MICHIGAN DEPARTMENT OF COMMUNITY HEALTH (MDCH)
CARDIAC CATHETERIZATION
STANDARD ADVISORY COMMITTEE (CCSAC) MEETING
APPROVED MINUTES

Wednesday December 1, 2010

Capitol View Building
MDCH Conference Center
201 Townsend Street
Lansing, Michigan 48913

I. Call to Order

Chairperson Eagle called the meeting to order @ 9:40 a.m.

A. Members Present:

Dagmar Raica, Marquette General Health System via conference call.
Lawerence O. Wells, Michigan League for Human Services
Roland Palmer, Vice-Chairperson, Alliance for Health arrived @ 9:49 a.m.
Kim Eagle, MD, Chairperson, University of Michigan Health System
Douglas W. Weaver, MD, Henry Ford Health System
Theodore Schreiber, MD, Detroit Medical Center
Bart Berndt, Lakeland Regional Medical Center arrived @ 9:54 a.m.
Fouad Ashkar, Garden City Hospital
Barry Lewis, DO, Botsford General Hospital
Frank D. Sotille, MD, Crittenton Hospital Medical Center
Kevin Donovan, Muskegon Construction arrived @ 9:53 a.m.
Arthur L. Riba, MD, Oakwood Healthcare, Inc.
David Dobies, MD, Genesys Regional Medical Center
Basil Dudar, MD, FACC, Beaumont Hospitals
John Heiser, MD, West MI Cardiothoracic Surgeons, PLC arrived @ 9:54 a.m.
Barton Buxton, Ed.D, Lapeer Regional Medical Center
Elizabeth J. Pielsticker, MD, Michigan Heart PC
Robert Goodman, MD, MHSA, FACEP, Blue Cross Blue Shield/Blue Care Network
Michelle Link, Bronson Methodist Hospital

B. Michigan Department of Community Health Staff Present:

Jessica Austin
William Hart Jr.
Stan Nash
Sallie Flanders
Tania Rodriguez
Brenda Rogers
Natalie Kellogg

II. Declaration of Conflicts of Interests

No conflicts of interests declared.

III. Review of Agenda

Motion by Buxton and seconded by Ashkar to modify current agenda by moving item V in place of IV. Motion Carried.

IV. Review of Minutes

Motion by Buxton and seconded by Dr.Schreiber to accept the draft minutes. Motion Carried.

V. Charge 2

Susan Heck and Dr. Tom Wharton presented on CON Commission SAC Cardiac Catheterization Standards (See Attachment A) Dr. Wharton also provided commentary on the following articles:

A. "The Current Status and Future Direction of Percutaneous Coronary Intervention without on-site Surgical Backup: An Expert Consensus."
T*he Society for Cardiovascular Angiography and Interventions*
(See Attachment B).

B. "Percutaneous Coronary Interventions in Facilities Without Cardiac Surgery: A Report from the *National Cardiovascular Data Registry (NCDR)" (*See Attachment C).

Discussion Followed.

Break @ 10:56 - 11:08 a.m.

1.) Dr. Schreiber gave a brief overview of the following articles**:**
"ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention: A Report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines" (See Attachment D)

a. 2005 pages 33, 35, 37, 38
b. 2006 pages 158, 160,
c. 2007 pages 476-477

"The Current Status and Future Direction of Percutaneous Coronary Intervention without On-site Surgical Back up: An Expert Consensus Document from the Society for Cardiovascular Angiography and Interventions" (See Attachment B)
"The Assessment and Maintenance of Proficiency in Coronary Interventional Procedures" (See Attachment E)

2.) Dr. Weaver volunteered to provide the SAC with the Weinberg Article regarding volume relationships and information on National volume requirements. Dr. Weaver will present his findings at the January SAC meeting.

Public Comment:
Dr. Tom Wharton

VI. Charge 5- Requirements to Initiate Primary PCI Services for Patients AMI

A. Dr. Riba gave a brief overview on the Comparative Effectiveness of STEMI Regionalization Strategies (See Attachment F).

B. Dr. Pielsticker gave a brief power point presentation on Michigan CON Requirements for Initiation of PPCI Program (See Attachment G).

C. Discussion Followed

Dr. Eagle would like the Department to provide annual compliance reports PCI and also identify how the number of primary PCI of 48 was chosen. Ms. Flanders will check into PCI data and compliance and report her findings at the next SAC meeting.

D. Dr. Sottile provided a brief written and verbal presentation on Hospital Bed Range (See Attachment H).

VII. Public Comment

Bob Meeker, Spectrum Health

VIII. Next Steps and Future Agenda Items

A. Dr. Sottile and Dr. Riba will work together on MI PCI Access paper specifically discussion with Eric Bates.
B. Dr. Riba also volunteered to obtain data from Blue Cross Blue Shield in regards to Michigan operators and if they are meeting current requirements.
C. The Department will be responsible for supplying information regarding PCI data and compliance reports along with the history of the number 48 for primary PCI.
D. Dr. Weaver will provide further data on the Mascucci paper from MI and internationals focusing on volumes and outcomes.
E. Dr. Schreiber volunteered to bring in a study that focused on meta-analysis of acute coronary syndrome study.
F. Dr. Dobies volunteered to bring in an abstract regarding gender disparities.

IX. Future Meeting Dates

A. January 11, 2011
B. February 8, 2011
C. March 10, 2011

D. April 6, 2011
E. May 4, 2011

X. Adjournment

Motion by Dobies and seconded by Buxton to adjourn the meeting @ 12:51 p.m. Motion Carried.

Attachment A

CON Commission Standard Advisory Committee

Cardiac Catheterization Standards

December 1, 2010

Coalition of Health Systems

MetroHealth

TRINITY HEALTH
Novi, Michigan

BOTSFORD HOSPITAL

Henry Ford HEALTH SYSTEM

SAINT MARY'S HEALTH CARE

MERCY HEALTH PARTNERS

GARDEN CITY HOSPITAL

DMC DETROIT MEDICAL CENTER

HURLEY MEDICAL CENTER

ST. MARY MERCY LIVONIA
SAINT JOSEPH MERCY HEALTH SYSTEM

Coalition Membership

- Coalition member hospitals and health systems who support and testimony being presented today
  - Botsford Hospital
  - Detroit Medical Center
  - Garden City Hospital
  - Henry Ford Health System
  - Hurley Medical Center
  - MetroHealth
  - Trinity Health

The Case for Elective PCI in Non-Open Heart Hospitals

Reconciling Policy with Practice

Our presentation shall establish the following:

- Patient safety and care will be improved
- Open heart hospitals have de facto de-linked open heart and elective PCI (no stand-by teams or OR's)
- Proposed standard will be substitutive or decrease, not additive to payor costs
- New standards will reinforce the concept of medical home and accountable care organizations

How can the CON program be flexible during the current health care transition?

- **Current reality:**
  - Fee for service (the more we do, the more we get paid)
  - Rewarded for high-tech
  - Specialty focus
  - "Build it and they will come" (brick and mortar)
  - Low accountability for outcomes
  - Extreme variation in care delivery

→

- **New reality:**
  - Pay for performance (at risk for managing cost, managing chronic conditions, and health outcomes)
  - Patient-centered medical homes
  - Primary care focus
  - Distributed model of care
  - Information-driven
  - Standardization to evidence-based practices

Technology Driving Change

The Cardiovascular (CV) Future—Clinical & Business

- New device technology (i.e. ICD, CRT-D) looming with expanded eligibility criteria

- Catheter–based valve replacement– update
  - PARTNER (Placement of AoRTic TraNscathetER Valve Trial) results released September 2010
  - Evaluated the safety & effectiveness of the transcatheter aortic valve implantation (TAVI) technique
  - Principle investigator (interventional cardiologist Martin Leon, MD) recommends its approval for use with patients with aortic stenosis, who are not surgical candidates

- Bundled payment pilot programs already in process with focus on CV case types
  - 28 cardiac procedures identified
  - Will require close affiliation with doctors to administrate payments—may be difficult if doctors who may not cross medical staffs

- Accountable Care Organization (ACOs)
  - Will require physician and hospital accountability beyond the acute care episode
  - Significant impact for CHF and other chronic CV conditions

Technology Driving Change---Regulations should NOT prevent advancements in the application of technology or processes that could provide better patient care

Shifts Are Already Occurring

- **Example: Michigan Blue Cross/Blue Shield's Physician Group Incentive Program (PGIP)**
  - Primary care and select specialty physicians on risk/reward programs for:
    - Patient-centered medical home behavior (open access, patient navigators, disease registries, e-prescribing, continuous improvement initiatives, etc.)
    - Patient satisfaction
      - Patient outcomes (e.g., chronic disease management)
    - Now includes gastro, ortho, rad oncology
  - Results:
    - 23% lower inpatient cost PMPM*, 20% lower admissions/1,000
    - 7% lower readmission cost PMPM*
    - 52% lower self-referral rate for low-tech imaging

* Per Member Per Month

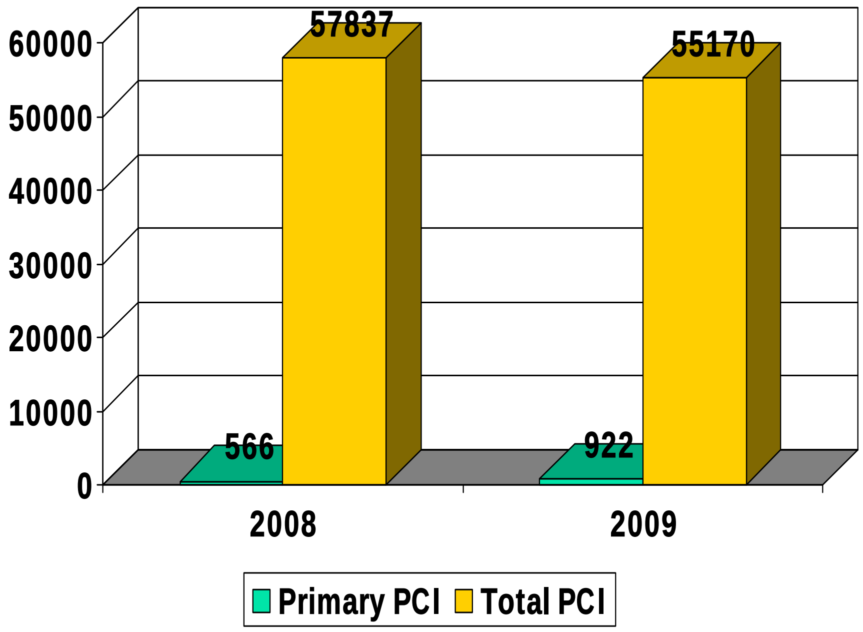
Impact of Closure of Low Volume OHS Programs on Access to PCI Care

- 7 hospitals not currently meeting OHS thresholds
- Represents 1254 OHS cases
- Represents 5683 PCI's

Closure of low volume OHS programs would require 5683 PCI patients to leave their medical homes for care if elective PCI without SOS is not approved.

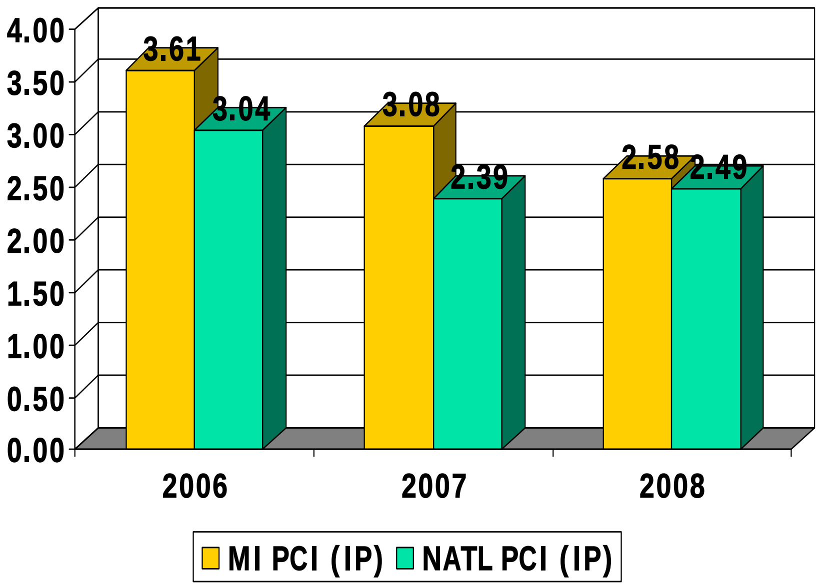
Based on 2009 data submitted to the State

Michigan PCI Volume & Utilization



Decreasing # of total PCI procedures with a growing # of PRIMARY PCI procedures at centers without SOS

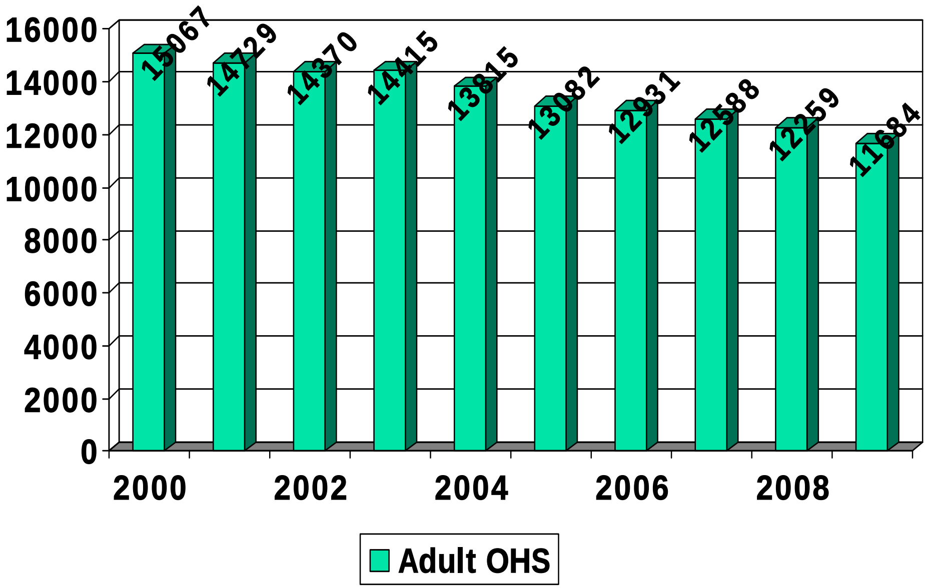
Source: 2008 and 2009 Certificate of Need Annual Survey



Decreasing Inpatient PCI Utilization *per 1000 population*

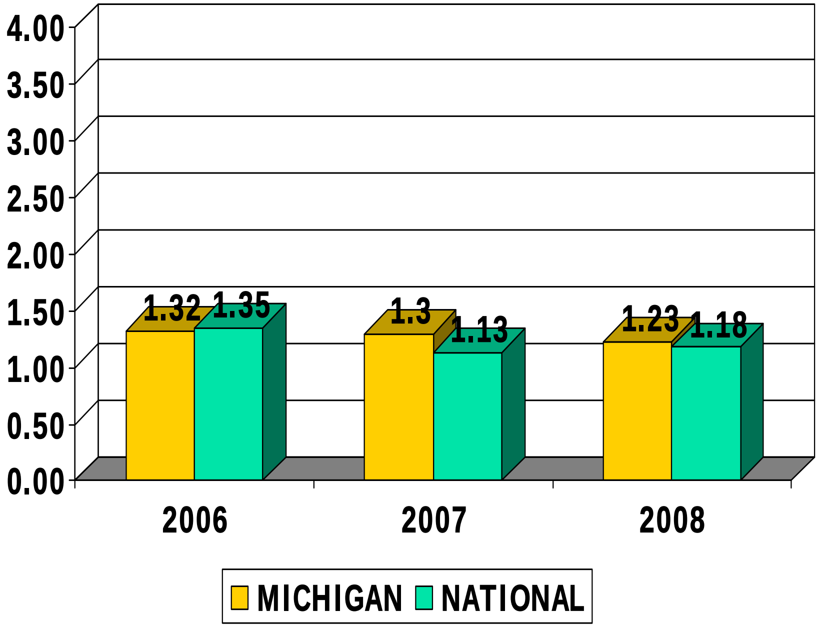
Source: The U.S. Department of Health & Human Services, Agency for Healthcare Research & Quality

Michigan OHS Volume & Utilization



Decreasing OHS Volumes

Source: 2008 and 2009 Certificate of Need Annual Survey



Decreasing OHS Utilization *per 1000 population*

Source: The U.S. Department of Health & Human Services, Agency for Healthcare Research & Quality

CV Mortality Rates per 100,000

Benchmarks from CDC

Age Adjusted Mortality Rates	2004	2005	2006
National	237.0	231.2	217.9
Michigan	256.4	260.8	246.3

Is this an access to care issue?

Source: CDC – most recent year available is 2006 – based on cardiovascular ICD-9 diagnosis codes

Shift of IP to OP

Benchmarks from Georgia

Reasons of Shift:

- Interqual removed Elective PCI from inpatient admission list
- CMS Recovery Audit Contractors (RAC) scrutinizes inappropriate admissions related to one-day length of stays; large focus on PCI

Georgia Case Study:

Georgia	2006		2007		2008		2009*	
IP vs. OP	Cases	%	Cases	%	Cases	%	Cases	%
IP	21,784	92%	21,173	94%	19,033	84%	16,118	72%
OP	1,803	**8%**	1,394	**6%**	3,567	**16%**	6,178	**28%**

Source: Georgia HeRMES Database (note: 2009 is annualized)

Introduction-- Dr. Thomas Wharton

CAREER SUMMARY

Dr. Thomas P. Wharton, Jr. is a board-certified interventional cardiologist and serves as both the Chief of Cardiology and Director of the Cardiac Cath Lab at Exeter Hospital in New Hampshire. His group has been providing primary angioplasty as first line therapy for the treatment of acute myocardial infarction 24-hours a day, 365 days a year for patients admitted with MI (heart attacks) since 1991. He has been a principal investigator in several national studies, and has authored numerous papers, abstracts, and textbook chapters on the subject of PCI.

He has lectured widely in the U.S. and abroad on primary angioplasty at hospitals without on-site surgery, and has contributed to setting up multiple new primary angioplasty programs. He has worked with many cardiologists in multiple states and countries trying to help change regulations which prohibit this procedure. His work has advanced this treatment modality to more communities. Dr. Wharton is a Fellow of the American College of Cardiology and of the Society of Cardiovascular Angiography and Intervention.

National Regulatory Climate

- Overview of the national regulatory climate related to elective PCI: clinical practice outpacing ACC guidelines
  - Only 4 states do not allow Primary or Elective PCI
  - Only 5 states including Michigan restrict to Primary only
  - 23 have no regulations governing practice
  - 16 states allow Primary and Elective with only 7 of 16 requiring study or trial participation

More than 500 centers in U.S. offer PCI without Surgery on Site (SOS)

Attachment A

41 States Allow Elective PCI with varying requirements

RECENT REGULATORY CHANGES

- **Kentucky**
  - September 20, 2010-now accepting applications for **all** cath services including PCI without SOS for Dec 1 batching cycle. Applications posted to public notice January 20, 2011.
- **California**
  - Allows primary PCI, in Jan '09 bill passed for a pilot to allow 6 hospitals to add elective PCI.
- **Florida**
  - In Jan '09 moved from CON to a 2-level licensure of adult cardiovascular services; Level 1 permits community hospitals meeting specific criteria to offer elective & emergent PCI services, Level 2 facilities provide open heart services.
- **Georgia**
  - In 2005, permitted 10 hospitals to participate in a national clinical trial to allow community hospitals to provide elective & emergent PCI without SOS. In July of '09 16 additional hospitals were granted approval to do primary & elective **without** participation in the C-PORT trial.
- **New York**
  - Engaged in project to allow 10 facilities to perform primary PCI. Regulatory changes signed in Nov of 09 that will allow elective PCI & prohibit the addition of diagnostic only labs.
- **Pennsylvania**
  - Beginning in 2001, 10 programs granted exceptions to pilot to provision of both primary and elective PCI without SOS. In '09 approved 5 new programs if they qualify for the C-PORT trial.
- **West Virginia**
  - In August '08, implemented 3 tiers of service: Tier 1 --must demonstrate a minimum diagnostic cath volume threshold; after 1 year of diagnostic caths, can apply to offer primary PCI under Tier 2. Hospitals that offer primary PCI for at least 2 years may apply to offer elective PCI under Tier 3.

PCI without Surgery on Site Regulations

State by State

- Not permitted
- Primary only
- Primary & Elective
- Permitted, not regulated

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International Practice and Experience

- England
  - The British Cardiac Society & British Cardiovascular Intervention Society 2005 guidelines approve PCI without SOS and emphasize common standards
- Germany
  - 1987 guidelines may not be relevant today- but PCI without SOS has been widely performed there for over 2 decades
- Spain
  - Spanish Society of Cardiology 1999 Guidelines_ PCI at hospitals without SOS is not prohibited provided a program meets certain requirements
- Brazil
  - Brazilian Society of Cardiac Hemodynamics and Intervention 2003 Guidelines similar to existing ACC Guidelines
- Australia and New Zealand
  - Cardiac Society of AU and NZ 2003 Policy Statement allows PCI without SOS with appropriate standards in place

Review of Science and Literature

- The American College of Cardiology's own database (ACC-NCDR) supports that primary and elective interventions can be performed as safely at programs without open heart surgery on site. Their study, published in the Journal of the American College of Cardiology (JACC) in 2009, analyzed data from the ACC National Cardiovascular Data Registry to show that patients who received elective or emergency percutaneous coronary intervention (PCI, aka angioplasty) at **hospitals without on-site cardiac surgery had no difference in procedural success, morbidity, emergency surgery, or mortality, compared with patients receiving the same procedure at hospitals with surgical backup on site**. This new study adds to the growing body of literature suggesting that PCI with off-site surgery backup can be done safely if off-site programs carefully monitor their results and follow rules about which patients are appropriate for PCI in facilities without on-site surgical backup. (5)
- Actual clinical practice evident in their own database supports the fact that practice is outpacing the ACC's endorsement.
  Sources: *http://www.seconds-count.org/Details.aspx?PAGE_ID=503;* *http://www.theheart.org/article/981347.do*
- Senior author on the study, **Dr Ralph G Brindis** (Northern California Kaiser Permanente, San Francisco, CA), told **heart*wire*** that while there is now an important randomized clinical trial under way, known as **C-PORT Elective**, looking at the feasibility and outcomes of performing elective "off-site" PCI (angioplasty without on-site surgical backup), these new data, culled from the **National Cardiovascular Data Registry** (NCDR), may be persuasive enough to convince guideline-writing groups to reassess some of their advice.
  Source: *http://www.theheart.org/article/981347.do*

Review of Science and Literature (cont'd)

- A recent Mayo Clinic study concluded: "Optimal outcomes with PCI have been observed at community hospitals without on-site cardiac surgical programs with application of a prospective, standardized quality assurance protocol. The in-hospital mortality rate at Immanuel St. Joseph's Hospital and Franciscan Skemp Healthcare was comparable to that at Saint Mary's Hospital for both elective (0.3%, 0.1%, 0.4%; *P*=.24) and nonelective PCI (2.6%, 2.4%, 3.1%; *P*=.49). No patient undergoing elective PCI required transfer for emergency cardiac surgery." (14) (http://www.mayoclinicproceedings.com/content/84/6/501.abstract)

- SCAI* Statement On Percutaneous Coronary Intervention (PCI) In Facilities Without On-Site Cardiac Surgery (http://www.seconds-count.org/Details.aspx?PAGE_ID=503) (1)
  - PCI without on-site surgical backup is being performed with acceptable outcomes and risks in the United States and many other countries.
  - "The ability to perform PCI in community hospitals often translates into an overall improved level of cardiovascular care, enabling the hospital to recruit the most skilled health care providers and offer overall better care to the people they serve."
  - "Advances resulting from the development of stents and the effectiveness of PCI in treating heart attacks, as well as the success of door-to-balloon time programs have led to a decrease in the need for open-heart surgery in patients with blocked arteries. Therefore, cardiac surgery is available at fewer hospitals than in the past."

- Additional References in Appendix demonstrate the safety and efficacy of off-site PCI.

* Society for Cardiovascular Angiography and Interventions

Position of Professional Societies

- Note that only 0.2% of patients suffer PCI complication requiring bypass surgery within 2 h. (16)
- American College of Cardiology (ACC)
  - Practice outpacing ACC's **very conservative position** in their guidelines
  - ACC led by **academic cardiologists** with vested interest in driving procedures to tertiary hubs, while community hospitals have a similar interest in expanding cardiology programs.
  - National (including ACC's own database) & international data points to safety in new practice
- Society for Cardiac Angiography and Interventions (SCAI)
  - Published an expert consensus document related to elective and primary PCI without SOS, endorsed by 12 international cardiology societies (1)

Position of SCAI Past President Greg Dehmer (23)

- “At the core of the debate over this issue *[PCI with off-site cardiac surgery backup]* are arguments that this practice is all being driven by desire for financial gain and market share.
- Some accuse those developing such programs of simply wanting a piece of the financial pie;
- in contrast, others say facilities that have programs with on-site surgery do not want their slice of the pie to disappear even if it is best for patient care.
- Although these debates may have an entertaining quality, the Society feels <u>the focus should be redirected toward providing quality PCI care to all patients and developing a delivery model that is best for the patients of each individual community.</u> “

Changing Clinical Practice

- Changing clinical practice is based on:
  - Technology advances — Improved catheters, wires and stents
  - Medication advances — Improved and safer anticoagulant and antiplatelet agents
  - Growing expertise of cardiologists to manage complications
  - Even tertiary centers no longer hold OR's open or keep staff on stand-by

- Practice of "coupling" diagnostic and PCI procedures in the same care setting is supported by quality and cost outcomes.

- When programs cannot provide ad hoc PCI:
  - Greater dye, radiation, infection and bleeding complication exposure from second procedure after transfer
  - Disconnect from their medical home
  - Impairs access to care for the economically disadvantaged populations

Access

- Changing clinical practice supports the "coupling" of diagnostic cath and PCI. Without the ability to perform "ad hoc" PCI at time of diagnostic cardiac catheterization, patients are forced to be transferred away from their medical home – which is the complete opposite approach of the current health care and payment reform efforts.

- Even highly regulated states such as New York are changing regulations to allow primary and elective PCI at centers without on-site surgery.
  - Further support to the changing clinical standards related to the coupling of diagnostic and interventional procedures, New York's new regulations **prohibit the addition of any new diagnostic only cath labs**.

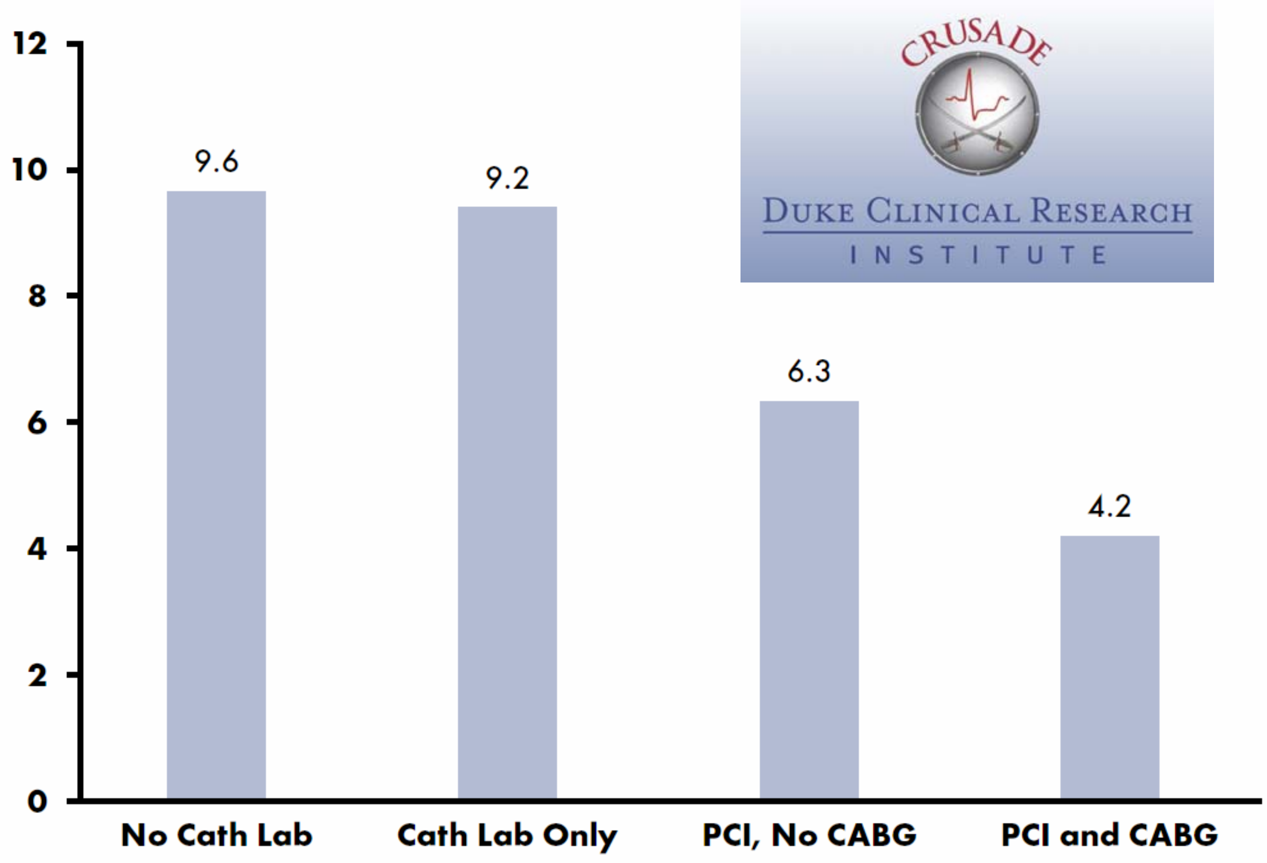
- The closing of low volume open heart surgery programs will impair access to PCI even more if elective PCI not allowed at hospitals without SOS

Does Michigan Have an Access Problem?

- 60% of pts with Acute Coronary Syndromes (ACS) in MI present to hospitals without cardiac surgery (17). Such pts require transfer for PCI, which has been shown to lead to underutilization of appropriate interventional procedures (18), particularly among women, ethnic minorities, the uninsured. (19,20).
- Broader availability of PCI should result in larger numbers of appropriate procedures, especially in patients with high-risk acute coronary syndromes (ACS).
- "Community hospitals without revascularization capabilities currently fail to transfer a large percentage of high-risk NSTE ACS patients to tertiary hospitals. . . Consequently, mortality rates for NSTE ACS patients are higher. . ." CRUSADE Registry. (21)
- The CRUSADE registry data on the following slide suggests the provocative possibility that 3 to 5 lives might be saved for every 100 patients with high-risk ACS that are admitted to hospitals that provide PCI on site.

Access to PCI is a Quality of Care Issue (ref 21)

FIGURE 2. In-Hospital Mortality by Hospital Capabilities (N = 57,039)*



Effect on Program Volumes and Quality?

- Will expansion of therapeutic cath labs dilute the volumes of existing tertiary centers and lead to more low-volume operators and centers?
- Since most operators perform PCI at multiple hospitals, a similar overall number of operators would likely handle the existing and growing load, covering both surgical and non-surgical hospitals.
- Given this operator crossover, there may be no correlation between operator volume and on-site vs off-site surgical backup.
- Regarding hospital volumes, the 2005 ACC/AHA/SCAI Guidelines give a Class IIa recommendation for an institutional volume of 200-400 PCI's per year.
- These guideline also state, "The documented relationships between activity level and outcome are statistical associations, and activity level is not a surrogate for quality."
- A study by Epstein (22) found absolutely no evidence of higher in-hospital mortality in patients undergoing PCI at hospitals performing 200-400 procedures per year vs those performing over 400/year.

Quality

- Current practice “couples” diagnostic caths with coronary intervention. Given prohibition to do elective caths without SOS (surgery on site), patients in Michigan may experience:
  - Exposure to increased/prolonged exposure to anticoagulants and increased x-ray dose;
  - Multiple invasive punctures which can lead to peripheral complications and increased chance of infections;
  - A disconnect from their medical home as their medical record and PCPs do not easily cross hospital boundaries at this time;
  - Dissatisfaction with transfer as the patient and family must navigate unfamiliar settings and meet new physicians.
  - Duplicate testing
  - Increased length of stay (LOS) due to transfer

Cost

- A review of the costs to **payors** for diagnostic cath & elective PCI being performed in staged settings:
  - The net difference between DX Cath and Elective PCI in same care setting vs. a staged procedure is approximately $7,350 per case based on a Medicare rate
  - Duplicate testing and redundant costs for dye, catheters, trays, and testing
  - Increase length of stay incumbent in the staged care process
  - Ambulance transfer fees average $400 per case
  - Given the groups estimate of about 1000 procedures— currently **paying over $7.35 million for less than standard care**

Payor Cost Avoidance Scenario

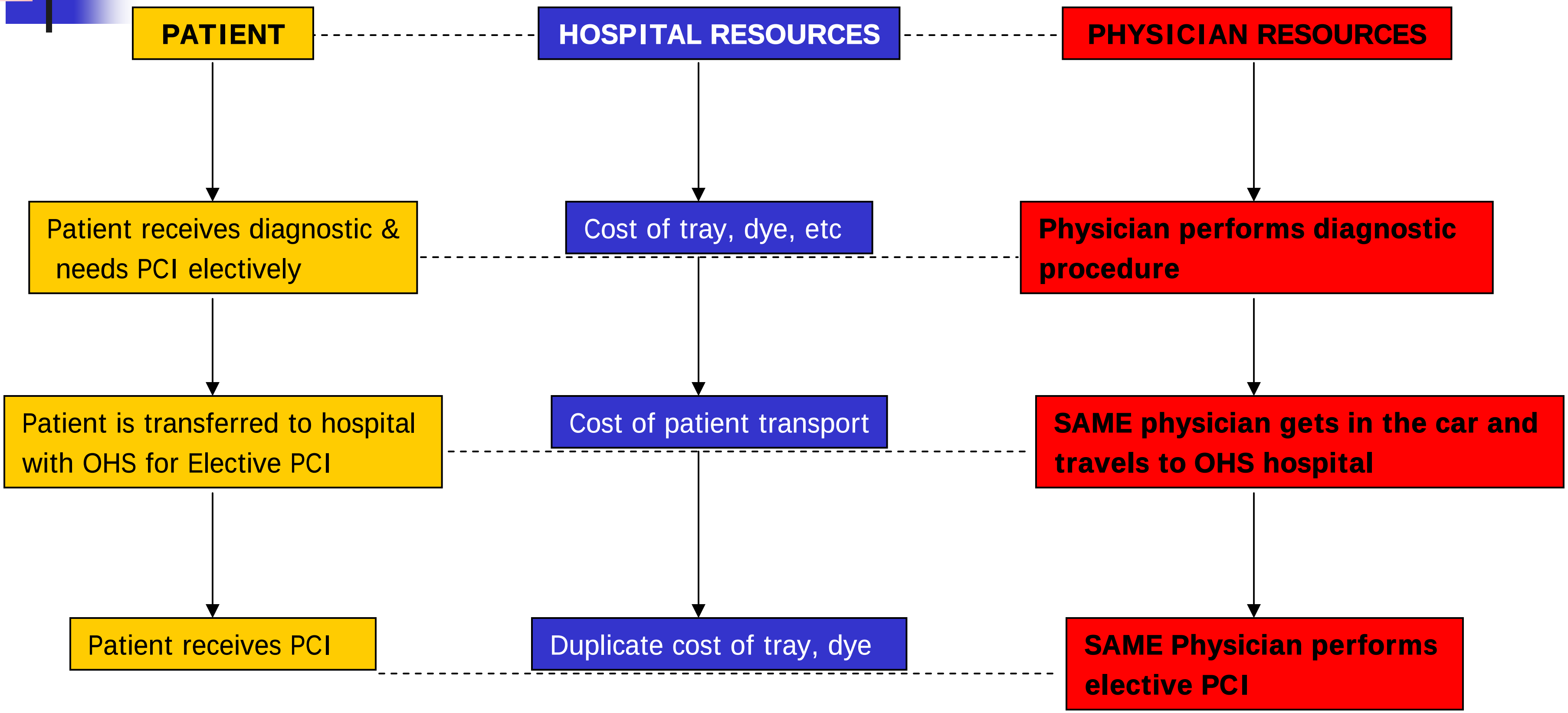
Sample based on Medicare— 2010

Medicare Costs	Hospital Component	Physician Component	Transport Component	Total
DX Cath and PCI in the same setting of Care	$ 11,454	$ 1,147	$ -	$ 12,600
DX cath with a Transfer to another facility for PCI	$ 18,197	$ 1,368	$ 386	$ 19,950
Difference	***$ 6,743***	***$ 221***	***$ 386***	***$ 7,350***

Sample Cost Avoidance	
Sample PCI Case Volume	1,000
Payor Cost Differential	$ 7,350
Total Cost Avoidance	***$ 7,350,136***

- Hospital component for PCI based on CMS 2010 split of case volume across DRGs 246-251
- Physician Pro-fee for dx cath based on CMS left heart cath & PCI blended payment rate based on 1.4 stents/case
- Transport based on Michigan ground rates + 10 miles & a blend of Advanced Life Support levels

Illogical Nature of Current System



- **Increased cost of care**
- **Patients leaving their medical homes**
- **Same doctors traveling to deliver care at different hospitals**

History of PCI Cost and Reimbursement

- True decrease of cost of procedure with increased technology and improved techniques
  - No more OR stand by for PCI
  - Stent prices decreased with more FDA approved vendors
  - Length of stay decreases with move to O/P care
- Dramatic ratcheting of reimbursement
- CMS creating codes for O/P PCI tracking
  - RAC auditors focused on converting 1 day LOS PCI's to Observation or O/P status
- Evidence of practice change in many regions
  - 28% of PCI cases in the State of GA are performed as O/P

The Massachusetts PCI Story

MASS COMM Trial: collaborative with Harvard Clinical Research Institute

- Primary PCI allowed via a pilot program in 1997. From abstract presented 2009: “No difference in mortality at 30 d and 1 yr" for primary PCI with and without SOS.
- June 2005--MASS COMM Trial initiated –collaborative with **Harvard Clinical Research Institute** (HCRI) and Massachusetts Data Analysis Center (MASS- DAC)
- Randomized trail to compare safety & long term outcomes for PCI between MASS hospitals with cardiac Surgery-on-Site and Community hospitals without Cardiac Surgery-on-Site
- Committees:
  - Massachusetts Chapter of the American College of Cardiology (MCACC) provides physician oversight with protocols to review operators
  - Data Adjudication Committee--reviews patient-specific data elements & corresponding data documentation submitted by hospitals to Mass-DAC in order to determine validity of coding.
  - Data Registry Publications Committee—facilitates utilization of shared data from the PCI data registry (must also submit to ACC-NCDR)

Questions

Appendix

Pertinent Literature

1. Dehmer GJ, Blankenship J, Wharton TP Jr, Seth A, Morrison DA, DiMario C, Muller D, Kellett M, Uretsky BF. The current status and future direction of percutaneous coronary intervention without on-site surgical backup: an expert consensus document from the Society for Cardiovascular Angiography and Interventions. Catheter Cardiovasc Interv 2007;69:471–478.
2. Mehta RH, Stalhandske EJ, McCargar PA, et al. Elderly patients at highest risk with acute myocardial infarction are more frequently transferred from community hospitals to tertiary centers: reality or myth? Am Heart J 1999;138:688-695.
3. Gibson. NRMI and current treatment patterns for ST-elevation myocardial infarction. Am Ht J 2004;148:S29.
4. Nallamothu BK, Bradley EH, Krumholz HM. Time to treatment in primary percutaneous coronary intervention. N Engl J Med 2007; 357:1631.
5. Kutcher MA, Klein LW, Ou FS, Wharton TP, et al, on behalf of the National Cardiovascular Data Registry (NCDR). Percutaneous coronary interventions in facilities without cardiac surgery on site: A report from the National Cardiovascular Data Registry (NCDR). J Am Col Cardiol. 2009;54;16-24.
6. Pride YB, Canto JG, Frederick PD, Gibson CM, for the NRMI investigators. Outcomes among patients with non ST-segment elevation myocardial infarction presenting to interventional hospitals with and without on-site cardiac surgery. J Am Coll Cardiol Intv 2009;2:944 –52.
7. Anis A, Normand ST, Wolf RE, Lovetet A, Mauri L, Jacobs AK. Primary PCI in Massachusetts: Outcomes following primary percutaneous coronary intervention: a comparison between hospitals with and without cardiac surgery on-site. Presented at AHA Scientific Sessions, November 2009.
8. Hannan EL, Zhong Y, Racz M, Jacobs AK, Walford G, Cozzens K, Holmes KR, Jones RH, Hibberd M, Doran D, Whalen D, King SB III. Outcomes for patients with ST-elevation myocardial infarction in hospitals with and without onsite coronary artery bypass graft surgery: the New York state experience. Circ Cardiovasc Intervent 2009; 2:00 published online Nov 17, 2009.

Pertinent Literature (cont'd)

9. Tebbe U, Hochadel M, Bramlage P, Kerber S, Hambrecht R, Grube E, Hauptmann KE, Gottwik M, Elsa¨sser A, Glunz H, Bonzel T, Carlsson JÆ, Zeymer U, Zahn R, Senges J. In-hospital outcomes after elective and non-elective percutaneous coronary interventions in hospitals with and without on-site cardiac surgery backup. Clin Res Cardiol Published online 14 July 2009.
10. Carlsson J, James SN, Stahle E, Ho¨fer S, Lagerqvist B. Outcome of percutaneous coronary intervention in hospitals with and without on-site cardiac surgery standby. Heart 2007;93:335-338.
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Attachment B

Catheterization and Cardiovascular Interventions 69:471–478 (2007)

EXECUTIVE SUMMARY

The Current Status and Future Direction of Percutaneous Coronary Intervention Without On-Site Surgical Backup: An Expert Consensus Document from the Society for Cardiovascular Angiography and Interventions

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*The full-length version of this article can be found on the **Catheterization and Cardiovascular Interventions** website (http://www.mrw.interscience.wiley.com/suppmat/1522-1946/suppmat/index.html) and on the SCAI website at www.scai.org.*

PREAMBLE

The Society for Cardiovascular Angiography and Interventions (SCAI) coauthored and cosponsored with the American College of Cardiology (ACC) and the American Heart Association (AHA) the percutaneous coronary intervention (PCI) guidelines update, released in November 2005 [1]. This guideline update continued to designate elective PCI without on-site surgery as a Class III indication, and primary PCI for ST-segment elevation myocardial infarction (STEMI) as a class IIb indication in the absence of on-site surgery. The performance of PCI without on-site surgical backup is currently the subject of debate. Although providing the highest quality of care and best outcomes to patients should always be the primary goal, debate on this topic has the potential to supersede quality of patient care issues. Within this context, SCAI developed this Expert Consensus document to determine the current status of PCI without on-site surgery not only in the United States, but globally, and make recommendations regarding the performance of PCI in this circumstance. The focus of this document is to provide a structure that provides the highest quality care to patients undergoing PCI in any circumstance.

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See Appendix Table

Endorsed by the following societies: Asian Pacific Society of Interventional Cardiology, Belgian Working Group of Interventional Cardiology, Brazilian Society for Interventional Cardiology, British Cardiovascular Intervention Society, Working Group on Interventional Cardiology of the Bulgarian Cardiology Society, Cardiac Society of Australia and New Zealand, Egyptian Society of Cardiology Working Group on Interventional Cardiology, Interventional Council of the Cardiological Society of India, Italian Society of Interventional Cardiology, Working Group on Interventional Cardiology of the Latvian Society of Cardiology, Polish Working Group on Interventional Cardiology of the Polish Cardiology Society, Sociedad Venezolana de Cardiología Intervencionista (Venezuelan Society of Interventional Cardiology).

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Received 18 December 2006; Accepted 20 December 2006

DOI 10.1002/ccd.21097
Published online 4 February 2007 in Wiley InterScience (www.interscience.wiley.com).

BACKGROUND

Over the past 20 years, the use and indications for PCI have greatly expanded. It is now well-recognized that PCI is safer and the need for urgent coronary artery bypass graft (CABG) surgery greatly reduced [2]. Primary PCI, when available, has eclipsed fibrinolytic therapy for reperfusion in the treatment of STEMI [3], but is adversely affected by time delays in initiating the PCI procedure [4]. Studies examining patient transport to PCI hospitals have shown suboptimal initial door-to-balloon times, especially in the United States [5]. Efforts to provide primary PCI services locally at community hospitals without on-site cardiac surgery have developed and demonstrate outcomes comparable to facilities that have on-site cardiac surgery [6]. Because it is difficult to sustain a PCI program solely on STEMI patients, elective PCIs are also being performed at facilities without on-site surgery [7], enhancing the debate regarding PCI without on-site surgery.

PREVALENCE AND TRENDS OF PCI WITHOUT ON-SITE SURGERY

Data on the prevalence of PCI performed without on-site surgical backup in the United States are not easily found and are changing rapidly. Data gathered from several sources and believed accurate as of July 2006 indicate primary PCI programs without on-site surgical backup exist in all but 10 states (Alaska, Arkansas, Delaware, Georgia, Mississippi, North Dakota, Rhode Island, South Dakota, Vermont, and Wyoming) plus the District of Columbia. Facilities performing both primary and elective PCI without on-site surgery currently exist in 28 states. A large (n = 18,000) randomized trial of elective PCI without on-site surgery (The Atlantic Cardiovascular Patient Outcomes Research Team Elective Angioplasty Study) is currently enrolling patients and includes facilities in several states where elective PCI without on-site backup has been prohibited.

The exact number of patients receiving PCI at facilities without on-site surgery is unknown. Data from facilities reporting to the CathPCI Registry™ of the ACC-National Cardiovascular Data Registry (ACC-NCDR®) show an increase in the number of both primary and elective PCIs performed without on-site surgical backup [8]. In 2005, 75 of the 463 facilities reporting to the ACC-NCDR were performing PCI without on-site surgical backup.

PCI without on-site surgical backup is being performed in 35 of 39 (90%) countries responding to requests for information and appears to be increasing. For example, 7% of PCI procedures performed in the United Kingdom in 1996 were at facilities without on-site cardiac surgery. By 2004, this increased to 15% with 26% of the PCI centers in the United Kingdom operating without on-site cardiac surgery.

EXISTING GUIDELINES AND COMPETENCY DOCUMENTS

ACC/AHA/SCAI Guidelines

In the 2005 update of this guideline, primary PCI without on-site surgical backup remained a Class IIb indication, and elective PCI without on-site surgery remained a Class III indication. Many other programmatic recommendations were made [1].

European Society of Cardiology Guidelines

In contrast to the ACC/AHA/SCAI guidelines, the 2005 European Society of Cardiology (ESC) guidelines do not comment on PCI without on-site cardiac surgery or issues related to institutional or operator competency [9].

British Cardiac Society and British Cardiovascular Intervention Society Guidelines

The British Cardiac Society and British Cardiovascular Intervention Society (BCIS) guideline, published in 2005, acknowledges and approves PCI without on-site surgical backup and emphasizes a common standard applied across facilities with and without on-site surgical backup so as to avoid two levels of service provision [10].

German Guidelines

The only German guidelines found were published in 1987 [11] and thus may not be relevant today. However, there is substantial evidence that PCI without on-site surgical backup is widely performed in Germany.

The Cardiac Society of Australia and New Zealand Guidelines

Policy statements on support facilities and on the performance of coronary angiography and PCI at rural sites in Australia and New Zealand were published (online) in 2003 and 2005, respectively [12,13]. The Cardiac Society of Australia and New Zealand (CSANZ) guidelines state that PCI is preferably performed in hospitals with on-site surgical support, but acknowledge that the requirements for on-site cardiac surgical facilities may be omitted in certain circumstances, and that appropriately trained individuals can perform coronary interventional procedures safely in hospitals without on-site surgical

Attachment B

backup. Furthermore, these documents acknowledge that rural patients have reduced access to diagnostic angiography and interventional procedures and further state that providing these services as close to the patient's place of residence as possible facilitates equity of access, which should result in improved quality of care.

Spanish Society of Cardiology Guidelines

Published in 1999 [14], these guidelines are specific for PCI at hospitals without on-site cardiac surgery. PCI performance without on-site cardiac surgery is not prohibited, provided a program meets certain requirements.

Sociedade Brasileira de Hemodinâmica e Cardiologia Intervencionista

Guidelines from the Brazilian Society of Cardiac Hemodynamics and Intervention (Sociedade Brasileira de Hemodinâmica e Cardiologia Intervencionista) [15] were published in 2003. They use a scheme similar to the ACC/AHA/SCAI guidelines [1] and classify elective PCI without on-site surgical backup as Class III. Primary PCI for STEMI in the absence of on-site surgery is a Class IIa indication; their guidelines do not have a IIb category.

Belgian Working Group on Invasive Cardiology Guidelines

Published in 2003, these guidelines acknowledge the increasing safety and diminishing risk of PCI but conclude that "the current standard practice for elective PCI remains the presence of on-site surgical standby" [16].

PEER-REVIEWED LITERATURE OF PCI WITHOUT ON-SITE SURGERY

There are over 30 published papers or abstracts reporting PCI results without on-site surgical backup. All published data for both primary and elective PCI were derived from retrospective reviews or registries, and thus are subject to unintentional bias and other methodological concerns. These are summarized and referenced in the on-line version of this document. These studies span a time period from 1990 to 2006, and thus incorporate changing treatment paradigms, including fibrinolytic therapy before PCI, glycoprotein IIb/IIIa inhibitors, and coronary artery stents. The total patient number within some of these reports is not easily derived because the studies listed are expanding experiences within the same registry; thus, simple aggregation of outcome data is not appropriate or meaningful. The more recent reports show that both primary and elective PCI without on-site surgical backup are performed with a high success rate, low in-hospital mortality rate, and a low rate of urgent cardiac surgery.

BEST PRACTICES FOR PCI WITHOUT ON-SITE SURGERY

Although no randomized or controlled studies exist and despite the current ACC/AHA/SCAI guideline recommendation, PCI without on-site surgery is being performed in many states and is accepted in many countries throughout the world. Moreover, data from many countries, including the United States, indicate that the use of PCI without on-site surgery is growing [8]. The purpose of this document is neither to challenge the ACC/AHA/SCAI guideline recommendations nor to support PCI without on-site surgery backup. However, with the reality that PCI without on-site surgery is growing, it is both appropriate and necessary to define the best standards of practice such that facilities and physicians operate within the highest possible quality standards.

Qualifications of the Physician

Simply performing a high volume of cases does not guarantee technical expertise or sound judgment on the part of the physician. More important than a specific case volume threshold is the accurate assessment of complication rates and patient outcomes. Recommendations for physicians performing PCI at facilities without on-site surgery include the following:

a. Only operators with complication rates and outcomes equivalent or superior to national benchmarks should perform PCI procedures with or without on-site surgery. The operator also must actively participate in a facility's quality improvement program. In addition to involvement in local continuous quality improvement efforts, participation in a national data registry if available and appropriate continuing medical education is mandatory.
b. A proven record of satisfactory outcomes is of greater importance than simply meeting an arbitrary case volume requirement. However, operators must have sufficient prior experience to allow assessment of their judgment and quality. The initial operators at a facility without on-site backup should not begin performing PCI in such facilities until they have a lifetime experience of >500 PCIs as primary operator after completing fellowship. Interventional cardiologists joining those already engaged in PCI without on-site surgery with <500 cases of lifetime experience should be mentored and monitored by existing physicians until it is determined and certi-

TABLE I. Personnel and Facility Requirements for PCI Programs Without On-Site Surgical Backup

Experienced nursing and technical laboratory staff with training in interventional laboratories. Personnel must be comfortable treating acutely ill patients with hemodynamic and electrical instability.
On-call schedule with operation of laboratory 24 hr/day, 365 days/year[a].
Experienced coronary care unit nursing staff, comfortable with invasive hemodynamic monitoring, temporary pacemaker operation, and intraaortic balloon pump management. Personnel capable of endotracheal intubation and ventilator management both on-site and during transfer if necessary.
Full support from hospital administration in fulfilling the necessary institutional requirements, including appropriate support services (e.g., respiratory care, blood bank, etc.).
Written agreements for the emergency transfer of patients to a facility with cardiac surgery. Transport protocols should be developed and tested a minimum of twice per year.
Well-equipped and maintained cardiac catheterization laboratory with high-resolution digital imaging capability and intraaortic balloon pump equipment compatible with transport vehicles. The ability for the real-time transfer of images and hemodynamic data (via T-1 transmission line) as well as audio and video images to review terminals for consultation at the facility providing surgical backup support is ideal.
Appropriate inventory of interventional equipment, including guide catheters, balloons, and stents in multiple sizes, thrombectomy and distal protection devices, covered stents, temporary pacemakers, pericardiocentesis trays. Pressure wire device and intravascular ultrasound equipment are optimal but not mandatory. Rotational or other atherectomy devices should be used cautiously in these facilities due to the greater risk of perforation.
Meticulous clinical and angiographic selection criteria for PCI (Tables II and III).
Performance of primary PCI as the treatment of first choice for STEMI to ensure streamlined care paths and increased case volumes. Door-to-balloon times should be tracked and be ≤90 min. Outlier cases should be carefully reviewed for process improvement opportunities.
On-site rigorous data collection, outcomes analysis, benchmarking, quality improvement, and formalized periodic case review.
Participation in a national data registry where available, such as the American College of Cardiology-National Cardiovascular Data Registry® in the United States.

CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation acute myocardial infarction.
[a]Required for the United States facilities, but this may not be possible for all facilities world-wide.
Adapted from Ref. 6.

TABLE II. Recommendations for Primary PCI and Emergency Aortocoronary Bypass Surgery at Hospitals Without On-Site Cardiac Surgery

Avoid intervention in:
Patients with >50% stenosis of left main artery proximal to infarct-related lesion especially if the area in jeopardy is relatively small and the overall LV function is not severely impaired.
Long, calcified or severely angulated target lesions at high-risk for PCI failure with TIMI grade 3 flow present during initial diagnostic angiography.
Lesions in other than the infarct artery (unless they appeared to be flow-limiting in patients with hemodynamic instability or ongoing symptoms).
Lesions with TIMI grade 3 flow that are not amenable to stenting in patients with left main or three-vessel disease that will require coronary bypass surgery.
Culprit lesions in more distal branches jeopardizing only a modest amount of myocardium when there is more proximal disease that could be worsened by attempted intervention.
Transfer emergently for coronary bypass surgery patients with:
High-grade left main or three-vessel coronary disease with clinical or hemodynamic instability after successful or unsuccessful PCI of an occluded vessel and preferably with intra-aortic balloon pump support.
Failed or unstable PCI result and ongoing ischemia, with intra-aortic balloon pump support during transfer.

LV, left ventricular; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction.
Adapted from Ref. 6.

fied formally by that hospital that their skills and judgment are excellent and outcomes equivalent or superior to the national benchmarks.

c. Operators performing PCI without on-site surgery should perform ≥100 total PCIs per year, including ≥18 primary PCIs per year. These numbers exceed those currently recommended in the ACC/AHA/SCAI guidelines to reflect the opinion of this writing group that a greater experience level is appropriate for PCI in this setting.
d. In the United States, board certification in interventional cardiology by the American Board of Internal Medicine is strongly recommended for all physicians performing PCI.

Facilities and Support Personnel

It is essential that all support personnel have adequate education regarding the management of PCI patients before, during, and after the procedure. This knowledge should include potential procedural complications and their management and the drug therapies used in PCI patients (Table I).

Facilities performing both primary and elective procedures without on-site surgery should perform a minimum of 200 PCI/year. Programs with <200 PCI/year should be reviewed on an individual basis. They should remain open only if they are in geographically isolated or under-served areas and their performance metrics are equivalent to accepted benchmarks. We recommend that each country or state review this issue, and establish an absolute minimum annual case volume below which a PCI program must close under any circumstance. In the United States, this minimum should be 150 PCI/year for a program offering both primary and elective PCIs and this must include a minimum of 36 primary PCI/year. Programs offering only primary PCIs must perform a minimum of 36 primary PCIs/year to remain operational. At the present time in the United States, there is no justification for a PCI

TABLE III. Recommendations for Patient and Lesion Selection and Backup Strategy for Nonemergent PCI at Hospitals Without On-site Cardiac Surgery and by Operators Performing ≥100 PCIs/Year

Patient Risk: expected clinical risk in case of occlusion caused by procedure.

High Patient Risk: Patients with any of the following:
- decompensated congestive heart failure (Killip Class 3) without evidence for active ischemia, recent CVA, advanced malignancy, known clotting disorders;
- left ventricular ejection fraction ≤25%;
- left main stenosis (≥50%) or three-vessel disease unprotected by prior bypass surgery (>70% stenoses in the proximal segment of all major epicardial coronary arteries);
- single target lesion that jeopardizes over 50% of remaining viable myocardium.

Lesion Risk: probability that procedure will cause acute vessel occlusion.

Increased Lesion Risk: lesions in open vessels with any of the following characteristics:
- diffuse disease (>2 cm in length) and excessive tortuosity of proximal segments;
- more than moderate calcification of a stenosis or proximal segment;
- location in an extremely angulated segment (>90°);
- inability to protect major side branches;
- degenerated older vein grafts with friable lesions;
- substantial thrombus in the vessel or at the lesion site;
- any other feature that may, in the operator's judgment, impede successful stent deployment.
- aggressive measures to open chronic total occlusions are also discouraged due to an increased risk of perforation.

Strategy for Surgical Backup Based on Lesion and Patient Risk:

High-Risk Patient with High-Risk Lesion should not undergo nonemergent PCI at a facility without on-site surgery.

High-Risk Patient with Not High-Risk Lesion: nonemergent patients with this profile may undergo PCI, but confirmation that a cardiac surgeon and operating room is immediately available is necessary.

Not High-Risk Patient with High-Risk Lesion requires no additional precautions.

Not High-Risk Patient with Not High-Risk Lesion requires no additional precautions. Best scenario for PCI without on-site surgery.

CVA, cerebrovascular accident; PCI, percutaneous coronary intervention. Adapted from Ref. 6.

TABLE IV. Requirements for Off-Site Surgical Backup

1. Interventional cardiologists establish a working relationship with cardiac surgeons at the receiving facility.
2. Cardiac surgeon must have privileges at the referring facility to allow review of treatment options as time allows.
3. Cardiac surgeons and receiving hospital agree to provide cardiac surgical backup for urgent cases at all hours and for elective cases at mutually agreed hours
4. Surgeon and receiving facility assure that patient will be accepted based on medical condition, capacity of surgeons to provide services at the time of request and availability of resources. If this cannot be assured before starting an elective procedure, the case should not be done at that time.
5. Interventional cardiologist must review with the surgeon the immediate needs and status of any patient transferred for urgent surgery.
6. Hospital administrations from both facilities endorse transfer agreement.
7. Transferring and receiving facility establish a rigorous protocol for the rapid transfer of patients, including the proper personnel with appropriate experience.
8. Transport provider is available to begin transport within 20 min of the request and provide vehicle/helicopter with necessary life-sustaining equipment, including IABP and monitoring capability.
9. Transferring physician obtains consent for surgery from patient or appropriate surrogate.
10. Initial informed consent for PCI discloses that procedure is being done without on-site surgical backup and acknowledges possibility of risks related to transfer. The consent process should include the risk of urgent surgery (~0.3%) and state that a written plan for transfer exists.
11. As part of the local continuous quality improvement program, a regular review of all patients transferred for emergency surgery with the outcome of surgery and identification of any improvement opportunities.

IABP, intraaortic balloon pump; PCI, percutaneous coronary intervention.

program without on-site surgery to perform only elective procedures or not provide availability to primary PCI 24 hr/day, but such a situation may exist in other countries and be appropriate. New programs should have 2 years to reach the absolute minimum volume, but after that programs failing to reach this volume for 2 consecutive years should not remain open under any circumstance.

Patient and Lesion Selection

Rigorous clinical and angiographic selection criteria are essential for programs performing PCI without on-site surgery. Since the clinical situation and risk-to-benefit ratio are different for primary versus elective PCI, different criteria and standards should apply (Table II). In elective PCI without on-site surgery, it is necessary to assess not only the likelihood of PCI failure, but also the potential patient risk if complications occur since it is possible to have a low-risk lesion in a high-risk patient and vice versa. It is important to consider both the patient and lesion risk when developing criteria for selection of appropriate patients for treatment in facilities without on-site surgery (Table III).

Requirements for Off-Site Surgery

A close alliance and cross-communication with cardiovascular surgeons with formalized agreements and periodically tested protocols for the emergency transfer of patients are essential (Table IV). Interventional cardiologists and cardiac surgeons must be actively involved in the program with attendance at regularly scheduled cardiac catheterization conferences and participation in risk management activities.

In hospitals with on-site surgery, it is no longer standard for a surgical suite to be held open awaiting the completion of a PCI. Because the need for urgent surgery is so infrequent, there are no current data regarding the actual time required to transport a patient to the operating room and initiate cardiopulmonary bypass should the need arise. Should a patient undergoing PCI at a facility without on-site surgery develop a complication requiring urgent transfer for surgery, it is unclear whether or by how much the facility-to-facility transport would add an additional delay in the current practice environment where operating rooms are not held open at on-site facilities. Minimizing the time to the initiation of cardiopulmonary bypass is the goal in this situation and more likely is feasible with on-site cardiac surgery if that surgery is immediately available. There is no acknowledged goal with supporting data similar to a door-to-balloon time for the initiation of cardiopulmonary bypass in this situation, but this should always be accomplished as rapidly as possible, with the goal of <120 min. Operators at facilities without on-site surgical backup should activate the emergency transport system at the first clear signs of a complication even if they attempt to salvage the situation using percutaneous techniques.

Monitoring of Programs

Providing the highest quality PCI services to patients mandates the collection of outcome data and comparison of these data to established benchmarks. Regardless of the mechanism, all PCI programs, with or without on-site surgical backup, must collect appropriate outcome data and compare their data to state, national or their country's performance standards. Data submitted must be audited by an independent authority periodically to insure integrity of the entire process.

UNRESOLVED ISSUES AND FUTURE DIRECTIONS

PCI without on-site surgery is a polarizing and emotional issue for many individuals both within and external to the interventional community. Although debate has focused on whether facilities that offer PCI without on-site surgery should exist, a more meaningful approach would focus on the goal of providing the best possible care to patients who require PCI, regardless of the setting. Recent publications suggest this goal is not being consistently met. Data indicate that the number of coronary artery bypass operations is declining. This trend is likely to continue, resulting in the closing of smaller surgical programs and the coalescence of cardiac surgical services to more centralized locations. If cardiac surgery programs begin to shrink, it will become more difficult for all PCI facilities to have on-site cardiac surgery.

It is inappropriate to open PCI centers if they are not based on the health needs of the community. Opening a low-volume PCI program within the same geographic area and thereby converting a high-volume program at another facility to a low-volume program is not necessarily in the best interests of patients in the community. There is clearly a potential for unnecessary or inappropriate PCI program development in the same geographic area and this is strongly discouraged. However, the factors that define a geographic area are not consistent throughout the United States or other countries. The level and availability of emergency transport services, response times of emergency medical transport, immediate availability of qualified cath lab personnel, and coverage by interventional cardiologists must be considered.

Desires for personal or institutional financial gain, prestige, market share, or other similar motives should not be part of the decision process in determining the need for a PCI program. These considerations apply equally to those wishing to start a new PCI program without on-site backup and those wishing to protect existing programs with on-site backup. In the final analysis, every PCI procedure, regardless of where it is performed, should be of the highest possible quality. This means the PCI is done for appropriate clinical indications, by a skilled operator with documented satisfactory outcomes in a laboratory with appropriate equipment and personnel that has careful tracking of patient outcomes and corrective mechanisms in place to manage individual operator or laboratory outcome data that fall below national standards. Ensuring that all PCI programs meet appropriate performance metrics is likely to save more lives than requiring all PCI programs have on-site surgery.

RECOMMENDATIONS

1. PCI without on-site surgical backup is being performed with acceptable outcomes and risks in the United States and many other countries. The recommendations outlined in this document are made to ensure patient safety and quality outcomes in such a work environment. This is not an open endorsement of PCI without on-site surgery and we do not support the wide-spread use of PCI without on-site surgery especially in the United States, but acknowledge that this practice may be appropriate in some circumstances.
2. The decision to begin or operate a PCI program without on-site surgical backup should be based on the health needs of a local area, not on desires for personal or institutional financial gain, prestige, market share, or other similar motives. Rural communities may have different health care delivery needs than urban centers and this should be considered.

3. It is the goal of SCAI to promote the highest possible program quality. Accordingly, PCI programs both with and without on-site surgical backup must evaluate their outcomes against their countries' benchmark for program performance or other acceptable standard.
4. Operators performing PCI without on-site surgery should perform ≥100 total PCIs per year, including ≥18 primary PCIs per year. The initial operators at a facility without on-site backup should not begin performing PCI in such facilities until they have a lifetime experience of >500 PCIs as primary operator after completing fellowship. Only operators with complication rates and outcomes equivalent or superior to national benchmarks should perform PCI procedures.
5. Independent program oversight should occur either within the context of a local facility's quality assurance program or through an independent government or external agency. Any program failing to perform adequately should close.
6. Further data collection and analysis should be done to more completely understand the role of PCI without on-site surgical backup as a strategy for the delivery of care.

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APPENDIX

TABLE SCAI Writing Committee for Expert Consensus Document Disclosures

Name	Do you perform elective PCIs in a hospital that has on-site surgical backup?	Do you have an ownership or other financial relationship with a hospital that performs elective PCIs and has on-site surgical backup?	Do you perform elective PCIs in a hospital that does not have on-site surgical backup?	Do you have an ownership or other financial relationship with a hospital that performs elective PCIs and does not have on-site surgical backup?	Comments
Dr. Gregory J. Dehmer	Yes	No	No	No	None
Dr. James Blankenship	Yes	No	No	No	None
Dr. Thomas P. Wharton, Jr.	Yes	No	Yes	No	None
Dr. Ashok Seth	Yes	No	No	No	None
Dr. Douglass A. Morrison	Yes	No	No	No	I perform PCI at one hospital with on-site surgery and primary PCI only at a different hospital without on-site surgery.
Dr. Carlo DiMario	Yes	No	No	No	
Dr. David Muller	Yes	No	No	No	I perform primary PCI at a hospital without on site surgery
Dr. Mirle Kellett	Yes	No	No	No	None
Dr. Barry F. Uretsky	Yes	No	No	No	None

PCI, percutaneous coronary intervention.

ADJUNCTIVE

Percutaneous Coronary Interventions in Facilities Without Cardiac Surgery On Site: A Report From the National Cardiovascular Data Registry (NCDR)

Michael A. Kutcher, Lloyd W. Klein, Fang-Shu Ou, Thomas P. Wharton, Jr, Gregory J. Dehmer, Mandeep Singh, H. Vernon Anderson, John S. Rumsfeld, William S. Weintraub, Richard E. Shaw, Matthew T. Sacrinty, Albert Woodward, Eric D. Peterson, Ralph G. Brindis, on behalf of the National Cardiovascular Data Registry (NCDR)

J. Am. Coll. Cardiol. 2009;54;16-24
doi:10.1016/j.jacc.2009.03.038

JACC
JOURNAL *of the* AMERICAN COLLEGE *of* CARDIOLOGY

Attachment C

Journal of the American College of Cardiology
© 2009 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 54, No. 1, 2009
ISSN 0735-1097/09/$36.00
doi:10.1016/j.jacc.2009.03.038

News from the NCDR

NCDR™
National Cardiovascular Data Registry

Percutaneous Coronary Interventions in Facilities Without Cardiac Surgery On Site: A Report From the National Cardiovascular Data Registry (NCDR)

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Since the introduction of percutaneous coronary intervention (PCI) in 1977 by Andreas Gruntzig (1), the presence of cardiac surgery backup on site has been a recommended practice to treat the potential of life-threatening complications. As a result of major improvements in technology and pharmacology, the need for emergency cardiac surgery is now infrequent (0.3% to 0.6%) (2,3). Moreover, primary PCI has been accepted as superior to fibrinolytic therapy for ST-segment elevation myocardial infarction (STEMI) (4). These developments have provided the justification for some hospitals without cardiac surgery to develop PCI programs based on a strategy to provide more rapid care for STEMI (5,6) and to increase the availability of PCI to patients in geographically underserved areas.

Favorable outcomes for primary PCI performed in facilities without cardiac surgery backup on site have been reported (7–9). In addition, smaller observational studies have extended this concept to both primary and elective PCI (10–14), and even PCI limited to elective cases (15). However, there are few large studies that have directly compared the procedural outcomes of both primary and elective PCI at facilities without cardiac surgery on site with those that have traditional surgery on site (16–18). Because of the conflicting literature on this subject, the American College of Cardiology (ACC), American Heart Association (AHA), and Society for Cardiovascular Angiography and Interventions (SCAI) 2005 PCI guidelines continue to designate primary PCI a Class IIb indication (may be considered), and elective PCI a Class III indication (not recommended) when performed at facilities without surgical backup on site (19). The 2007 PCI guideline focused update did not address or change these designations (20). Despite

From the *Wake Forest University School of Medicine, Winston-Salem, North Carolina; †Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois; ‡Duke Clinical Research Institute, Durham, North Carolina; §Exeter Hospital, Exeter, New Hampshire; ||Texas A&M University College of Medicine, Scott & White HealthCare, Temple, Texas; ¶Mayo Clinic, Rochester, Minnesota; #University of Texas Health Science Center, Houston, Texas; **Denver VA Medical Center, Denver, Colorado; ††Christiana Health Care System, Newark, Delaware; ‡‡Sutter Pacific Heart Centers, San Francisco, California; §§National Cardiovascular Data Registry, Washington, DC; and ||||Northern California Kaiser Permanente, San Francisco, California. Data analysis was performed by the Duke Clinical Research Institute with funding from the National Cardiovascular Data Registry. Drs. Kutcher and Klein perform percutaneous coronary intervention (PCI) at facilities that have on-site cardiac surgery. Dr. Wharton is a consultant to Corazon, The Heart and Vascular Experts, and performs PCI at a facility that does not have on-site cardiac surgery. Dr. Dehmer is Chief, Division of Cardiology, Texas A&M College of Medicine, Scott & White HealthCare, which includes facilities that have on-site cardiac surgery and facilities that do not. Dr. Singh performs PCI at Mayo Clinic facilities that have on-site cardiac surgery and facilities that do not. Dr. Anderson performs PCI at a facility that has on-site cardiac surgery.

these classifications, the number of PCI programs in the U.S. without surgery on site has increased significantly over the past several years (21). Recently, a SCAI expert panel outlined practical consensus principles for PCI performed at facilities without surgery on site, while not specifically encouraging or endorsing this practice (22).

The National Cardiovascular Data Registry (NCDR) was established by the ACC to proactively monitor and assess the clinical practice of cardiology in the U.S. (23). The NCDR CathPCI Registry, cosponsored by the ACC and SCAI, offers its participant institutions data field definitions, uniform data entry, secure transmission requirements, a data quality program, and risk-adjustment algorithms (24–26). Therefore, this registry provides an excellent resource of comparative data, in a relative contemporary clinical setting, to address the controversy over PCI at facilities without surgical backup on site.

Methods

Study population. Clinical characteristics and in-hospital outcomes were assessed in consecutive PCI cases reported to the NCDR CathPCI Registry from January 1, 2004, to March 30, 2006. Standardized NCDR version 3.04 definitions and data fields were used by all participating sites (27). The analysis cohort consisted of 308,161 patients from 465 PCI-capable facilities. Of these, 8,736 patients had PCI performed at 60 institutions in which it was verified there was no surgical backup on site within the buildings or campus that constituted the facility (off-site facility). The remaining 299,425 patients underwent PCI at 405 facilities that had cardiac surgery on site (on-site facility). Off-site PCI facilities comprised 13% of sites and 3% of patients in the NCDR CathPCI Registry during the study period.

Definitions. The primary outcomes for analysis were the incidence of emergency surgery and in-hospital death from all causes after PCI. Emergency surgery was defined as coronary artery bypass graft (CABG) surgery performed after PCI in which there was evidence of active ischemia or mechanical dysfunction (emergency), or if the patient required cardiopulmonary resuscitation en route to the operating room or before anesthesia (emergent/salvage). Secondary outcomes included procedure success, total complications (any general, bleeding, or vascular complications), and reperfusion time in cases of primary PCI for STEMI.

Off-site data clarification. During initial analysis, variations in 2 data fields unique to off-site PCI programs were noted. The field "CABG during this admission" permitted entry of only 1 category. In off-site centers, there was a disproportionately low incidence of "emergency" surgery, but a proportionately large number of patients "transferred for CABG" entered in this field. In addition, "transfer" patients could be counted as "alive" in the data field "discharge status" from an off-site center, but this opened the potential that a subsequent death after emergency surgery at the outside surgical center may not have been captured.

To resolve these issues, we conducted a data clarification project. Off-site centers with specific data points in question were queried to clarify whether a "transfer for CABG" data point was for elective or emergency surgery, and to verify the eventual survival at the off-site surgical center. This effort also provided an opportunity to gather additional information by a Capabilities Survey to reaffirm a true off-site status and to assess organization, staffing, and logistics. All of the off-site programs were invited to fill out the survey form, even those sites in which data clarification was not necessary.

Abbreviations and Acronyms

ACC = American College of Cardiology

AHA = American Heart Association

CABG = coronary artery bypass graft surgery

IABP = intra-aortic balloon pump

MI = myocardial infarction

NSTEMI = non–ST-segment myocardial infarction

PCI = percutaneous coronary intervention

SCAI = Society for Cardiovascular Angiography and Interventions

STEMI = ST-segment elevation myocardial infarction

Of the 8,736 patients undergoing PCI in off-site centers, 172 (2%) patients from 43 sites required data clarification regarding transfer surgery or mortality status. Of these 43 sites, 38 (88%) sites were able to clarify CABG status and/or mortality information for 154 of the 172 (90%) patients. For the 18 patients (0.2% of 8,736) whose transfer or mortality data were not clarified, if CABG status was uncertain, the original record entry was used for the CABG status-related analysis. If the subsequent mortality at the receiving surgery center could not be clarified, these patients were not included in the analysis of observed or risk-adjusted mortality.

Statistical analysis. Data analysis was performed by the Duke Clinical Research Institute. For descriptive analyses, institutional comparisons between off- and on-site PCI centers were made based on hospital characteristics. Comparisons between patients were made based on clinical characteristics, treatment profiles, procedural details, and clinical outcomes. These aggregates were further divided and analysis performed in patients who underwent primary PCI as first-line therapy for reperfusion in the presence of STEMI, and to the remainder of patients who underwent PCI in a nonprimary setting. Continuous variables are presented as mean with SD or as frequencies with percentages in each pre-specified category. Categorical variables are expressed as frequencies with percentages. To test for independence of patients' baseline characteristics, in-hospital care patterns and outcomes with respect to off-site versus on-site centers, the Wilcoxon rank-sum test was used for continuous variables, and the Pearson chi-square test was used for categorical variables.

A multivariable logistic regression model was then used to estimate the risk-adjusted association between on-site versus off-site PCI center surgical status and primary outcomes. Variables adjusted to mortality in-

JACC Vol. 54, No. 1, 2009
June 30, 2009:16–24

cluded age, sex, insulin-treated diabetes mellitus, hypercholesterolemia, hypertension, dialysis, cerebrovascular disease, chronic lung disease, peripheral vascular disease, congestive heart failure, prior CABG, prior PCI, prior myocardial infarction (MI), cardiogenic shock at presentation, MI status (STEMI, non–ST-segment myocardial infarction [NSTEMI], and no MI), pre-operative intra-aortic balloon pump (IABP), PCI status (rescue, emergent, urgent, and elective), subacute thrombosis in a major artery, any treated lesion in left main artery, any treated lesion with pre-procedure stenosis 100%, any treated lesion with pre-procedure Thrombolysis In Myocardial Infarction (TIMI) flow grade 0, any treated lesion with high/C risk characteristics (see definition, bottom legend, Table 1), and total number of lesions treated. Variables adjusted to emergency CABG included cardiogenic shock, MI status (STEMI, NSTEMI, and no MI), pre-operative IABP, PCI status (rescue, emergent, urgent, and elective), and any treated left main artery lesion.

The Generalized Estimate Equation method (28) was applied to account for within-hospital clustering, considering patients at the same hospital are more likely to have similar responses relative to patients in other hospitals (i.e., within-center correlation for response). This method produces estimates comparable to those from ordinary logistic regression, but estimated variances are adjusted for the correlation of outcomes within each hospital.

Because not all off-site PCI center patient mortality data could be clarified, a sensitivity analysis was performed. This analysis utilized the same multivariable logistic regression model but imputed data to either of the following: patients with missing mortality data were considered either as all had died (worst scenario) or as all were alive (best scenario) on discharge.

Results

Institutional characteristics. Institutional characteristics are shown in Table 2. Compared with on-site centers, off-site PCI facilities had smaller bed capacity, were more likely to be located in nonurban areas, and had lower annual total PCI and primary PCI volume ($p < 0.001$). Overall, 43 (72%) of the off-site programs performed <200 total PCIs per year, and only 3 sites (5%) had >400 cases, suggesting that it was unlikely the outcomes were preferentially influenced by a few large-volume centers. The recommended volume standard of 36 or more primary PCIs per year (19) was achieved by 42% of the off-site programs compared with 80% of the on-site centers ($p < 0.001$).

Off-site capabilities survey. The survey (Table 3) was completed by 53 of the 60 off-site PCI facilities (88%). Approximately one-quarter of the centers had travel distances >40 miles and transit times (estimated driving or flight) >30 min. This information also reaffirmed that these were true off-site programs and did not have surgery back-up nearby in the next building. Full 24-h, 7-day coverage for PCI was provided by 92% of the sites. Both primary and elective PCI were performed in 79% of the centers, and none of the programs performed only elective PCI. Descriptive demographics regarding the organization of technical staff, interventional cardiologists, and transpor-

Table 1 Clinical Characteristics by PCI Status

	All PCI Patients			Primary PCI Patients			Nonprimary PCI Patients		
Characteristic	Off-Site (n = 8,736)	On-Site (n = 299,425)	p Value	Off-Site (n = 1,934)	On-Site (n = 31,099)	p Value	Off-Site (n = 6,802)	On-Site (n = 268,312)*	p Value
Age, yrs, mean ± SD	63.5 ± 12	64.1 ± 12	<0.001	61.2 ± 13	60.6 ± 13	0.194	64.2 ± 12	64.4 ± 12	0.062
Male	5,817 (67)	198,656 (66)	0.639	1,384 (72)	21,958 (71)	0.371	4,433 (65)	176,688 (66)	0.243
Previous MI >7 days	2,285 (26)	87,521 (29)	<0.001	327 (17)	5,440 (17)	0.509	1,958 (29)	82,077 (31)	0.001
Previous CHF	839 (9.6)	30,953 (10.3)	0.026	80 (4)	1,442 (5)	0.308	759 (11)	29,510 (11)	0.675
Diabetes	2,534 (29)	95,160 (32)	<0.001	361 (19)	6,514 (21)	0.016	2,173 (32)	88,642 (33)	0.058
Previous renal failure	367 (4)	15,868 (5)	<0.001	56 (3)	1,033 (3)	0.308	311 (4.6)	14,835 (5.5)	<0.001
Cerebrovascular disease	817 (9)	33,865 (11)	<0.001	105 (5)	2,165 (7)	0.010	712 (10)	31,700 (12)	<0.001
Peripheral vascular disease	895 (10)	35,519 (12)	<0.001	123 (6)	2,019 (6)	0.818	772 (11)	33,500 (12)	0.005
Hypertension	6,226 (71)	225,404 (75)	<0.001	1,069 (55)	18,275 (59)	0.002	5,157 (76)	207,120 (77)	0.007
Dyslipidemia	5,827 (67)	220,220 (74)	<0.001	974 (50)	17,432 (56)	<0.001	4,853 (71)	202,780 (76)	<0.001
Previous PCI	2,711 (31)	105,133 (35)	<0.001	321 (17)	5,254 (17)	0.735	2,390 (35)	99,875 (37)	<0.001
Previous CABG	1,068 (12)	56,815 (19)	<0.001	99 (5)	1,810 (6)	0.199	969 (14)	55,000 (21)	<0.001
Lesion characteristics									
≥2 lesions in laboratory visit	2,503 (29)	99,309 (33)	<0.001	478 (25)	8,463 (27)	0.048	2,025 (30)	90,843 (34)	<0.001
Segment in SVG	396 (5)	20,644 (7)	<0.001	55 (3)	989 (3)	0.657	341 (5)	19,675 (7)	<0.001
High-risk C lesion†	3,426 (39)	123,207 (41)	<0.001	1,106 (57)	18,933 (61)	0.001	2,320 (34)	104,270 (39)	<0.001

Data are n (%) unless otherwise indicated. *14 patients not included due to missing value for variable "Acute PCI." †High risk C lesion includes any of the following: diffuse (length >20 mm), excessive tortuosity of proximal segment, extremely angulated segments >90 degrees, total occlusions >3 months old and/or bridging collaterals, inability to protect major side branches, and degenerated vein grafts with friable lesions.

CABG = coronary artery bypass grafting; CHF = congestive heart failure; MI = myocardial infarction; PCI = percutaneous coronary intervention; SVG = saphenous vein graft.

tation modalities are further outlined in Table 3. Of note, 81% of the off-site programs reported that their interventional operators also rotated and performed PCI at on-site facilities.

Clinical characteristics. Clinical characteristics are shown in Table 1. In aggregate, on-site PCI centers generally treated patients with more risk factors and performed a greater percentage of PCI in multiple-lesion (33% vs. 29%, $p < 0.001$), saphenous vein graft (7% vs. 5%, $p < 0.001$), and higher lesion-risk cases (41% vs. 39%, $p = 0.001$). This difference was more pronounced in patients who underwent nonprimary PCI. In contrast, off-site facilities had a greater incidence of patients who had a clinical presentation of STEMI or NSTEMI (41% vs. 29%, $p < 0.001$) (Fig. 1).

Observed unadjusted procedural outcomes. Observed unadjusted procedural outcomes are shown in Table 4. Off-site facilities had slightly higher aggregate procedural success (94% vs. 93%, $p = 0.010$), predominantly due to higher success rates in nonprimary PCI cases. Aggregate total complications were similar in both off- and on-site facilities (6.5% vs. 6.3%), but off-site programs tended to have more bleeding events, and on-site more vascular complications. Off-site programs had fewer total complications in primary PCI (11.6% vs. 13.4%, $p = 0.029$) and had lower general (2.6% vs. 3.3%, $p = 0.001$) and vascular (0.8% vs. 1.1%, $p = 0.017$) complication rates in nonprimary PCI patients compared with on-site facilities.

In the overall PCI cohort, there was no significant difference in the incidence of emergency CABG surgery (0.3% vs. 0.4%, $p = 0.271$) or mortality with emergency CABG (13.6% vs. 12.8%, $p = 0.907$) between off- and on-site facilities, respectively. There was no difference in

Table 2 Institutional Characteristics

Variable	Off-Site (n = 60)	On-Site (n = 405)	p Value
Number of CMS-certified beds			
Median	198	371	<0.001
Mean ± SD	212 ± 109	403 ± 188	
<200	31 (52%)	40 (10%)	<0.001
≥200 and <400	27 (45%)	178 (44%)	
≥400	2 (3%)	185 (46%)	
Location/community type			
Rural	21 (35%)	67 (17%)	<0.001
Suburban	24 (40%)	115 (28%)	
Urban	15 (25%)	223 (55%)	
Average annual PCI volume			
Median	134	612	<0.001
Mean ± SD	166 ± 138	745 ± 551	
<200	43 (72%)	23 (6%)	<0.001
≥200 and <400	14 (23%)	98 (24%)	
≥400	3 (5%)	284 (70%)	
Average annual primary PCI volume			
Median	32	66	<0.001
Mean ± SD	35 ± 22	78 ± 52	
≥36	25 (42%)	324 (80%)	<0.001

Two sites had missing Centers for Medicare and Medicaid Services (CMS) bed data. Primary percutaneous coronary intervention (PCI) indicates PCI performed as first-line therapy for reperfusion in the presence of ST-segment elevation myocardial infarction (STEMI), and does not include rescue or facilitated PCI or PCI for non-STEMI.

Table 3 Off-Site Capabilities Survey

Characteristic	Off-Site (n = 53)
Average travel distance to surgical facility, miles	
Mean ± SD	36 ± 59
<10	11 (21%)
≥10 and <20	18 (34%)
≥20 and <40	11 (21%)
≥40	13 (25%)
Average transit time to surgical facility, min	
Mean ± SD	25 ± 17
<10	4 (8%)
≥10 and <20	16 (30%)
≥20 and <30	19 (36%)
≥30	14 (26%)
Predominant transportation mechanism	
Ground ambulance	28 (53%)
Helicopter	11 (21%)
Fixed wing aircraft	1 (2%)
Combination of ground or air	13 (25%)
Dedicated staff and facilities for PCI	
24 h, 7 days a week	49 (92%)
Daytime during weekdays only	3 (6%)
Variable time frames	1 (2%)
Type of PCI provided	
Only primary PCI for acute MI	11 (21%)
Both primary PCI and elective PCI	42 (79%)
Only elective PCI	0 (0%)
Catheterization laboratory staff experience*	
Work only at off-site PCI center	41 (77%)
Rotate between off- and on-site PCI centers	11 (21%)
Interventional operators at facility	
Mean ± SD	5 ± 4
1	5 (9%)
2 to 3	18 (34%)
4 to 5	11 (21%)
6 or more	19 (36%)
Interventional operators' experience*	
Work only at off-site PCI center	9 (17%)
Rotate between off- and on-site PCI centers	43 (81%)

*One site did not respond.
Abbreviations as in Table 1.

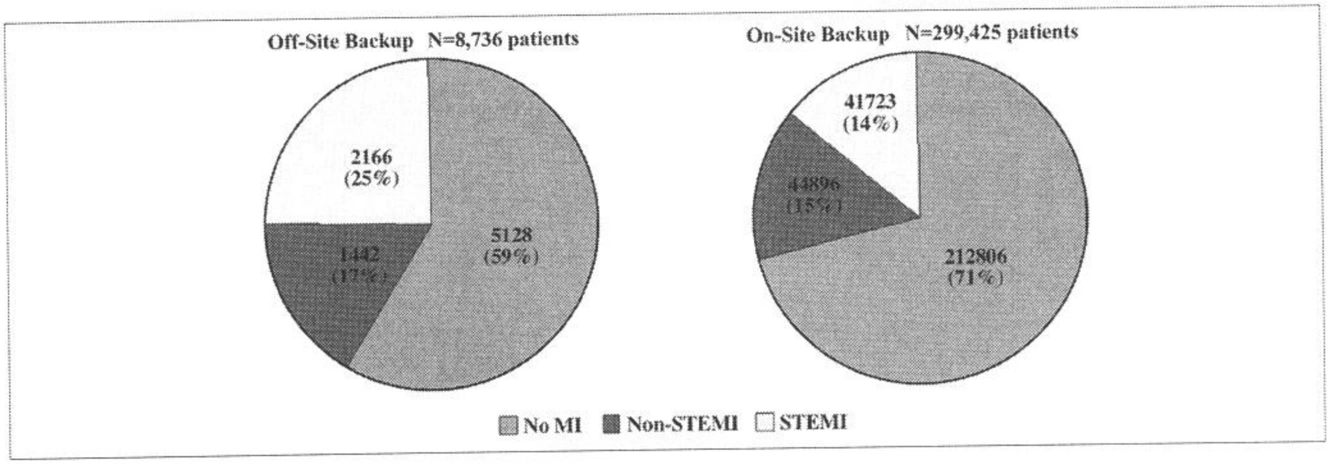
either of these variables when the analysis was stratified into primary PCI and nonprimary PCI patients. Although the unadjusted aggregate mortality rate was higher in off-site facilities (1.7% vs. 1.2%, $p < 0.001$) and appeared to be confined to patients who did not require emergency surgery, this difference did not persist when stratified by primary or nonprimary PCI. This increased unadjusted aggregate mortality was most likely due to a higher proportion of primary PCI patients (22% vs. 10%, $p < 0.001$) and STEMI and NSTEMI presentations (41% vs. 29%, $p < 0.001$) in off-site compared with on-site programs, respectively.

Primary PCI reperfusion times in nontransferred patients were significantly shorter in off-site PCI centers (mean 2.1 ± 5.1 h, median 1.4 h) compared with on-site (mean 2.6 ± 8.4 h, median 1.5 h, $p < 0.001$). These "reperfusion times" were defined as the time of arrival at the facility to the time of first treatment device deployment (27). Although both groups followed the same definition, these data were collected before there were major national quality

JACC Vol. 54, No. 1, 2009
June 30, 2009:16–24

Figure 1 MI Presentation Status

Pie charts showing the relative distribution of myocardial infarction (MI) presentation within centers with on- or off-site surgical backup.
Blue areas indicate no MI; **purple areas** indicate non–ST-segment elevation myocardial infarction (non-STEMI); **yellow areas** indicate STEMI. $p < 0.001$.



improvement initiatives and attention to the detailed measurements of true "door-to-balloon" times. Therefore, these times do not reflect the current door-to-balloon standards.

Risk-adjusted outcomes. After risk adjustment, there were no mortality differences between off- and on-site facilities among total PCI patients, primary PCI patients, nonprimary PCI patients, or patients who did not require emergency surgery (Fig. 2). There was a higher risk-adjusted odds of emergency surgery in on-site PCI centers (odds ratio: 0.60 [95% confidence interval: 0.37 to 0.98], $p = 0.042$).

A sensitivity analysis was performed comprising models that imputed missing mortality from off-site centers to 2 potential scenarios. Although the point estimate changed from 0.88 to 1.21, the confidence intervals surrounding these estimates were not statistically significant between off- and on-site facilities under either of these extreme assumptions.

Discussion

This study represents the largest and most comprehensive clinical comparison of PCI centers in the U.S. with and without cardiac surgery support on site. Despite lower annual PCI procedural volumes and more patients presenting with MI subsets, off-site PCI facilities reporting to the NCDR CathPCI Registry had similar rates of procedural success, morbidity, emergency surgery, and risk-adjusted mortality when compared with on-site PCI centers. These results persisted whether PCI was performed as primary therapy for STEMI or in a less urgent nonprimary PCI setting. In addition, the off-site Capabilities Survey in this study provided more descriptive information than has been previously reported in the literature regarding the organization and logistics of established off-site PCI programs.

It is important to contrast this study with the few large comparative reports in the literature. Wennberg et al. (16) found no difference in risk-adjusted mortality for primary PCI at facilities without surgery backup on site, but an increase in mortality for nonprimary/rescue PCI, particularly at very low-volume programs (<50 Medicare PCIs per year). Although their study had more hospitals without surgery on site (n = 178) and similar patient volumes (n = 8,168), the time period was from 1999 to 2001, and the data were derived from coded admission/discharge billing diagnoses confined to the Medicare population. In contrast, our study was based on well-defined contemporary clinical parameters and included clarification of ambiguous transfer data from the off-site PCI programs. We found no significant difference for risk-adjusted mortality between centers with and without surgery on site, in either primary or nonprimary PCI patients.

Ting et al. (17) previously reported comparable acute and long-term outcomes for both primary and elective PCI in a propensity score analysis of 1,007 cases from a PCI center without surgery on site matched to the same number of patients from a center with surgery on site. Of note, these Mayo Clinic facilities did not participate in the NCDR, and thus their patients were not included in our analysis.

Finally, in a recent report based on SCAAR (Swedish Coronary Angiography and Angioplasty Registry), Carlsson et al. (18) compared 8,838 PCI procedures from 14 PCI facilities that did not have cardiac surgery on site to 25,525 procedures from 10 PCI centers that did have surgery on site. Their analysis was adjusted for baseline variables, and demonstrated comparable 30-day and 1-year mortality and morbidity outcomes for both primary PCI and nonacute PCI. Although different variables were used in our risk-

Table 4 Observed Unadjusted Procedural Outcomes

Outcome	All PCI Patients Off-Site (n = 8,736)	All PCI Patients On-Site (n = 299,425)	p Value	Primary PCI Patients Off-Site (n = 1,934)	Primary PCI Patients On-Site (n = 31,099)	p Value	Nonprimary PCI Patients Off-Site (n = 6,802)	Nonprimary PCI Patients On-Site (n = 268,312)*	p Value
PCI procedure success	8,194 (94)	278,844 (93)	0.010	1,756 (92)	27,909 (91)	0.139	6,438 (95)	250,923 (94)	<0.001
Total complications	567 (6.5)	18,796 (6.3)	0.399	222 (11.6)	4,104 (13.4)	0.029	345 (5.1)	14,692 (5.5)	0.150
General complications	320 (3.7)	11,629 (3.9)	0.304	144 (7.5)	2,792 (9.1)	0.021	176 (2.6)	8,837 (3.3)	0.001
Bleeding complications	261 (3.0)	7,036 (2.4)	<0.001	104 (5.4)	1,620 (5.3)	0.749	157 (2.3)	5,416 (2.0)	0.093
Vascular complications	66 (0.8)	3,198 (1.1)	0.005	14 (0.7)	344 (1.1)	0.115	52 (0.8)	2,854 (1.1)	0.017
Overall mortality	151 (1.7)	3,632 (1.2)	<0.001	97 (5.1)	1,607 (5.2)	0.869	54 (0.8)	2,025 (0.8)	0.700
Emergency CABG	26 (0.3)	1,110 (0.4)	0.271	14 (0.7)	357 (1.2)	0.091	12 (0.2)	753 (0.3)	0.107
Mortality									
Emergency CABG	3/22† (13.6)	142/1,110† (12.8)	0.907	2/12† (16.7)	59/357† (16.5)	0.990	1/10† (10.0)	83/753† (11.0)	0.918
No emergency CABG	148/8,669† (1.7)	3,488/298,293† (1.2)	<0.001	95/1,894† (5.0)	1,547/30,741† (5.0)	0.975	53/6,775† (0.8)	1,941/267,538† (0.7)	0.587
Reperfusion times (h), nontransfer patients				(n = 1,678)	(n = 19,708)				
Mean ± SD				2.1 ± 5.1	2.6 ± 8.4	<0.001			
Median				1.4	1.5				

Procedure success was defined as residual stenosis <50% with Thrombolysis in Myocardial Infarction flow grade 3 and minimal decrease in stenosis ≤20% in all lesions attempted. Total complications was defined as any of the following complications: general complications: periprocedural MI, cardiogenic shock, congestive heart failure, cerebrovascular accident, tamponade, thrombocytopenia, contrast reaction, renal failure; bleeding complications: bleeding at the access site, retroperitoneal, gastrointestinal, genitourinary, or other; vascular complications: access site occlusion, peripheral embolization, arterial dissection, arterial pseudoaneurysm, or arterio-venous fistula. Primary PCI was defined as PCI performed as first-line therapy for reperfusion in the presence of STEMI; does not include rescue or facilitated PCI or PCI for non-STEMI. Reperfusion time indicates time of arrival to facility to time of first intracoronary treatment device deployment. *14 patients not included due to missing value for variable "Acute PCI." †Clarified data.

Abbreviations as in Tables 1 and 2.

adjusted model, the in-hospital mortality/morbidity results are similar to these 2 studies.

The nonprimary PCI patient cohort in our study is not a reflection of purely elective PCI, as this group includes some patients who presented with acute coronary syndromes, NSTEMI, or after STEMI. However, the consideration of this group as "nonurgent" and a reasonable surrogate for elective PCI is consistent with the analyses done in the literature cited in the preceding text. In our study, the differentiation of patients in off-site versus on-site PCI centers into primary PCI and nonprimary PCI permitted a more comprehensive assessment and risk-adjustment analysis of the major clinical end points.

Within our study cohort, the aggregate incidence of emergency surgery was comparably low at off- and on-site PCI facilities (0.3% to 0.4%, respectively) and consistent with contemporary studies (2,3). When emergency surgery was necessary, the mortality rate was similarly high between off- (13.6%) and on-site (12.8%) facilities, and comparable to that reported in prior literature (2,3).

There have been concerns that off-site PCI facilities may tend to keep some borderline stable patients with suboptimal procedural results rather than initiate the logistics of emergency transfer to an outside surgical center. These patients may have adverse outcomes, as seems to be suggested by the aggregate unadjusted mortality rate in our study. However, in the risk-adjusted analyses, there was comparable in-hospital mortality for those off-site patients who were not transferred for emergency surgery.

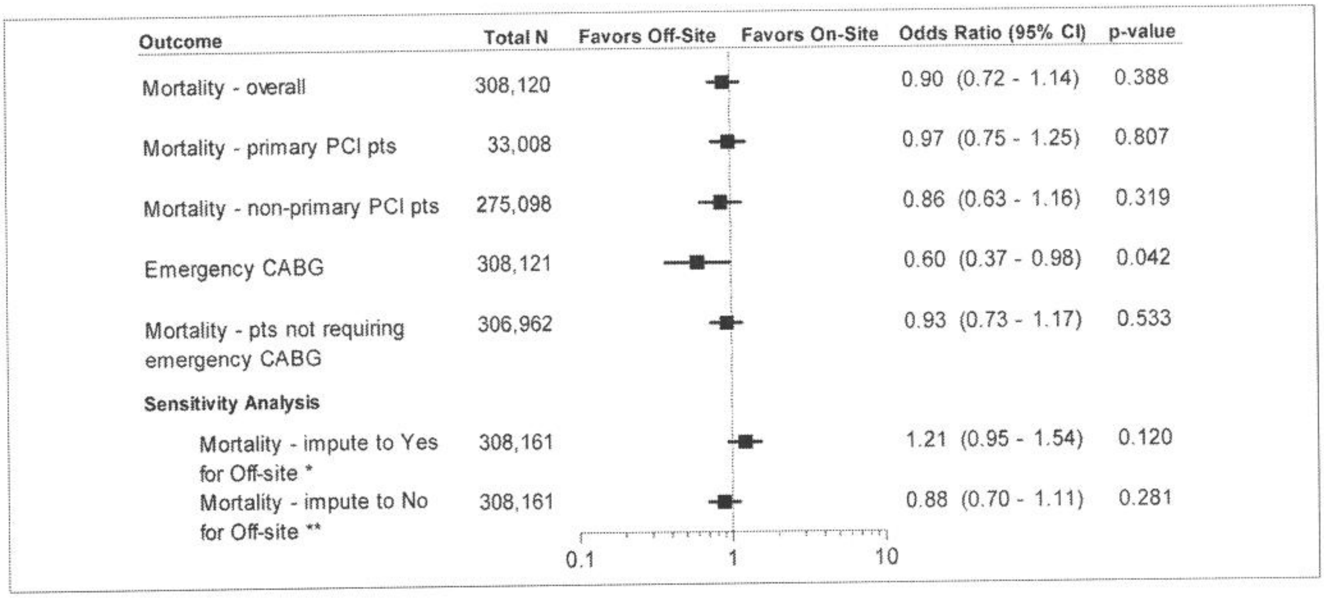
Conversely, the 1.5-fold higher risk-adjusted incidence of emergency surgery at on-site PCI centers could reflect a lower threshold to opt for emergency surgery if there is any doubt about a suboptimal result, as surgery is available without the added logistics of transfer. An alternative explanation could be that on-site centers perform higher risk elective cases, as is suggested by the clinical and lesion characteristics profiles in this study. In addition, it is possible that patients may have had initial angiography at off-site facilities, found to have complex coronary anatomy and/or high-risk MI subsets with a higher predisposition to emergency surgery, then deferred and transferred to an on-site center for PCI. These complicated potential scenarios and the detailed reasons for case selection were beyond the scope of the NCDR database elements. Regardless, the increased risk-adjusted incidence of emergency surgery at on-site PCI programs did not translate into an increase in mortality.

Data from the Capabilities Survey revealed a mean transit time of 25 ± 17 min from off-site facilities. The British Cardiovascular Interventional Society has recommended a 90 min to emergency surgery standard (29).

JACC Vol. 54, No. 1, 2009
June 30, 2009:16–24

Figure 2 Risk-Adjusted Analysis of Outcomes

Odds ratio plot of risk-adjusted outcomes, including sensitivity analysis for missing mortality data. Odds ratio: outcomes for patients at off-site (vs. on-site) facilities, adjusting for within site correlations and potential confounding variables. *Worst case scenario: all patients with missing mortality data were considered to have died. **Best case scenario: all patients with missing mortality data were considered as alive. CABG = coronary artery bypass graft surgery; CI = confidence interval; PCI = percutaneous coronary intervention; pts = patients.



This includes not only the transit time, but also the total time from the initial decision to transport (including call time, transfer of patient from catheterization laboratory to vehicle, vehicle to operating suite), to the actual time of initiating cardiopulmonary bypass at the receiving surgical center. The transit time in the NCDR survey was an estimate of basic travel time and did not include the above additional time elements. However, based on the transit time, most off-site PCI programs in our study may be able to meet this global standard of 90 min by having a clear decision process and heightened logistical coordination with ambulance services and the receiving surgical center.

The demographics of the off-site centers in our study suggests these facilities conform to the stated goals of lowering geographic barriers and facilitating access to PCI, particularly for those patients presenting with STEMI (5,6). The Capabilities Survey also indicates these programs are well staffed and organized with good logistical plans. The fact that 81% of the off-site center operators rotated to an on-site PCI center suggests that most of the off-site facilities were hub-and-spoke centers staffed by large group practices. Overall, the information suggests that the off-site PCI programs in this study have demonstrated a strong commitment to the classic Donabedian triad of structure, process, and outcomes measurements (30).

Study limitations. First, this study is subject to the usual concerns regarding observational registry data. There may be an inherent bias in off-site PCI programs that are either mandated by regulatory agencies or choose on their own to participate in the NCDR. Participants in any registry may be prone to "game" the system, particularly if score carding and public disclosure is an issue.

Second, this study includes outcomes up to the time of hospital discharge. Data regarding long-term outcomes are not currently captured in the NCDR CathPCI Registry. In addition, outcomes are assessed and analyzed on an institutional level, not on an individual operator level.

Third, specific in-depth details regarding clinical presentation, case selection, procedural complications, morbidity, and mortality were sometimes beyond the purview of the basic datasets. However, a special data clarification effort was utilized to resolve the 172 of 8,736 off-site patients (2%) for whom mortality or transfer data were questioned, resulting in clarification of 154 of these patients (90%), leaving 18 of 8,736 (0.2%) not clarified. A sensitivity analysis confirmed that the unclarified data would not have affected the risk-adjusted mortality analysis results.

Fourth, although this NCDR study indicates that nonprimary PCI can be done safely at off-site facilities, the efficacy of truly elective PCI at off-site facilities can perhaps be best addressed by a large randomized prospective trial such as the C-PORT (Cardiovascular Patient Outcome Research Team) Elective Angioplasty Study, which is under way. However, such studies are difficult to conduct, and results may not be forthcoming for some time. In the interim, a comprehensive large database such as the NCDR CathPCI Registry offers a realistic and relative contemporary quality assurance standard to monitor these issues. Based on the experiences gained with this current study, the NCDR plans to sponsor a proactive comprehensive working group of off-site PCI centers to further communicate and track outcomes. This effort will coincide with the upcoming transition to the next CathPCI database version 4.0.

Finally, a participation bias cannot be excluded. The total number of PCI centers in the U.S. that do not have surgery on site is not definitively known (22) but may number ≈250. Of these, it is estimated that one-third submit data to another peer-reviewed registry, a spoke and hub partner database, or a multicenter trial. Thus, the 60 off-site PCI facilities in this NCDR study may represent a minority of such programs in the nation and are probably in the upper tier of quality. With this perspective, the results reported here may not be applicable to all PCI centers without surgical backup on site, particularly those that do not participate in any formal data registry or clinical trial.

Conclusions

Compared with on-site PCI centers, off-site PCI programs in the NCDR were predominantly located in nonurban areas, had lower annual PCI volume, treated a higher percentage of patients who presented with subsets of MI, and had better reperfusion times in primary PCI. Off-site PCI centers had similar observed procedure success, morbidity, emergency cardiac surgery rates, and mortality in cases that required emergency surgery. The risk-adjusted mortality rates in off-site PCI facilities were comparable to those of PCI centers that had cardiac surgery on site, regardless of whether PCI was performed as primary therapy for STEMI or in a nonprimary setting.

These findings should not be extrapolated to encourage the widespread proliferation of more PCI programs without surgery on site to fulfill a political or an economic agenda. Rather, our study does confirm the safety of an off-site strategy at PCI centers where rigorous clinical, operator, and institutional criteria are in place and where data are submitted and reviewed in a comprehensive multicenter registry such as the NCDR.

Acknowledgments

The authors would like to thank Jessica Morris, MBA, and Kristi Mitchell, MA, MPH, of the NCDR for their tireless work and outstanding efforts in the conduct of the data clarification project. Tammy Davis and Susan Queen of Wake Forest University School of Medicine deserve special thanks for their expertise in the preparation of this paper.

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JACC Vol. 54, No. 1, 2009
June 30, 2009:16–24

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Key Words: percutaneous coronary intervention ▪ cardiac surgery ▪ outcomes analysis.

APPENDIX

For supplemental NCDR information, please see the online version of this article.

Attachment C

Percutaneous Coronary Interventions in Facilities Without Cardiac Surgery On Site: A Report From the National Cardiovascular Data Registry (NCDR)

Michael A. Kutcher, Lloyd W. Klein, Fang-Shu Ou, Thomas P. Wharton, Jr, Gregory J. Dehmer, Mandeep Singh, H. Vernon Anderson, John S. Rumsfeld, William S. Weintraub, Richard E. Shaw, Matthew T. Sacrinty, Albert Woodward, Eric D. Peterson, Ralph G. Brindis, on behalf of the National Cardiovascular Data Registry (NCDR)

J. Am. Coll. Cardiol. 2009;54;16-24
doi:10.1016/j.jacc.2009.03.038

 Attachment D

ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention)

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Acknowledgement: The ACC and AHA recognize Dr J. Ward Kennedy for his dedicated service on developing ACC/AHA guidelines for PTCA and PCI since their inception in 1986 and for his counsel and advice in the preparation of this guideline.

This document was approved by the American College of Cardiology Foundation Board of Trustees in August 2005, by the American Heart Association Science Advisory and Coordinating Committee in August 2005, and by the Society for Cardiovascular Angiography and Interventions Board of Trustees in August 2005.

When citing this document, the American College of Cardiology Foundation requests that the following citation format be used: Smith SC Jr, Feldman TE, Hirshfeld JW Jr, Jacobs AK, Kern MJ, King SB III, Morrison DA, O'Neill WW, Schaff HV, Whitlow PL, Williams DO. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). American College of Cardiology Web Site. Available at: http://www.acc.org/clinical/guidelines/percutaneous/update/index.pdf.

Copies: This document is available on the World Wide Web sites of the American College of Cardiology (www.acc.org), the American Heart Association (www.americanheart.org), and the Society for Cardiovascular Angiography and Interventions (www.scai.org). Single copies of this document are available by calling 1-800-253-4636 or writing the American College of Cardiology Foundation, Resource Center, at 9111 Old Georgetown Road, Bethesda, MD 20814-1699. Ask for reprint number 71-0347. To obtain a copy of the Summary Article published in the January 3, 2006 issue of the *Journal of the American College of Cardiology*, the January 3, 2006 issue of *Circulation*, and the January 2006 issue of *Catheterization and Cardiovascular Interventions*, ask for reprint number 71-0346. To purchase bulk reprints (specify version and reprint number): Up to 999 copies, call 1-800-611-6083 US only) or fax 413-665-2671; 1000 or more copies, call 214-706-1789, fax 214-691-6342, or e-mail pubauth@heart.org.

TABLE OF CONTENTS

PREAMBLE

It is important that the medical profession play a significant role in critically evaluating the use of diagnostic procedures and therapies as they are introduced and tested in the detection, management, or prevention of disease states. Rigorous and expert analysis of the available data documenting relative benefits and risks of those procedures and therapies can produce helpful guidelines that improve the effectiveness of care, optimize patient outcomes, and favorably affect the overall cost of care by focusing resources on the most effective strategies.

The American College of Cardiology (ACC) and the American Heart Association (AHA) have jointly engaged in the production of such guidelines in the area of cardiovascular disease since 1980. This effort is directed by the ACC/AHA Task Force on Practice Guidelines, whose charge is to develop and revise practice guidelines for important cardiovascular diseases and procedures. The Task Force is pleased to have this guideline cosponsored by the Society for Cardiovascular Angiography and Interventions (SCAI). Experts in the subject under consideration have been selected from all three organizations to examine subject-specific data and write guidelines. The process includes additional representatives from other medical practitioner and specialty groups where appropriate. Writing groups are specifically charged to perform a formal literature review, weigh the strength of evidence for or against a particular treatment or procedure, and include estimates of expected health outcomes where data exist. Patient-specific modifiers, comorbidities, and issues of patient preference that might influence the choice of particular tests or therapies are considered, as well as frequency of follow-up and cost-effectiveness. When available, information from studies on cost will be considered; however, review of data on efficacy and clinical outcomes will be the primary basis for preparing recommendations in these guidelines.

The ACC/AHA Task Force on Practice Guidelines makes every effort to avoid any actual, potential, or perceived conflicts of interest that might arise as a result of an outside relationship or personal interest of a member of the writing panel. Specifically, all members of the writing panel are asked to provide disclosure statements of all such relationships that might be perceived as real or potential conflicts of interest. These statements are reviewed by the parent task force, reported orally to all members of the writing panel at each meeting, and updated and reviewed by the writing committee as changes occur.

The practice guidelines produced are intended to assist healthcare providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis, management, or prevention of specific diseases or conditions. These guidelines attempt to define practices that meet the needs of most patients in most circumstances. These guideline recommendations reflect a consensus of expert opinion after a thorough review of the available, current scientific evidence and are intended to improve patient care. If these guidelines are used as the basis for regulatory/payer decisions, the ultimate goal is quality of care and serving the patient's best interests. The ultimate judgment regarding care of a particular patient must be made by the healthcare provider and patient in light of all of the circumstances presented by that patient.

These guidelines were approved for publication by the governing bodies of the ACCF, AHA, and SCAI. The guidelines will be reviewed annually by the ACC/AHA Task Force on Practice Guidelines and will be considered current unless they are revised or withdrawn from distribution. The summary article and recommendations are published in the January 3, 2006 issue of the *Journal of the American College of Cardiology*, the January 3, 2006 issue of *Circulation*, and the January 2006 issue of *Catheterization and Cardiovascular Interventions*. The full-text guideline is posted on the World Wide Web sites of the ACC (www.acc.org), the AHA (www.americanheart.org), and the SCAI (www.scai.org). Copies of the full text and the executive summary are available from the ACC, AHA, and the SCAI.

Elliott M. Antman, MD, FACC, FAHA
Chair, ACC/AHA Task Force on Practice Guidelines

1. INTRODUCTION

The ACC/AHA Task Force on Practice Guidelines was formed to gather information and make recommendations about appropriate use of technology for the diagnosis and treatment of patients with cardiovascular disease. Percutaneous coronary interventions (PCIs) are an important group of technologies in this regard. Although initially limited to balloon angioplasty and termed percutaneous transluminal coronary angioplasty (PTCA), PCI now includes other new techniques capable of relieving coronary narrowing. Accordingly, in this document, implantation of intracoronary stents and other catheter-based interventions for treating coronary atherosclerosis are considered components of PCI. In this context, PTCA will be used to refer to those studies using only balloon angioplasty, whereas PCI will refer to the broader group of percutaneous techniques. These new technologies have impacted the effectiveness and safety profile initially established for balloon angioplasty. Moreover, additional experience has been gained in the use of adjunctive pharmacological treatment with glycoprotein (GP) IIb/IIIa receptor antagonists and the use of bivalirudin, thienopyridines, and drug-eluting stents (DES). In addition, since publication of the guidelines in 2001, greater experience in the performance of PCI in patients with acute coronary syndromes and in community hospital settings has been gained. In view of these developments, an update of these guidelines is warranted. This document reflects the opinion of the ACC/AHA/SCAI writing committee charged with updating the 2001 guidelines for PCI (1).

Several issues relevant to the Writing Committee's process and the interpretation of the guidelines have been noted previously and are worthy of restatement. First, PCI is a technique that has been continually refined and modified; hence, continued, periodic guideline revision is anticipated. Second, these guidelines are to be viewed as broad recommendations to aid in the appropriate application of PCI. Under unique circumstances, exceptions may exist. These guidelines are intended to complement, not replace, sound medical judgment and knowledge. They are intended for operators who possess the cognitive and technical skills for performing PCI and assume that facilities and resources required to properly perform PCI are available. As in the past, the indications are categorized as class I, II, or III on the basis of a multifactorial assessment of risk and expected efficacy viewed in the context of current knowledge and the relative strength of this knowledge.

These classes summarize the recommendations for procedures or treatments as follows:

Class I: Conditions for which there is evidence for and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.

Class IIb: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful.

In addition, the weight of evidence in support of the recommendation is listed as follows:

- Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses.
- Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies.
- Level of Evidence C: Only consensus opinion of experts, case studies, or standard-of-care.

A recommendation with level of evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful and effective.

In instances where recommendations of class III, level of evidence C, occur, it is recognized that the bases of these recommendations are opinion and the consensus of the writing group. In this setting, it is not unreasonable for clinical trials to be conducted to further investigate the validity of this consensus opinion. The schema for classification of recommendations and level of evidence is summarized in Table 1, which also illustrates how the grading system provides an estimate of the size of the treatment effect and an estimate of the certainty of the treatment effect.

The committee conducted comprehensive searching of the scientific and medical literature on PCI, with special emphasis on randomized controlled trials and meta-analyses published since 2001. In addition to broad-based searching on PCI, specific targeted searches were performed on the following subtopics: catheter-based intervention, stents (drug-eluting and bare-metal), cardiac biomarkers (e.g., creatine kinase and troponins), pharmacological therapy (aspirin, thienopyridines, GP IIb/IIIa inhibitors, heparin, and direct thrombin inhibitors), special populations (women, patients with diabetes, elderly), coronary artery bypass grafting (CABG), high-risk PCI, quality, outcomes, volume, left main PCI (protected and unprotected), distal embolic protection, intravascular ultrasound (IVUS), fractional flow reserve (FFR), vascular closure, and secondary prevention/risk factor modification. The complete list of keywords is beyond the scope of this section. The committee reviewed all compiled reports from computerized searches and conducted additional searching by hand. Literature citations were generally restricted to published manuscripts appearing in journals listed in Index Medicus. Because of the scope and importance of certain ongoing clinical trials and other emerging information, published abstracts were cited when they were the only published information available. Additionally, the Committee reviewed and incorporated recommendations and/or text from published ACC/AHA or SCAI documents to maintain consistency, as appropriate.

Initially, this document describes the background information that forms the foundation for specific recommendations. Topics fundamental to coronary intervention are reviewed, followed by separate discussions relating to unique technical and operational issues. This format is designed to enhance the usefulness of this document for the assessment and care of patients with coronary artery disease (CAD). Formal recommendations for the use of PCI according to clinical presentation are included in Section 5. A clear distinction is drawn between the emergency use of PCI for patients with ST-segment elevation myocardial infarction (STEMI), termed "primary PCI," and all other procedures, which are included under the term "elective PCI" (see Section 4.2 for further discussion).

This committee includes cardiologists with and without involvement in interventional procedures, and a cardiac surgeon. This document was reviewed by 2 official reviewers nominated by ACC; 2 official reviewers nominated by AHA;

Table 1. Applying Classification of Recommendations and Level of Evidence

"Size of Treatment Effect" (columns); "Estimate of Certainty (Precision) of Treatment Effect" (rows)

	Class I *Benefit >>> Risk* Procedure/Treatment SHOULD be performed/administered	Class IIa *Benefit >> Risk* *Additional studies with focused objectives needed* IT IS REASONABLE to perform procedure/administer treatment	Class IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; Additional registry data would be helpful* Procedure/Treatment MAY BE CONSIDERED	Class III *Risk ≥ Benefit* *No additional studies needed* Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL
Level A *Multiple (3-5) population risk strata evaluated** *General consistency of direction and magnitude of effect*	• Recommendation that procedure or treatment is useful/effective • Sufficient evidence from multiple randomized trials or meta-analyses	• Recommendation in favor of treatment or procedure being useful/effective • Some conflicting evidence from multiple randomized trials or meta-analyses	• Recommendation's usefulness/efficacy less well established • Greater conflicting evidence from multiple randomized trials or meta-analyses	• Recommendation that procedure or treatment not useful/effective and may be harmful • Sufficient evidence from multiple randomized trials or meta-analyses
Level B *Limited (2-3) population risk strata evaluated**	• Recommendation that procedure or treatment is useful/effective • Limited evidence from single randomized trial or non-randomized studies	• Recommendation in favor of treatment or procedure being useful/ effective • Some conflicting evidence from single randomized trial or non-randomized studies	• Recommendation's usefulness/efficacy less well established • Greater conflicting evidence from single randomized trial or non-randomized studies	• Recommendation that procedure or treatment not useful/effective and may be harmful • Limited evidence from single randomized trial or non-randomized studies
Level C *Very limited (1-2) population risk strata evaluated**	• Recommendation that procedure or treatment is useful/effective • Only expert opinion, case studies, or standard-of-care	• Recommendation in favor of treatment or procedure being useful/ effective • Only diverging expert opinion, case studies, or standard-of-care	• Recommendation's usefulness/efficacy less well established • Only diverging expert opinion, case studies, or standard-of-care	• Recommendation that procedure or treatment not useful/effective and may be harmful • Only expert opinion, case studies, or standard-of-care
Suggested phrases for writing recommendations †	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/ beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown /unclear/uncertain or not well established	is not recommended is not indicated should not is not useful/effective/beneficial may be harmful

*Data available from clinical trials or registries about the usefulness/efficacy in different sub-populations, such as gender, age, history of diabetes, history of prior MI, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

†In 2003, the ACC/AHA Task Force on Practice Guidelines developed a list of suggested phrases to use when writing recommendations. All recommendations in this guideline have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendations), would still convey the full intent of the recommendation. It is hoped that this will increase readers' comprehension of the guidelines and will allow queries at the individual recommendation level.

2 official reviewers nominated by SCAI; 1 official reviewer from the ACC/AHA Task Force on Practice Guidelines; and 8 content reviewers, including members from the AHA Committee on Diagnostic and Interventional Cardiac Catheterization and the ACCF Cardiac Catheterization and Intervention Committee.

2. GENERAL CONSIDERATIONS AND BACKGROUND

Coronary angioplasty was first introduced by Andreas Gruentzig in 1977 (2) as a nonsurgical method for coronary arterial revascularization. Fundamentally, the technique involved advancing a balloon-tipped catheter to an area of coronary narrowing, inflating the balloon, and then removing the catheter after deflation. Early reports demonstrated that balloon angioplasty could reduce the severity of coronary stenosis and diminish or eliminate objective and subjective manifestations of ischemia (3-5). Although angioplasty was clearly feasible and effective, the scope of coronary disease to be treated was quite narrow. Also, because angioplasty could result in sudden arterial occlusion and subsequent myocardial infarction (MI), immediate access to coronary bypass surgery was essential (6). With experience and time, however, the cognitive and technical aspects as much as the equipment used to perform angioplasty became more refined. Observational reports of large numbers of patients confirmed that coronary angioplasty could be applied to broad groups of coronary patients with higher rates of success and lower rates of complications than seen in initial experiences (7,8). More than 1 000 000 PCI procedures are performed yearly in the United States (9), and it has been estimated that nearly 2 000 000 procedures are performed annually worldwide.

The value of coronary angioplasty was further defined by comparing its results to those of alternative methods of treatment. Randomized clinical trials have assessed the outcomes of patients treated by a strategy of initial angioplasty to one of medical therapy alone or to coronary artery bypass surgery (10-14). The results of these trials have clarified the utility of angioplasty in terms of effectiveness, complications, and patient selection. The technique of coronary angioplasty has also been expanded by the development of devices that replace or serve as adjuncts to the balloon catheter. These "new devices" have been evaluated and have had a variable impact in enhancing the immediate- and long-term efficacy and safety of coronary angioplasty. The following section of this report expands on this background and describes the practice of PCI as it is applied today.

Advances in coronary-based interventions, especially the use of bare-metal stents (BMS) and drug-eluting stents (DES), have improved the efficacy and safety profile of percutaneous revascularization observed for patients undergoing PTCA. For example, stents reduce both the acute risk of major complications and late-term restenosis. The success of new coronary devices in meeting these goals is reflected in part by the rapid transition from the use of PTCA alone (less than 30%) to the high use of PCI with stenting, which was greater than 70% by the late 1990s (Figure 1) (15). Atherectomy devices and stenting, associated with improved acute angiographic and clinical outcomes compared with PTCA alone in specific subsets, continue to be applied to a wider patient domain that includes multivessel disease and complex coronary anatomy. However, strong evidence (level A data from multiple randomized clinical trials) is primarily available for stenting over PTCA in selected patients undergoing single-vessel PCI.

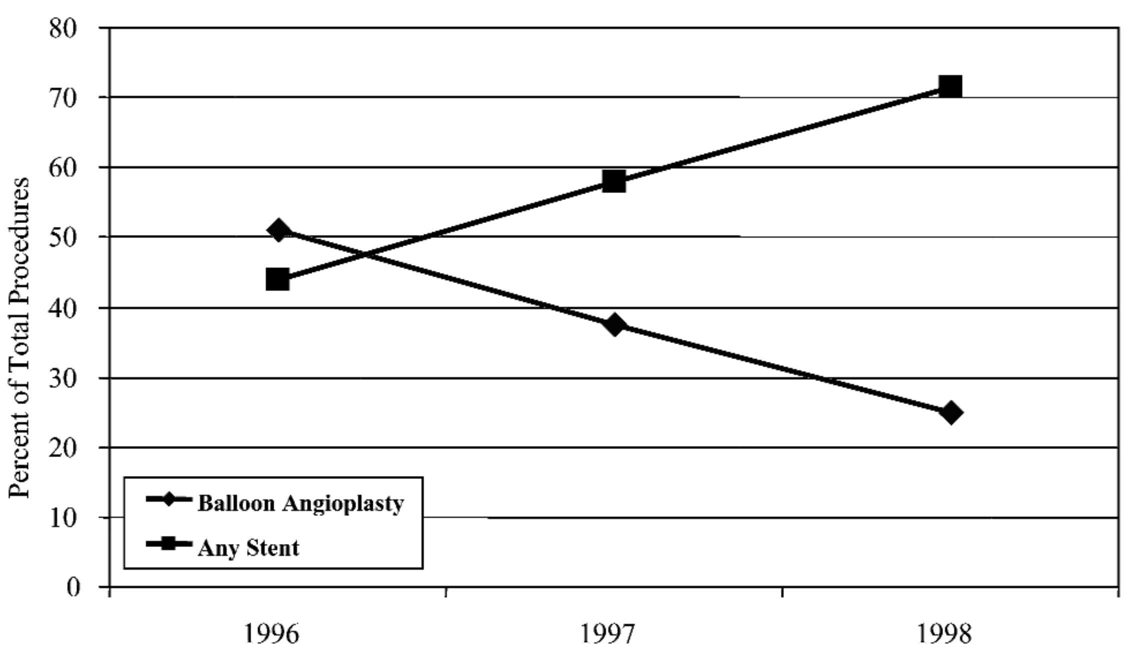

Figure 1. Frequency of device use in the SCAI registry. Source data from Laskey et al. Catheter Cardiovasc Interv 2000;49:19-22 (15).

The range of non-balloon revascularization technology approved by the Food and Drug Administration (FDA) for use in native and/or graft coronary arteries includes balloon expandable stents, DES, extraction atherectomy, directional coronary atherectomy, rotational atherectomy, rheolytic thrombectomy catheter, proximal and distal embolic protection devices, excimer laser coronary atherectomy, and local radiation devices to reduce in-stent restenosis (ISR) (16,17). A variety of devices are under investigation, including new designs of balloon or self-expanding stents and mechanical thrombectomy devices. This guideline update will focus on the FDA-approved balloon-related and non-balloon coronary revascularization devices.

3. OUTCOMES

The outcomes of PCI are measured in terms of success and complications and are related to the mechanisms of the employed devices, as well as the clinical and anatomic patient-related factors. Complications can be divided into 2 categories: (a) those common to all arterial catheterization procedures and (b) those related to the specific technology used for the coronary procedure. Specific definitions of success and complications exist, and where appropriate, the definitions used herein are consistent with the ACC-National Cardiovascular Data Registry (NCDR®) Catheterization Laboratory Module version 3.0 (18). The committee recommends such standards whenever feasible in order to accommodate the common database for the assessment of outcomes. With increased operator experience, new technology, and adjunctive pharmacotherapy, the overall success and complication rates of angioplasty have improved.

3.1. Definitions of PCI Success

The success of a PCI procedure may be defined by angiographic, procedural, and clinical criteria.

3.1.1. Angiographic Success

A successful PCI produces substantial enlargement of the lumen at the target site. The consensus definition before the widespread use of stents was the achievement of a minimum stenosis diameter reduction to less than 50% in the presence of grade 3 Thrombolysis In Myocardial Infarction (TIMI) flow (assessed by angiography) (1). However, with the advent of advanced adjunct technology, including coronary stents, a minimum stenosis diameter reduction to less than 20% has been the clinical benchmark of an optimal angiographic result. Frequently, there is a disparity between the visual assessment and computer-aided quantitative stenosis measurement (19,20), and, thus, the determination of success may be problematic when success rates are self-reported.

3.1.2. Procedural Success

A successful PCI should achieve angiographic success without major clinical complications (e.g., death, MI, emergency coronary artery bypass surgery) during hospitalization (1,3). Although the occurrence of emergency coronary artery bypass surgery and death are easily identified end points, the definition of procedure-related MI has been debated. The development of Q waves in addition to a threshold value of creatine kinase (CK) elevation has been commonly used. Most agree that the definition of MI as put forth by the ACC/European Society of Cardiology document on the redefinition of MI (21) should be the accepted standard. However, the clinical significance and definition of cardiac biomarker elevations in the absence of Q waves remains the subject of investigation and debate (21a). Several reports have identified non–Q-wave MIs with CK-MB elevations 3 to 5 times the upper limit of normal as having clinical significance (22,23). One report suggests that a greater than 5 times increase in CK-MB is associated with worsened outcome (24). Thus, this degree of increase in CK-MB without Q waves is considered by most to qualify as an associated complication of PCI. Troponin T or I elevation occurs frequently after PCI. The timing of the peak elevation after PCI is unclear (25). Minor elevations do not appear to have prognostic value, whereas marked (greater than 5 times) elevations are associated with worsened 1-year outcome (Table 2) (26-40). Troponin T or I elevation occurs more frequently than CK-MB increase after PCI (34).

3.1.3. Clinical Success

In the short term, a clinically successful PCI includes anatomic and procedural success with relief of signs and/or symptoms of myocardial ischemia after the patient recovers from the procedure. The long-term clinical success requires that the short-term clinical success remain durable and that the patient have persistent relief of signs and symptoms of myocardial ischemia for more than 6 months after the procedure. Restenosis is the principal cause of lack of long-term clinical success when a short-term clinical success has been achieved. Restenosis is not considered a complication but rather an associated response to vascular injury. The incidence of clinically important restenosis may be judged by the frequency with which subsequent revascularization procedures are performed on target vessels after the index procedure.

3.2. Acute Outcome: Procedural Complications

Class I

All patients who have signs or symptoms suggestive of MI during or after PCI and those with complicated procedures should have CK-MB and troponin I or T measured after the procedure. ***(Level of Evidence: B)***

Class IIa

Routine measurement of cardiac biomarkers (CK-MB and/or troponin I or T) in all patients undergoing PCI is reasonable 8 to 12 hours after the procedure. ***(Level of Evidence: C)***

Table 2. Incidence of Troponin Elevations After Percutaneous Coronary Intervention in the Published Literature

First Author of Study (Reference)	n	Marker	% Positive	Positive Definition	Prognostic Information
Hunt (29)	22	Troponin I	0	Greater than 6 ng per mL	N/A
Ravkilde (30)	23	Troponin T	13	Greater than 0.12 ng per mL	N/A
Karim (31)	25	Troponin T	44	Greater than 0.2 ng per mL	N/A
La Vecchia (32)	19 (Stent) 25 (balloon PCI)	Troponin T and troponin I	37 cTnI; 21 cTnT 14 cTnI; 0 cTnT	N/A	N/A
Johansen (33)	75	Troponin T	28	Greater than 0.1 ng per mL	N/A
Shyu (34)	59 (Stent) 61 (balloon PCI)	Troponin T	29 13	Greater than 0.1 ng per mL	Significantly higher incidence of elevated cTnT in patients undergoing stenting than angioplasty alone.
Bertinchant (35)	105	Troponin I	22	Greater than 0.1 ng per mL	No difference in incidence of recurrent angina, MI, cardiac death, or RR after 12 months between patients positive or negative for cTnI. Stenting not associated with more minor myocardial damage than angioplasty.
Garbarz (36)	109	Troponin I	27	Greater than 0.3 ng per mL	No association between post-PCI cTnI and adverse ischemic events.
Fuchs (37)	1129	Troponin I	31	Greater than 0.15 ng per mL	cTnT levels greater than 3× normal limit associated with increased risk of major in-hospital complications, but no association with adverse intermediate-term (8 months) clinical outcomes.
Cantor (26)	481	Troponin I	48 overall; 26 after excluding positive or unknown pre-PCI cTnI	Greater than 1.5 ng per mL	Significantly higher 90-day rates of MI and the composite of MI or death in patients with positive cTnI.
Wu (38)	98	Troponin T	26	Greater than 0.1 ng per mL	At a mean of 77 months follow-up, no increase in risk of major adverse events detected in relation to post-PCI cTnT elevation.
Kizer (27)	212	Troponin T	40 positive prior to PCI; 18 of baseline negative were positive post-PCI	Greater than or equal to 0.1 ng per mL	Pre-PCI cTnT elevation was significantly related to event-free survival during 6-year follow-up; in baseline negative patients, positive cTnT was the only independent predictor of major adverse events at 1 year; post-PCI elevations of cTnT greater than or equal to 5× normal was the strongest long-term predictor of major adverse events at 6 years.
Ricciardi (39)	286	Troponin I	13.6	Greater than 2.3 ng per mL	cTnI elevations greater than 3-fold care predictive of future major adverse cardiac events (MACE). Increased incidence of MACE is accounted for by higher rate of early RR and not late cardiac events.
Kini (40)	2873	Troponin I	38.9	Greater than 2 ng per mL	Neither cTnI peak elevations nor any subgroup predicted mid-term mortality in low- to medium-risk patients.

cTnI indicates cardiac troponin I; cTnT, cardiac troponin T; N/A, not applicable; PCI, percutaneous coronary intervention; and RR, repeat revascularization.

Complications associated with PCI are similar to those resulting from diagnostic cardiac catheterization, but their prevalence is more frequent. Complications have been categorized as major (death, MI, and stroke) or minor (transient ischemic attack, access site complications, renal insufficiency, or adverse reactions to radiographic contrast). Additional specific complications include intracoronary thrombosis, coronary perforation, tamponade, and arrhythmias.

Reported rates for death after diagnostic catheterization range from 0.08% to 0.14%, whereas analyses of large registries indicate overall unadjusted in-hospital rates for PCI of 0.4% to 1.9% (Table 3) (41-52). This range is greatly influenced by the clinical indication for which PCI is performed, with the highest mortality rates occurring among patients with STEMI and cardiogenic shock. Death in such patients may not be a direct result of the PCI procedure but rather a consequence of the patient's underlying illness. For example, in a combined analysis of PCI as primary reperfusion therapy for STEMI, the short-term mortality rate was 7% (53). Even after exclusion of patients with cardiogenic shock, in-hospital mortality was 5%.

Myocardial infarction can be a direct result of PCI, most commonly due to abrupt coronary occlusion or intracoronary embolization of obstructive debris. Determining and comparing the incidence of MI after PCI is difficult because the definition of MI as a result of PCI is controversial. The conventional definition requires 2 of the following: a) prolonged chest discomfort or its equivalent; b) development of pathologic Q waves; and c) rise in serum cardiac biomarkers above a critical level. Rates of periprocedural MI using this definition have ranged from 0.4% to 4.9%. Using a consistent definition for MI, the incidence of this complication has declined approximately 50% with the routine use of intracoronary stents (21,21a,50).

More recently, an isolated rise and fall in either CK-MB or troponin is considered to be a marker of myocardial necrosis (21). The relationship between cardiac biomarker elevation and myocardial cell death and evidence of subendocardial infarction on magnetic resonance imaging (MRI) support this position (54,55). Furthermore, large rises in cardiac biomarkers are associated with an increased risk for late death (26,56,57). Whether death in such patients is a consequence of the myonecrosis or a marker of patients who are at increased risk for death because of more advanced coronary disease is unclear. Complicating our understanding of the implications of this definition is the very frequently observed mild to modest elevation of serum CK-MB among patients with apparently uncomplicated PCI. When troponin is measured after PCI, more than 70% of patients exhibit elevated values after an otherwise successful intervention (58). Such patients may have no symptoms or electrocardiographic (ECG) abnormalities to suggest ischemia yet are "enzyme positive." One study has suggested a postprocedural increase in troponin T of 5 times normal is predictive for adverse events at 6 years. The long-term prognostic significance of smaller postprocedural troponin T elevations awaits further investigation (27) (Table 2) (26-40).

Another study indicated that more extensive stent expansion resulted in CK release but did not increase adverse cardiac events (59). Accordingly, it is important to acknowledge that the significance of mild biomarker rises after clinically successful PCI should be distinguished from situations wherein patients experience an unequivocal "clinical" infarction manifested by chest pain and diagnostic ECG findings (60).

Routine measurement of CK-MB is advocated by some (21) and actually mandated by certain healthcare systems. In this regard, the current Committee supports the recommendations of the 2001 Guidelines and recommends that all patients who have signs or symptoms suggestive of MI during or after PCI and those with complicated procedures should have CK-MB and troponin I or T measured after the procedure. In addition, the Committee recommends that routine measurement of cardiac biomarkers (CK-MB and/or troponin I or T) in every patient undergoing PCI is reasonable 8 to 12 h after the procedure. In such patients, a new CK-MB or troponin I or T rise greater than 5 times the upper limit of normal would constitute a clinically significant periprocedural MI.

The need to perform emergency coronary artery bypass surgery (CABG) has been considered as a potential complication of PCI. Typically, CABG is performed as a rescue revascularization procedure to treat acute ischemia or infarction resulting from PCI-induced acute coronary occlusion. In the era of balloon angioplasty, the rate of emergency CABG was 3.7% (49). In a more contemporary time period, with the availability of stents, the reported rate was 0.4% among a similar cohort of patients.

Various definitions have been proposed for stroke. A common feature to definitions has been a loss of neurologic function of vascular cause that lasts more than 24 h. More recently, attention has been directed to refining the definition of transient ischemic attack (TIA), which indirectly broadens that of stroke (61). The time-based definition of a TIA is a sudden, focal neurologic deficit that lasts less than 24 h that is of presumed vascular origin and confined to an area of the brain or eye perfused by a specific artery. The new definition of TIA is a brief episode of neurologic dysfunction caused by brain or retinal ischemia, with clinical symptoms typically lasting less than 1 hour and without evidence of infarction. Presence of cerebral infarction by imaging techniques constitutes evidence of stroke regardless of the duration of symptoms.

Bleeding is a complication of increasing concern with the more frequent use of potent antithrombin and antiplatelet agents. A frequently used definition for bleeding developed by the TIMI group includes classification as major, moderate, or minor. Major bleeding is defined as intracranial, intraocular, or retroperitoneal hemorrhage or any hemorrhage requiring a transfusion or surgical intervention or that results in a hematocrit decrease of greater than 15% or hemoglobin decrease of greater than 5 g per dL (62). Episodes of hemorrhage of lesser magnitude would fall into the moder-

Table 3. Unadjusted In-Hospital Outcome Trends After Percutaneous Coronary Interventions

Registry	Years	Reference	n	Clinical Success, %	In-Hospital Mortality, %	Q-Wave MI, %	Emergency CABG, %
NHLBI (I)‡	1977-1981	(41)	3079*	61	1.2	NR	5.8
NHLBI (II)§	1985-1986	(41)	2311*	78	1.0	4.8	5.8
BARI Registry‖	1988-1991	(42)	1189*	NR	0.7	2.8	4.1
Northern New England¶	1990-1993	(43)	13 014†	88.8	1.0	2.4	2.2
SCAI#	1990-1994	(44)	4366†	91.5	2.5	NR	3.4
NACI**	1990-1994	(45)	4079*	NR	1.6	1.6	1.9
NY State Database	1991-1994	(46,47)	62 670*	NR	0.9	NR	3.4
Northern New England¶	1994-1995	(43)	7248†	89.2	1.1	2.1	2.3
NCN	1994-1997	(48)	76 904†	NR	1.3	NR	1.7
Northern New England¶	1995-1997	(43)	14 490†	91.5	1.2	2.0	1.3
NHLBI Dynamic Registry‡‡	1997-1998	(49)	1559*	92	1.9	2.8	0.4
NHLBI Dynamic	1997-1999	(50)	857	91	0.9	0.8	1.9
ACC-NCDR	1998-2000	(51)	100 292	96.5	1.4	0.4	1.9
NY State Database	1997-2000	(52)	22 102	NR	0.68	NR	NR

CABG indicates coronary artery bypass graft surgery; MI, myocardial infarction; NACI, New Approaches in Coronary Interventions; NCN, National Cardiovascular Network; and NR, not reported.

*N indicates number of patients.

†N indicates number of procedures.

‡In NHLBI (I), emergency CABG was defined as in-hospital CABG.

§In NHLBI (II), MI was defined as the presence of at least 2 of the 3 criteria: clinical symptoms, Q waves on ECG (Minnesota code), or elevated cardiac enzyme level (double the normal levels for CK or its MB fraction without Q waves). Emergency CABG was defined as in-hospital CABG.

‖In BARI, MI was defined as the appearance of ECG changes (new pathologic Q waves) supported by abnormal CK-MB elevations.

¶In Northern New England, a new MI was defined as a clinical event, ECG changes, and a creatinine phosphokinase rise at least 2 times normal levels with positive isozymes. Emergency CABG was defined as surgery performed to treat acute closure, unstable angina, or congestive heart failure requiring intravenous nitroglycerin or ABP, or tamponade resulting from the intervention.

#In SCAI, a new MI was defined as any significant infarction (greater than 3 times normal rise in MB fraction).

**In NACI, MI was defined as a Q-wave MI.

††MI was defined as 2 or more of the following: 1) typical chest pain greater than 20 min not relieved by nitroglycerin; 2) serial ECG recordings showing changes from baseline or serially in ST-T and/or Q waves in at least 2 contiguous leads; or 3) serum enzyme elevation of CK-MB greater than 5% of total CK (total CK more than 2 times normal; lactate dehydrogenase subtype 1 greater than lactate dehydrogenase subtype 2).

ate/minor categories. A listing of other bleeding classifications has been developed for use by the ACC-NCDR® (18).

3.3. Acute Outcome: Success Rates

Success has been described on both a lesion and patient basis. In early studies of PTCA, lesion success is defined as an absolute 20% reduction in lesion severity with final stenosis less than 50%. When describing the results of multiple attempted lesions, success is classified as either partial (some but not all attempted lesions successfully treated) or total (each attempted lesion successfully treated). Procedural success is defined as the achievement of either partial or total angiographic success without death, MI, or emergency CABG (49).

Reported rates of angiographic success now range between 82% and 98% depending on the device used and the types of lesions attempted. Formal comparisons demonstrate that success rates are now higher (91% to 92%) in the era of new technology, which includes stents and contemporary drug therapies, than in the era of conventional balloon angioplasty (72% to 74%) (49). The types of lesions attempted strongly influence success rates. The chance of dilating a chronic total occlusion averages 65%, and specific clinical and anatomic factors have been identified that affect this rate (63). Quite different are the success rates for total occlusions associated with STEMI. Success rates over 90% can be expected in this subgroup (64).

With an increase in angiographic success rates and a decline in periprocedural MI and the need for emergency CABG, procedural success rates have risen from a range of 80% to 85% to a range of 90% to 95% (Table 3) (41-52).

3.4. Long-Term Outcome and Restenosis

Although improvements in technology, such as stents, have resulted in an improved acute outcome of the procedure, the impact of these changes on long-term (5 to 10 years) outcome may be less dramatic because factors such as advanced age, reduced left ventricular (LV) function, and progression of complex multivessel disease in patients currently undergoing PCI may have a more important influence. In addition, available data on long-term outcome are mostly limited to patients undergoing PTCA. Ten-year follow-up of the initial cohort of patients treated with PTCA revealed an 89.5% survival rate (95% in patients with single-vessel disease, 81% in patients with multivessel disease) (65). In patients undergoing PTCA within the 1985-1986 National Heart, Lung, and Blood Institute (NHLBI) PTCA Registry (66), 5-year survival was 92.9% for patients with single-vessel disease, 88.5% for those with 2-vessel disease, and 86.5% for those with 3-vessel disease. In patients with multivessel disease undergoing PTCA in the Bypass Angioplasty Revascularization Investigation (BARI) (10), 5-year survival was 86.3%, and infarct-free survival was 78.7%. Specifically, 5-year survival was 84.7% in patients with 3-vessel disease and 87.6% in patients with 2-vessel disease.

In addition to multivessel disease, other clinical factors adversely impact late mortality. In randomized patients with treated diabetes undergoing PTCA in BARI, the 5-year survival was 65.5%, and the cardiac mortality rate was 20.6% compared with 5.8% in patients without treated diabetes (67), although among eligible but not randomized diabetic patients treated with PTCA, the 5-year cardiac mortality rate was 7.5% (68). In the 1985-1986 NHLBI PTCA Registry, 4-year survival was significantly lower in women (89.2%) than in men (93.4%) (69). In addition, although LV dysfunction was not associated with an increase in in-hospital mortality or nonfatal MI in patients undergoing PTCA in the same registry, it was an independent predictor of a higher long-term mortality (70).

A major determinant of event-free survival after coronary intervention is the incidence of restenosis, which had, until the development of stents, remained fairly constant despite multiple pharmacologic and mechanical approaches to limit this process (Table 4) (71-95). The incidence of restenosis after coronary intervention varies depending on the definition, i.e., whether clinical or angiographic restenosis or target-vessel revascularization is measured (96). Data from multiple randomized clinical trials and prospective registries suggest that DES incorporating either rapamycin or paclitaxel with a timed-release polymer are associated with a reduction in restenosis rates to less than 10% across a wide spectrum of clinical and angiographic subsets.

The pathogenesis of the response to mechanical coronary injury is thought to relate to a combination of growth factor stimulation, smooth muscle cell migration and proliferation, organization of thrombus, platelet deposition, and elastic recoil (97,98). In addition, change in vessel size (or lack of compensatory enlargement) has been implicated (99). It has been suggested that attempts to reduce restenosis have failed in part because of lack of recognition of the importance of this factor (100). Although numerous definitions of restenosis have been proposed, greater than 50% diameter stenosis at follow-up angiography has been most frequently used because it was thought to correlate best with maximal flow and therefore ischemia. However, it is now recognized that the response to arterial injury is a continuous rather than a dichotomous process, occurring to some degree in all patients (101). Therefore, cumulative frequency distributions of the continuous variables of minimal lumen diameter or percent diameter stenosis are frequently used to evaluate restenosis in large patient populations (102) (Figure 2) (80).

Although multiple clinical factors (diabetes, unstable angina [UA]/NSTEMI, STEMI, and prior restenosis) (103,104), angiographic factors (proximal left anterior descending artery [LAD], small vessel diameters, total occlusion, long lesion length, and saphenous vein grafts [SVGs]) (105), and procedural factors (higher postprocedure percent diameter stenosis, smaller minimal lumen diameter, and smaller acute gain) (102) have been associated with an increased incidence of restenosis, the ability to integrate these factors and predict the risk of restenosis in individual patients after the procedure remains difficult. The most promising potential

Table 4. Selected Trials of Pharmacological and Mechanical Approaches to Limit Restenosis

Study	Year	Reference	n	Agent	Restenosis Rate, %	
					Placebo or Control	Agent
Schwartz	1988	(71)	376	Aspirin and dipyridamole	39	38
Ellis	1989	(72)	416	Heparin	37	41
Pepine	1990	(73)	915	Methylprednisolone	39	40
CARPORT	1991	(74)	649	Vapiprost	19	21
O'Keefe	1992	(75)	197	Colchicine	22	22
MERCATOR	1992	(76)	735	Cilazapril	28	28
CAVEAT*	1993	(77)	500	DCA versus PTCA	57	50
CCAT	1993	(78)	136	DCA versus PTCA	43	46
Serruys	1993	(79)	658	Ketanserin	32	32
BENESTENT*	1994	(80)	520	Stent versus PTCA	32	22
ERA	1994	(81)	458	Enoxaparin	51	52
Leaf	1994	(82)	551	Fish oil	46	52
STRESS*	1994	(83)	410	Stent versus PTCA	42	32
Weintraub	1994	(84)	404	Lovastatin	42	39
BOAT*	1998	(85)	492	DCA versus PTCA	40	31
Wantanabe*	1996	(86)	118	Probucol	40	20
Tardif*	1997	(87)	317	Probucol	39	21
BENESTENT II*	1998	(88)	823	Stent versus PTCA	31	17
TREAT*	1999	(89)	255	Tranilast	39	18
PRESTO*	2000	(90)	192	DCA and Tranilast	26	11
ARTIST*	2002	(91)	298	Rotablation (in-stent) versus PTCA	51	65
START*	2002	(92)	476	Radiation (in-stent)	45	29
SIRIUS*	2003	(93)	1058	Sirolimus-coated stent versus bare stent	36	9
TAXUS-IV*	2004	(94)	1314	Paclitaxel-coated stent versus bare stent	27	8
RESCUT	2004	(95)	428	Cutting balloon (in-stent) versus PTCA	31	30

DCA indicates directional coronary atherectomy; n, number of patients; and PTCA, percutaneous transluminal coronary angioplasty.
**P* less than 0.05.

approaches to favorably impact the restenosis process are stents and, more recently, DES and catheter-based radiation. More than 6300 patients have been studied in 12 randomized clinical trials to assess the efficacy of PTCA versus stents to reduce restenosis (Table 5) (80,83,88,106-114).

The pivotal BENESTENT (BElgian NEtherlands STENT study) (80) and STRESS (STent REStenosis Study) trials (83) documented that stents significantly reduce angiographic restenosis compared with balloon angioplasty (BENESTENT: 22% vs 32%; STRESS: 32% vs 42%, respectively). These results were further corroborated in the BENESTENT II trial, in which the angiographic restenosis rate was reduced by almost half (from 31% to 16% in patients treated with balloon angioplasty versus heparin-coated stents, respectively) (88).

In addition, randomized studies in patients with ISR have shown that both intracoronary gamma and beta radiation significantly reduced the rate of subsequent angiographic and clinical restenosis by 30% to 50% (92,115-117). Late subacute thrombosis was observed in some of these series (117), but this syndrome has resolved with judicious use of stents and extended adjunct antiplatelet therapy with ticlopidine or clopidogrel. The development of DES has significantly reduced the rate of ISR (see Section 7.3.6 for full discussion).

3.5. Predictors of Success/Complications

3.5.1. Lesion Morphology and Classification

Target lesion anatomic factors related to adverse outcomes have been widely examined. Lesion morphology and absolute stenosis severity were identified as the prominent predictors of immediate outcome during PTCA in the prestent era (118,119). Abrupt vessel closure, due primarily to thrombus or dissection, was reported in 3% to 8% of patients and was associated with certain lesion characteristics (120-122). The risk of PTCA in the prestent era relative to anatomic subsets has been identified in previous NHLBI PTCA Registry data (7) and by the ACC/AHA Task Force on Practice Guidelines (1,123). The lesion classification based on severity of characteristics proposed in the past (123-125) has been principally altered using the present PCI techniques, which capitalize on the ability of stents to manage initial and subsequent complications of coronary interven-

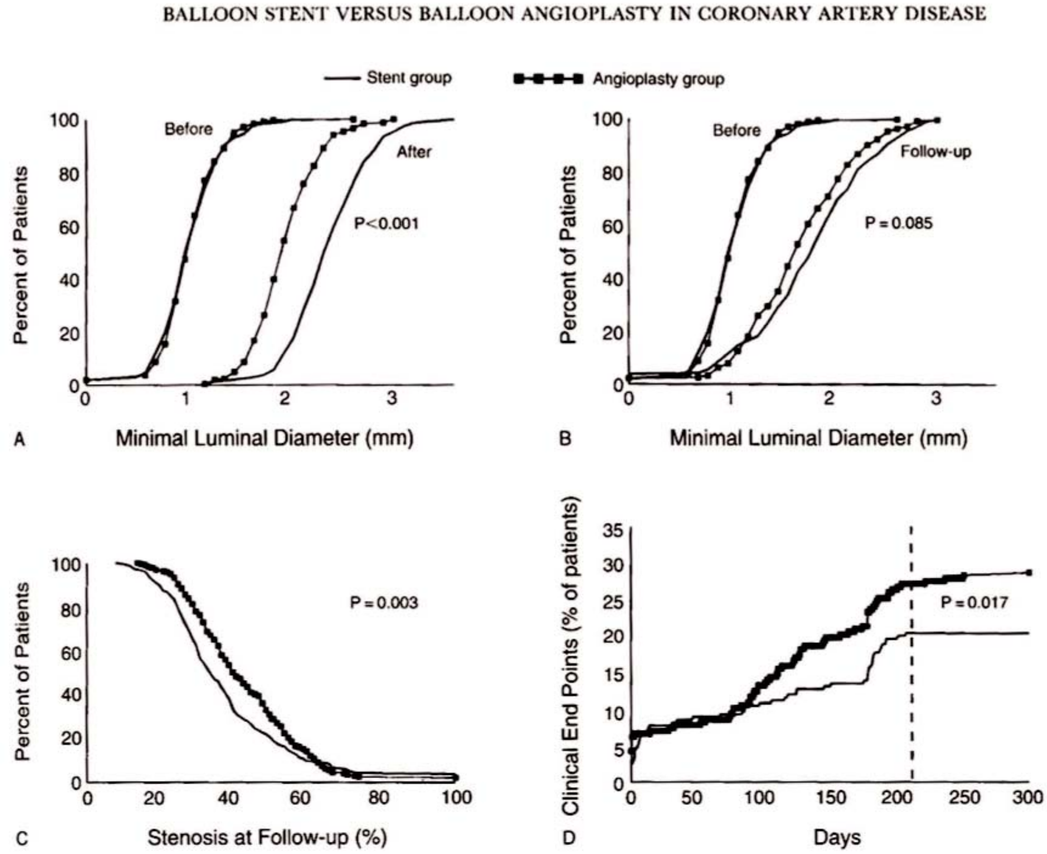

Figure 2. Balloon stent vs balloon angioplasty in coronary artery disease. Cumulative frequency distribution curves for the 2 study groups, showing minimum lumen diameters measured before and after intervention and follow-up (B), the percentage of stenosis at follow-up, and the percentage of patients with clinical end points. Significant differences were apparent that consistently favored the stent group over the angioplasty group with respect to the increased minimal lumen diameter at intervention (A) and follow-up (B), the percentage of stenosis at follow-up (C), and the incidence of major clinical events (D). The vertical dashed line in D indicated the end of the study. Reprinted with permission from Serruys et al. N Engl J Med 1994;331:489-95 (80). Copyright 2004 Massachusetts Medical Society. All rights reserved.

tions (126). As a result, the Committee has revised the previous ACC/AHA lesion classification system to reflect high-risk (at least 1 type C lesion characteristic) and non–high-risk (no type C lesion characteristic) lesions (Table 6) in accordance with the PCI Clinical Data Standards from the ACC-NCDR® (18). Studies (127-130) have confirmed that complex coronary lesions remain predictive of adverse events after PCI. However, although the risk of restenosis and technical failure remains high for chronic total occlusions, the risk of acute complications is not increased.

The SCAI proposed a new lesion classification using 7 lesion characteristics (131). This system dichotomizes lesions by the presence or absence of a type C characteristic and vessel patency versus total occlusion, yielding 4 lesion classes (Table 7) (132). Utilizing data from the voluntary ACC-NCDR®, the SCAI group presented analyses that showed that the more simplified SCAI lesion classification provided better discrimination for success and complications than the ACC/AHA lesion classification system (132,133).

The SCAI lesion classification system was validated from a voluntary registry, which imposes a potential bias because the operator classified the lesion after finishing the case and knowing whether the case was successful or had complications. No prospective studies using core laboratory analysis have validated this system. Nonetheless, the SCAI classification system utilizing vessel patency in addition to C and non-C class appears promising to categorize the risk of success and complications with PCI.

3.5.1.1. Clinical Factors

Coexistent clinical conditions can increase the complication rates for any given anatomic risk factor. For example, complications occurred in 15.4% of patients with diabetes versus 5.8% of patients without diabetes undergoing balloon angioplasty in a multicenter experience (119,122). Several studies have reported specific factors associated with increased risk of adverse outcome after PTCA. These factors include advanced age, female gender, UA, congestive heart failure (HF), diabetes, and multivessel CAD (10,118,119,127-130,134,135). Elevated baseline C-reactive protein (CRP) has recently also been shown to be predictive of 30-day death and MI (128,136). Other markers of inflammation, such as

Table 5. Studies Comparing Balloon Angioplasty with Stents for Native Coronary Artery Lesions

Study (Ref)	Year	Follow-Up, mo	n, Stent/ Angioplasty	Angiographic Restenosis, % Stent	Angiographic Restenosis, % Angioplasty	Angiographic Restenosis, % *P* value	TVR, % Stent	TVR, % Angioplasty	TVR, % *P* value	Death, % Stent	Death, % Angioplasty	Death, % *P* value
STRESS (83)	1994	6	205/202	31.6	42.1	0.046	10.2	15.4	0.06	1.5	1.5	NS
BENESTENT (80,107)	1996	7/12*	259/257	22	32	0.02	10	21	0.001	1.2	0.8	NS
Versaci et al. (108)	1997	12	60/60	19	40	0.02	6.6	22	NA	NA	NA	NA
STRESS II (109)	1998	12	100/89	NA	NA	NA	10	20	NA	17‖	34‖	NA
BENESTENT II (88)	1998	6	413/410	16	31	Less than 0.001	8†	13.7	0.02	0.2%	0.5%	NS
OCBAS (110)	1998	7	57/59	18.8	16.6	NA	17.5	9.2	NA	0	1.6	NS
EPISTENT (111,112)‡	1998	6	794/796	NA	NA	NA	8.7	15.4	Less than 0.001	0.5	1.8	0.02
START (113)	1999	6/48§	229/223	22	37	Less than 0.002	12	24.6	Less than 0.002	2.7	2.4	NS
OPUS (114)	2000	6	479 (Overall)	NA	NA	NA	3.0	10.1	0.003	0.4	1.2	NS

mo indicates months; NA, data not reported for that category, NS, not significant; and TVR, target vessel revascularization. Data are for lesions in coronary arteries with vessel diameter greater than or equal to 3.0 mm.
*6-7 months angiographic follow-up and 12 months clinical follow-up.
†Any repeat procedure.
‡Stent plus abciximab versus percutaneous transluminal angioplasty plus abciximab.
§6 months angiographic follow-up and 48 months clinical follow-up.
‖End point of death/any MI/CABG/target lesion percutaneous transluminal angioplasty.
Modified with permission from Al SJ et al. JAMA 2000;284:1828-36 (106).

Table 6. Lesion Classification System

Descriptions of a High-Risk Lesion (Type C Lesion)
Diffuse (length greater than 2 cm)
Excessive tortuosity of proximal segment
Extremely angulated segments, greater than 90°
Total occlusions more than 3 months old and/or bridging collaterals*
Inability to protect major side branches
Degenerated vein grafts with friable lesions*

*The high risk with these criteria is for technical failure and increased restenosis, not for acute complications.

interleukin-6 and other cytokines, have also been shown to be predictive of outcome (137). The BARI trial found that patients with diabetes and multivessel CAD had an increased periprocedural risk of ischemic complications and increased 5-year mortality compared with patients without diabetes or patients with diabetes undergoing bypass surgery using internal mammary artery (IMA) grafts (10,42). Patients with impaired renal function, especially those with diabetes, are at increased risk for contrast nephropathy (138) and increased 30-day and 1-year mortality (139,140). Renal insufficiency is a strong predictor of outcome in both primary and elective PCI (141-143). Increased risk for death or severe compromise in LV function may occur in association with a complication involving a vessel that also supplies collateral flow to viable myocardium. Certain variables were used to prospectively identify patients at risk for significant cardiovascular compromise during PTCA (144,145). These resulted in a composite 4-variable scoring system, prospectively validated to be both sensitive and specific in predicting cardiovascular collapse for failed PTCA, which includes: 1) percentage of myocardium at risk (e.g., greater than 50% viable myocardium at risk and LV ejection fraction of less than 25%), 2) preangioplasty percent diameter stenosis, 3) multivessel CAD, and 4) diffuse disease in the dilated segment (124) or a high myocardial jeopardy score (125). Patients with higher preprocedural jeopardy scores were shown to have a greater likelihood of cardiovascular collapse when abrupt vessel closure occurred during PTCA (144).

Table 7. SCAI Lesion Classification System: Characteristics of Class I-IV Lesions

Type I lesions (highest success expected, lowest risk)
- (1) Does not meet criteria for C lesion
- (2) Patent

Type II lesions
- (1) Meets any of these criteria for ACC/AHA C lesion
  - Diffuse (greater than 2 cm length)
  - Excessive tortuosity of proximal segment
  - Extremely angulated segments, greater than 90°
  - Inability to protect major side branches
  - Degenerated vein grafts with friable lesions
- (2) Patent

Type III lesions
- (1) Does not meet criteria for C lesion
- (2) Occluded

Type IV lesions
- (1) Meets any of the criteria for ACC/AHA C lesion
  - Diffuse (greater than 2 cm length)
  - Excessive tortuosity of proximal segment
  - Extremely angulated segments, greater than 90°
  - Inability to protect major side branches
  - Degenerated vein grafts with friable lesions
  - Occluded for more than 3 months
- (2) Occluded

Reprinted from Krone et al. Evaluation of the American College of Cardiology/American Heart Association and the Society for Coronary Angiography and Interventions lesion classification system in the current "stent era" of coronary interventions (from the ACC-National Cardiovascular Data Registry®). Am J Cardiol 2003;92:394 (Appendix B) (132).

3.5.1.2. Left Main CAD

CABG has long been considered the "gold standard" for revascularization of lesions in the unprotected left main (ULM) coronary artery (146). With the advent of newer technology utilizing BMS and DES, experience has been gained in performing PCI in ULM coronary artery lesions. Some studies have demonstrated that stenting of the ULM is feasible and appears to be a promising strategy in selected patients (147-152). Patients treated for ULM disease have varied from those presenting with stable angina to those with MI and shock. However, despite the feasibility and high procedural success rate of ULM PCI in the pre-DES era, there are reports of an unacceptably high incidence of long-term adverse events (153-155). This may be attributed to the inclusion of high-risk patients, such as those not considered good surgical candidates. The experience with BMS for ULM PCI in the multicenter ULTIMA (Unprotected Left Main Trunk Intervention Multicenter Assessment) registry suggested a high early mortality (2% per month among hospital survivors over the first 6 months after hospital discharge), and careful surveillance with coronary angiography was recommended (153) (see Section 6.3.4). Patients presenting with MI, ULM occlusion, and cardiogenic shock have lower successful PCI rates (69.7% vs 100%, P equals 0.040), higher in-hospital mortality (71.4% vs 10%, P equals 0.0008), and higher 1-year mortality rates (P equals 0.0064) than stable MI patients regardless of performance of primary PCI with stents (155).

More recently, published studies of left main PCI using DES have reported 6-month or 1-year death rates ranging from 0% to 14% (Table 8) (147-150,152-161). Furthermore, ISR appears to be improved with the use of DES versus BMS. One of the larger studies performed to date showed that the 6-month angiographic restenosis rate was signifi-

Table 8. Published Trials and Selected Registry Experiences of PCI for Unprotected Left Main Coronary Artery Stenosis

First Author, Year (Reference)	Device Used	n	In-Hospital Mortality, %	Mortality, % (Follow-Up Period)	Restenosis, %	TVR, %	Comments
Ellis 1994-1996 (147)	50% BMS	107	20.6	66.0 plus or minus 4.7 (9 mo)	20.8	N/A	Survival to hospital discharge 31% in acute MI patients; in elective patients, in-hospital mortality 5.9% in good candidates for CABG, 30.4% in poor CABG candidates; in-hospital survival strongly correlated with LVEF
Silvestri 1993-1998 (148)	100% BMS	140	9% high CABG risk; 0% low CABG risk	2% high CABG risk; 2.6% low CABG risk (6 mo)	23	17.4	Good immediate results of PCI in ULM stenosis, especially in good CABG candidates
Black 1994-1998 (149)	100% BMS	92	4.3	10.8 (7.3 plus or minus 5.8 mo)	N/A	7.3	PCI to ULM appears better in candidates for CABG than in patients in whom CABG is contraindicated; trend toward cardiac mortality with 3-vessel disease and low LVEF; low final stent lumen diameter only significant predictor of cardiac mortality
ULTIMA 1993-1998 (153)	68.8% BMS	279	13.7	24.2 (1 y)	N/A	33.6*	46% of patients were deemed inoperable or at high risk for CABG; in patients less than 65 y old with LVEF greater than 30% and no shock, 0% periprocedural deaths and 1-year mortality 3.4%; 2% per month death rate among hospital survivors over 6 months after discharge; careful surveillance with coronary angiography recommended
Park 1995-2000 (150)	100% BMS	127	0	3.1 (25.5 plus or minus 16.7 mo)	19	11.8	Elective stenting in patients with normal LVEF; IVUS may optimize immediate results; significantly lower restenosis rate with debulking before stenting
Takagi 1993-2001 (154)	96% BMS	67	0	16.4 (31 plus or minus 23 mo)	31.4	23.9	High rate of restenosis and RR; 11.9% cardiac mortality; significantly higher cardiac mortality in patients with Parsonnet score greater than 15 at 3 years
Park 1995-2000 (152)	100% BMS	270	0	7.4 (32.3 plus or minus 18.5 mo)	21.1	16.7†	Good overall long-term (3-year) survival in selected patients with normal LVEF; combined CAD and post-procedural lumen diameter significant predictors of MACE
Sakai 1992-2000 (155)	65% to 74% BMS	38	71.4% with shock; 10% without shock	71.4% with shock; 20% without shock (1 y)	N/A	N/A	Patients with acute MI due to ULM stenosis and shock have poor survival regardless of performance of PCI with stents

Continued on next page

Table 8. *Continued*

First Author, Year (Reference)	Device Used	n	In-Hospital Mortality, %	Mortality, % (Follow-Up Period)	Restenosis, %	TVR, %	Comments
de Lezo 2002-2004 (156)	100% SES	52	0	0 (12 plus or minus 4 mo)	3.8	1.9	Treatment with SES appears feasible and safe; promising midterm results
Agostoni 2002-2003 (158)	100% DES	58	2	5 (1 y)	N/A	7	Rate of events did not differ significantly between IVUS and angiographically guided procedures; Anatomic location of atherosclerotic disease in ULM artery only independent predictor of events at follow-up
Chieffo 2002-2004 (159)	100% DES	85	0	3.5 (6 mo)	19	19	Despite higher risk profile, patients receiving DES had significant advantage in the incidence of MACE compared with historical control group receiving BMS
Park 2003-2004 (160)	100% SES	102	0	0 (1 y)	7	2	SES implantation in ULM and normal LVEF associated with low in-hospital and 1-year mortality; SES more effective in preventing in-stent restenosis than historical BMS control
RESEARCH/ 2003 T-SEARCH 2002- (161)	100% DES	95 (15 protected LM)	11	14 (1 y)	N/A	6	More than 50% of study population at high surgical risk by Parsonnet classification; 47% relative risk reduction in MACE in DES group compared with BMS control, driven by significantly lower incidence of MI and TVR

*1-Year estimate; †32.3 plus or minus 18.5 mo.
n indicates number of patients; LVEF, LV ejection fraction; MACE, major adverse cardiac events; RR, repeat revascularization; SES, sirolimus-eluting stent; TVR, target-vessel revascularization; and ULM, unprotected left main.

cantly lower in the ULM group receiving DES than in those who received BMS (7.0% vs 30.3%, *P* less than 0.001) (160). The lower rate of restenosis of DES compared with BMS has been confirmed in other studies of ULM PCI (159).

There have been some attempts to predict success of ULM PCI using customary risk factors such as age, renal failure, coronary calcification, and location of the lesion in the left main coronary artery. In general, younger patients with preserved LV function, noncalcified coronary arteries, and complete delivery of stent, fare better. Maintenance of antiplatelet therapy after the procedure is critical, as is the implementation of secondary prevention therapies. Careful postprocedure surveillance with coronary angiography is needed to prevent fatal MI or sudden death that may be associated with ISR with a large area of myocardium in jeopardy; however, the frequency and best method of follow-up are unknown (162). One study's authors from the BMS era suggested routine surveillance angiography at 2 and 4 months after PCI (153). Others advocate routine stress testing or cardiac catheterization at 3 and 6 months even in asymptomatic patients (148,150). Studies from the DES era have reported performing routine angiography 4 to 8 months after PCI or earlier if clinically indicated by symptoms or documented myocardial ischemia (159,160). Other issues that remain to be resolved are technical issues (e.g., optimal bifurcation stenting technique, stent size), degree of revascularization necessary, cost-effectiveness, and the selection of patients best suited for DES.

In conclusion, CABG using IMA grafting is the "gold standard" for treatment of ULM disease and has proven benefit on long-term outcomes. The use of DES has shown encouraging short-term outcomes, but long-term follow-up is needed. Nevertheless, the use of PCI for patients with significant ULM stenosis who are candidates for revascularization but not suitable for CABG can improve cardiovascular outcomes and is a reasonable revascularization strategy in carefully selected patients. Recommendations for ULM PCI in specific angina subsets can be found in Sections 5.1, 5.2, 5.3, and 5.4 and in Section 6.3.4 for post-PCI follow-up.

3.5.2. Risk of Death

In the majority of patients undergoing elective PCI, death as a result of PCI is directly related to the occurrence of coronary artery occlusion and is most frequently associated with pronounced LV failure (144,145). The clinical and angiographic variables associated with increased mortality include advanced age, female gender, diabetes, prior MI, multivessel disease, left main or equivalent coronary disease, a large area of myocardium at risk, pre-existing impairment of LV or renal function, post-PCI worsening of renal function, and collateral vessels supplying significant areas of myocardium that originate distal to the segment to be dilated (10,118,120,122,134,135,138,139,140,144,163-167). Periprocedural stroke also increases in-hospital and 1-year mortality (168). PCI in the setting of STEMI is associated with a significantly higher death rate than is seen in elective PCI.

3.5.3. Women

An estimated 33% of the more than 1 million PCIs performed in the United States annually are in women. The need for more data concerning outcomes from PCI in women has led the AHA to issue a scientific statement summarizing available studies (169). Compared with men, women undergoing PCI are older and have a higher incidence of hypertension, diabetes mellitus, hypercholesterolemia, and comorbid disease (69,170-174). Women also have more UA and a higher functional class of stable angina (Canadian Cardiovascular Society [CCS] class III and IV) for a given extent of disease (175). Yet, despite the higher-risk profile in women, the extent of epicardial coronary disease is similar to (or less than) that in men. In addition, although women presenting for revascularization have less multivessel disease and better LV systolic function, the incidence of HF is higher in women than in men. The reason for this gender paradox is unclear, but it has been postulated that women have more diastolic dysfunction than men (176).

Early reports of patients undergoing PTCA revealed a lower procedural success rate in women (172); however, subsequent studies have noted similar angiographic outcome and incidence of MI and emergency CABG in women and men (69). Although reports have been inconsistent, in several large-scale registries, in-hospital mortality is significantly higher in women (177), and an independent effect of gender on acute mortality after PTCA persists after adjustments for the baseline higher-risk profile in women (69,178). The reason for the increase in mortality is unknown, but small vessel size (179) and hypertensive heart disease in women have been thought to play a role. Although a few studies have noted that gender is not an independent predictor of mortality when body surface area (a surrogate for vessel size) is accounted for (171), the impact of body size on outcome has not been thoroughly evaluated. The higher incidence of vascular complications, coronary dissection, and perforation in women undergoing coronary intervention has been attributed to the smaller vasculature in women than in men. In addition, diagnostic IVUS studies have not detected any gender-specific differences in plaque morphology or luminal dimensions once differences in body surface area were corrected, which suggests that differences in vessel size account for some of the apparent early and late outcome differences previously noted in women (180). It has also been postulated that the volume shifts and periods of transient ischemia during PTCA are less well tolerated by the hypertrophied ventricle in women, and HF has shown to be an independent predictor of mortality in both women and men undergoing PTCA (181).

Women continue to have increased bleeding and vascular complications compared with men, but these rates have decreased with the use of smaller sheath sizes and early sheath removal, weight-adjusted heparin dosing, and less aggressive anticoagulation regimens (169). Use of IIb/IIIa platelet receptor antagonists during PCI is not associated with an increased risk of major bleeding in women

(182,183), and the direct thrombin inhibitor bivalirudin during elective PCI appears to reduce the risk of bleeding (combined major and moderate bleeding) in both women and men compared with unfractionated heparin (184).

Improved outcomes have been reported in more recently treated women undergoing both PTCA and PCI, despite the fact that the women are older and have more complex disease than women treated previously (Table 9) (69,170,185-189). In fact, in the 1993-1994 NHLBI PTCA Registry (open to women only), procedural success was higher and major complications lower than in women treated in the 1985-1986 registry (190). Additionally, in patients undergoing PTCA in BARI, in-hospital mortality, MI, emergency coronary artery bypass surgery rates, and 5-year mortality were similar in women and men, although women had a higher incidence of periprocedural HF and pulmonary edema (188).

The widespread use of stents and adjunctive pharmacologic therapy has improved outcomes in patients undergoing contemporary PCI (80,83,112,191-202). Early studies of drug-eluting stents in small vessels (less than or equal to 2.75 mm), of particular importance in women, report favorable long-term results in both women and men (203). The hope that stents would eliminate the difference in outcomes between women and men has not been realized. Gender differences in mortality have persisted for patients treated with stents both in the setting of acute and nonacute MI (204). In a meta-analysis of invasive versus conservative therapy of patients with UA/NSTEMI, men demonstrated a clear survival advantage using routine invasive therapy with GP IIb/IIIa inhibitors and intracoronary stents; however, using similar therapy, the results for women were not significantly improved (205), although it has been shown that the benefits of an invasive strategy have been limited to high-risk women (206).

In women with STEMI, the relative benefit of primary PCI compared with fibrinolytic therapy is similar to that in men, but there is a larger absolute benefit in women owing to their higher event rate (207). In patients with shock complicating acute MI, the benefit of revascularization is similar in women and men (208).

In general, the risks and benefits of adjunctive pharmacotherapy in women are similar to those in men, although an increased rate of minor bleeding has been reported in women treated with abciximab (183). When IIb/IIIa platelet receptor antagonists are used with unfractionated heparin, a lower dose of the latter should be considered to decrease the risk of bleeding in women (Table 9) (69,170,185-189).

Few gender-specific data are available on the outcomes of other percutaneous coronary devices. Although directional coronary atherectomy has been associated with lower procedural success and higher bleeding complications in women (209), similar benefit to that in men has been reported from embolic protection devices used in saphenous vein PCI (210) and from vascular brachytherapy (169).

Table 9. Gender-Specific Mortality Risk

Study	Years	Reference	Women Versus Men (n)	Follow-Up (years)	Device	Mortality, Men Versus Women (%)	*P*	Adjusted OR (95% CI)
Mayo Clinic	1979-1990	(186)	3027 (824 vs 2203)	5.5	PTCA	27 versus 22	0.06	0.94 (0.76 to 1.15)
Emory University	1980-1991	(187)	10 785 (2845 vs 7940)	5	PTCA	8 versus 5	0.0002	1.08 (0.84 to 1.39)
NHLBI PTCA Registry	1985-1986	(69)	2136 (546 vs 1590)	4	PTCA	6.6 versus 10.8	0.001	1.20 (0.84 to 1.73)
BARI	1988-1994	(188)	1829 (489 vs 1340)	5	PTCA	12.8 versus 12.0	NS	0.60 (0.43 to 0.84)
NACI	1990-1994	(189)	2855 (975 vs 1880)	1	PCI	5.7 versus 5.9	NS	NS
Northern New England	1994-1999	(170)	33 666 (10 997 vs 22 689)	In-hospital	PCI	1.21 versus 1.06	0.096	1.24 (0.96 to 1.60)
NHLBI Dynamic Registry	1997-1998	(185)	2524 (895 vs 1629)	1	PCI	4.3 versus 6.5	0.022	1.26* (0.85 to 1.87)

CI indicates confidence interval; NS, not significant; n, number of patients; OR, odds ratio; PCI, percutaneous coronary intervention; and PCTA, percutaneous transluminal coronary angioplasty. For expansion of study names, see corresponding reference.
*Expressed as relative risk (RR).

3.5.4. The Elderly Patient

Age greater than 75 years is one of the major clinical variables associated with increased risk of complications (211-214). In the elderly population, the morphologic and clinical variables are compounded by advanced years, with the very elderly having the highest risk of adverse outcomes (215). In octogenarians, although feasibility has been established for most interventional procedures, the risks associated with both percutaneous and nonpercutaneous revascularization are increased (216-218). Octogenarians undergoing PCI have a higher incidence of prior MI, lower LV ejection fraction, and more frequent HF (219,220). In the stent era, procedural success and restenosis rates are comparable to those for nonoctogenarians, albeit with higher incidences being reported for in-hospital and long-term mortality and for vascular and bleeding complications (221). A multicenter study compared an early invasive strategy versus an early conservative strategy in 2220 patients hospitalized for UA/NSTEMI. Among patients 65 years or older, the early invasive strategy conferred a 4.8% absolute risk reduction (39% Relative Risk Reduction [RRR]) in death or MI at 6 months. In a post hoc analysis, patients aged 75 years or older experienced a 10.8% reduction (56% RRR) in 6-month death or MI with an early invasive strategy. However, there was a significant major bleeding rate in patients aged 75 years or older assigned to an invasive versus a conservative strategy (16.6% vs 6.5%, *P* equals 0.009) (222). For patients enrolled in the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial of PCI for STEMI using routine stenting versus balloon angioplasty, with or without abciximab administration in both revascularization strategies, 1-year mortality increased exponentially for each decile of age after 65 years (1.6% for patients less than 55 years, 2.1% for 55 to 65 years, 7.1% for 65 to 75 years, 11% for greater than 75 years; *P* less than 0.0001). The incidence of stroke and major bleeding was also increased in the elderly at 1 year. Abciximab administration did not confer a benefit in elderly patients but was deemed safe. In contrast, routine stent implantation in elderly patients reduced 1-year rates of ischemic target-vessel revascularization (7.0% vs 17.6%, *P* less than 0.0001) and subacute or late thrombosis (0% vs 2.2%, *P* equals 0.005) compared with balloon angioplasty. The authors acknowledged that additional risks/benefits of stent or IIb/IIIa inhibitor use in elderly patients with STEMI might have become evident had more patients been enrolled in this study (223). Thus, with rare exception (primary PCI for cardiogenic shock in patients greater than 75 years of age), a separate category has not been created in these guidelines for the elderly (224). However, their higher incidence of comorbidities and risk for bleeding complications should be taken into account when considering the need for PCI (218,225).

3.5.5. Diabetes Mellitus

In the TIMI-IIB study of MI, patients with diabetes mellitus had significantly higher 6-week (11.6% vs 4.7%), 1-year (18.0% vs 6.7%), and 3-year (21.6% vs 9.6%) mortality rates than nondiabetic patients (226). Patients with diabetes with a first MI who were randomly assigned to the early invasive strategy faired worse than those managed conservatively (42-day mortality: death or MI, or death alone, 14.8% vs 4.2%; *P* less than 0.001) (227). An early catheterization and intervention strategy after fibrinolysis was of little benefit in these patients with diabetes. Although adjusted in-hospital mortality was not different in diabetic and nondiabetic patients, data from the NHLBI registry showed that at 1 year, adjusted mortality and repeat revascularization were significantly higher in diabetics (228). Thus, routine catheterization and PCI in this patient subgroup should be based on clinical need and ischemic risk stratification.

Stenting decreases the need for target-vessel revascularization procedures in diabetic patients compared with PTCA (229). The efficacy of stenting with GP IIb/IIIa inhibitors was assessed in the diabetic population compared with those without diabetes in a substudy of the EPISTENT (Evaluation of IIb/IIIa Platelet Inhibitor for Stenting) trial (230). One hundred seventy-three diabetic patients were randomized to stent/placebo combination, 162 patients to stent/abciximab combination, and 156 patients to PTCA/abciximab combination. For the composite end point of death, MI, or target-vessel revascularization, the rates were as follows: 25%, 23%, and 13% for the stent/placebo, PTCA/abciximab, and stent/abciximab groups (*P* equals 0.005). Irrespective of revascularization strategy, abciximab significantly reduced 6-month death and MI rate in patients with diabetes for all strategies. Likewise, 6-month target-vessel revascularization was reduced in the stent/abciximab group approach. One-year mortality for diabetics was 4.1% for the stent/placebo group and 1.2% for the stent/abciximab group. Although this difference was not significant, the combination of stenting and abciximab among diabetics resulted in a significant reduction in 6-month rates of death and target-vessel revascularization compared with stent/placebo or PTCA/abciximab therapy (230). Similar results in 1-year target-vessel revascularization and mortality have been reported with abciximab and the small-molecule GP IIb/IIIa inhibitor tirofiban (231). (See Section 6.2.2 Glycoprotein IIb/IIIa Inhibitors.) The BARI trial, in which stents and abciximab were not used, showed that survival was better for patients with treated diabetes undergoing CABG with an arterial conduit than for those undergoing PTCA (232). The benefit of CABG in patients with diabetes may be related to lessened mortality after subsequent Q-wave MI among patients with diabetes. In the BARI trial, the benefit of bypass surgery in diabetic patients was greater in those patients with more extensive disease (e.g., more than 4 lesions). This advantage was largely due to a lower mortality for subsequent MI (233).

Since the BARI trial was completed, several studies have assessed the use of PCI with stenting versus CABG in patients with multivessel disease. Patients with diabetes were assessed specifically in studies from the ARTS (Arterial Revascularization Therapies Study) and AWESOME (Angina

With Extremely Serious Operative Mortality Evaluation) groups. Glycoprotein IIb/IIIa inhibitors were used in approximately 11% of AWESOME PCI patients and were not incorporated into the ARTS protocol. At 3 years of follow-up, the survival rates of the diabetic subsets treated with CABG and PCI were not significantly different in either ARTS or AWESOME. Repeat revascularization was higher with PCI in the subsets of patients with diabetes in both trials.

Randomized trials, meta-analysis of trials, and epidemiological studies have shown the superiority of DES over BMS in terms of reducing late repeat revascularization (234-236). There are, as yet, inadequate data from which to infer impact on long-term survival after PCI for patients with diabetes. The sum effect of DES and GP IIb/IIIa inhibitors will be assessed against contemporary CABG in multivessel-disease patients with diabetes in the upcoming National Institutes of Health (NIH)–sponsored Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM trial) (237). A discussion about the selection of patients with diabetes for surgical revascularization or PCI may be found in Section 3.6, Comparison With Bypass Surgery. Preliminary data suggest late outcomes in diabetic patients after PCI are similar to nondiabetics if the hemoglobin A1C can be maintained less than 7.0% (238). Management of other risk factors, particularly lipid abnormalities, in patients with diabetes has also been shown to have a very significant effect on long-term outcome (239-242). These observations emphasize the importance of diabetes management and secondary prevention therapies after PCI.

3.5.6. PCI After Coronary Artery Bypass Surgery

Although speculated to be at higher risk, patients having PCI of native vessels after prior coronary bypass surgery have, in recent years, nearly equivalent interventional outcomes and complication rates compared with patients having similar interventions without prior surgery. For PCI of SVG, studies indicate that the rate of successful angioplasty exceeds 90%, the death rate is less than 1.2%, and the rate of Q-wave MI is less than 2.5% (Table 10) (243-248). The incidence of non–Q-wave MI may be higher than that associated with native coronary arteries (249-251).

In consideration of PCI for SVG, the age of the SVG and duration and severity of myocardial ischemia should be taken into consideration. Use of GP IIb/IIIa blockers has not been shown to improve results of angioplasty in vein grafts (252). However, preliminary studies of 2 different distal embolic protection devices (Percusurge and GuideWire) (253-255) are associated with promising results (254,255) (see Section 5.5.2, Late Ischemia After CABG). The native vessels should be treated with PCI if feasible. Patients with older and/or severely diseased SVGs may benefit from elective repeat CABG surgery rather than PCI (256,257).

In some circumstances, PCI of a protected left main coronary artery stenosis with a patent and functional LAD or left circumflex coronary conduit can be considered. PCI should be recognized as a palliative procedure with the potential to delay the ultimate application of repeat CABG surgery.

3.5.7. Specific Technical Considerations

Certain outcomes of PCI may be specifically related to the technology utilized for coronary recanalization. Periprocedural CK-MB elevation appears to occur more frequently after use of ablative technology such as rotational or directional atherectomy (23,77,85,243,258). Antecedent UA appears to be a clinical predictor of slow flow and periprocedural infarction after ablative technologies (259), and direct platelet activation has been demonstrated to occur with both directional and rotational atherectomy (260). In support of the premise that platelets play a pathophysiologic role in periprocedural MI are observations that the presence and magnitude of CK-MB elevation after ablative technologies can be reduced to levels observed after PTCA by the administration of prophylactic platelet GP IIb/IIIa receptor blockade (261,262).

Coronary perforation may occur more commonly after the use of atheroablative devices, including rotational, directional, or extraction atherectomy, and excimer laser coronary angioplasty. However, the incidence of perforation has been reported variably to be 0.10% to 1.14% with balloon angioplasty, 0.25% to 0.70% with directional coronary atherectomy, 0.0% to 1.3% with rotational atherectomy, 1.3% to 2.1% with extraction atherectomy, and 1.9% to 2.0% after excimer laser coronary angioplasty (263,264). Coronary perforation complicates PCI more frequently in the elderly and in women. Although 20% of perforations may be secondary to the coronary guidewire, most are related to the specific technology used. Perforation is usually (80% to 90%) evident at the time of the interventional procedure and should be a primary consideration in the differential diagnosis for cardiac tamponade manifest within 24 h of the procedure. Perforations may be classified on the basis of angiographic appearance as type I (extraluminal crater without extravasation), type II (pericardial and myocardial blush without contrast jet

Table 10. Probability of Success, Complications, and Restenosis After Balloon Angioplasty or Stenting in Patients After Coronary Bypass Surgery

Conduit Site	Reference	Success Rate	Death Rate	MI Rate*	Restenosis Rate†
Saphenous vein graft	(243-246)	Greater than 92%	Less than 2%	15%	20% to 35%
Internal mammary artery	(247)	97%	Less than 1%	12.5%	7% anastomotic, 25% ostial site
Left main	(248)	95%	Less than 2%	10%	25%

MI indicates myocardial infarction.
*Greater than 3 times normal CK-MB on serial determinations after intervention..
†Restenosis measured as target-vessel revascularization.

extravasation), and type III (extravasation through a frank [1 mm] perforation) (263). In the absence of extravasation (type III), the majority of perforations may be effectively managed without urgent surgical intervention. Type III perforations have been successfully managed nonoperatively with pericardiocentesis, reversal of anticoagulation, and either prolonged perfusion balloon inflation at the site of perforation or deployment of a covered stent. Perforations caused by atheroablative devices usually require surgical repair.

3.5.8. Issues of Hemodynamic Support in High-Risk PCI

Controversy exists about the ability to predict hemodynamic compromise during PCI. Hemodynamic compromise, defined as a decrease in systolic blood pressure to an absolute level less than 90 mm Hg during balloon inflation, was often associated with LV ejection fraction less than 35%, greater than 50% of myocardium at risk, and PTCA performed on the last remaining vessel (120,163).

Early feasibility studies of high-risk PTCA using percutaneous cardiopulmonary support (CPS) indicated that although initial likelihood of success was high, vascular morbidity was also high, with an incidence of 43% (265,266). However, no study has published data to validate commonly used high-risk categorizations.

Elective high-risk PCI can be performed safely without intra-aortic balloon pump (IABP) or CPS in most circumstances. Emergency high-risk PCI such as primary PCI for STEMI can usually be performed without IABP or CPS. CPS for high-risk PCI should be reserved only for patients at the extreme end of the spectrum of hemodynamic compromise, such as those patients with extremely depressed LV function and patients in cardiogenic shock. However, in patients with borderline hemodynamics, ongoing ischemia, or cardiogenic shock, insertion of an intra-aortic balloon just before coronary instrumentation has been associated with improved outcomes (267,268). Furthermore, it is reasonable to obtain vascular access in the contralateral femoral artery before the procedure in patients in whom the risk of hemodynamic compromise is high, thereby facilitating intra-aortic balloon insertion, if necessary.

For high-risk patients, clinical and anatomic variables influencing complications and outcome should be assessed before the performance of PCI to determine procedural risk, the risk of abrupt vessel closure, and potential for cardiovascular collapse. In patients having a higher-risk profile (such as those with LV dysfunction, single patent vessel or ULM, degenerated SVG, or high thrombus burden in the obstructed vessel), consideration of alternative therapies, particularly coronary bypass surgery, formalized surgical standby, or periprocedural hemodynamic support should be addressed before proceeding with PCI. Several small retrospective studies have evaluated the use of elective balloon pump support before high-risk PCI. These studies generally reveal successful reperfusion by PCI, with improved procedural or in-hospital morbidity and mortality (267,269,270). An alternative approach is to use standby IABP, which results in slightly greater complications for patients undergoing standby IABP than for those in whom the IABP was in place before the procedure (271). Available data for the use of IABP in high-risk patients involve retrospective analyses of relatively small numbers of patients; therefore, no formal recommendations are suggested. The decision to proceed with IABP before PCI remains a clinical judgment made by the physician based on the high-risk characteristics of coronary anatomy and overall status of the patient.

3.6. Comparison With Bypass Surgery

The major advantage of PCI is its relative ease of use and avoidance of general anesthesia, thoracotomy, extracorporeal circulation, central nervous system complications, and prolonged convalescence. Repeat PCI can be performed more easily than repeat bypass surgery, and revascularization can be achieved more quickly in emergency situations. The disadvantages of PCI are early restenosis and the inability to relieve many totally occluded arteries and/or those vessels with extensive atherosclerotic disease.

Coronary artery bypass surgery has the advantages of greater durability (graft patency rates exceeding 90% at 10 years with arterial conduits) (272) and more complete revascularization regardless of the morphology of the obstructing atherosclerotic lesion. Generally speaking, the greater the extent of coronary atherosclerosis and its diffuseness, the more compelling the choice of coronary artery bypass surgery, particularly if LV function is depressed. Patients with a lesser extent of disease and localized lesions are good candidates for endovascular approaches.

PTCA and coronary artery bypass surgery have been compared in many nonrandomized and randomized studies. Whereas randomized controlled trials are the only way to completely eliminate bias between comparative therapies, large prospective registries can best extend observations to broad segments of the population who might be excluded from randomized trials. Through risk-adjustment methodologies, large groups of patients can be evaluated between therapies to attempt to eliminate the impact of baseline differences. A number of registries have compared coronary bypass graft surgery with PCI (52). New York State mandates a registry of all patients undergoing PCI and CABG that is monitored by audit and provides survival data on all New York State residents. Patients with multivessel disease treated between January 1, 1997, and December 31, 2000, were followed up for 3 years (52). During this period when stent utilization was common, the adjusted hazard ratio favored surgery for all subsets of multivessel disease patients. The surgical advantage was greatest for patients with 3-vessel disease with involvement of the proximal LAD and least for patients with 2-vessel disease without anterior descending involvement. One important factor differentiating the techniques was significantly more complete revascularization in the surgery group. By identifying trends such as these, registries can provide important insight for clinical improvement.

The most accurate comparisons of outcomes are best made from prospective randomized trials of patients suitable for either treatment. Although results of these trials provide useful information for selection of therapy in several patient subgroups, prior studies of PTCA may not reflect outcome of current PCI practice, which includes frequent use of stents and antiplatelet drugs. Similarly, many previous studies of CABG may not reflect outcome of current surgical practice, in which arterial conduits are used whenever practicable. Beating heart bypass operations are also employed for selected patients with single-vessel disease with reduced morbidity (273). In addition, patients are selected for PCI (with or without stenting) because of certain lesion characteristics, and these anatomic criteria are not required for CABG.

Randomized trials also must be interpreted carefully. It is unethical to withhold subsequent PCI or CABG from patients solely because they fail an earlier treatment; thus, comparative prospective studies can only compare initial strategies of revascularization. This critically important point is frequently overlooked by those who claim that a randomized study proves equally good outcome of one method of revascularization over the other.

Despite these limitations, some generalizations can be made from comparative trials of PTCA and CABG. First, for most patients with single-vessel disease, late survival is similar with either revascularization strategy, and this might be expected given the generally good prognosis of most patients with single-vessel disease managed medically (274-276).

Two prospective clinical trials have evaluated PTCA and CABG for revascularization of isolated disease of the LAD. Investigators in the Medicine, Angioplasty or Surgery Study (MASS) used a combined end point of cardiac death, MI, or refractory angina requiring repeat revascularization by surgery; at 3 years of follow-up, this combined end point occurred in 24% of PTCA patients, 17% of medical patients, and 3% of surgical patients (277). Importantly, there was no difference in overall survival in the 3 groups. In the Lausanne trial of 134 patients with isolated LAD disease treated by either PTCA (68 patients) or bypass with an IMA, survival was similar in the 2 groups, and 94% of PTCA patients and 95% of CABG patients were free of limiting symptoms (278). However, patients in the PTCA group took more antianginal drugs than surgical patients, and at median follow-up of 2.5 years, 86% of CABG-treated versus 43% of PTCA-treated patients were free from late events (*P* less than 0.01); this difference was primarily due to restenosis (32%) requiring subsequent CABG (16%) or PTCA (15%). Neither of the 2 aforementioned trials included stenting, a technique that would be expected to reduce rates of early restenosis by as much as 50% in appropriately selected lesions (108,279,280).

In a similar manner, the 3-year follow-up of the Argentine randomized trial of PTCA versus CABG multivessel disease (ERACI study) (279) demonstrated that in patients randomized to PTCA or bypass surgery, the 1-, 3-, and 5-year follow-up results indicated that freedom from combined cardiac events was significantly greater for bypass surgery than for the PTCA group (77% vs 47%; *P* less than 0.001). However, there were no differences in overall and cardiac mortality or in the frequency of MI between the 2 groups. Patients who had bypass surgery were more frequently free of angina (79% vs 57%) and had fewer additional reinterventions (6.3% vs 37%) than patients who had PTCA. This study indicated that freedom from combined cardiac events at 3-year follow-up was greater in bypass patients than in those who had PTCA and that the PTCA group had a higher incidence of recurrence of angina and need for repeat procedures. Cumulative cost at 3 years was greater for surgery than for the PTCA group.

In the ARTS trial, the first trial to compare stenting with surgery, there was no significant difference in mortality between PCI and surgical groups at 1 and 3 years (281,282). The main difference compared with previous PTCA and CABG trials was an approximate 50% reduction in the need for repeat revascularization in a group randomized to PCI with stent placement (281).

Similar results were reported by the Stent or Surgery (SoS) trial. In this trial, 988 patients with multivessel disease were randomized to PCI (78% received stents) or CABG. At a median follow-up of 2 years, 21% of the PCI group required repeat revascularization compared with 6% of the CABG group (hazard ratio 3.85, 95% confidence interval [CI] 2.56-5.79, *P* less than 0.0001). The incidence of death or Q-wave MI was similar in both groups (hazard ratio 0.95, 95% CI 0.63-1.42, *P* equals 0.80). Mortality was higher in the PCI group, but this was influenced by a particularly low surgical mortality and a high rate of noncardiovascular deaths in the PCI group (283).

The ERACI II study randomized 450 patients with multivessel disease (91% UA) to PCI or CABG. At a mean follow-up of 18.5 months, survival was 96.9% in PCI group versus 92.5% in the CABG group (*P* less than 0.017). Freedom from MI was also better in the PCI group than in the CABG group (97.7% vs 93.4%, *P* less than 0.017). Similar to other studies, the need for repeat revascularization was higher in the PCI group (16.8% vs 4.8%, *P* less than 0.002) (284).

In the AWESOME study, 454 patients with medically refractory myocardial ischemia and high-risk features for adverse outcomes with surgery were randomized to either PCI (54% received stents) or CABG. High-risk features included: prior open heart surgery, age greater than 70 years, LV ejection fraction less than 0.35, MI within 7 days, or IABP required. Comparable survival was observed between the PCI and CABG groups at 3 years (80% vs 79%), with more frequent repeat revascularization in the PCI group. Additionally, survival free of UA in the PCI group was within 90% of that in the CABG group (285).

Direct comparison of initial strategies of PCI or CABG in patients with multivessel coronary disease is possible only by randomized trials because of selection criteria of patients for PCI. There have been 5 large (more than 300 patients) randomized trials of PTCA versus CABG and 2 smaller studies and 5 large trials of PCI using stents versus CABG (10-12,279,281,283-289). Characteristics of the studies are summarized in Table 11 (11,12,279,282-290). These trials demonstrate that in appropriately selected patients with multivessel coronary disease, an initial strategy of standard PCI with BMS yields similar overall outcomes (e.g., death, MI) to initial revascularization with coronary artery bypass.

An important exception to the conclusion of the relative safety of PCI in multivessel disease is the subgroup of patients with treated diabetes mellitus. In BARI, the only trial with a sufficiently large patient enrollment to examine survival alone, the data showed that among treated diabetic patients assigned to PTCA, 7-year survival was 55.7% compared with 76.4% for patients having CABG (*P* equals 0.0011); the improved outcome with CABG was due to reduced cardiac mortality (5.8% vs 20.6%, *P* equals 0.0003), which was confined to those receiving at least 1 IMA graft (10,67,290). There was no mortality difference at 7 years in the remainder of the patients, those without diabetes and patients with diabetes not undergoing medical treatment (290). Better survival of diabetic patients with multivessel disease treated initially with CABG has also been observed in a large retrospective study from Emory (291) and in the 8-year results of Emory Angioplasty Surgery Trial (EAST) (292). In the BARI trial, the benefit of bypass surgery in diabetic patients was greater in those patients with more extensive disease (e.g., more than 4 lesions). This advantage was largely due to a lower mortality for subsequent MI (233,293). As compelling as these reports may be, it is of interest that treated diabetic patients enrolled in the BARI registry did not show a similar advantage for CABG over PCI, which suggests that physician judgment in the selection of diabetic patients for PCI may be an important factor (42,68).

Patients with diabetes have been evaluated specifically in studies from the ARTS and AWESOME groups, which included the use of stents (294,295). GP IIb/IIIa inhibitors were used in approximately 11% of AWESOME PCI patients and were not incorporated into the ARTS protocol. After 3 years of follow-up, the survival rates of the diabetic subsets treated with CABG and PCI were not significantly different in either ARTS or AWESOME. Repeat revascularization was higher with PCI in the subsets of patients with diabetes in both trials. The sum effect of DES and GP IIb/IIIa inhibitors will be assessed against contemporary CABG in multivessel disease patients with diabetes in the upcoming NIH-sponsored FREEDOM trial.

Overall, 6 trials have been published comparing PCI using stents with CABG in single-vessel or multivessel disease. Both revascularization techniques relieve angina. In aggregate, these trials have not shown a difference between CABG and PCI in terms of mortality or procedural MI among the populations studied, which have mostly included low-risk patients. Stents appear to have narrowed the late repeat revascularization difference that favored CABG in the balloon era. Randomized trials, meta-analysis of trials, and epidemiological studies have shown the superiority of DES over BMS in terms of reducing late repeat revascularization (234-236) (see also Section 7.3.5 on DES). At this writing, no published studies are available comparing PCI with DES to CABG; thus, the impact of contemporary therapy with DES compared with CABG requires further evaluation. The ARTS II study compared outcomes for 600 surgically treated patients in ARTS II with 600 similar patients prospectively treated with multistent, sirolimus-eluting stent (SES) implantation [P.W. Serruys, oral presentation, American College of Cardiology Scientific Session, Orlando, Fla, March 2005]. Preliminary data from that study showed a lower rate of perioperative MI for the stent group. The surgery group still had fewer repeat revascularization procedures; however, the difference was markedly attenuated compared with the ARTS I BMS group. Furthermore, medical management of atherosclerosis, both before and after revascularization, has continued to evolve with the increased use of beta-blockers, inhibitors of the renin-angiotensin-aldosterone system, and lipid-lowering agents. Other changes in patient management that may influence these conclusions are the use of GP IIb/IIIa inhibitors, as mentioned above, and the use of direct thrombin inhibitors during PCI, the more frequent use of IMA grafts, and the emergence of less invasive surgical approaches. It is likely that during the progress of their disease, many patients will benefit from a combined application of percutaneous and surgical techniques, taking advantage of the low morbidity of percutaneous methods and the established long-term benefit of surgical revascularization with arterial conduits. Recommendations for revascularization in various patient subsets are presented in Section 5.

3.7. Comparison With Medicine

There has been a considerable effort made to evaluate the relative effectiveness of bypass surgery compared with PCI for coronary artery revascularization. In contrast to this, very little effort has been directed toward comparing medical therapy with PCI for the management of stable and UA. Several randomized trials are currently available comparing PCI with the medical management of angina (Table 12) (289,296-302). Most trials comparing PCI with medical therapy have utilized PTCA, not stents, in comparison with medical therapy, and no major trials are available comparing DES with medical therapy. The ACME (Angioplasty Compared to Medicine) investigators randomized 212 patients with single-vessel disease, stable angina pectoris, and ischemia on treadmill testing to PTCA or medical therapy. This trial demonstrated superior control of symptoms and better exercise capacity in patients managed with PTCA than in those given medical therapy. Death and MI were infrequent occurrences, and their incidence was similar in both groups. The Veterans Administration ACME trial investigators provided long-term results in an additional 101 randomized patients with double-vessel disease not previously reported (300) that indicated that patients randomized to medical therapy or PTCA had similar improvement in exercise duration, freedom from angina, and improvement in quality of life at the

Table 11. Summary of Randomized Trials of PTCA and Stents Versus CABG for Multivessel Disease

Trial	Years	Ref	Location	n	Follow-Up, y	End Point	Comments
PTCA Trials							
RITA	1989-1991	(11)	U.K. multicenter	1011	2.5	Death or MI	45% of patients had SVD
EAST	1987-1990	(286)	Emory University	392	3	Death, Q-wave MI, or large ischemic defect on thallium	Repeat revascularization in 5.4% of PTCA group compared with 13% of patients having CABG
GABI	1986-1991	(12)	Germany multicenter	359	1	Freedom from angina	IMA used in only 37% of CABG patients; more than 80% of patients had 2-vessel disease
CABRI	1988-1993	(287)	Europe multicenter	1054	1	Mortality, symptom status	Complete revascularization with PTCA was not required
ERACI	1988-1990	(279)	Argentina	127	3.8	Event-free survival (MI, angina, and RR)	Similar in-hospital and 1-year survival and freedom from MI; less angina and fewer repeat procedures after CABG
BARI	1988-1991	(290)	North American multicenter	1829	7	Death	Overall survival similar with PTCA and CABG, but late survival of treated diabetic patients better with CABG when IMA grafts were used
Toulouse	1989-1993	(288)	France	152	2.8	Freedom from angina 1 year after revascularization	Similar survival with PTCA and CABG at 5 years, but better event-free survival with CABG (fewer repeat procedures)
Stent Trials							
ARTS	1997-1998	(282)	Europe multicenter	1205	3	Freedom from major adverse cardiac and CV events	No significant difference between PCI and CABG in terms of death, stroke, or MI; PCI was associated with greater need for RR
AWESOME	1995-2000	(285)	Veterans Affairs multicenter	454	3	Death	Comparable survival between PCI and CABG in patients with medically refractory myocardial ischemia, with higher RR in PCI group
ERACI II	1996-98	(284)	Argentina	450	1.5	MACE (death, Q-wave MI, stroke, RR)	Better survival and freedom from MI with PCI than with CABG; RR higher in PCI group
SoS	1996-99	(283)	Europe, Canada multicenter	988	1	RR	Significantly higher number of RRs with PCI; no difference in composite measure of death and Q-wave MI; fewer deaths in the CABG group
MASS II	1995-2000	(289)	Brazil single center	611	1	Cardiac death, nonfatal acute MI, and unstable angina	Included medical therapy arm; no difference in cardiac death or MI among patients in the CABG, PCI, or medical therapy groups; significantly greater need for RR procedures in patients who underwent PCI

CABG indicates coronary artery bypass graft surgery; CV, cerebrovascular; IMA, internal mammary artery; MACE, major adverse cardiac events; MI, myocardial infarction; n, number of patients; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; Ref, reference; RR, repeat revascularization; SVD, single-vessel disease; and y, year.

Table 12. PCI Comparison With Medical Therapy

Study	Year	Ref	n	Patient Population	Treatment	Follow-Up	Results: PCI	Results: Medical Therapy	Results: Significance (*P*)	Comments
ACME	1992	(296)	212	Patients with single-vessel disease	Medical therapy vs balloon angioplasty	6 mo	64% less angina	46% less angina	Less than 0.01	The PTCA group had less angina, better exercise performance, and more improvement in quality-of-life scores but had more complications (emergency bypass 2 patients, MI in 5, and repeat PTCA in 16)
VA ACME	1997	(300)	328	Patients with documented chronic stable angina 227 single-vessel disease 101 double-vessel disease	Medical therapy vs balloon angioplasty	3 y	63% less angina	48% less angina	0.02	Among patients with single-vessel disease, the PTCA group had less angina, better exercise performance, and more improvement in quality-of-life scores
ACIP	1997	(301)	558	Patients with documented CAD and asymptomatic ischemia 183 angina-guided drug therapy 183 angina- plus ischemia-guided drug therapy 192 revascularization by PTCA or CABG	Angina-guided drug therapy vs angina- plus ischemia guided drug therapy vs revascularization	2 y	4.7% death or MI	8.8% death or MI for ischemia-guided drug therapy 12.1% death or MI for angina-guided drug therapy	Less than 0.01	40% of patients had previous MI, 23% had prior PTCA or CABG, and 38% had triple-vessel disease
AVERT	1999	(298)	341	Patients with stable CAD, normal LV function, and angina class I/II; patients required to complete 4 min on Bruce protocol	Medical therapy with atorvastatin vs PTCA	18 mo	21% ischemic events	13% ischemic events	0.048; 0.045 needed for significance due to interim analysis	Only 2 deaths among 341 patients in 18 months; significant improvement in angina in patients treated with PTCA compared with medical therapy

Continued on next page

Table 12. *Continued*

Study	Year	Ref	n	Patient Population	Treatment	Follow-Up	Results: PCI	Results: Medical Therapy	Results: Significance (*P*)	Comments
RITA-2	2003	(299)	1018	53% with Class II angina 47% with prior angina 7% with triple-vessel disease	Medical therapy vs balloon angioplasty	7 y	14.5% death or MI	12.3% death or MI	0.21	PTCA group had increased rates of death and MI but had 6.4% less class II angina or worse at 5 years and longer exercise treadmill time at 3 years
RITA-3	2002	(302)	1810	Suspected cardiac chest pain at rest with documented CAD (at least 1 of the following: ECG changes, pathological Q waves, previous arteriogram)	Medical therapy and either early invasive or conservative (selectively invasive) treatment strategy; both groups received enoxaparin in addition to standard medical therapy	1 y	7.6% death or MI	8.3% death or MI	NS	Similar results for death or MI between treatment groups; significant difference in primary end point (death, MI, refractory angina) due to halving of refractory angina in intervention group
MASS-II	2004	(289)	611	Stable angina, multivessel disease, preserved LV function	Medical therapy, CABG, or PCI	1 y	4.5% death	1.5% death	NS	Aggressive medical management for multivessel disease has low incidence of early events, including death and Q-wave MI, but is inferior to PCI (and CABG) for control of angina

n indicates number of patients; CABG, coronary artery bypass graft; CAD, coronary artery disease; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; and PCI, percutaneous coronary intervention.

time of 6-month follow-up. Thus, these patients with double-vessel PTCA did not demonstrate superior control of their symptoms as compared with medical therapy, as was experienced by the ACME patients with single-vessel disease. This small study suggests that PTCA is less effective in controlling symptoms in patients with double-vessel disease and stable angina than in those with single-vessel disease.

The Randomized Intervention Treatment of Angina (RITA)-2 investigators randomized 1018 patients with stable angina to PTCA or conservative (medical) therapy (297,299). Patients who had inadequate control of their symptoms with optimal medical therapy were allowed to cross over to myocardial revascularization. The combined end point of the trial was all-cause mortality and nonfatal MI. The 504 PTCA and 514 medically treated patients were followed up for a mean of 7 years. Death due to all causes occurred in 43 (8.5%) of the PTCA patients and 43 (8.4%) of the medical patients. Of the 86 deaths, only 8 were due to heart disease. Angina improved in both groups, but there was a 16.5% absolute excess of grade 2 or worse angina in the medical group at 3 months after randomization (*P* less than 0.001). These differences in angina narrowed over time, with the PTCA group always having less angina than the medically treated patients. Thus, RITA-2 demonstrated that PTCA results in better control of symptoms of ischemia and improves exercise capacity compared with medical therapy but is associated with a higher combined end point of death and periprocedural MI. It is important to remember that although the patients in this trial were asymptomatic or had only mild angina, 62% of them had multivessel CAD, and 34% had significant disease in the proximal segment of the LAD (301). Thus, most of these patients had severe anatomic CAD.

The Asymptomatic Cardiac Ischemia Pilot (ACIP) study provides additional information comparing medical therapy with PTCA or CABG revascularization in patients with documented CAD and asymptomatic ischemia by both stress testing and ambulatory ECG monitoring (301). This trial randomized 558 patients suitable for revascularization by PTCA or CABG to 3 treatment strategies: angina-guided drug therapy (n equals 183), angina- plus ischemia-guided drug therapy (n equals 183), and revascularization by PTCA or CABG surgery (n equals 192). Of the 192 patients who were randomized to revascularization, 102 were selected for PTCA and 90 for CABG. At 2 years of follow-up, death or MI had occurred in 4.7% of the revascularization patients compared with 8.8% of the ischemia-guided group and 12.1% of the angina-guided group (*P* less than 0.01). Because a large portion of the patients underwent CABG surgery instead of PTCA to achieve complete revascularization, it is not appropriate to directly compare these results with RITA-2. Nonetheless, the ACIP study suggests that outcomes of revascularization with CABG surgery and PTCA are very favorable compared with medical therapy in patients with asymptomatic ischemia with or without mild angina. It should be emphasized that aggressive lipid-lowering therapy was not widely employed in either treatment arm of ACIP.

The Atorvastatin Versus Revascularization Treatment (AVERT) trial (298) randomly assigned 341 patients with stable CAD, normal LV function, and class I and/or II angina to PTCA or medical therapy with 80 mg of atorvastatin daily (mean low-density lipoprotein cholesterol equals 77 mg per dL). At 18 months of follow-up, 13% of the medically treated group had ischemic events compared with 21% of the PTCA group (*P* equals 0.048). Angina relief was greater in those treated with PTCA. Although not statistically different when adjusted for interim analysis, these data suggest that in low-risk patients with stable CAD, aggressive lipid-lowering therapy can be as effective as PTCA in reducing ischemic events.

During the MASS-II trial (289), 611 patients with stable angina, multivessel disease, and preserved LV function were randomized to 3 treatment groups: medical therapy, CABG, or PCI (medical therapy n equals 203, CABG n equals 203, and PCI n equals 205). One-year survival was similar in the 3 groups at 98.5%, 96.0%, and 95.6%, respectively. At 1 year of follow-up, a Q-wave MI had occurred in 2% of CABG patients, 8% of the PCI patients, and 3% of the medical therapy patients. By 1 year, additional revascularization procedures were performed in 8.3% of medical therapy patients, 13.3% of PCI patients, and only 0.5% of CABG patients. More patients were free of angina at 1 year in the CABG and PCI groups (88% and 79%, respectively) than in the medical therapy groups, in which only 46% were free of angina. This small contemporary trial utilizing aggressive medical management demonstrated that medical therapy for multivessel disease has a low incidence of early events including death and Q-wave MI but is inferior to PCI and CABG for the control of angina.

Given the limited data available from randomized trials comparing medical therapy with PCI, it seems prudent to consider medical therapy for the initial management of most patients with CCS classification class I and II stable angina and to reserve PCI and CABG for those patients with more severe symptoms and ischemia. The symptomatic patient who wishes to remain physically active, regardless of age, will usually require PCI or CABG to accomplish this.

The Clinical Outcomes Utilization Revascularization and Aggressive Drug Evaluation (COURAGE) trial was designed to compare intensive medical therapy with PCI plus intensive medical therapy. Enrollment has been completed, and results are expected to be available in the next few years. This trial will provide further valuable information about the relative merits of medical treatment plus PCI versus medical treatment alone and will also give us a detailed assessment of outcomes relative to quality of life and economic cost (303). The Bypass Angioplasty Revascularization trial in patients with diabetes (BARI 2d) was designed to compare revascularization in addition to aggressive medical therapy in patients with diabetes compared with aggressive medical therapy alone. Enrollment was completed in the first quarter of 2005.

Patients with UA and NSTEMI have been randomized to medical therapy or PCI in the FRagmin and Fast

Revascularisation during InStability in Coronary artery disease (FRISC) II and Treat Angina with Aggrastat and determine the Cost of Therapy with an Invasive or Conservative Strategy (TACTICS) TIMI 18 trials, as well as in RITA-3. These trials utilizing stenting as the primary therapy have favored the invasive approach (206,302,304). They are discussed in Section 5.3.

4. INSTITUTIONAL AND OPERATOR COMPETENCY

4.1. Quality Assurance

Class I

1. **An institution that performs PCI should establish an ongoing mechanism for valid peer review of its quality and outcomes. Review should be conducted both at the level of the entire program and at the level of the individual practitioner. Quality-assessment reviews should take risk adjustment, statistical power, and national benchmark statistics into consideration. Quality-assessment reviews should include both tabulation of adverse event rates for comparison with benchmark values and case review of complicated procedures and some uncomplicated procedures. *(Level of Evidence: C)***
2. **An institution that performs PCI should participate in a recognized PCI data registry for the purpose of benchmarking its outcomes against current national norms. *(Level of Evidence: C)***

Definition of Quality in PCI

Satisfactory quality in PCI may be defined as the appropriate selection of patients for the procedure and the achievement of risk-adjusted outcomes that are comparable to national benchmark standards in terms of procedure success and adverse event rates. To achieve optimal quality and outcomes in PCI, it is necessary that both the physician operator and the supporting institution be appropriately skilled and experienced.

Institutional Quality-Assurance Requirement

PCI is a demanding, technically complex procedure. The potential exists for substantial quality variation among both operators and institutions.

In the United States, responsibility for quality assurance is vested in the healthcare institution, which is responsible to the public to ensure that patient care conducted under its jurisdiction is of acceptable quality. Thus, the institution has the responsibility to monitor its PCI program's quality with respect to process, appropriateness, and outcomes in order to identify and correct any circumstances in which quality falls below accepted norms. Quality-assessment review should be conducted both at the level of the entire program and at the level of the individual practitioner.

Each institution that performs PCI must establish an ongoing mechanism for valid peer review of its quality and outcomes. The program should provide an opportunity for interventionalists, as well as for physicians who do not perform angioplasty but are knowledgeable about it, to review its overall results on a regular basis. The review process should tabulate the results achieved both by individual physician operators and by the overall program and compare them with national benchmark standards with appropriate risk adjustment. Valid quality assessment requires that the institution maintain meticulous records that include the patient demographic and clinical characteristics necessary to assess appropriateness and to conduct risk adjustment.

Role of Risk Adjustment in Assessing Quality

A raw adverse event rate that is not appropriately risk adjusted has little meaning. Data compiled from large registries of procedures performed in recent years have generated multivariate risk-adjustment models for adverse event rates for PCI in the current era. Six multivariate models of the risk of mortality after PCI have been published (43,47,305-308).

Although these models differ somewhat, they are consistent in identifying acute MI, shock, and age as important risk-stratification variables for mortality. The ACC-NCDR reported a univariate mortality rate of 0.5% for patients undergoing elective PCI, a mortality rate of 5.1% for patients undergoing primary PCI within 6 h of the onset of STEMI, and a mortality rate of 28% for patients undergoing PCI for cardiogenic shock (305). Thus, it is clear that to assess PCI mortality rates, patients should be stratified by whether they are undergoing elective PCI, primary PCI for acute STEMI without shock, or primary PCI for STEMI with shock.

Challenges in Determining Quality

As discussed above, given the complexity of case selection and procedure conduct, quality is difficult to measure in PCI and is not determined solely by adverse event rates even when properly adjusted for risk. Accurate assessment of quality becomes more problematic for low-volume operators and institutions, because absolute event rates are expected to be small. Thus, particularly in low-volume circumstances, quality may be better assessed by an intensive case review process conducted by recognized experts who can properly judge all of the facets of the conduct of a case. Case review also has merit in high-volume situations, because it can identify subtleties of case selection and procedure conduct that may not be reflected in pooled statistical data.

Requirement for Institutional Resources and Support

A high-quality PCI program requires appropriately trained and experienced skilled physician operators. However, the operator does not work in a vacuum. An operator needs a well-maintained, high-quality cardiac catheterization facility to practice effectively. In addition, the operator depends on a multidisciplinary institutional infrastructure for support and response to emergencies. Thus, to provide quality PCI services, the institution must ensure that its catheterization facility is properly equipped and managed and that all of its necessary support services are of high quality and are readily available.

The Quality-Assessment Process

Quality assessment is a complex process that includes more than mere tabulation of success and complication rates. Components of quality in coronary interventional procedures include appropriateness of case selection, quality of procedure execution, proper response to intraprocedural problems, accurate assessment of procedure outcome, and appropriateness of postprocedure management. It is important to consider each of these parameters when conducting a quality-assessment review. A quality program performs appropriately selected procedures that achieve risk-adjusted outcomes, in terms of procedure success and complication rates, that are comparable to national benchmark standards. Patient characteristics that determine appropriateness are discussed elsewhere in this document. Multivariate models that predict risk have been published previously (43,47,305-308).

It is accepted that quality-assurance monitoring is best conducted through the peer review process despite the political challenges associated with colleagues evaluating each other. There has been a considerable controversy surrounding efforts to define standards, criteria, and methodologies for conducting quality assessment. There are many challenges to conducting this process in a fair and valid manner.

The cornerstone of quality-assurance monitoring is the assessment of procedural outcomes in terms of success and adverse event rates. Other components of quality-assurance monitoring include establishment of criteria for assessing procedure appropriateness and application of proper risk adjustment to interpret adverse event rates. Because adverse events should be rare, a valid estimate of a properly risk-adjusted adverse event rate generally requires tabulation of the results of a large number of procedures. This adds an additional challenge to the valid assessment of low-volume operators and institutions. The responsible supervising authority should monitor the issues outlined in Table 13 (309).

Initial Physician Operator Credentialing Criteria

The institutional credentialing committee should document that an interventionalist wishing to initiate practice meets the established training criteria, including those of the ACC Task Force on Training in Cardiac Catheterization and Interventional Cardiology (310-312). The ACC Training Statement (312) for coronary invasive training requires a 3-year comprehensive cardiac program with 12 months of training in diagnostic catheterization, during which the trainee performs 300 diagnostic catheterizations, with at least 200 of those as the primary operator. Interventional training requires a fourth year of fellowship, during which the trainee should perform more than 250 but not more than 600 interventional procedures (312). The physician's training program director should certify that the candidate has completed the program and has achieved the necessary competence to perform coronary interventional procedures independently. The certification should also include whether the candidate has achieved requisite competence in related interventional techniques such as rotational atherectomy, balloon valvuloplasty, and closure of patent foramen ovale and atrial septal defect.

It is recommended that an interventional cardiology operator be certified by the American Board of Internal Medicine in interventional cardiology. Ideally, board certification in interventional cardiology should be required for credentialing. The American Board of Internal Medicine certifying examination in interventional cardiology has been administered annually since 1999. As of the 2004 administration, a total of 4718 individuals have been certified.

Privilege Renewal

Criteria for practitioner privilege renewal should be based on both activity level and outcomes. The assessment process should ascertain whether a physician operator's activity level is sufficient to maintain competence. In addition, the assessment process should assess the appropriateness of the operator's case selection and compare the operator's risk-adjusted outcomes with established national benchmark standards (310). This is discussed in depth in Section 4.2. Current benchmark standards for mortality, complication rates, and risk adjustment will be subject to future revision as procedure technique is refined and newer data emerge. It is important that institutions assist with these efforts by participating in active database efforts to track clinical and procedural information for individual operators and their institutions.

Outcome Data Tabulation and Reporting

Institutions performing PCI should gather data needed to monitor their outcomes and should submit their data to a national registry for benchmarking purposes. Institutions should conduct meticulous record keeping that details the cases performed-patient demographics and comorbidities,

Table 13. Key Components of a Quality-Assurance Program

Clinical proficiency
General indications/contraindications
Institutional and individual operator complication rates, mortality and emergency CABG
Institutional and operator procedure volumes
Training and qualifications of support staff
Equipment maintenance and management
Quality of laboratory facility [See ACC/SCAI Expert Consensus Document on Catheterization Laboratory Standards (309)]
Quality improvement process
Establishment of an active concurrent database to track clinical and procedural information and patient outcomes for individual operators and the institution. The ACC-NCDR® or other databases are strongly recommended for this purpose
Radiation safety
Educational program in the diagnostic use of X-ray
Patient and operator exposure

ACC indicates American College of Cardiology; CABG, coronary artery bypass graft surgery; NCDR®, National Cardiovascular Data Registry; and SCAI, Society for Cardiovascular Angiography and Interventions.

cardiovascular characteristics including type of presentation, coronary anatomy, ventricular function, procedures performed, and periprocedural complications. These data are necessary to permit appropriate risk adjustment. Institutions should carefully monitor their risk-adjusted outcomes at the level of the institution and of the individual operators and should ascertain that their outcomes fall within national norms. One example is the ACCF CathKit®, a tool that provides templates and guidance for the quality assessment process.

This Writing Committee agrees with the ACC Task Force recommendations for the Assessment and Maintenance of Proficiency in Coronary Interventional Procedures (310). Institutions and healthcare providers performing PCI should meet the standards outlined in Table 14 (309,310,312) and in Section 4.2.

4.2. Operator and Institutional Volume

Class I

1. **Elective PCI should be performed by operators with acceptable annual volume (at least 75 procedures) at high-volume centers (more than 400 procedures) with onsite cardiac surgery (310,312).** ***(Level of Evidence: B)***
2. **Elective PCI should be performed by operators and institutions whose historical and current risk-adjusted outcomes statistics are comparable to those reported in contemporary national data registries.** ***(Level of Evidence: C)***
3. **Primary PCI for STEMI should be performed by experienced operators who perform more than 75 elective PCI procedures per year and, ideally, at least 11 PCI procedures for STEMI per year. Ideally, these procedures should be performed in institutions that perform more than 400 elective PCIs per year and more than 36 primary PCI procedures for STEMI per year.** ***(Level of Evidence B)***

Class IIa

1. **It is reasonable that operators with acceptable volume (at least 75 PCI procedures per year) perform PCI at low-volume centers (200 to 400 PCI procedures per year) with onsite cardiac surgery (310,312).** ***(Level of Evidence: B)***
2. **It is reasonable that low-volume operators (fewer than 75 PCI procedures per year) perform PCI at high-volume centers (more than 400 PCI procedures per year) with onsite cardiac surgery (310,312). Ideally, operators with an annual procedure volume less than 75 should only work at institutions with an activity level of more than 600 procedures per year. Operators who perform fewer than 75 procedures per year should develop a defined mentoring relationship with a highly experienced operator who has an annual procedural volume of at least 150 procedures per year.** ***(Level of Evidence: B)***

Table 14. Considerations for the Assessment and Maintenance of Proficiency in Coronary Interventional Procedures

Institutions
Quality-assessment monitoring of privileges and risk-stratified outcomes
Provide support for a quality-assurance staff person (e.g., nurse) to monitor complications
Minimal institutional performance activity of 200 interventions per year, with ideal minimum of 400 interventions per year
Interventional program director who has a career experience of more than 500 PCI procedures and who is board certified by the ABIM in interventional cardiology
Facility and equipment requirements to provide high-resolution fluoroscopy and digital video processing
Experienced support staff to respond to emergencies (see Section 4.3, Role of On-Site Cardiac Surgical Backup for discussion)
Establishment of a mentoring program for operators who perform fewer than 75 procedures per year by individuals who perform at least 150 procedures per year
Physicians
Procedural volume of 75 per year or more
Continuation of privileges based on outcome benchmark rates, with consideration of not granting privileges to operators who exceed adjusted case mix benchmark complication rates for a 2-year period
Ongoing quality assessment comparing results with current benchmarks, with risk stratification of complication rates
Board certification by ABIM in interventional cardiology

ABIM indicates American Board of Internal Medicine; and PCI, percutaneous coronary intervention.

Class IIb

The benefit of primary PCI for STEMI patients eligible for fibrinolysis when performed by an operator who performs fewer than 75 procedures per year (or fewer than 11 PCIs for STEMI per year) is not well established. ***(Level of Evidence: C)***

Class III

It is not recommended that elective PCI be performed by low-volume operators (fewer than 75 procedures per year) at low-volume centers (200 to 400) with or without onsite cardiac surgery (310,312). An institution with a volume of fewer than 200 procedures per year, unless in a region that is underserved because of geography, should carefully consider whether it should continue to offer this service. ***(Level of Evidence: B)***

Operator and Institution Volume-Outcome Relationships

Threshold activity level standards for institutions and operators have been particularly controversial. Such standards are derived from the principle that proper skill maintenance requires a requisite activity level. It is logical that both a threshold experience and an ongoing activity level are necessary to achieve and maintain requisite proficiency in PCI.

Standards originally formulated for the earliest versions of these guidelines were based on opinion (Level of Evidence: C) drawing on the well-documented existence of volume-outcome relationships for other complex surgical procedures. Initially, a panel of experts identified a threshold activity level of 75 procedures per year as necessary for maintenance of competence in PCI (313). Subsequent studies of PCI continue to identify annual procedural volume both at the program level and at the operator level as strongly correlated with complication rates. Most studies' findings are consistent with the operator threshold of 75 procedures per year (47, 306,309,314-320).

Most studies of the PCI volume-outcome relationship focus on mortality and emergent bypass surgery as quality-determining outcome variables. These variables, while important, encompass only a portion of the overall quality determinants for PCI.

McGrath et al. examined volume outcome relationships using procedures performed on 167 208 Medicare recipients in 1997 (321). Procedures performed by low-volume physicians (fewer than 30 Medicare procedures per year) had a greater emergency CABG rate (2.25%) than procedures performed by high-volume physicians (more than 60 Medicare procedures per year; 1.55%, *P* less than 0.001). An increased 30-day mortality rate was found for low-volume programs (fewer than 80 Medicare procedures per year) versus high-volume programs (more than 160 Medicare procedures per year; 4.29% vs 3.15%, *P* less than 0.001).

Kimmel et al., using data from the SCAI, found that an inverse relationship existed between the number of angioplasty procedures performed at a hospital and the rate of major complications (315). These results were risk stratified and independent of the patient-risk profile. Significantly fewer complications occurred in laboratories that performed at least 400 angioplasty procedures per year.

Jollis et al. found that low-volume hospitals were associated with higher rates of emergency coronary artery bypass surgery and death (316). Improved outcomes were identified with a threshold volume of 75 Medicare angioplasties per physician and 200 Medicare angioplasty procedures per hospital. Using a 35% to 50% ratio of Medicare patients, the threshold value was 150 to 200 angioplasty procedures per cardiologist and 400 to 600 angioplasty procedures per institution (322).

Epstein et al., using an administrative data set, analyzed risk-adjusted mortality in 362 748 admissions to 1000 United States hospitals between 1997 and 2000 during which a PCI was performed (323). They found a consistent trend of decreasing risk-adjusted mortality with increasing hospital volume. The differences between groups were small, and there was considerable heterogeneity within groups, which indicates that hospital volume is not the sole determinant of outcome.

Other studies have also supported the relationship of complication rate to procedural volume (47,306,314). Although some investigators have suggested that low procedure volume does not contribute to poor outcomes (44,309), these studies are small in number and underpowered for analysis (318).

Progress in technique and instrumentation has reduced absolute complication rates, which makes the procedure safer and more effective. This has fueled the opinion that the volume-outcome relationship has weakened, justifying advocacy that PCI be diffused to smaller-volume institutions and lower-volume operators. Although it is possible to consider earlier studies anachronistic because of the lack of availability of coronary stents and other adjunctive therapies, studies based on data sets accumulated in the stent era continue to show a volume-outcome relationship (albeit with lower absolute event rates).

Brown evaluated the outcomes of PCI at all hospitals in California in 1997 (324). Mortality for PCI in which a stent was used was 1.5% in hospitals performing fewer than 400 procedures per year compared with 1.1% in hospitals performing more than 400 procedures per year. The rate of emergent CABG was 1.2% in hospitals performing fewer than 400 procedures per year compared with 0.8% in hospitals that performed more than 400 procedures per year.

Moscucci et al. studied the outcomes of 18 504 consecutive PCIs performed at 14 hospitals in Michigan in 2002 (325). Operator volume was divided in quintiles (1-33, 34-89, 90-139, 140-206, and 207-582 procedures per year). The primary end point was a composite of MACE including death, CABG, stroke or TIA, MI, and repeat PCI at the same site during the index hospitalization. The unadjusted MACE rate was significantly higher in quintiles 1 and 2 of operator volume than in quintile 5 (7.38% and 6.13% vs 4.15%, *P* equals 0.002 and *P* equals 0.0001, respectively). A similar trend was observed for in-hospital death. After adjustment for comorbidities, patients treated by low-volume operators had a 63% increased odds of MACE (adjusted odds ratio [OR] 1.63, 95% CI 1.29-2.06, *P* less than 0.0001 for quintile 1; adjusted OR 1.63, 95% CI 1.34-1.90, *P* less than 0.0001 for quintile 2 vs quintile 5) but not of in-hospital death. Overall, high-volume operators had better outcomes than low-volume operators in both low-risk and high-risk patients (325).

Distinction Between Elective PCI and Primary PCI for STEMI

Elective PCI and primary PCI for STEMI are different, although related, disciplines. Experience in elective PCI translates only partially to experience with primary PCI for STEMI. Throughout this guideline, a distinction is drawn between primary PCI, which is performed under emergency circumstances, and all other PCI procedures, which are included under the term "elective." The volume-outcome relationship exists for both elective procedures and primary angioplasty for STEMI (326-328) but has important differences. Available data indicate that the best results are obtained by operators who are highly experienced both in elective PCI and in primary PCI for STEMI who work in institutions that have established an active program for performing primary PCI for STEMI.

Operator experience in elective PCI is not sufficient to confer expertise in primary PCI for STEMI. This finding is not surprising, because there are aspects of procedure conduct that are unique to primary PCI for STEMI.

Vakili et al., analyzing primary PCI procedures for STEMI performed in New York State, found no relationship between physician total angioplasty procedure volume and mortality after primary PCI for STEMI but did find an association between an operator's primary PCI activity level and the outcome of primary PCI for STEMI that was independent of the operator's experience in elective PCI (328,329). Low-volume physicians, who performed 1 to 10 primary PCI procedures per year, had an unadjusted mortality rate of 7.1% compared with 3.8% for physicians who performed 11 or more primary PCI procedures per year.

Magid et al. analyzed the National Registry of Myocardial Infarction (NRMI) database and grouped acute-care hospitals by volume tertiles of primary PCI for STEMI procedures (327). They found a reduction in risk-adjusted mortality with increasing hospital volume of PCI: low volume (fewer than 16 procedures), 6.2%; intermediate volume (17 to 48 procedures), 4.5%; and high volume (more than 49 procedures), 3.4% (327). Canon et al. analyzed or reviewed 20 080 consecutive patients with STEMI in the NRMI-2 database (330). A multivariate model was used to show that overall adjusted mortality was lower as volume increased, with the greatest reduction in mortality occurring at hospitals performing more than 3 angioplasties per month (330). Different studies identified different cutpoints. The relationship between the studies is graded, and the individual cutpoints are artifacts of analysis methodology.

Vakili et al. found a doubling of mortality in STEMI patients who underwent PCI in hospitals that performed fewer than 400 total PCI procedures per year compared with hospitals that performed more than 400 (8.1% vs 4.3%) (329). Furthermore, they found that high-volume hospitals that performed more than 56 primary PCI procedures per year had a nonsignificant trend toward a lower crude mortality rate (4.0% vs 5.8%), with a multivariate OR for mortality of 0.53 (0.29 to 1.1). The best outcomes were achieved by high-volume physicians working in high-volume hospitals (crude mortality rate 3.7% compared with 7.1% for low-volume physicians in low-volume hospitals; adjusted relative risk 0.51, 95% CI 0.26 to 0.99).

Canto et al. (331) also found a graded relationship between hospital volume and mortality after PCI for STEMI. The highest quartile of hospital volume performed more than 33 primary PCIs for STEMI per year and achieved a 28% reduction in mortality compared with the lowest-volume hospitals.

Appropriateness of Activity Levels as a Surrogate for Quality

The documented relationships between activity level and outcome are statistical associations, and activity level is not a surrogate for quality. The heterogeneity within hospital volume groups found by Epstein et al. (323) validates that activity level is an incomplete surrogate for quality. An activity level above a threshold value does not guarantee good quality, and an activity level below a threshold value may not necessarily indicate lower quality. Thus, high-volume operators and institutions are not necessarily of uniformly high quality, and low-volume operators and institutions are not, by definition, poor.

However, an activity level below a threshold necessarily raises the question of whether an operator or institution has sufficient ongoing experience to maintain expertise and skills. In particular, it is plausible that an operator or institution that is below a threshold activity level cannot accrue the necessary ongoing experience to perform complex procedures skillfully, to acquire experience with new techniques and devices, and to respond effectively to adverse and emergency situations. The emergency response consideration is particularly relevant, because the likelihood of a serious complication cannot be predicted from patient baseline characteristics.

Quality Assessed by Outcomes: Statistical Power Considerations and the Importance of Case Reviews

The quality of both institutions and operators should ultimately be judged through the quality-assessment process as outlined in Section 4.1. Because expected adverse event rates are low, a large number of procedures are required to achieve the requisite statistical power to assign an interpretable confidence interval to an operator's or a program's adverse event rate estimate. Furthermore, adverse event rates cannot be interpreted without appropriate risk adjustment.

The first approximation in assessing an operator's or a program's quality is to compare the actual adverse event rate to an expected rate as predicted by an accepted risk-prediction model (ACC-NCDR® model or Dynamic Registry model). Calculation of an expected adverse event rate can be conducted by entering the characteristics of the group of patients treated into the model. The model yields an expected adverse event rate with confidence intervals that can then be compared with the actual event rate. Interpretation of the expected adverse event rate is complex because of the precision of the estimate. An arbitrary criterion will need to be applied to determine whether a particular actual adverse event rate is an outlier when compared with the expected event rate. For example, 50% of operators may be expected to have an adverse event rate above the expected value purely by chance. Thus, merely being above the predicted mean value does not automatically identify an operator or a program as an outlier.

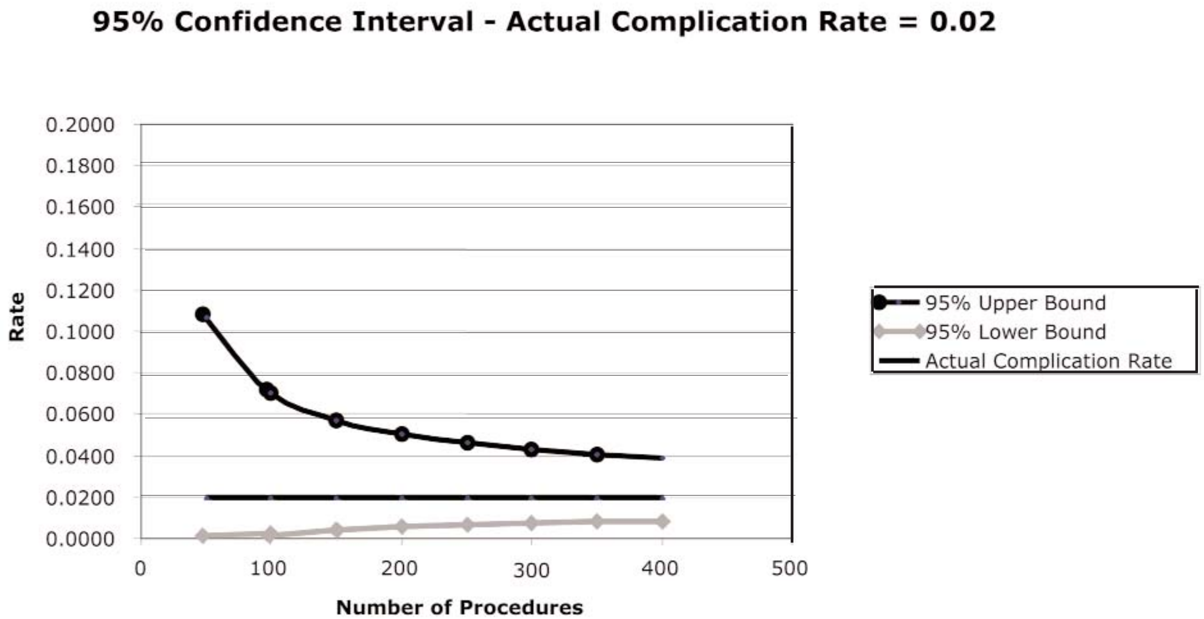

Figure 3. Plot of an actual adverse event rate of 2% over a procedure number range from 25 to 400. The horizontal line at 0.02 represents the actual adverse event rate. The curved lines above and below the horizontal line represent the upper and lower bounds of the 95% confidence interval of the estimate of the adverse event rate. Note that as the number of procedures decreases, the range between the upper and lower bounds increases, which indicates lack of stability of any adverse event rate estimate at procedure numbers below 200.

Furthermore, valid assessment of an operator's or an institution's actual adverse event rate becomes problematic if the number of procedures available for analysis is small. The statistical basis for this issue is illustrated in Figures 3 and 4.

Figure 3 plots the upper and lower 95% CI bounds of an observed adverse event rate of 2% (1 adverse event per 50 procedures) as a function of the number of procedures available for analysis. It demonstrates that if only 50 cases are available, the upper bound of the confidence interval is 10.6%. Thus, if 50 cases are performed with 1 adverse event, it is possible that the true adverse event rate is as high as 10.6%. However, it is also possible that it is as low as 0.05%. The upper-bound value decreases as the number of cases increases such that if 400 cases are available, it is only 3.9%.

If only a small number of cases are available, even if no adverse events occur, it may be difficult to exclude that an increased risk of adverse events exists. Figure 4 plots the upper bound of the 95% CI for very low numbers of cases

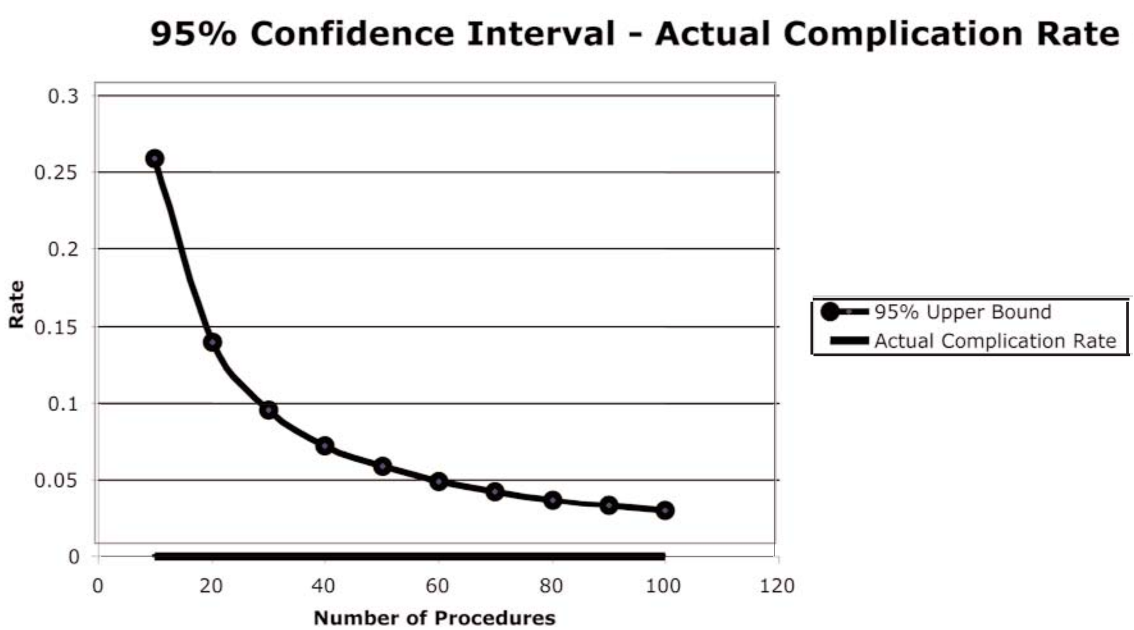

Figure 4. Plot of an actual complication rate of 0% over a procedure number range from 10 to 100. The format is similar to Figure 3. The horizontal line at 0 represents the actual complication rate. The curved line above the horizontal line represents the upper bound of the 95% confidence interval of the estimate of the complication rate. Note that if 50 procedures are performed without a complication, the upper bound of the 95% confidence interval of the estimated rate is 6%.

performed with a zero adverse event rate. It demonstrates that if 10 consecutive cases are performed without a complication, the upper bound of the 95% CI is 25%. If 50 cases are performed without an adverse event, the upper bound is 5.8%.

Thus, although it is likely that certain low-volume operators and institutions perform procedures with acceptable quality, satisfactory quality is difficult to prove unless a sufficient number of procedures are compiled for analysis. The quality-assessment process must take the above issues into consideration. This means that it is essential that institution and operator outcomes be tracked over sufficiently long periods of time to assemble a sufficient number of procedures to permit a satisfactory analysis.

In addition, mere tabulation of adverse event rates, even with appropriate risk adjustment, is inadequate to judge operator or program quality. Such tabulations do not address numerous other quality issues, in particular, appropriateness. Thus, the quality-assessment process should also conduct detailed reviews both of cases that have adverse outcomes (to determine the cause(s) of the adverse event) and of uncomplicated cases (to judge case selection appropriateness and procedure execution quality). These reviews should be conducted by recognized experienced interventionalists drawn either from within the institution or externally if a requisite number of appropriately qualified, unconflicted individuals are not available.

Role of Low-Volume PCI Programs

There is an ongoing debate as to whether PCI services should be diffused widely to be available in most healthcare institutions or whether the service should be regionalized and concentrated in specialized high-volume centers. Given the widespread availability of sophisticated interventional/surgical programs in the United States, it is difficult to demonstrate a need for additional low-volume programs to perform elective angioplasty except in underserved areas that are geographically distant from major centers. At this writing, outcome data that link activity level to outcomes indicate that the development of small cardiovascular surgical programs to support angioplasty is a poor use of resources that will likely lead to suboptimal results (320). In general, the proliferation of small angioplasty or small surgical programs to support such angioplasty programs is not needed to improve patient access to PCI services and would appear not to be in the interest of fostering optimal quality; thus, it should be discouraged. An exception to this principle should be when geographic considerations become important determinants of patient access.

These data support the conclusion that not every cardiologist desiring to perform PCI should perform these procedures, and not every hospital that would like to have an interventional program should start one (322). This caveat is particularly true where high-volume programs and operators are already nearby.

The Writing Committee, therefore, recommends that elective PCI be performed by higher-volume operators (75 cases per year) with advanced technical skills (e.g., subspecialty certification) at institutions with fully equipped interventional laboratories and an experienced support staff. This setting is optimally a high-volume center (more than 400 cases per year) with an onsite cardiovascular surgical program (332).

It is recommended that primary PCI for STEMI be performed by higher-volume operators experienced in both elective PCI and primary PCI for STEMI with ongoing activity levels of more than 75 elective PCI procedures per year and, ideally, annual PCI for STEMI activity levels of at least 11 per year. It is clear that an effective PCI for STEMI program, irrespective of whether cardiac surgery is available onsite, requires appropriate physician operator expertise, appropriate institutional commitment, and the achievement of the requisite utilization levels. The nursing and technical catheterization laboratory staff must be experienced in handling acutely ill patients, must be skilled in all aspects of interventional equipment, and must participate in a 24-hours-per-day, 365-days-per-year call schedule. Ideally, these procedures should be performed in institutions that perform more than 400 elective PCIs per year and more than 36 primary PCIs for STEMI per year and that achieve risk-adjusted outcomes that are comparable to national benchmark standards.

The Writing Committee cannot recommend angioplasty by low-volume operators (fewer than 75 cases per year) working in low-volume institutions (200 to 400 cases per year) with or without onsite surgical coverage. As noted earlier, ongoing investigational experience and clinical data are mandatory if these recommendations are to be modified. Any change in this recommendation awaits further data assessing the safety and outcomes for patients treated in various settings.

4.3. Role of Onsite Cardiac Surgical Back-Up

Class I

1. **Elective PCI should be performed by operators with acceptable annual volume (at least 75 procedures per year) at high-volume centers (more than 400 procedures annually) that provide immediately available onsite emergency cardiac surgical services.** ***(Level of Evidence: B)***
2. **Primary PCI for patients with STEMI should be performed in facilities with onsite cardiac surgery.** ***(Level of Evidence: B)***

Class III

Elective PCI should not be performed at institutions that do not provide onsite cardiac surgery. ***(Level of Evidence: C)****

*Several centers have reported satisfactory results based on careful case selection with well-defined arrangements for immediate transfer to a surgical program (333-337,348-353). A small, but real fraction of patients undergoing elective PCI will experience a life-threatening complication that could be managed with the immediate onsite availability of cardiac surgical support but cannot be managed effectively by urgent transfer. Wennberg, et al., found higher mortality in the Medicare database for patients undergoing elective PCI in institutions without onsite cardiac surgery (356). This recommendation may be subject to revision as clinical data and experience increase.

The purpose of cardiac surgical backup for PCI is to provide emergent hemodynamic support and revascularization to salvage complications that cannot be addressed by catheter-based techniques. PCI can be complicated by life-threatening hemodynamic and ischemic emergencies that can be addressed only by the availability of emergency cardiac surgery. The role of onsite cardiac surgical backup is 2-fold: onsite cardiac surgical backup provides prompt availability of cardiac surgical support in the event of a hemodynamic or ischemic emergency, and onsite cardiac surgical backup is a surrogate for an institution's overall capability to provide a highly experienced and promptly available team to respond to a catheterization laboratory emergency.

Cardiac surgical backup for PCI has evolved from a formal surgical standby in the 1980s to an informal arrangement of first-available operating room and, in some cases, off-site surgical backup (44,333-337). With the advent of intracoronary stenting, there has been a decrease in the need for emergency CABG ranging between 0.4% and 2% (49,305,338-342). Not surprisingly, emergency CABG surgery for a patient with an occluded or dissected coronary artery is associated with a higher mortality than elective surgery (146,343-347). Emergency procedures are also associated with high rates of perioperative infarction and less frequent use of arterial conduits. Complex CAD intervention, hemodynamic instability, and prolonged time to reperfusion are contributing factors to the increased risk of emergency bypass surgery.

Technical improvements in PCI instruments and technique have led to the concept that the requirement for emergency cardiac surgery is sufficiently rare that PCI can be performed safely without onsite surgery. This has led to the development of elective angioplasty programs without onsite surgical coverage. Several centers have reported satisfactory results based on careful case selection with well-defined arrangements for immediate transfer to a surgical program (333-337,348-352). These studies of angioplasty without onsite surgical coverage have not identified significant differences in the outcomes, which recalls the infrequent rate of complications (353). Despite many reported successful angioplasty series without onsite surgical backup and a very low percentage of need for off-site surgery in failed angioplasty, some clinicians have expressed concern (354,355) about the appropriateness of elective angioplasty in centers without onsite surgical coverage.

Even with current interventional techniques, life-threatening complications requiring surgical intervention still occur. Such complications include left main coronary dissection, spiral coronary trunk dissection, and coronary perforation. Many emergency surgery patients did not receive a coronary stent, which indicates that either a stent delivery was not feasible or a stent would not solve the problem that required surgical intervention. Data from the ACC-NCDR® indicate that PCI programs staffed by highly experienced practitioners still experience a 0.4% likelihood of a patient requiring emergency cardiac surgery for a complication that developed during a procedure. Roughly half of patients who require emergency surgery are severely hemodynamically unstable at the time of transfer to the operating room. Furthermore, analyses of series of patients requiring emergency cardiac surgery indicate that patient baseline characteristics do not predict the risk of the need for emergency surgery (305,342).

It has been argued that a well-planned strategy to provide rapid transfer to a surgical center in the event of a complication is tantamount to providing onsite surgical backup support. Such strategies are unrealistic because they are logistically difficult to achieve and require that a critically ill patient be transported outside of a hospital environment, possibly without a physician in attendance. Furthermore, if an institution without cardiac surgery is sufficiently close to one that provides surgery to permit sufficiently timely transfer, there is little justification for not transferring the patient electively in the first place.

Although individual programs have reported successful results, the national experience with PCI programs at institutions that do not offer onsite cardiac surgery has been less satisfactory. Wennberg et al. (356) analyzed the Medicare database for a 2-year period from 1999 to 2001 (when stents and IIb/IIIa inhibitors were in widespread use). They identified 178 hospitals without onsite cardiac surgical facilities and 943 hospitals with onsite cardiac surgery that performed PCI during that period. After adjusting for baseline differences, they found similar mortality rates in patients who underwent primary PCI for STEMI. However, for the larger nonprimary/rescue PCI population, mortality was higher in hospitals without onsite cardiac surgery (adjusted OR 1.38; 95% CI 1.14 to 1.67; *P* equals 0.001). This increase in mortality was primarily confined to hospitals that performed 50 or fewer Medicare PCIs per year. This experience is consistent with the concept that expansion of PCI services outside of large, full-service centers creates small, low-volume programs with inadequate infrastructure that are not able to perform PCI at the same level of sophistication and quality that a larger institution can.

This Writing Committee concludes that performance of elective PCI in a setting without immediately available onsite cardiac surgery potentially compromises patient safety and is not recommended. Although the frequency of PCI complications for which the outcome is favorably affected by prompt surgery is small, it is nonetheless finite. Consequently, performance of PCI in such a setting exposes the patient to a small but very real additional and medically unnecessary risk. In addition, an institution without an established cardiac surgery program is likely to be a low-volume institution less able to offer as high quality PCI service as a larger, full-service institution. Therefore, at this time, the

Writing Committee continues to support the recommendation that elective PCI should not be performed in facilities without onsite cardiac surgery. Mere convenience should not replace safety and efficacy in establishing an elective PCI program without onsite surgery. As with many dynamic areas in interventional cardiology, these recommendations may be subject to revision as clinical data and experience increase.

4.4. Primary PCI for STEMI Without Onsite Cardiac Surgery

Class IIb

Primary PCI for patients with STEMI might be considered in hospitals without onsite cardiac surgery, provided that appropriate planning for program development has been accomplished, including appropriately experienced physician operators (more than 75 total PCIs and, ideally, at least 11 primary PCIs per year for STEMI), an experienced catheterization team on a 24 hours per day, 7 days per week call schedule, and a well-equipped catheterization laboratory with digital imaging equipment, a full array of interventional equipment, and intra-aortic balloon pump capability, and provided that there is a proven plan for rapid transport to a cardiac surgery operating room in a nearby hospital with appropriate hemodynamic support capability for transfer. The procedure should be limited to patients with STEMI or MI with new or presumably new left bundle-branch block on ECG and should be performed in a timely fashion (goal of balloon inflation within 90 minutes of presentation) by persons skilled in the procedure (at least 75 PCIs per year) and at hospitals performing a minimum of 36 primary PCI procedures per year. *(Level of Evidence: B)*

Class III

Primary PCI should not be performed in hospitals without onsite cardiac surgery and without a proven plan for rapid transport to a cardiac surgery operating room in a nearby hospital or without appropriate hemodynamic support capability for transfer. *(Level of Evidence: C)*

Fibrinolytic trials in STEMI have demonstrated that early reperfusion saves myocardium and reduces mortality (357-360). Randomized trials comparing primary PCI for STEMI have shown that primary PCI performed by a highly experienced team achieves superior results. Primary PCI, compared with fibrinolytic therapy, has achieved modest reductions in overall mortality, but its overall benefit is chiefly leveraged by a reduction in early recurrent ischemic events (361-364).

In patients who have a contraindication to fibrinolytic therapy, or when there are complications such as cardiogenic shock, catheter-based therapy may limit infarct size (365,366). Thus, the potential overall superiority and greater applicability of primary PCI for the treatment of STEMI has raised the question of whether primary PCI should be performed at institutions with diagnostic cardiac catheterization laboratories that do not perform elective PCI or have onsite cardiac surgery. For this reason, the establishment of PCI programs at institutions without onsite cardiovascular surgery has been promoted as necessary to maintain quality of care (333-335,367-376).

PCI in the early phase of a STEMI requires a cognitive knowledge base and technical skill set that is somewhat different from that required to perform elective PCI. Primary PCI for STEMI can be technically difficult and requires even more skill and experience than routine PCI in the stable patient. The linkage between experience in performing elective PCI and primary PCI is incomplete (328). A successful primary PCI program requires an experienced operator and an experienced laboratory technical staff accustomed to managing critically ill patients (377). In addition, it is necessary to have available a broad range of catheters, guidewires, stents, and other devices (e.g., IABP) that are required to achieve results in an acutely ill patient (Table 15) (368).

Observational data from large, multi-institutional data sets have demonstrated that patients with STEMI who are treated with primary PCI performed by interventionalists with limited experience at institutions with low volume experience outcomes comparable to those achieved by fibrinolytic therapy (331). Thus, the benefits of primary PCI for STEMI require the infrastructure of a well-organized program with requisite experience and capabilities. In the absence of such capabilities, either onsite fibrinolytic therapy or transfer to a center that routinely performs complex PCI will often be a more effective and efficient course of action (123). The Danish Myocardial Infarction Study (DANAMI-2) demonstrated superior results in patients with STEMI who were urgently transferred to an experienced PCI center compared with those for whom fibrinolytic therapy was administered locally. In addition, the results in patients emergently transferred for primary PCI were comparable to those achieved in patients receiving primary PCI who initially presented to the PCI center institution (378). Nonetheless, fibrinolysis remains an acceptable form of therapy (379) and is likely preferable to acute PCI by an inexperienced team (62,379).

There are important institutional considerations in creating an effective program of primary PCI for STEMI. An institution must commit its catheterization facility to be capable of a 24-hours-per-day, 7-days-per-week rapid response to a patient presenting with STEMI. In addition, the institution's catheterization facility staff must be sufficiently trained and experienced in the management of the seriously ill patient with STEMI. In general, this means that the institution best positioned to provide effective PCI for STEMI is the institution with an active high-quality elective PCI program.

It has been demonstrated that institutions without an elective PCI program that care for a large number of patients with STEMI can create high-quality programs of PCI for STEMI. These programs require the 24-hours-per-day, 7-days-per-week availability of experienced interventionalists and an institutional commitment to invest in the physical and

Table 15. Criteria for the Performance of Primary PCI at Hospitals Without On-Site Cardiac Surgery

The operators must be experienced interventionalists who regularly perform elective PCI at a surgical center (greater than or equal to 75 cases per year). The catheterization laboratory must perform a minimum of 36 primary PCI procedures per year.
The nursing and technical catheterization laboratory staff must be experienced in handling acutely ill patients and must be comfortable with interventional equipment. They must have acquired experience in dedicated interventional laboratories at a surgical center. They participate in a 24-hours-per-day, 365-days-per-year call schedule.
The catheterization laboratory itself must be well-equipped, with optimal imaging systems, resuscitative equipment, and IABP support, and must be well-stocked with a broad array of interventional equipment.
The cardiac care unit nurses must be adept in hemodynamic monitoring and IABP management.
The hospital administration must fully support the program and enable the fulfillment of the above institutional requirements.
There must be formalized written protocols in place for immediate and efficient transfer of patients to the nearest cardiac surgical facility that are reviewed/tested on a regular (quarterly) basis.
Primary PCI must be performed routinely as the treatment of choice around the clock for a large proportion of patients with AMI, to ensure streamlined care paths and increased case volumes.
Case selection for the performance of primary PCI must be rigorous. Criteria for the types of lesions appropriate for primary PCI and for the selection for transfer for emergency aortocoronary bypass surgery are shown in Table 14.
There must be an ongoing program of outcomes analysis and formalized periodic case review.
Institutions should participate in a 3- to 6-month period of implementation, during which time development of a formalized primary PCI program is instituted that includes establishment of standards, training of staff, detailed logistic development, and creation of a quality-assessment and error-management system.

AMI indicates acute myocardial infarction; IABP, intra-aortic balloon pump; and PCI, percutaneous coronary intervention.
Adapted with permission from Wharton et al. J Am Coll Cardiol 1999;33:1257-65 (368).

cognitive resources needed to support a high-quality program. The feasibility of such an undertaking was first demonstrated by Wharton et al. in a 2-center study (368) and subsequently confirmed in multicenter studies by Aversano et al. (380) and Wharton et al. (375).

Before the use of stenting and GP receptor blockers, primary angioplasty in certain hospitals had been associated with acute mortality rates greater than those reported from centers with established primary angioplasty programs. Overall, in-hospital mortality rates have ranged from 1.4% to 13% (334,335,370).

Criteria have been suggested for the performance of primary PCI at hospitals without onsite cardiac surgery (Tables 15 and 16) (319,368,381). Of note, large-scale registries have shown an inverse relationship between the number of primary angioplasty procedures performed and in-hospital mortality (321,327,331). These data suggest that both door-to-balloon time and in-hospital mortality are significantly lower in institutions that perform more than 36 primary angioplasty procedures per year (330). It is important to point out that these data were achieved in hospitals with established elective PCI programs, and the numerical data may not extrapolate directly to hospitals that perform only primary PCI.

As an alternative to establishing numerous freestanding, modest-sized, primary PCI-only programs, a community may choose to concentrate PCI in a subset of its healthcare institutions, identifying well-qualified and experienced centers to perform this procedure. Suboptimal results may relate to operator/staff inexperience and capabilities and delays in performing angioplasty for logistical reasons (382).

From clinical data and expert consensus, the Writing Committee recommends that primary PCI for STEMI performed at hospitals without established elective PCI programs be restricted to those institutions capable of performing a requisite minimum number of primary angioplasty procedures (36 per year) by highly experienced operators after careful program development according to the procedures used by the C-PORT (Cardiovascular Patient Outcomes Research Team trial) and PAMI-No SOS (PAMI with No Surgery On Site) studies, including a proven plan for rapid and effective PCI and rapid access to cardiac surgery in a nearby facility (383). Although some experience suggests that an institution can develop an effective stand-alone primary PCI program, currently available data also indicate that concentration rather than diffusion of this capability will provide the most effective patient care. Thus, a strategy of emergency transfer to an established center with a well-developed primary PCI program is preferred to the development of new freestanding primary PCI programs.

Table 16. Patient Selection for Primary PCI and Emergency Aortocoronary Bypass at Hospitals Without On-Site Cardiac Surgery

Avoid intervention in hemodynamically stable patients with:
Significant (greater than or equal to 60%) stenosis of an unprotected left main coronary artery upstream from an acute occlusion in the left coronary system that might be disrupted by the angioplasty catheter
Extremely long or angulated infarct-related lesions with TIMI grade 3 flow
Infarct-related lesions with TIMI grade 3 flow in stable patients with 3-vessel disease (319, 381)
Infarct-related lesions of small or secondary vessels
Hemodynamically significant lesions in other than the infarct artery
Transfer for emergency aortocoronary bypass surgery patients with:
High-grade residual left main or multivessel coronary disease and clinical or hemodynamic instability present after primary PCI of occluded vessels, preferably with IABP support.

IABP indicates intra-aortic balloon pump; PCI, percutaneous coronary intervention; and TIMI, Thrombolysis In Myocardial Infarction.

Adapted with permission from Wharton et al. J Am Coll Cardiol 1999;33:1257-65 (368).

4.5. Elective PCI Without Onsite Surgery

Class III

Elective PCI should not be performed at institutions that do not provide onsite cardiac surgery. ***(Level of Evidence: C)****

*Several centers have reported satisfactory results based on careful case selection with well-defined arrangements for immediate transfer to a surgical program (333-337,348-353). A small, but real fraction of patients undergoing elective PCI will experience a life-threatening complication that could be managed with the immediate onsite availability of cardiac surgical support but cannot be managed effectively by urgent transfer. Wennberg et al., found higher mortality in the Medicare database for patients undergoing elective PCI in institutions without onsite cardiac surgery (356). This recommendation may be subject to revision as clinical data and experience increase.

Technical improvements in interventional cardiology have led to the development of elective angioplasty programs without onsite surgical coverage. Several centers have reported satisfactory results based on careful case selection with well-defined arrangements for immediate transfer to a surgical program (333-337,348-353). The studies of angioplasty without onsite surgical coverage have not identified significant differences in outcomes, which recalls the infrequent rate of complications (353). Despite many reported successful angioplasty series without onsite surgical backup and a very low percentage need for off-site surgery in failed angioplasty, some clinicians have expressed concern (354,355) about the appropriateness of elective angioplasty in centers without onsite surgical coverage. Life-threatening complications of elective PCI are, fortunately, rare but have not been reduced to negligible levels. A small but valid fraction of patients undergoing elective PCI will experience a life-threatening complication that could be managed with the immediate onsite availability of cardiac surgical support but cannot be managed effectively by urgent transfer. Lotfi et al. reported the experience of a large, high-quality coronary interventional center (384). Of 6582 PCI procedures performed between 1996 and 2000, 45 (0.7%) required emergency cardiac surgery. Of the 45 patients, 11 (0.2%) required truly emergent surgery because they were too unstable to tolerate an interhospital transfer. Thus, under the best of circumstances 1 in 500 patients undergoing elective PCI will experience a life-threatening complication that can be salvaged by immediate access to onsite cardiac surgery. As previously noted, Section 4.4, Wennberg, et al., found higher mortality in the Medicare database for patients undergoing elective PCI in institutions without onsite cardiac surgery (356). Furthermore, the availability of onsite cardiac surgery is a surrogate for overall program size and capability, as well as for the availability of many other experienced support services.

Caution is warranted before an unrestricted policy for PCI in hospitals without appropriate facilities is endorsed. Several outstanding and critically important clinical issues, such as timely management of ischemic complications, adequacy of specialized postinterventional care, logistics for managing cardiac surgical or vascular complications and operator/laboratory volumes, and accreditation, must be addressed. Mere convenience should not replace safety and efficacy in the establishment of an elective PCI program without onsite surgery.

At this time, the Writing Committee, therefore, continues to support the recommendation that elective PCI should not be performed in facilities without onsite cardiac surgery. As with many dynamic areas in interventional cardiology, these recommendations may be subject to revision as clinical data and experience increase.

5. CLINICAL PRESENTATIONS

A broad spectrum of clinical presentations exists wherein patients may be considered candidates for PCI, ranging from asymptomatic to severely symptomatic or unstable, with variable degrees of jeopardized myocardium. In this guideline, the CCS classification system for grading angina pectoris is used to summarize the severity of angina, as shown below (Table 17) (385).

Each time a patient is considered for revascularization, the potential risk and benefits of the particular procedure under consideration must be weighed against alternative therapies (Table 18). When PCI is considered, the benefits and risks of surgical revascularization and medical therapy always deserve thoughtful discussion with the patient and family. The initial simplicity and associated low morbidity of PCI compared with surgical therapy is always attractive, but the patient and family must understand the limitations inherent in current PCI procedures, including a realistic presentation

Table 17. Grading of Angina Pectoris According to CCS Classification

Class	Description of Stage
I	"Ordinary physical activity does not cause…angina," such as walking or climbing stairs. Angina occurs with strenuous, rapid, or prolonged exertion at work or recreation.
II	"Slight limitation of ordinary activity." Angina occurs on walking or climbing stairs rapidly; walking uphill; walking or stair climbing after meals; in cold, in wind, or under emotional stress; or only during the few hours after awaking. Angina occurs on walking more than 2 blocks on the level and climbing more than 1 flight of ordinary stairs at a normal pace and under normal conditions.
III	"Marked limitations of ordinary physical activity." Angina occurs on walking 1 to 2 blocks on the level and climbing1 flight of stairs under normal conditions and at a normal pace.
IV	"Inability to carry on any physical activity without discomfort—anginal symptoms may be present at rest."

CCS indicates Canadian Cardiovascular Society.
Adapted with permission from Campeau. Circulation 1976;54:522-3 (385).

of the likelihood of restenosis and the potential for incomplete revascularization compared with CABG surgery. In patients with CAD who are asymptomatic or have only mild symptoms, the potential benefit of antianginal drug therapy along with an aggressive program of risk reduction must also be understood by the patient before a revascularization procedure is performed. In those clinical settings in which PCI is recommended without evidence that it will reduce cardiovascular mortality but in which it does hold a promise to reduce symptoms, a class IIa or IIb classification has been chosen, which indicates a role for patient preference.

5.1. Patients With Asymptomatic Ischemia or CCS Class I or II Angina

Class IIa

1. **PCI is reasonable in patients with asymptomatic ischemia or CCS class I or II angina and with 1 or more significant lesions in 1 or 2 coronary arteries suitable for PCI with a high likelihood of success and a low risk of morbidity and mortality. The vessels to be dilated must subtend a moderate to large area of viable myocardium or be associated with a moderate to severe degree of ischemia on noninvasive testing.** ***(Level of Evidence: B)***
2. **PCI is reasonable for patients with asymptomatic ischemia or CCS class I or II angina, and recurrent stenosis after PCI with a large area of viable myocardium or high-risk criteria on noninvasive testing.** ***(Level of Evidence: C)***
3. **Use of PCI is reasonable in patients with asymptomatic ischemia or CCS class I or II angina with significant left main CAD (greater than 50% diameter stenosis) who are candidates for revascularization but are not eligible for CABG.** ***(Level of Evidence: B)***

Table 18. Provider Checklist: Key Areas for Consideration

Patients at High Risk
Assess key clinical and anatomic variables
Consider alternative therapies such as CABG in consultation with the patient
Ensure that formalized surgical standby is available
Ensure periprocedural hemodynamic support is available
Patients at Low Risk
Assess key clinical and anatomic variables
Consider alternative therapies such as medical therapy in consultation with the patient

CABG indicates coronary artery bypass graft surgery.

Class IIb

1. **The effectiveness of PCI for patients with asymptomatic ischemia or CCS class I or II angina who have 2- or 3-vessel disease with significant proximal LAD CAD who are otherwise eligible for CABG with 1 arterial conduit and who have treated diabetes or abnormal LV function is not well established.** ***(Level of Evidence: B)***
2. **PCI might be considered for patients with asymptomatic ischemia or CCS class I or II angina with nonproximal LAD CAD that subtends a moderate area of viable myocardium and demonstrates ischemia on noninvasive testing.** ***(Level of Evidence: C)***

Class III

PCI is not recommended in patients with asymptomatic ischemia or CCS class I or II angina who do not meet the criteria as listed under the class II recommendations or who have 1 or more of the following:

a. **Only a small area of viable myocardium at risk** ***(Level of Evidence: C)***
b. **No objective evidence of ischemia.** ***(Level of Evidence: C)***
c. **Lesions that have a low likelihood of successful dilatation.** ***(Level of Evidence: C)***
d. **Mild symptoms that are unlikely to be due to myocardial ischemia.** ***(Level of Evidence: C)***
e. **Factors associated with increased risk of morbidity or mortality.** ***(Level of Evidence: C)***
f. **Left main disease and eligibility for CABG.** ***(Level of Evidence: C)***
g. **Insignificant disease (less than 50% coronary stenosis).** ***(Level of Evidence: C)***

In the previous ACC/AHA guidelines for PCI, specific recommendations were made separately for patients with single-vessel or multivessel disease (1,123). The current techniques of PCI have matured to the point at which, in patients with favorable anatomy, the competent practitioner can perform either single-vessel or multivessel PCI with low risk and with a high likelihood of initial success. For this reason, in this update of the guidelines, recommendations have been made largely based on the patient's clinical condition, specific coronary lesion morphology and anatomy, LV function, and associated medical conditions, and less emphasis has been placed on the number of lesions or vessels requiring PCI. The CCS classification of angina (I to IV) is used to define the severity of symptoms. The categories described in this section refer to an initial PCI procedure in a patient without prior CABG surgery. The randomized trials comparing PCI and medical therapy have been discussed (Table 12) (11,12,279,282-290).

The Writing Committee recognizes that the majority of patients with CCS class I or II angina should be treated medically. The published ACIP study (301) casts some doubt on the wisdom of medical management for those higher-risk patients who are asymptomatic or have mild angina but have objective evidence by both treadmill testing and ambulatory monitoring of significant myocardial ischemia and CAD. In addition, a substantial portion of the middle-aged and older-age populations in the United States remain physically active, participating in sports, such as tennis and skiing, or performing regular and vigorous physical exercise, such as jogging, have CAD. For such individuals with moderate or severe ischemia and few symptoms, revascularization with PCI or CABG surgery may reduce their risk of serious or fatal cardiac events (301). For this reason, patients in this category of higher-risk asymptomatic ischemia or mild symptoms and severe anatomic CAD are placed in class IIa or IIb recommendations. PCI may be considered if there is a high likelihood of success and a low risk of morbidity or mortality. The judgment of the experienced physician is deemed valuable in assessing the extent of ischemia.

5.2. Patients With CCS Class III Angina

Class IIa

1. **It is reasonable that PCI be performed in patients with CCS class III angina and single-vessel or multivessel CAD who are undergoing medical therapy and who have 1 or more significant lesions in 1 or more coronary arteries suitable for PCI with a high likelihood of success and low risk of morbidity or mortality.** ***(Level of Evidence: B)***
2. **It is reasonable that PCI be performed in patients with CCS class III angina with single-vessel or multivessel CAD who are undergoing medical therapy with focal saphenous vein graft lesions or multiple stenoses who are poor candidates for reoperative surgery.** ***(Level of Evidence: C)***
3. **Use of PCI is reasonable in patients with CCS class III angina with significant left main CAD (greater than 50% diameter stenosis) who are candidates for revascularization but are not eligible for CABG.** ***(Level of Evidence: B)***

Class IIb

1. **PCI may be considered in patients with CCS class III angina with single-vessel or multivessel CAD who are undergoing medical therapy and who have 1 or more lesions to be dilated with a reduced likelihood of success.** ***(Level of Evidence: B)***
2. **PCI may be considered in patients with CCS class III angina and no evidence of ischemia on noninvasive testing or who are undergoing medical therapy and have 2- or 3-vessel CAD with significant proximal LAD CAD and treated diabetes or abnormal LV function.** ***(Level of Evidence: B)***

Class III

PCI is not recommended for patients with CCS class III angina with single-vessel or multivessel CAD, no evidence of myocardial injury or ischemia on objective testing, and no trial of medical therapy, or who have 1 of the following:

a. **Only a small area of myocardium at risk.** ***(Level of Evidence: C)***
b. **All lesions or the culprit lesion to be dilated with morphology that conveys a low likelihood of success.** ***(Level of Evidence: C)***
c. **A high risk of procedure-related morbidity or mortality.** ***(Level of Evidence: C)***
d. **Insignificant disease (less than 50% coronary stenosis).** ***(Level of Evidence: C)***
e. **Significant left main CAD and candidacy for CABG.** ***(Level of Evidence: C)***

The primary benefit of PCI among patients with CCS class III angina and single-vessel or multivessel CAD resides in the relief of symptoms, which may be accomplished with medical therapy. However, many patients with moderate or severe stable angina do not respond adequately to medical therapy and often have significant coronary artery stenoses that are suitable for revascularization with CABG surgery or PCI. In addition, a proportion of these patients have reduced LV systolic function, which places them in a group that is known to have improved survival with CABG surgery and possibly with revascularization by PCI (386-389). In patients without diabetes with 1- or 2-vessel disease in whom angioplasty of 1 or more lesions has a high likelihood of initial success, PCI is the preferred approach. In a minority of such patients, CABG surgery may be preferred, particularly for those in whom the LAD can be revascularized with the IMA or in those with left main coronary disease. (See Section 3.5.1.2 on left main CAD.)

5.3. Patients With UA/NSTEMI

Class I

An early invasive PCI strategy is indicated for patients with UA/NSTEMI who have no serious comorbidity and coronary lesions amenable to PCI. Patients must have any of the following high-risk features:

a. **Recurrent ischemia despite intensive anti-ischemic therapy.** ***(Level of Evidence: A)***
b. **Elevated troponin level.** ***(Level of Evidence: A)***
c. **New ST-segment depression.** ***(Level of Evidence: A)***
d. **HF symptoms or new or worsening MR.** ***(Level of***

Evidence: A)

e. **Depressed LV systolic function. *(Level of Evidence: A)***

f. **Hemodynamic instability. (Level of Evidence: A)**

g. **Sustained ventricular tachycardia. *(Level of Evidence: A)***

h. **PCI within 6 months. *(Level of Evidence: A)***

i. **Prior CABG. *(Level of Evidence: A)***

Class IIa

1. **It is reasonable that PCI be performed in patients with UA/NSTEMI and single-vessel or multivessel CAD who are undergoing medical therapy with focal saphenous vein graft lesions or multiple stenoses who are poor candidates for reoperative surgery. *(Level of Evidence: C)***
2. **In the absence of high-risk features associated with UA/NSTEMI, it is reasonable to perform PCI in patients with amenable lesions and no contraindication for PCI with either an early invasive or early conservative strategy. *(Level of Evidence: B)***
3. **Use of PCI is reasonable in patients with UA/NSTEMI with significant left main CAD (greater than 50% diameter stenosis) who are candidates for revascularization but are not eligible for CABG. *(Level of Evidence: B)***

Class IIb

1. **In the absence of high-risk features associated with UA/NSTEMI, PCI may be considered in patients with single-vessel or multivessel CAD who are undergoing medical therapy and who have 1 or more lesions to be dilated with reduced likelihood of success. *(Level of Evidence: B)***
2. **PCI may be considered in patients with UA/NSTEMI who are undergoing medical therapy who have 2- or 3-vessel disease, significant proximal LAD CAD, and treated diabetes or abnormal LV function. *(Level of Evidence: B)***

Class III

In the absence of high-risk features associated with UA/NSTEMI, PCI is not recommended for patients with UA/NSTEMI who have single-vessel or multivessel CAD and no trial of medical therapy, or who have 1 or more of the following:

a. **Only a small area of myocardium at risk. *(Level of Evidence: C)***

b. **All lesions or the culprit lesion to be dilated with morphology that conveys a low likelihood of success. *(Level of Evidence: C)***

c. **A high risk of procedure-related morbidity or mortality. *(Level of Evidence: C)***

d. **Insignificant disease (less than 50% coronary stenosis). *(Level of Evidence: C)***

e. **Significant left main CAD and candidacy for CABG. *(Level of Evidence: B)***

Clinical investigations have evaluated the use of routine catheterization and PCI for patients with UA or NSTEMI and have yielded inconsistent results. TIMI-IIIB was the first trial to compare strategies of routine catheterization and revascularization in addition to medical therapy and selective use of aggressive treatment. In TIMI-IIIB, there was no difference in the incidence of death or recurrent MI at 1 year between the 2 strategies, but patients treated by the aggressive strategy experienced less angina and repeat hospitalizations for ischemia and required fewer medications (390). In the VANQWISH trial (Veterans Affairs Non–Q-Wave Infarction Strategies in Hospital) performed by the US Veterans Administration, no difference in death or death and MI was observed between the 2 strategies at late follow-up, but the minority of patients in the aggressive strategy received revascularization, and the mortality rate for those having CABG was high (391). The FRISC II trial compared medical and revascularization approaches among patients after 6 days of low-molecular-weight heparin therapy before a decision regarding PCI (304). Those randomized to the conservative therapy only underwent PCI if they had at least 3 mm of ST-segment depression on stress testing. Compared with prior studies, patients assigned to the aggressive strategy in FRISC II experienced a 22% reduction (*P* equals 0.031) in the incidence of death or MI at 6 months (9.4%) compared with conservatively treated patients (12.1%). In addition, there was a significant decrease in the MI rate alone and a nonsignificantly lower mortality rate in the treated group (1.9% vs 2.9%; *P* equals 0.10). Symptoms of angina and hospital readmission were decreased 50% by the invasive strategy. These findings were supported by long-term follow-up from the FRISC II study that indicated that low-molecular-weight heparin and early intervention lowered the risk of death, MI, and revascularization in unstable coronary syndromes, at least during the first month of therapy. Early protective therapy could be used to reduce the risk of late events in patients waiting for definitive PCI (392). This treatment benefit was most pronounced for high-risk patients. The FRISC II trial (304) results support the use of catheterization and revascularization for selected patients with an acute coronary syndrome. The TACTICS trial randomized 2220 patients to an early invasive strategy in which cardiac catheterization and revascularization were performed 4 to 48 h after randomization or to a conservative strategy in which revascularization was reserved for those patients who developed recurrent ischemia after medical stabilization (393). All patients were treated with aspirin, heparin, beta-blockers, cholesterol-lowering therapy, and tirofiban. The primary end point, a composite of death, MI, and rehospitalization for worsening chest pain by 6 months, was lower in patients assigned to the invasive strategy (15.9% vs 19.4% in patients assigned to conservative therapy; *P* equals 0.0025). The rate of death or MI was also significantly reduced at 6 months in the invasive strategy arm (7.3% vs 9.5% in patients assigned to conservative therapy; *P* less than 0.05) (393). The TIMI-TACTICS group (394) has proposed a new risk stratification. The early invasive strategy was particularly effective for patients at moderate to high risk. The greater benefits derived from PCI in the TACTICS and FRISC trials compared with the TIMI III and VANQWISH trials can be explained in part by the use of stents and GP-receptor blockers and lower periprocedural complications in the TACTICS and FRISC II trials. In several studies published to date, the use of routine invasive therapy in patients with UA/NSTEMI, accompanied by IIb/IIIa receptor antagonists, has been shown to improve survival (205,302,393,395-397). New trials such as RITA-3 (302) further demonstrate the safety and effectiveness of an early invasive strategy.

It is recognized by the Committee that the assessment of risk of unsuccessful PCI or serious morbidity or mortality must always be made with consideration of the alternative therapies available for the patient, including more intensive or prolonged medical therapy or surgical revascularization (Table 19) (302,304,390,391,393), especially in patients with UA/NSTEMI.

When CABG surgery is a poor option because of high risk due to special considerations or other organ system disease, patients otherwise in class IIb may be appropriately managed with PCI. Under these special circumstances, formal surgical consultation is recommended.

5.4. Patients With STEMI

5.4.1. General and Specific Considerations

Class I

General considerations:

1. **If immediately available, primary PCI should be performed in patients with STEMI (including true posterior MI) or MI with new or presumably new left bundle-branch block who can undergo PCI of the infarct artery within 12 hours of symptom onset, if performed in a timely fashion (balloon inflation goal within 90 minutes of presentation) by persons skilled in the procedure (individuals who perform more than 75 PCI procedures per year, ideally at least 11 PCIs per year for STEMI). The procedure should be supported by experienced personnel in an appropriate laboratory environment (one that performs more than 200 PCI procedures per year, of which at least 36 are primary PCI for STEMI, and that has cardiac surgery capability).** ***(Level of Evidence: A)*** **Primary PCI should be performed as quickly as possible, with a goal of a medical contact-to-balloon or door-to-balloon time within 90 minutes.** ***(Level of Evidence: B)***

Specific Considerations:

2. **Primary PCI should be performed for patients less than 75 years old with ST elevation or presumably new left bundle-branch block who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock, unless further support is futile because of the patient's wishes or contraindications/unsuitability for further invasive care.** ***(Level of Evidence: A)***
3. **Primary PCI should be performed in patients with severe congestive heart failure and/or pulmonary edema (Killip class 3) and onset of symptoms within 12 hours. The medical contact-to-balloon or door-to-balloon time should be as short as possible (i.e., goal within 90 minutes).** ***(Level of Evidence: B)***

Class IIa

1. **Primary PCI is reasonable for selected patients 75 years or older with ST elevation or left bundle-branch block or who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock. Patients with good prior functional status who are suitable for revascularization and agree to invasive care may be selected for such an invasive strategy.** ***(Level of Evidence: B)***
2. **It is reasonable to perform primary PCI for patients with onset of symptoms within the prior 12 to 24 hours and 1 or more of the following:**
   a. **Severe congestive heart failure** ***(Level of Evidence: C)***
   b. **Hemodynamic or electrical instability** ***(Level of Evidence: C)***
   c. **Evidence of persistent ischemia** ***(Level of Evidence: C)***

Class IIb

The benefit of primary PCI for STEMI patients eligible for fibrinolysis when performed by an operator who performs fewer than 75 PCI procedures per year (or fewer than 11 PCIs for STEMI per year) is not well established. ***(Level of Evidence: C)***

Class III

1. **Elective PCI should not be performed in a non-infarct-related artery at the time of primary PCI <u>of</u> the infarct related artery in patients without hemodynamic compromise.** ***(Level of Evidence: C)***
2. **Primary PCI should not be performed in asymptomatic patients more than 12 hours after onset of STEMI who are hemodynamically and electrically stable.** ***(Level of Evidence: C)***

Acute STEMI results from a severe and sudden cessation of myocardial blood flow, most commonly due to atherosclerotic-thrombotic occlusion of a major epicardial coronary artery. PCI is a very effective method for re-establishing coronary perfusion and is suitable for 90% of patients. Considerable data support the use of PCI for patients with STEMI (53,364,398). Reported rates of achieving TIMI 3 flow, the goal of reperfusion therapy, range from 70% to 90% (399). Late follow-up angiography demonstrates that 87% of infarct arteries remain patent (400). Although most studies of primary PCI have been in patients who are eligible to receive fibrinolytic therapy, considerable experience supports the

Attachment D

Table 19. Invasive Versus Conservative Strategies in Unstable Angina Patients

Study	Years	Ref	n	Patient Population	Treatment	Follow-Up	Results: PCI	Results: Medical Therapy	Results: P	Comments
TIMI-IIIB	1989-1992	(390)	1473	Patients 21 to 76 years of age presenting within 24 h of ischemic discomfort at rest consistent with unstable angina or non–Q-wave MI	Medical therapy (tPA vs placebo) and early invasive or conservative strategy	6 wk	16.2% combined primary end points	18.1% combined primary end points	NS	Although no difference was found in combined primary end points (death, MI, positive ETT), the early invasive strategy was associated with shorter hospital stay and lower incidence of rehospitalization
						1 y	12.4 %	10.6%		
VANQWISH	1993-1996	(391)	920	Patients with an evolving MI	Invasive vs conservative	Average 23 mo	32.9% death and MI	30.3% death and MI	0.35	Fewer patients treated conservatively had death plus MI or death at hospital discharge at 1 month and at 1 year; the invasive group had a higher CABG mortality rate (11.6% vs 3.4%)
FRISC II	1996-1998	(304)	2457	Patient's ischemic symptoms in previous 48 hours accompanied by ECG changes or elevated markers	Early invasive therapy or noninvasive treatment strategy. Patients also received dalteparin or placebo for 3 months	6 mo	9.4% death or MI	12.1% death or MI	0.031	Invasive strategy was associated with 50% lower recurrent angina and hospital readmission rates
TACTICS-TIMI 18	1997-1999	(393)	2220	UA and NSTEMI with ECG changes, elevated levels of cardiac biomarkers, a history of CAD, or all 3 findings	Medical therapy (aspirin, heparin, tirofiban) and either early invasive or conservative (selectively invasive) treatment strategy	6 mo	7.3% death or MI	9.5% death or MI	Less than 0.05	Significant 22% relative risk reduction in composite end point of death, nonfatal MI, and rehospitalization
RITA-3	1997-2001	(302)	1810	Suspected cardiac chest pain at rest with documented evidence of CAD (at least 1 of the following: ECG changes, pathological Q waves, previous arteriogram)	Medical therapy and either early invasive or conservative (selectively invasive) treatment strategy; both groups received enoxaparin in addition to standard medical therapy	1 y	7.6% death or MI	8.3% death or MI	NS	Similar results for death or MI between treatment groups; significant difference in primary end point (death, MI, refractory angina) due to halving of refractory angina in the intervention group

CABG indicates coronary artery bypass graft surgery; CAD, coronary artery disease; ECG, electrocardiography; ETT, exercise treadmill test; MI, myocardial infarction; mo, month; n, number; NS, not significant; NSTEMI, non–ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; Ref, reference; tPA, alteplase; UA, unstable angina; wk, week; and y, year.

value of PCI for patients who may not be suitable for fibrinolytic therapy owing to an increased risk of bleeding (401).

Primary PCI has been compared with fibrinolytic therapy in 23 randomized clinical trials (361-363,378,380,381,402-415), including the SHOCK (SHould we emergently revascularize Occluded Coronaries in cardiogenic shocK?) trial (366). The recommendations for primary PCI in patients with cardiogenic shock are discussed and summarized separately in Section 5.4.6. These investigations consistently demonstrate that PCI-treated patients experience lower short-term mortality rates (7.0% vs 9.0%, relative risk 0.73, 96% CI 0.62 to 0.86, *P* equals 0.0002, and 5.0% vs 7.0%, relative risk 0.70, 95% CI 0.58 to 0.85, *P* equals 0.003 excluding the SHOCK trial), fewer nonfatal reinfarctions (3.0% vs 7.0%, relative risk 0.35, 95% CI 0.27 to 0.45, *P* equals 0.0003), and fewer hemorrhagic strokes (0.05% vs 1.0%, relative risk 0.05, 95% CI 0.006 to 0.35, *P* equals 0.0001) than those treated by fibrinolysis (53), albeit with an increased risk of bleeding (7.0% vs 5.0%, RR 1.3, 95% CI 1.02 to 1.65, *P* equals 0.032). These results have been achieved in medical centers and by providers experienced in the performance of primary PCI and under circumstances in which angioplasty can be performed promptly after patient presentation. The magnitude of the treatment differences for death, nonfatal reinfarction, and stroke vary depending on whether PCI is compared with streptokinase or a fibrin-specific lytic. The short- and long-term outcomes of patients with STEMI treated by fibrinolysis versus PCI and the numbers of patients who need to be treated to prevent 1 event or to cause a harmful complication when PCI is selected instead of fibrinolysis as the reperfusion strategy are shown in Figure 5 (53,416,417).

Time from symptom onset to reperfusion is an important predictor of patient outcome. Two studies (330,418) have reported increasing mortality rates with increasing door-to-balloon times. Other studies have shown better LV function and fewer complications when reperfusion occurs before PCI (419,420). An analysis of the randomized controlled trials comparing fibrinolysis with primary PCI suggests that the mortality benefit with PCI exists when treatment is delayed by no more than 60 min (Figure 6) (421). Mortality increases significantly with each 15-minute delay in the time between arrival and restoration of TIMI-3 flow (door-to–TIMI-3 flow time), which further underscores the importance of timely reperfusion in patients who undergo primary PCI (422). Given that the door-to-needle time goal is 30 min, this Writing Committee joins the Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology (423) and the ACC/AHA STEMI Guidelines Writing Committee (332) in lowering the door-to-balloon time goal from 120 to 90 min in an attempt to maximize the benefits for reperfusion by PCI (Figure 7) (418). Importantly, after adjustment for baseline characteristics, time from symptom onset to balloon inflation is significantly correlated with 1-year mortality in patients undergoing primary PCI for STEMI (relative risk equals 1.08 for each 30-minute delay from symptom onset to balloon inflation, *P* equals 0.04) (424).

The enthusiasm for primary PCI has led to the concept of emergency interhospital transfer for catheter-based reperfusion rather than fibrinolytic therapy in the initial hospital (425-427). Five randomized trials have enrolled 2466 patients with favorable results for PCI versus fibrinolytic therapy (378,381,407,412). Mortality was reduced with PCI (6.8% vs 9.6%, relative risk 0.69, 95% CI 0.51 to 0.0.92, *P* equals 0.01), as was the combined end point of death, nonfatal reinfarction, and stroke (8.5% vs 15.5%, relative risk 0.51, 95% CI 0.39 to 0.65, *P* less than 0.0001). Importantly, mean time to treatment was delayed only 44 min in these studies (Figure 8) (378,415). In contrast, first hospital door-to-balloon time, as recorded in 1346 patients undergoing hospital transfer before PCI in NRMI-4, was 185 min in the United States in 2002 (Figure 9) (428). Emergency transport in Europe is centrally organized and more efficient than in the United States (Table 20) (378,381,407,412,415). Delays in door-to-balloon time versus door-to-needle time of more than 60 min because of interhospital transfer might negate the potential mortality benefit of transfer for primary PCI over immediate intravenous fibrinolysis demonstrated in these trials (421). However, transfer of patients to PCI-capable centers should be accomplished when fibrinolytic therapy is contraindicated or unsuccessful, when cardiogenic shock ensues, when the anticipated delay is less than 60 min, or when symptoms have been present for more than 2 to 3 h (410,415). To achieve optimal results, a systems approach for rapid triage and transfer must be established. Time from first hospital door to balloon inflation in the second hospital should be as short as possible, with a goal within 90 min. Significant reductions in door-to-balloon times might be achieved by transporting patients directly to PCI centers, rather than transporting them to the nearest hospital, if interhospital transfer will subsequently be required to obtain primary PCI. Central to the success of all of the acute reperfusion strategies is a well-developed process of triage, as discussed in the STEMI guidelines (332,429).

Primary PCI with stenting has been compared with fibrinolytic therapy in 12 randomized clinical trials (366,378,380,381,407-412,415,430). These investigations demonstrate that PCI-treated patients experience lower mortality rates (5.9% vs 7.7%, OR 0.75, 95% CI 0.60 to 0.94, *P* equals 0.013), fewer reinfarctions (1.6% vs 5.1%, OR 0.31, 95% CI 0.21 to 0.44, *P* equals 0.0001), and fewer hemorrhagic strokes than those treated by fibrinolysis (53). Compared with PTCA, intracoronary stents achieve a better immediate angiographic result with a larger arterial lumen, less reclosure of the infarct-related artery, and fewer subsequent ischemic events (431-433). Primary stenting has been compared with primary angioplasty in 9 studies (64,106,433-440) (Table 21). There were no differences in mortality (3.0% vs 2.8%) or reinfarction (1.8% vs 2.1%) rates. However, subsequent target-vessel revascularization rates were lower with stenting (440).

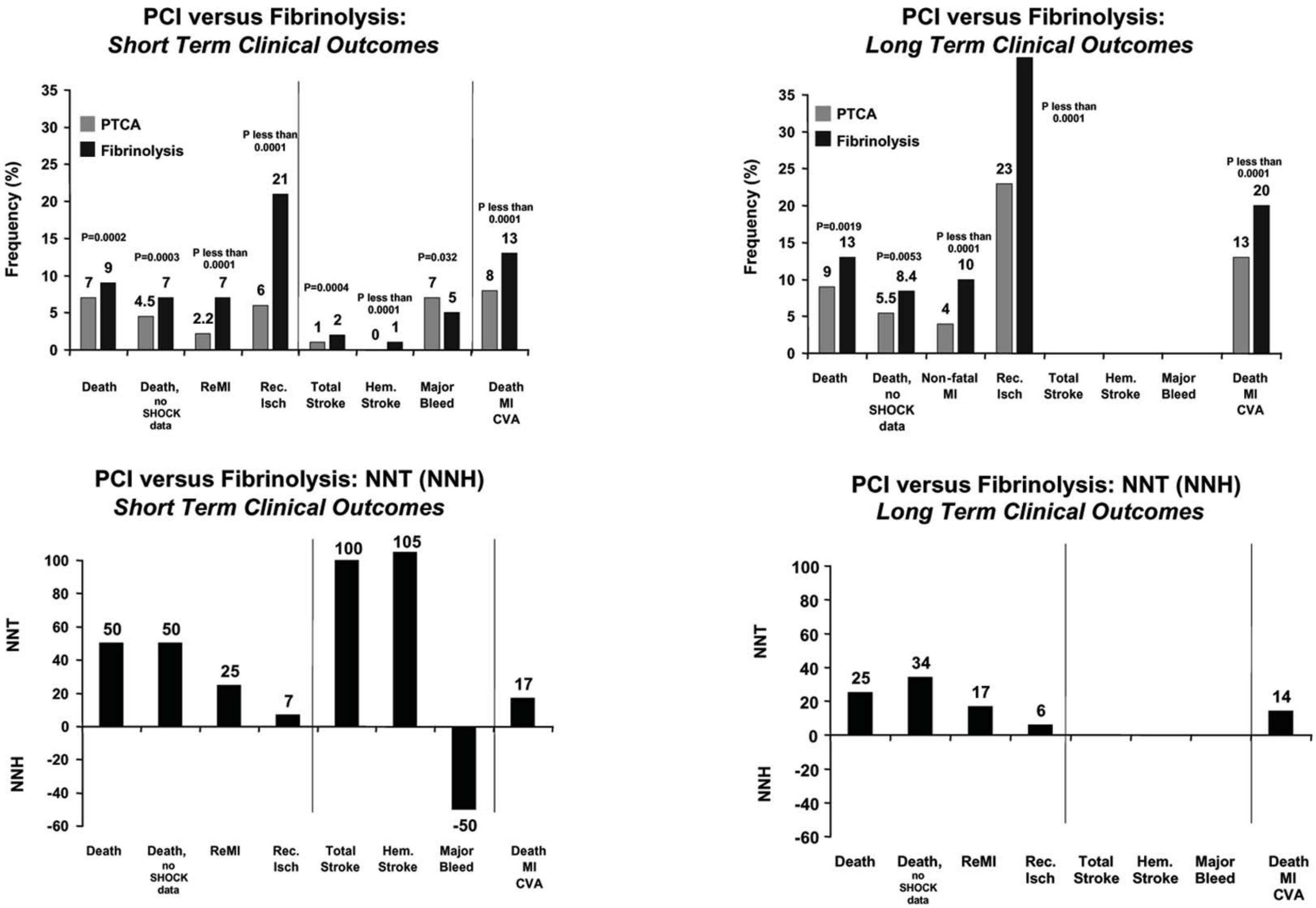

Figure 5. Percutaneous coronary intervention vs fibrinolysis for STEMI. The short-term (4 to 6 weeks; top left) and long-term (top right) outcomes for the various end points shown are plotted for STEMI patients randomized to PCI or fibrinolysis for reperfusion in 23 trials (n=7739). Based on the frequency of events for each end point in the 2 treatment groups, the number needed to treat (NNT) or number needed to harm (NNH) is shown for the short-term (bottom left) and long-term (bottom right) outcomes. Modified with permission from Elsevier (Keeley et al. The Lancet, 2003, 361, 13-20). Note: The magnitude of the treatment differences for death, nonfatal reinfarction, and stroke vary depending on whether PCI is compared with streptokinase or a fibrin-specific lytic. For example, when primary PCI is compared with alteplase (tPA) and the SHOCK trial is excluded, the mortality rate is 5.5% vs 6.7% (OR 0.81, 95% CI 0.64 to 1.03, *P* equals 0.081). Source: Melandri. Circulation 2003;108:e162. CVA indicates cerebrovascular accident; Hem. Stroke, hemorrhagic stroke; MI, myocardial infarction; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; Rec. Isch, recurrent ischemia; ReMI, recurrent MI; and STEMI, ST-elevation myocardial infarction.

Preliminary reports suggest that compared with conventional BMS, DES are not associated with increased risk when used for primary PCI in patients with STEMI. Postprocedure vessel patency, biomarker release, and the incidence of short-term adverse events were similar in patients receiving SES or BMS. Thirty-day event rates of death, reinfarction, or revascularization were 7.5% versus 10.4%, respectively (*P* equals 0.4) (441).

Furthermore, the impact of IIb/IIIa platelet receptor antagonists in the setting of primary PCI has undergone considerable evaluation. In a randomized trial of stents plus abciximab compared with fibrinolysis plus abciximab in patients with STEMI, myocardial salvage and salvage index measured by technetium-99m sestamibi scintigraphy was significantly greater in the stent group (430). In a similar study comparing primary PCI with stent plus abciximab to fibrinolysis with alteplase, infarct size was smaller and the cumulative incidence of death, reinfarction, or stroke at 6 months significantly lower in the primary PCI group (411).

However, results of studies comparing primary PCI with stents with or without IIb/IIIa platelet receptor antagonists have been less consistent. In the CADILLAC trial, a composite of death, reinfarction, disabling stroke, and ischemia-driven target-vessel revascularization was similar in patients treated with stents with or without abciximab (64). Yet, in a similar randomized comparison of stent plus abciximab versus stent alone in patients with STEMI (ADMIRAL trial; Abciximab before Direct angioplasty and stenting in Myocardial Infarction Regarding Acute and Long-term follow-up), a composite of death, reinfarction, or urgent target-

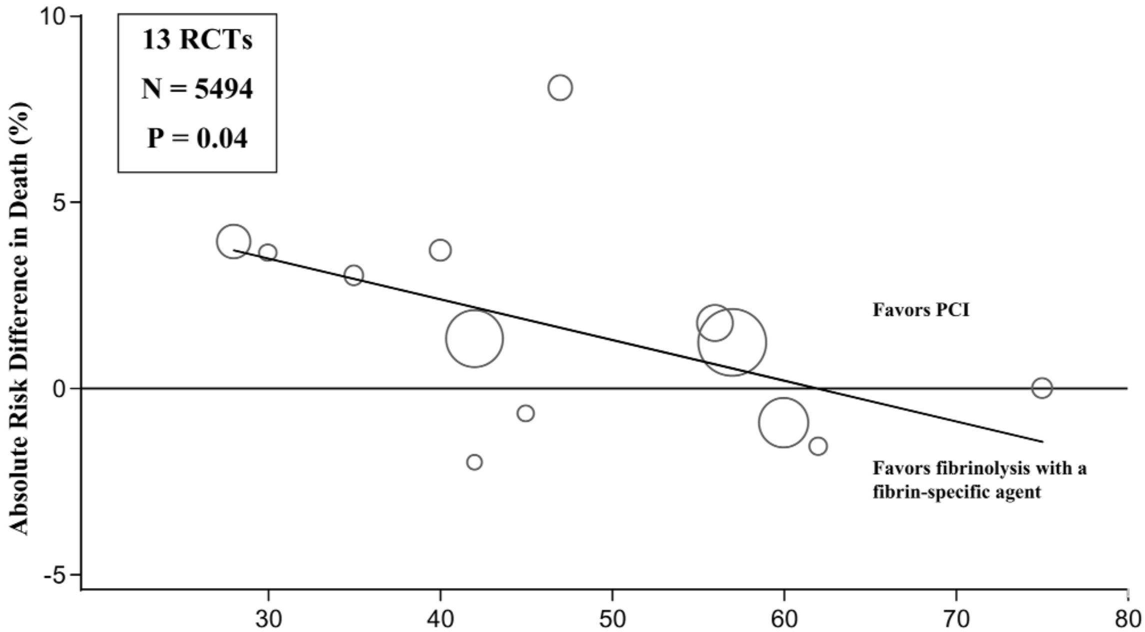

Figure 6. PCI versus fibrinolysis with fibrin-specific agents: is timing (almost) everything? PCI indicates percutaneous coronary intervention. Modified with permission from Nallamothu and Bates. Am J Cardiol 2003;92:824-6 (421).

vessel revascularization at 30 days occurred significantly less often in the abciximab group than in the control group (6.0% vs 14.6%, *P* equals 0.01), a difference that was sustained at 6 months of follow-up (442). The less favorable comparable clinical outcomes in patients treated with abciximab in the CADILLAC trial compared with those in the ADMIRAL trial have been attributed to the earlier administration of abciximab in the latter trial. The results of a pooled analysis of these 2 trials plus 3 similar trials (RAPPORT, ISAR-2, and ACE) (443-445) suggest that early (before coronary angiography) administration of abciximab will be associated with the most favorable clinical outcomes (446).

PCI appears to have its greatest mortality benefit in high-risk patients. In patients with cardiogenic shock, an absolute 9% reduction in 30-day mortality with mechanical revascularization instead of immediate medical stabilization was reported in the SHOCK trial (366) (see Section 5.4.6, PCI for Cardiogenic Shock). In NRMI-II, patients with HF had a

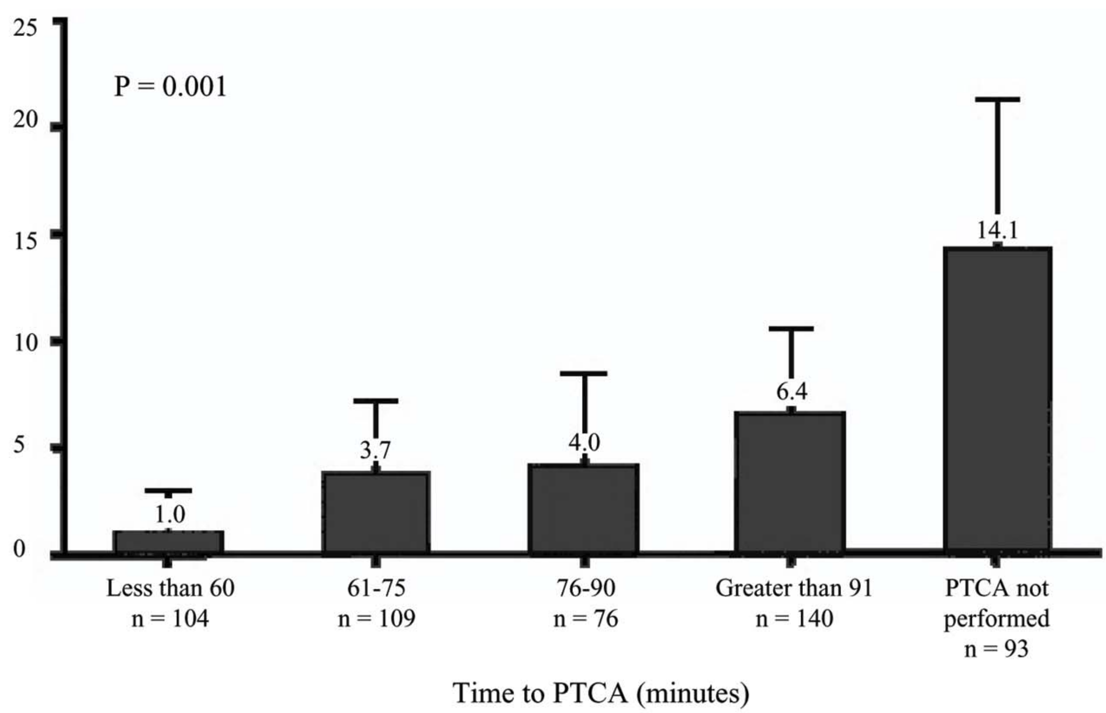

Figure 7. Relationship between 30-day mortality and time from study enrollment to first balloon inflation. Patients assigned to angioplasty in whom angioplasty was not performed are also shown. n indicates number of patients; and PTCA, percutaneous transluminal coronary angioplasty. Reprinted with permission from Berger et al. Circulation 1999;100:14-20 (418).

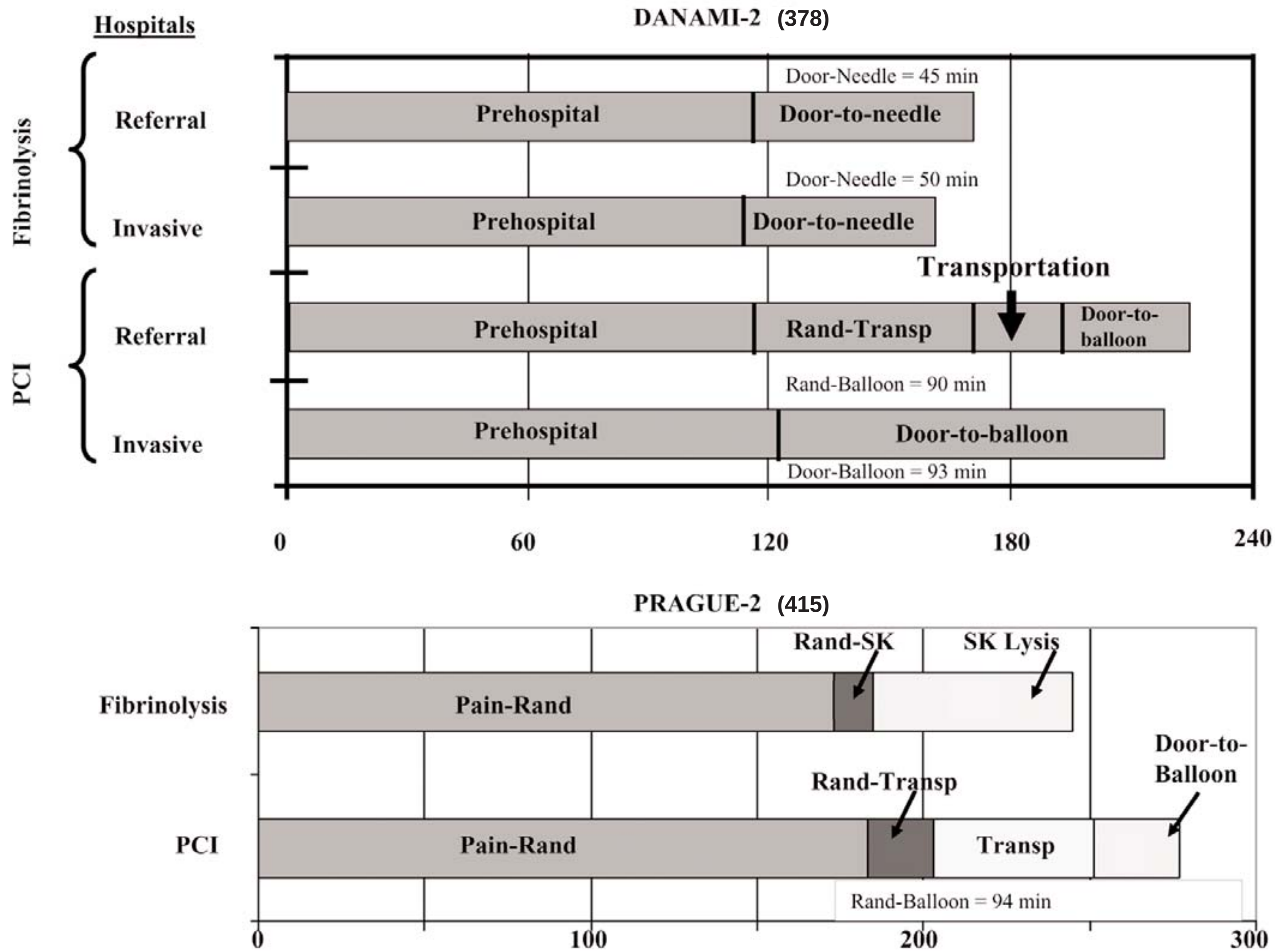

Figure 8. Comparison of elapsed time to fibrinolysis versus primary PCI. Time is presented as a continuous variable in minutes on the horizontal axis. For DANAMI-2, times reflect components of delay from symptom onset to randomization (vertical bar) and are further separated according to whether patients presented at community referral hospitals or those equipped for primary PCI. For those patients randomized to PCI at a referral hospital, the 3 components of delay after randomization are related to duration of stay at referral hospital, time for transport to PCI hospital, and delay from arrival at PCI hospital to balloon inflation. Lysis indicates fibrinolysis; PCI, percutaneous coronary intervention; Rand, randomization; SK, streptokinase; and Transp, transportation. Top graph reprinted with permission from Anderson et al. N Engl J Med 2003;349:733-42 (378). Copyright 2003 Massachusetts Medical Society. All rights reserved. Bottom graph reprinted from Widimsky et al. Eur Heart J 2003;24:94-104 (415) with permission from the European Society of Cardiology.

33% relative risk reduction with primary PCI compared with a 9% relative risk reduction with fibrinolytic therapy (447-449). Primary PCI in patients with anterior STEMI reduces mortality compared with fibrinolytic therapy, but there is no difference in patients with nonanterior STEMI (450,451).

Despite the evidence supporting primary PCI in the treatment of STEMI, there is serious concern that a routine policy of primary PCI for patients with STEMI will result in unacceptable delays in achieving reperfusion in a substantial number of patients and less than optimal outcomes if performed by less experienced operators. The mean time delay for PCI instead of fibrinolysis in the randomized trials was only 40 min (364). Strict performance criteria must be mandated for primary angioplasty programs so that excessive delays in reperfusion and performance by low-volume or poor-outcome operators/centers do not occur. The physicians, nursing, and technical catheterization laboratory staff must be experienced in handling acutely ill patients, must be skilled in all aspects of interventional equipment and procedures, and must participate in a 24-hours-per-day, 365-days-per-year call schedule. Interventional cardiologists and centers should strive for 1) balloon dilation within 90 min of admission and diagnosis of STEMI (452); 2) TIMI 2 to 3 flow attained in more than 90% of patients; 3) emergency CABG rate less than 2% among all patients undergoing the procedure; 4) actual performance of PCI in 85% of patients brought to the laboratory; and 5) a risk-adjusted in-hospital mortality rate less than 7% in patients without cardiogenic

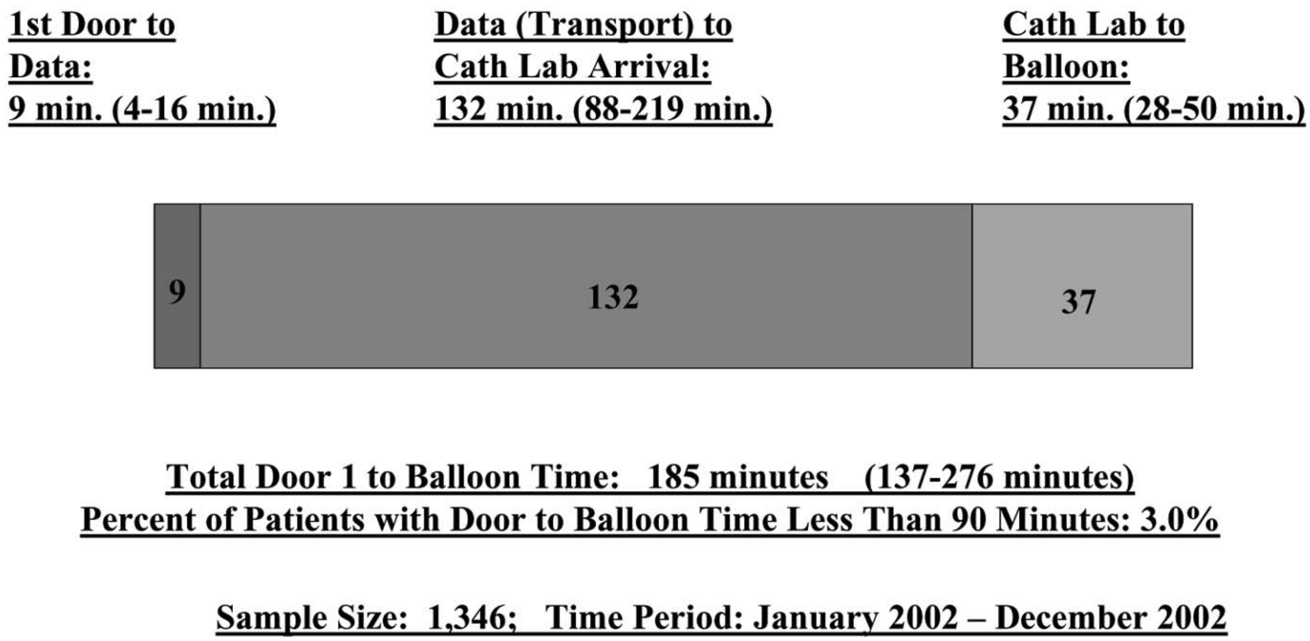

Figure 9. Door-to-balloon times: patients transferred in NRMI 4. Data are expressed in minutes as median time (25th percentile to 75th percentile). Cath Lab indicates catheterization laboratory. Modified, with permission, from NRMI-4 Investigators: The National Registry of Myocardial Infarction-4 Quarterly Report. Genentech, South San Francisco, Calif; March, 2003:2 (428).

shock. Otherwise, the focus of treatment should be the early use of fibrinolytic therapy, with further referral to PCI when indicated.

5.4.2. PCI in Fibrinolytic-Ineligible Patients

Class I

Primary PCI should be performed in fibrinolytic-ineligible patients who present with STEMI within 12 hours of symptom onset. ***(Level of Evidence: C)***

Class IIa

It is reasonable to perform primary PCI for fibrinolytic-ineligible patients with onset of symptoms within the prior 12 to 24 hours and 1 or more of the following:

a. **Severe congestive heart failure.** ***(Level of Evidence: C)***
b. **Hemodynamic or electrical instability.** ***(Level of Evidence: C)***
c. **Evidence of persistent ischemia.** ***(Level of Evidence: C)***

Randomized, controlled clinical trials evaluating the outcome of PCI for patients who present with STEMI but who are ineligible for fibrinolytic therapy have not been performed. Nevertheless, these patients are at increased risk for mortality (453), and there is a general consensus that PCI is an appropriate means for achieving reperfusion in those who cannot receive fibrinolytic drugs because of an increased risk of bleeding (401,454-456). Other reasons also exclude STEMI patients from fibrinolytic therapy, and the outcome of PCI in these patients may differ from those eligible for fibrinolytic therapy. Few data are available to characterize the value of primary PCI for this subset of STEMI patients (Table 22) (332,401).

Table 20. Transport of Patients With STEMI for Primary PCI

Study (Reference)	Number Transported	Distance, km	Time Between Randomization and First Balloon Inflation, min
Vermeer et al. (412)	75	25 to 50	85*
PRAGUE-1 (407)	101	5 to 74	80*
AIR-PAMI (381)	71	52*	155†
PRAGUE-2 (415)	429	5 to 120	97*
DANAMI-2 (378)	567	3 to 150	90†
Total	1243	3 to 150	

min indicates minutes; km, kilometer; PCI, percutaneous coronary intervention; and STEMI, ST-elevation myocardial infarction.
*Mean.
†Median.

Table 21. Studies Comparing PTCA with Stents in Acute Myocardial Infarction

					Early Events (0-30 days), %					Late Events (Cumulative) %				
Study	Year	Follow-Up (mo)	n, Stent/PTCA	Success (%)	Crossover	Death	Reinfarction	TVR	Any Event	Restenosis	Death	Reinfarction	TVR	Any Event
FRESCO (434)	1998	6	75/75	99*	NA	0/0	1.3/2.6	1.3/12	3/15	17/43	1/0	1/3	7/25	13/32
GRAMI (438)	1998	12	52/52	98/94.2	25*	3.8/7.6	0/7.6	0/5.7	3.8/19.2	NA	NA	NA	14/21	17/35
Suryapranata et al. (439)	2001	4	112/115	98/96	2/13	2/3	1/4	NA	NA	NA	3/3	1/9	13/34	16/38
PASTA (436)	1999	12	67/69	99/97	1/10	3/7	3/4	6/13	6/19	17/37.5	5/9	NA	NA	22/49
Stent-PAMI (433)	1999	6	452/448	89.4/92.7	1.5/15	3.5/1.8	0.4/1.1	1.8/3.8	4.6/5.8	20.3/33.5	4.2/2.7	2.4/2.2	7.7/1.7	12.6/20.1
STENTIM-2 (435)	2000	12	101/110	95/94.5	3/36.4	1/0	4/3.6	5/5.4	5/5.4	25.3/39.6	3/1.9	4.0/5.5	17.8/28.2	12.9/20.0
PSAAMI (437)	2001	710 plus or minus 282 days	44/44	NA	1/27	2/5	0/2	0/9	5/11	24/61	9/18	2/9	16/34	23/43
CADILLACa (64)	2002	6	512/518	94.5/94.7	16†	2.2/2.5	1.0/0.8	3.2/5.6	5.7/8.3	22.2/40.8§	3.0/4.5	1.6/1.8	8.3/15.7	11.5/20.0
CADILLACb (64)	2002	6	524/528	96.9/96.1	14‡	2.7/1.1	0.8/0.8	1.6/3.4	4.4/4.8	NA	4.2/2.5	2.2/2.7	5.2/13.8	10.2/16.5

n indicates number of patients; NA, data not gathered for that category; and TVR, target-vessel revascularization. All data are presented as values for stent/PTCA groups.
CADILLACa = Stent alone and PTCA alone arms.
CADILLACb = Stent plus abciximab and PTCA plus abciximab arms.
*Success rate of 99% before randomization.
†Values for crossovers from PTCA to stent treatment.
‡Values for crossovers from PTCA or stenting alone to combination with abciximab treatment.
§7-month follow-up; n = 636; independent of abciximab use.
Modified from Al SJ et al. JAMA 2000;284:1828-36 (106).

Table 22. Contraindications and Cautions for Fibrinolysis in STEMI*

Absolute contraindications
Any prior intracranial hemorrhage
Known structural cerebral vascular lesion (e.g., AVM)
Known malignant intracranial neoplasm (primary or metastatic)
Ischemic stroke within 3 months, EXCEPT acute ischemic stroke within 3 hours
Suspected aortic dissection
Active bleeding or bleeding diathesis (excluding menses)
Significant closed head or facial trauma within 3 months
Relative contraindications
History of chronic severe, poorly controlled hypertension
Severe uncontrolled hypertension on presentation (SBP greater than 180 mm Hg or DBP greater than 110 mm Hg)†
History of prior ischemic stroke greater than 3 months, dementia, or known intracranial pathology not covered in contraindications
Traumatic or prolonged (greater than 10 minutes) CPR or major surgery (less than 3 weeks)
Recent (within 2 to 4 weeks) internal bleeding
Noncompressible vascular punctures
For streptokinase/anistreplase: prior exposure (more than 5 days ago) or prior allergic reaction to these agents
Pregnancy
Active peptic ulcer
Current use of anticoagulants: the higher the INR, the higher the risk of bleeding

AVM indicates arteriovenous malformation; CPR, cardiopulmonary resuscitation; DBP, diastolic blood pressure; INR, international normalized ratio; SBP, systolic blood pressure; and STEMI, ST-elevation myocardial infarction.

*Viewed as advisory for clinical decision making and may not be all inclusive or definitive.

†Could be an absolute contraindication in low-risk patients with STEMI (see Section 6.3.1.6.3.2 in the ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction, available at: http://www.acc.org/clinical/guidelines/stemi/index.pdf).

Reprinted from Antman et al. J Am Coll Cardiol 2004;44:e1-e211 (332).

5.4.3. Facilitated PCI

Class IIb

Facilitated PCI might be performed as a reperfusion strategy in higher-risk patients when PCI is not immediately available and bleeding risk is low. ***(Level of Evidence: B)***

Facilitated PCI refers to a strategy of planned immediate PCI after an initial pharmacological regimen such as a full-dose fibrinolytic, a half-dose fibrinolytic, a GP IIb/IIIa inhibitor, or a combination of reduced-dose fibrinolytic therapy and a platelet GP IIb/IIIa inhibitor. Facilitated PCI should be differentiated from primary PCI without fibrinolysis; from primary PCI with a GP IIb/IIIa inhibitor started at the time of PCI; from immediate, early, or delayed PCI after successful full-dose fibrinolysis; and from rescue PCI after unsuccessful fibrinolysis. Potential advantages include earlier time to reperfusion, improved patient stability, greater procedure success rates, higher TIMI flow rates, and improved survival rates (419,420,442,457-460). However, preliminary studies have not demonstrated any benefit in reducing infarct size or improving outcomes. It is unlikely that this strategy would be beneficial in low-risk patients.

A strategy of facilitated PCI holds promise in higher-risk patients when PCI is not immediately available. Potential risks include increased bleeding complications, especially in older patients, and potential limitations include added cost. Several randomized trials of facilitated PCI with a variety of pharmacological regimens are in progress.

5.4.4. PCI After Failed Fibrinolysis (Rescue PCI)

Class I

1. **Rescue PCI should be performed in patients less than 75 years old with ST elevation or left bundle-branch block who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock, unless further support is futile because of the patient's wishes or contraindications/unsuitability for further invasive care.** ***(Level of Evidence: B)***
2. **Rescue PCI should be performed in patients with severe congestive heart failure and/or pulmonary edema (Killip class 3) and onset of symptoms within 12 hours.** ***(Level of Evidence: B)***

Class IIa

1. **Rescue PCI is reasonable for selected patients 75 years or older with ST elevation or left bundle-branch block or who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock. Patients with good prior functional status who are suitable for revascularization and agree to invasive care may be selected for such an invasive strategy.** ***(Level of Evidence: B)***
2. **It is reasonable to perform rescue PCI for patients with 1 or more of the following:**
   a. **Hemodynamic or electrical instability.** ***(Level of Evidence: C)***
   b. **Evidence of persistent ischemia.** ***(Level of Evidence: C)***

Class III

Rescue PCI in the absence of 1 or more of the above class I or IIa indications is not recommended. ***(Level of Evidence: C)***

PCI Immediately After Failed Fibrinolysis

Intravenous fibrinolytic therapy successfully restores antegrade coronary flow at 90 min in 50% to 80% of patients with acute STEMI (461). In those in whom it is unsuccessful, antegrade coronary flow can usually be restored with PCI. Several studies have demonstrated the marked beneficial effect of infarct-related artery patency (obtained via endogenous, pharmacological, or mechanical recanalization) on survival in patients with acute STEMI (462). Survivors of STEMI with a patent infarct-related artery demonstrated at 90 min after treatment have an improved long-term outcome compared with those with an occluded infarct-related artery, even when LV systolic function is similar (463,464). The REACT trial (Rapid Early Action for Coronary Treatment) was a randomized trial comparing medical therapy, immediate PCI, or repeat fibrinolytic in patients previously treated with fibrinolytic therapy. Preliminary data at 30 days demonstrated a significant advantage to rescue PCI [A.H. Gershlick, oral presentation, American Heart Association Scientific Sessions, New Orleans, LA, November 2004.]

Rescue (also known as salvage) PCI is defined as PCI within 12 h after failed fibrinolysis for patients with continuing myocardial ischemia. Rescue PCI has resulted in higher rates of early infarct-artery patency, improved regional infarct-zone wall motion, and greater freedom from adverse in-hospital clinical events compared with a deferred PCI strategy or medical therapy (465). The Randomized Evaluation of Rescue PCI with Combined Utilization Endpoints (RESCUE) trial demonstrated a reduction in rates of in-hospital death and combined death and HF that was maintained up to 1 year after study entry for patients presenting with anterior wall STEMI who failed fibrinolytic therapy when performed a mean of 8 h after symptom onset (466,467). Improvement in TIMI grade flow from 2 to 3 may offer additional clinical benefit. Similar data are not available for patients with nonanterior STEMI.

A major problem in adopting a strategy of rescue PCI lies in the limitation of accurate identification of patients in whom fibrinolytic therapy has not restored antegrade coronary flow. Unless unsuccessful fibrinolysis is recognized and corrected quickly (within 3 to 6 h of onset of symptoms), salvage of ischemic myocardium is unlikely. Unfortunately, clinical markers of reperfusion, such as relief of ischemic-type chest discomfort, partial resolution of ST-segment elevation, and reperfusion arrhythmias, have limited predictive value in identifying failure of fibrinolysis (468). Immediate catheterization of all patients after fibrinolytic therapy to identify those with an occluded infarct-related artery in a prior era in which the practice of PCI was less mature failed to show a significant benefit and was associated with bleeding complications. However, there was no specific study using stents and current pharmacotherapy. This strategy is being re-evaluated in clinical trials testing facilitated PCI in the contemporary PCI setting.

Even in the patient with documented failure of fibrinolysis, rescue PCI has limitations. First, because extensive myocardial necrosis occurs when coronary occlusion has been present for more than 3 h (469), PCI may not salvage a substantial amount of myocardium, considering the time delay associated with presentation of the patient to the hospital after onset of symptoms, infusion of the fibrinolytic agent, recognition of failed fibrinolysis, and subsequent initiation of PCI. Second, rescue PCI fails to reestablish antegrade coronary flow in about 10% of patients, and reocclusion of the infarct-related artery occurs in as many as 20% of the remainder (470), although GP IIb/IIIa inhibitors and stent implantation may have improved these results. Third, unsuccessful rescue PCI is associated with a high mortality (471,472). Finally, coronary reperfusion occurs over the subsequent h after fibrinolytic therapy in many patients. Although infarct-related artery patency is achieved in only 50% to 85% of patients 90 min after fibrinolytic therapy, it rises to 90% by 24 h (473). Such "late" reperfusion may improve survival without the risk of invasive procedures coupled with fibrinolytic therapy. Confounding the issue, both fibrinolysis and PCI may successfully restore flow in the epicardial artery but fail to improve microvascular perfusion.

Hours to Days After Failed Fibrinolysis

Patency of the infarct-related artery is an important predictor of mortality in survivors of STEMI (462,463,474). Compared with those with a patent infarct artery, survivors of STEMI with a persistently occluded artery after fibrinolysis, PCI, or no reperfusion therapy have 1) increased LV dilatation (475), 2) a greater incidence of spontaneous and inducible ventricular arrhythmias (476), and 3) a poorer prognosis (477). On the basis of observational and experimental data, it has been hypothesized that infarct artery patency may favorably influence LV remodeling and electrical stability, even if accomplished at a time when salvage of ischemic myocardium is unlikely (i.e., more than 12 h to days after coronary artery occlusion). Five small randomized trials, which enrolled a total of 562 patients, have directly tested the hypothesis that mechanical opening of persistent total occlusions late after MI will improve long-term LV remodeling and clinical outcomes (the late open artery hypothesis). Most studies enrolled a combination of patients, including those who had failed fibrinolysis and those who had not received reperfusion therapy (478-480), with a range from almost no fibrinolytic therapy (481) to fibrinolytic therapy in nearly all patients (482). There was wide variation in the effect of routine PCI compared with medical therapy only on LV size and function. Most studies showed no significant differences between the treatment groups (478,479). One single-center study of 83 patients with LAD occlusions reported improved LV volumes and clinical outcomes (composite of HF, MI, and death) at 6 months in the PCI group (481). In contrast, a multicenter study of 66 patients with LAD occlusions reported significantly worse LV remodeling, with progressive LV dilation at 1 year and more clinical events in the PCI group than in those assigned to optimal medical therapy alone (482). The latter included very high rates of beta-blocker and angiotensin converting enzyme inhibitor use. The largest multicenter study, DECOPI (DEsobstruction COronaire en Post-Infarctus), enrolled 212 patients and reported no difference in the primary end point, the composite of death, ventricular tachycardia, and MI at 6 months (483). Stents were used in 80% of patients in the PCI group, and GP IIb/IIIa antagonists were used in 9%. The study reached less than one third of the target sample size and was severely underpowered, as were all the other studies, to assess clinical events.

Selection of patients for revascularization based on viability testing has gained a great deal of investigational support, i.e., delayed enhancement or low-dose dobutamine cardiac

MRI assessment. If viability is shown, outcomes are excellent, whereas if transmural MI is present, it is not, and revascularization is not recommended (484-486).

There are no convincing data to support the routine use of late adjuvant PCI days after failed fibrinolysis or for patients who do not receive reperfusion therapy. Nevertheless, this is being done in some STEMI patients as an extension of the invasive strategy for NSTEMI patients. The Occluded Artery Trial (OAT) is currently randomizing patients to test whether routine PCI days to weeks after MI improves long-term clinical outcomes in asymptomatic high-risk patients with an occluded infarct-related artery (487).

5.4.5. PCI After Successful Fibrinolysis or for Patients Not Undergoing Primary Reperfusion

Class I

1. **In patients whose anatomy is suitable, PCI should be performed when there is objective evidence of recurrent MI. *(Level of Evidence: C)***
2. **In patients whose anatomy is suitable, PCI should be performed for moderate or severe spontaneous or provocable myocardial ischemia during recovery from STEMI. *(Level of Evidence: B)***
3. **In patients whose anatomy is suitable, PCI should be performed for cardiogenic shock or hemodynamic instability. *(Level of Evidence: B)***

Class IIa

1. **It is reasonable to perform routine PCI in patients with LV ejection fraction less than or equal to 0.40, HF, or serious ventricular arrhythmias. *(Level of Evidence: C)***
2. **It is reasonable to perform PCI when there is documented clinical heart failure during the acute episode, even though subsequent evaluation shows preserved LV function (LV ejection fraction greater than 0.40). *(Level of Evidence: C)***

Class IIb

PCI might be considered as part of an invasive strategy after fibrinolytic therapy. *(Level of Evidence: C)*

PCI Immediately After Successful Fibrinolysis

In early studies, asymptomatic patients undergoing routine PCI of the stenotic infarct-related artery immediately after successful fibrinolysis showed no benefit with regard to salvage of jeopardized myocardium or prevention of reinfarction or death. In addition, in some studies, this approach was associated with an increased incidence of adverse events, including bleeding, recurrent ischemia, emergency CABG surgery, and death (488-491). However, these studies have not been repeated in the modern interventional era with improved equipment, improved antiplatelet and anticoagulant therapy, and coronary stents. Notwithstanding this, routine PCI immediately after fibrinolysis may increase the chance for vascular complications at the catheterization access site and hemorrhage into the infarct-related vessel wall (491).

Hours to Days After Successful Fibrinolysis

It was initially suggested that elective PCI of the stenotic infarct-related artery hours to days after fibrinolysis might allow sufficient time for development of a more stable hemostatic milieu at the site of previous thrombotic occlusion. In this setting, PCI would be safer and more effective in reducing the incidence of reocclusion and improving survival. Two large randomized, prospective trials from an earlier PCI era tested this hypothesis, with both concluding that 1) there are fewer complications if PCI is delayed for several days after fibrinolytic therapy, and 2) routine PCI in the absence of spontaneous or provocable ischemia does not improve LV function or survival (226,489,490,492). Thus, in unselected patients receiving fibrinolytic therapy, PCI of the stenotic infarct-related artery in the absence of evidence of recurrent ischemia within 48 h did not appear to be beneficial.

Great improvements in equipment, operator experience, and adjunctive pharmacotherapy have increased PCI success rates and decreased complications. More recently, the invasive strategy for patients with NSTEMI has been given a class I recommendation by the ACC/AHA 2002 Guideline Update for the Management of Patients With UA/NSTEMI (493). Patients with STEMI are increasingly being treated similarly as an extension of this approach. Although 7 published reports (474,480,494-498) support this strategy, randomized studies similar to those in NSTEMI are needed.

One study supports the policy of performing catheterization and subsequent revascularization for patients who do have spontaneous or inducible angina after STEMI. The DANAMI trial (499) randomly assigned 1008 survivors of a first acute MI treated with fibrinolytic therapy within 12 h of onset of symptoms to catheterization and subsequent revascularization or standard medical therapy if they showed evidence of spontaneous or inducible angina. Those who underwent revascularization had less UA and fewer nonfatal MIs during a 2.5-year period of follow-up than those patients randomly assigned to medical treatment only (18% and 5.6% vs 30% and 10.5%, respectively). Among 500 patients undergoing fibrinolysis for STEMI, the GRACIA-1 (randomized trial comparing stenting within 24 hours of thrombolysis versus ischemia-guided approach to thrombolysed acute myocardial infarction with ST elevation) trial compared a strategy of angiography and intervention within 6 to 24 h of fibrinolysis to an ischemia-guided conservative approach for intervention. Eighty percent of patients assigned to angiography and intervention underwent stenting of the culprit artery compared with 20% in the ischemia-guided group. At 1 year, patients in the invasive group had a lower frequency of the primary end point (death, reinfarction, or revascularization; 9% vs 21%, *P* equals 0.008), and they tended to have a reduced rate of death or reinfarction (7% vs 12%, *P* equals

0.07). In the angiography and intervention group, 81% had TIMI-3 flow before PCI was performed (494).

Days to Weeks After Successful Fibrinolysis

Continued thrombus lysis and remodeling of the infarct artery stenosis occur over the days to weeks after successful fibrinolysis, which makes the underlying residual coronary stenosis more stable and less prone to rethrombosis and reocclusion. Thus, a delay in performing PCI for days to weeks after fibrinolysis might improve survival, even though earlier routine PCI does not. To date, there have not been adequately sized trials to evaluate this treatment strategy. Two older, small, randomized trials (488,500) demonstrated similar LV function, rates of reinfarction, and mortality in patients randomized to PCI or conservative therapy.

5.4.6. PCI for Cardiogenic Shock

Class I

Primary PCI is recommended for patients less than 75 years old with ST elevation or left bundle-branch block who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock, unless further support is futile because of the patient's wishes or contraindications/unsuitability for further invasive care. *(Level of Evidence: A)*

Class IIa

Primary PCI is reasonable for selected patients 75 years or older with ST elevation or left bundle-branch block who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock. Patients with good prior functional status who are suitable for revascularization and agree to invasive care may be selected for such an invasive strategy. *(Level of Evidence: B)*

Observational studies support the value of PCI for patients who develop cardiogenic shock in the early hours of MI. For patients who do not have mechanical causes of shock, such as acute mitral regurgitation or septal or free wall rupture, mortality among those having PCI is lower than among those treated by medical means (366). However, undergoing cardiac catheterization alone, with or without PCI, is associated with a lower mortality because of patient selection bias (501).

Two randomized clinical trials (366,502) have further clarified the role of emergency revascularization in STEMI complicated by cardiogenic shock. Both showed a statistically insignificant, but clinically important, absolute 9% reduction in 30-day mortality. In the SHOCK trial (366), the survival curves continued to progressively diverge such that at 6 months and 1 year, there was a significant mortality reduction with emergency revascularization (53% vs 66%, *P* less than 0.03) (503). The prespecified subgroup analysis of patients less than 75 years old showed an absolute 15% reduction in 30-day mortality (*P* less than 0.02), whereas there was no apparent benefit for the small cohort (n equals 56) of patients more than 75 years old. These data strongly support the approach that patients younger than 75 years with STEMI complicated by cardiogenic shock should undergo emergency revascularization and support measures. Three registries (504-506) have demonstrated a marked survival benefit for elderly patients who are clinically selected for revascularization (approximately 1 of 5 patients), so age alone should not disqualify a patient for early revascularization (see Section 3.5.9).

Several additional discussions elsewhere in this guideline are important to consider in these patients. Intra-aortic balloon pump support or ventricular assist devices can stabilize hemodynamics so that revascularization procedures can be performed (see Section 3.5.8). Post hoc analyses (507-509) have suggested that GP IIb/IIIa inhibitors may reduce mortality, but the studies are limited by lower than expected mortality rates, larger than expected mortality reduction, and small sample sizes. Although PCI in a noninfarct artery is not recommended in stable patients, it can be beneficial in hemodynamically compromised patients if the stenotic artery perfuses a large area of myocardium and the procedure can be performed efficiently. In patients with significant left main disease or severe 3-vessel disease and without right ventricular infarction or major comorbidities such as renal insufficiency or severe pulmonary disease, CABG can be considered as the revascularization strategy (Figure 10) (510).

5.4.7. PCI in Selected Patient Subgroups

5.4.7.1. Young and Elderly Postinfarct Patients

Although not supported by randomized trials, routine cardiac catheterization after fibrinolytic therapy for STEMI has been a frequently performed strategy in all age groups. Young patients (less than 50 years old) often undergo cardiac catheterization after fibrinolytic therapy owing to a "perceived need" to define coronary anatomy and thus establish psychological as well as clinical outcomes. In contrast, older patients (greater than 75 years of age) have higher in-hospital and long-term mortality rates and enhanced clinical outcomes when treated with primary PCI (511-514). In addition, patients thought to be candidates for implantable cardioverter-defibrillator placement and those with small infarcts may undergo cardiac catheterization for further evaluation after STEMI.

In a secondary analysis of the TIMI-IIB study that compared angiographic findings and clinical outcomes among 841 young (aged less than 50 years) and 859 older (aged 65 to 70 years) patients randomly assigned to an invasive or conservative post-lytic management strategy (515), the younger patients assigned to the invasive strategy commonly had insignificant (i.e., less than 60% diameter stenosis) and single-vessel CAD. Severe 3-vessel or left main coronary disease findings were infrequent (3-vessel incidence, 4%; left main, 0%). Fatal and nonfatal MI and death through-

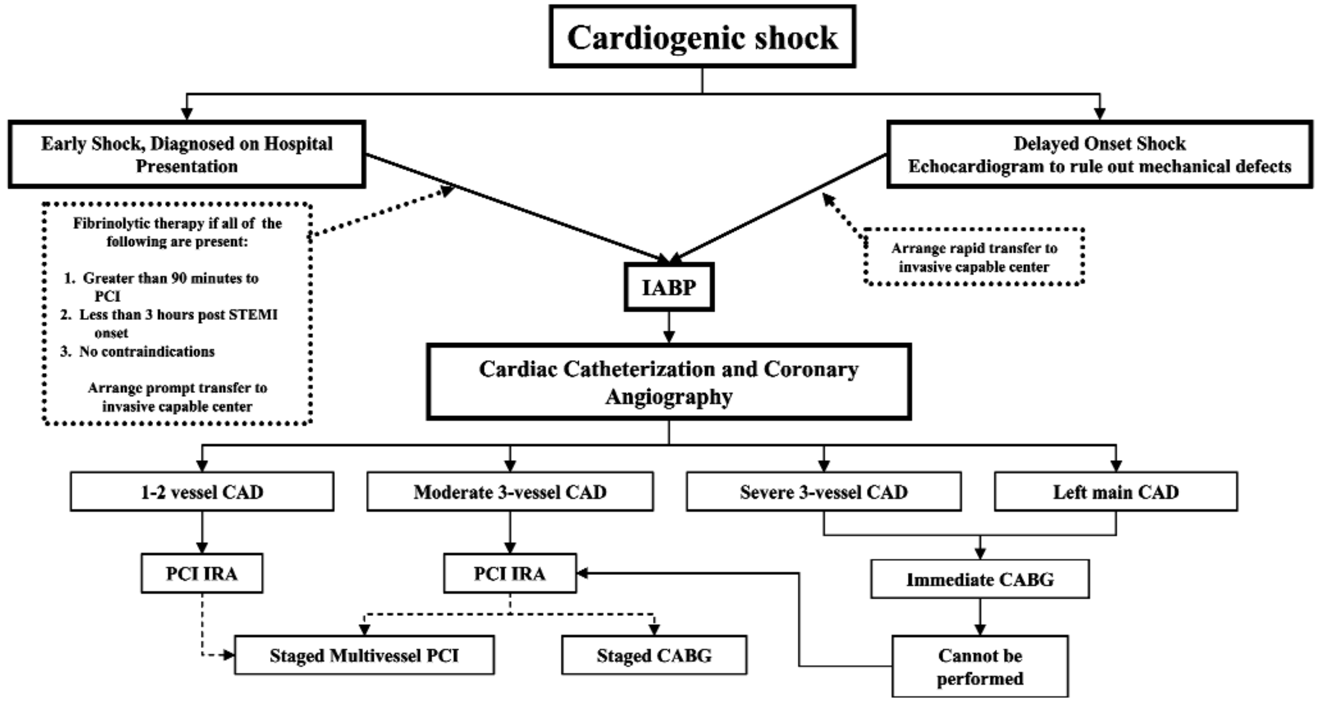

Figure 10. Recommendations for initial reperfusion therapy when cardiogenic shock complicates STEMI. Early mechanical revascularization with PCI/CABG is a Class I recommendation for candidates less than 75 years of age with ST elevation or left bundle-branch block who develop shock less than 36 hours from STEMI and in whom revascularization can be performed within 18 hours of shock, and it is a Class IIa recommendation for patients 75 years of age or older with the same criteria. Eighty-five percent of shock cases are diagnosed after initial therapy for STEMI, but most patients develop shock within 24 hours. IABP is recommended when shock is not quickly reversed with pharmacological therapy, as a stabilizing measure for patients who are candidates for further invasive care. Dashed lines indicate that the procedure should be performed in patients with specific indications only. Recommendations for staged CABG and PCI are discussed in the text, as are definitions of moderate and severe 3-vessel CAD. CABG indicates coronary artery bypass graft surgery; CAD, coronary artery disease; IABP, intra-aortic balloon pump; IRA, infarct-related artery; and STEMI, ST-elevation myocardial infarction. Modified with permission from Hochman. Circulation 2003;107:2998-3002 (510).

out the first year after study entry were also infrequent. There were no differences in the rates of in-hospital recurrent ischemia, reinfarction, or death among patients assigned to the conservative strategy of selective cardiac angiography and coronary revascularization compared with an invasive strategy, which consisted of routine post-lytic coronary angiography. Compared with younger patients, older patients had a higher prevalence of multivessel CAD (i.e., 44%) and higher 42-day rates of reinfarction and death.

In spite of these observations, there was no difference in the 42-day rates of reinfarction or death among the older patient subgroup, regardless of the post-lytic management strategy. The TIMI-II data of younger and older infarct patients are consistent with the overall results of other randomized trials of fibrinolysis/PTCA. More recent studies have examined PCI compared with fibrinolysis in young and elderly patients. The Primary Angioplasty in Myocardial Infarction (PAMI) investigators reviewed 3362 patients with ST-elevation MI enrolled in the various PAMI trials. All underwent primary angioplasty. Hospital mortality was higher for older patients, but the improvement in survival was also significant. Patients with high-risk infarction, including those with age greater than 70 years, had an improved outcome when treated with primary PTCA compared with fibrinolysis (512). In a review of more than 37 000 patients with STEMI from a national cohort of the Medicare database, after age adjustment, fibrinolytic therapy was not associated with a better 30-day survival than no therapy, whereas primary angioplasty was (OR 0.79, 95% CI 0.66 to 0.94). The benefit of primary angioplasty was noted at 1 year as well (513). In the GUSTO-IIB (Global Use of Strategies to Open occluded coronary arteries in acute coronary syndromes) angioplasty study, 1138 patients were randomized to receive primary angioplasty or fibrinolytic therapy. Irrespective of treatment, the risk of hospital mortality increased with age. For each 10-year increment in patient age, outcome was improved with angioplasty compared with fibrinolytic therapy. After adjustment for baseline characteristics, each increment of 10 years of age increased the risk of death or MI by a factor of 1.3 (95% CI 1.04 to 1.76, *P* equals 0.022). Advancing age was found to be associated with worse outcomes, and the risks increased in proportion to age. Primary angioplasty improved outcome compared with fibrinolysis but was not incrementally better in older than in younger patient groups (514). Given the current data, with the exception of patients presenting with cardiogenic shock, use of

PCI should be determined by clinical need without special consideration of age.

5.4.7.2. Patients With Prior MI

A prior MI is an independent predictor of death, reinfarction, and need for urgent coronary bypass surgery (516). In fibrinolytic trials, 14% to 20% of enrolled patients had a history of prior MI (490,517,518), and patients with prior MI have higher rates of reinfarction after fibrinolytic therapy (519).

In the TIMI-II study, patients with a history of prior MI had a higher 42-day mortality (8.8% vs 4.3%; *P* less than 0.001), higher prevalence of multivessel CAD (60% vs 28%; *P* less than 0.001), and a lower LV ejection fraction (42% vs 48%; *P* less than 0.001) than patients with a first MI (520). Among patients assigned to the conservative post-lytic strategy, those with a prior MI had a significantly higher 42-day mortality than patients with a first MI (11.5% vs 3.5%; *P* less than 0.001), whereas in the invasive strategy, the mortality outcome was essentially the same in the 2 patient groups. Mortality tended to be lower among patients with a prior MI undergoing the invasive versus the conservative strategy, a benefit that persisted up to 1 year after study entry (492).

In a registry involving almost 12 000 patients with acute coronary syndromes, with and without ST-segment elevation, a history of prior MI was noted in almost one third of patients. There was no significant increase in relative risk for hospital mortality in this group (521). Some analyses of predictors of mortality for angioplasty after fibrinolytic therapy have found relatively little importance for prior infarction and emphasized the much greater importance of time delays in achieving reperfusion among patients with failed fibrinolysis (418).

Given the above findings and current practice, PCI should be based on clinical need. The presence of prior MI places the patient in a higher-risk subset and should be considered in the PCI decision.

5.5. Percutaneous Intervention in Patients With Prior Coronary Bypass Surgery

Class I

1. **When technically feasible, PCI should be performed in patients with early ischemia (usually within 30 days) after CABG.** ***(Level of Evidence: B)***
2. **It is recommended that distal embolic protection devices be used when technically feasible in patients undergoing PCI to saphenous vein grafts.** ***(Level of Evidence: B)***

Class IIa

1. **PCI is reasonable in patients with ischemia that occurs 1 to 3 years after CABG and who have preserved LV function with discrete lesions in graft conduits.** ***(Level of Evidence: B)***
2. **PCI is reasonable in patients with disabling angina secondary to new disease in a native coronary circulation after CABG. (If angina is not typical, objective evidence of ischemia should be obtained.)** ***(Level of Evidence: B)***
3. **PCI is reasonable in patients with diseased vein grafts more than 3 years after CABG.** ***(Level of Evidence: B)***
4. **PCI is reasonable when technically feasible in patients with a patent left internal mammary artery graft who have clinically significant obstructions in other vessels.** ***(Level of Evidence: C)***

Class III

1. **PCI is not recommended in patients with prior CABG for chronic total vein graft occlusions.** ***(Level of Evidence: B)***
2. **PCI is not recommended in patients who have multiple target lesions with prior CABG and who have multivessel disease, failure of multiple SVGs, and impaired LV function unless repeat CABG poses excessive risk due to severe comorbid conditions.** ***(Level of Evidence: B)***

5.5.1. Early Ischemia After CABG

Recurrent ischemia early (less than 30 days) postoperatively usually reflects graft failure, often secondary to thrombosis (522-524), and may occur in both saphenous vein and arterial graft conduits (525). Incomplete revascularization and unbypassed native vessel stenoses or stenoses distal to a bypass graft anastomosis may also precipitate recurrent ischemia. Urgent coronary angiography is indicated to define the anatomic cause of ischemia and to determine the best course of therapy. Emergency PCI of a focal graft stenosis (venous or arterial) or recanalization of an acute graft thrombosis may successfully relieve ischemia in the majority of patients. Balloon dilatation across suture lines has been accomplished safely within days of surgery (526-528). Intracoronary fibrinolytic therapy should be administered with caution during the first week postoperatively (529-532), and if required, residual thrombus may be “targeted” in low doses through a local drug delivery system. Conversely, mechanical thrombectomy with newer catheter technologies may be effective without the attendant risk of fibrinolysis (533). Adjunctive therapy with abciximab for percutaneous intervention during the first week after bypass surgery has been limited but intuitively may pose less risk for hemorrhage than fibrinolysis. Because flow in vein graft conduits is pressure dependent, IABP support should be considered in the context of systemic hypotension or severe LV dysfunction. If feasible, PCI of both bypass graft and native vessel offending stenoses should be attempted, particularly if intracoronary stents can be deployed successfully.

When ischemia occurs 1 to 12 months after surgery, the cause is usually perianastomotic graft stenosis. Distal anastomotic stenoses (both arterial and venous) respond well to balloon dilation alone and have a more favorable long-term prognosis than stenoses involving the midshaft or proximal vein graft anastomosis (250,251,534-537). Midshaft vein graft stenoses occurring during this time frame are usually due to intimal hyperplasia. Restenosis may be less frequent and event-free survival may be enhanced after angioplasty of SVGs dilated within 6 months of surgery compared with grafts of older age. The immediate results of PCI in midshaft ostial or distal anastomotic vein graft stenoses may be enhanced by coronary stent deployment (537,538). Ablative technologies such as directional atherectomy or excimer laser coronary angioplasty may facilitate angioplasty and stent deployment in patients with aorto-ostial vein graft stenoses (539,540).

Stenoses in the midportion or origin of the IMA graft are uncommon but respond to balloon dilation (541,542) with stent deployment as feasible. Long-term follow-up of patients after IMA angioplasty has demonstrated sustained benefit and relief of ischemia in the majority of patients (543,544). Balloon angioplasty with or without stent deployment can be performed successfully in patients with distal anastomotic stenoses involving the gastroepiploic artery bypass graft and in patients with free radial artery bypass grafts (545). Percutaneous intervention has also been effective in relieving ischemia for patients with stenosis of the subclavian artery proximal to the origin of a patent left IMA bypass graft (546,547).

5.5.2. Late Ischemia After CABG

Ischemia occurring more than 1 year postoperatively usually reflects the development of new stenoses in graft conduits and/or native vessels that may be amenable to PCI (548). At 3 years or more after SVG implantation, atherosclerotic plaque is frequently evident and is often progressive. These lesions may be friable and often have associated thrombus formation, which may contribute to the occurrence of slow flow, distal embolization, and periprocedural MI after attempted percutaneous intervention (56). Slow flow occurs more frequently in grafts that have diffuse atherosclerotic involvement, angiographically demonstrable thrombus, and irregular or ulcerative lesion surfaces, and with long lesions that have large plaque volume (549,550). Although a reduced incidence of distal embolization has been reported after the use of the extraction atherectomy catheter to recanalize stenoses in older vein graft conduits (551-555), embolization may still complicate adjunctive balloon dilation. Distal embolic protection devices have significantly reduced the occurrence of complications of embolization in SVGs and should be used when possible (254,255). Slow flow with signs and symptoms of myocardial ischemia may be ameliorated by the intragraft administration of agents such as adenosine, diltiazem, nitroprusside, and verapamil (549,556-559). The adjunctive administration of abciximab during vein graft intervention was evaluated in a meta-analysis of 5 studies that demonstrated no improvement in outcomes after PCI and in the absence of distal protection and was associated with a high incidence of death and nonfatal ischemic events (252).

Although postprocedural minimum lumen diameter is larger after directional coronary atherectomy (243,560,561) or stent deployment (244,245,562-569) than with balloon angioplasty of SVG stenoses, long-term prognosis remains guarded, and late recurrent ischemic events may be due to both restenosis of the target lesion and diffuse vein graft disease (570-572). Final patency after PCI is greater for distal SVG lesions than for ostial or mid-SVG lesions (535), and stenosis location appears to be a better determinant of final patency than graft age or the type of interventional device used.

Percutaneous intervention for chronic vein graft occlusion has been problematic. Balloon angioplasty alone has been associated with high complication rates and low rates of sustained patency (572). Although prolonged intragraft infusion of fibrinolytic therapy was reported to successfully recanalize 69% of a selected group of patients with chronic SVG occlusion of less than 6 months' duration, long-term patency rates with or without adjunctive stent deployment were low (573-575). In addition, prolonged fibrinolytic therapy has been associated with thromboembolic MI (576-579), intracranial hemorrhage (580), and intramyocardial hemorrhage (581), as well as vascular access-site complications. Favorable results have been obtained with both local "targeted" and more prolonged infusion of fibrinolytic agents for nonocclusive intragraft thrombus (582,583). Fibrinolytic catheter-based systems appear to successfully treat SVG thrombosis as well as or better than fibrinolytic agents (584).

5.5.3. Early and Late Outcomes of Percutaneous Intervention

Before the general availability of coronary stenting, overall angioplasty procedural success rates exceeded 90%, and adverse outcomes of emergency repeat coronary bypass surgery (2.3%) and death (0.8%) were infrequent as reported in combined series of over 2000 patients with prior bypass surgery undergoing percutaneous intervention (250,585-597). These results are comparable to those achieved in patients without prior bypass surgery, an observation confirmed by NHLBI registry data (7). The most common complications observed in this population are NSTEMI and atheroembolism, particularly after SVG intervention (538,598).

Patients with prior bypass surgery who undergo successful PCI have a long-term outcome that is dependent on patient age, the degree of LV dysfunction, and the presence of multivessel coronary atherosclerosis. The best long-term results are observed after recanalization of distal anastomotic stenoses occurring within 1 year of operation. Angioplasty of distal anastomotic stenoses involving IMA grafts has been associated with similar, favorable long-term patency rates (543,544). Conversely, event-free survival is less favorable after angioplasty of totally occluded SVGs, ostial vein graft stenoses, or grafts with diffuse or multicentric disease (570-572). Coexistent multisystem disease, the presence of which may have prompted the choice of a percutaneous revascularization strategy, may also influence long-term outcomes in this population.

5.5.4. General Considerations

Aged, diffuse, friable, and degenerative SVG disease in the absence of a patent arterial conduit to the LAD represents a prime consideration for repeat surgical revascularization. In contrast, the presence of a patent arterial conduit to the LAD favors a percutaneous interventional approach to other vessels (599). The overall risk of repeat operation, especially the presence of comorbidities such as concomitant cerebrovascular, renal, or pulmonary disease and the potential for jeopardizing patent, nondiseased bypass conduits, must be considered carefully. Isolated, friable stenoses in vein grafts may be approached with primary stenting or the combination of extraction atherectomy and stenting in an attempt to reduce the likelihood of distal embolization. Distal embolic protection devices have reduced the occurrence of complications of embolization significantly and should be used when possible (254,255) (see Sections 5.5.2 and 6.1.1).

Another therapeutic option for patients with prior coronary bypass surgery that has become available is grafting with the IMA through a "minimally invasive" surgical approach (273,600-604). This strategy, which avoids both the risk of cardiopulmonary bypass (stroke or coagulopathy) and repeat median sternotomy, may be particularly applicable to patients with chronic native-vessel LAD coronary occlusion and friable atherosclerotic disease that involves a prior SVG to this vessel. The role of combining a minimally invasive surgical approach with PCI requires further study (605,606).

In general, patients with multivessel disease, failure of multiple SVGs, and moderately impaired LV function derive the greatest benefit from the durability provided by surgical revascularization with arterial conduits. Regardless of repeat revascularization strategy, risk factor modification with cessation of smoking (607,608) and lipid-lowering therapy (609,610) should be implemented in patients with prior CABG surgery. An aggressive lipid-lowering strategy that targets a low-density lipoprotein cholesterol level substantially less than 100 mg per dL (optional therapeutic target for low-density lipoprotein cholesterol less than 70 mg per dL in very-high-risk patients) (611) can be effective in reducing recurrent ischemic events and the need for subsequent revascularization procedures (610).

5.6. Use of Adjunctive Technology (Intracoronary Ultrasound Imaging, Flow Velocity, and Pressure)

The limitations of coronary angiography for diagnostic and interventional procedures can be reduced by the use of adjunctive technology such as intracoronary ultrasound imaging, flow velocity, and pressure. Information obtained from the adjunctive modalities of intravascular imaging and physiology can improve PCI methods and outcomes.

5.6.1. Intravascular Ultrasound Imaging

Class IIa

IVUS is reasonable for the following:

a. **Assessment of the adequacy of deployment of coronary stents, including the extent of stent apposition and determination of the minimum luminal diameter within the stent.** ***(Level of Evidence: B)***
b. **Determination of the mechanism of stent restenosis (inadequate expansion versus neointimal proliferation) and to enable selection of appropriate therapy (vascular brachytherapy versus repeat balloon expansion).** ***(Level of Evidence: B)***
c. **Evaluation of coronary obstruction at a location difficult to image by angiography in a patient with a suspected flow-limiting stenosis.** ***(Level of Evidence: C)***
d. **Assessment of a suboptimal angiographic result after PCI.** ***(Level of Evidence: C)***
e. **Establishment of the presence and distribution of coronary calcium in patients for whom adjunctive rotational atherectomy is contemplated.** ***(Level of Evidence: C)***
f. **Determination of plaque location and circumferential distribution for guidance of directional coronary atherectomy.** ***(Level of Evidence: B)***

Class IIb

IVUS may be considered for the following:

a. **Determination of the extent of atherosclerosis in patients with characteristic anginal symptoms and a positive functional study with no focal stenoses or mild CAD on angiography.** ***(Level of Evidence: C)***
b. **Preinterventional assessment of lesional characteristics and vessel dimensions as a means to select an optimal revascularization device.** ***(Level of Evidence: C)***
c. **Diagnosis of coronary disease after cardiac transplantation.** ***(Level of Evidence: C)***

Class III

IVUS is not recommended when the angiographic diagnosis is clear and no interventional treatment is planned. ***(Level of Evidence: C)***

IVUS imaging provides a tomographic 360-degree sagittal scan of the vessel from the lumen through the media to the vessel wall. IVUS measurements of arterial dimensions (minimal and maximal diameters, cross-sectional area, and plaque area) complement and enhance angiographic information. IVUS has been used to refine device selection through plaque characterization (e.g., calcified) and artery sizing. IVUS has contributed to the understanding of the mechanisms of coronary angioplasty in general and specifically to the advancement of coronary stenting without long-term anticoagulation (612-617). In a large observational study, IVUS-guided angioplasty resulted in a decreased final residual plaque area from 51% to 34%, despite a final angiographic percent stenosis of 0% (612). IVUS-facilitated stent deployment was associated with a subacute thrombosis rate of 0.3% without systemic anticoagulation, although antiplatelet agents are still required for stenting (612). In the placement of coronary stents, because radiographic contrast material can be located between stent struts and the vascular wall, an angiographic appearance of a large lumen may exist when the stent has not been fully deployed. IVUS documents full apposition of stent struts to the vessel wall (612).

IVUS is not necessary for all stent procedures. The results of the French Stent Registry study of 2900 patients treated without warfarin and without IVUS reported a subacute closure rate of 1.8% (618). In the Stent Anticoagulation Regimen Study (STARS) (619), a subacute closure rate of 0.6% in patients having optimal stent implantation supports the approach that IVUS does not appear to be required routinely in all stent implantations. However, the use of IVUS to evaluate results in high-risk procedures (e.g., those patients with multiple stents, impaired TIMI grade flow or coronary flow reserve, and marginal angiographic appearance) appears warranted.

The long-term outcomes when adjunctive IVUS is used are currently under study. In the Multicenter Ultrasound Stent In Coronaries (MUSIC) trial of 161 patients (620), which evaluated optimal stent expansion (defined as complete apposition of the stent over its length) with symmetrical expansion (defined as a ratio of minimum to maximum luminal diameter greater than 0.7) and minimal luminal area (compared with greater than 80% of the reference area), the subacute closure rate was 1.3% with monotherapy of aspirin. The angiographic restenosis rate was less than 10% when stent cross-sectional areas were greater than 9.0 mm^2.

Fitzgerald et al. reported that the degree of stent expansion as measured by IVUS directly correlates to clinical outcomes in the CRUISE (Can Routine Ultrasound Influence Stent Expansion) study (621). This multicenter study compared 270 patients with IVUS-guided stent implantation with IVUS-documented, but not guided, stent implantation in 229 patients. At 9-month follow-up, there was no difference in rates of death or MI, but the target-lesion revascularization rate was substantially lower in the IVUS-guided group (8.5% vs 15.3%; *P* equals 0.019). These data suggest that ultrasound guidance of stent implantation may result in more effective stent expansion than angiographic guidance alone and subsequently reduce the need for late target-lesion revascularization.

In several instances, IVUS has been useful in determining the reason for reduced efficacy of new technology. In the RESCUT (REStenosis CUTting balloon evaluation) trial comparing cutting balloon with PTCA for ISR, IVUS examinations showed that there was stent underexpansion when a cutting balloon was used at low pressure compared with high-pressure balloons (91).

IVUS has also identified complications of PCI that require further therapy. Postprocedure hematomas that were not identifiable by angiography were identified by IVUS (622).

Stent underexpansion was also shown to be common in diabetic patients assessed with angiography. This can be revealed by IVUS so that further expansion of the stent can be accomplished (623). IVUS increasingly is also being used to measure the volume of intimal hyperplasia in experimental studies to evaluate the efficacy of systemic and locally delivered antirestenotic therapies (624-628) or in clinical research trials to assess the effect of therapies for dyslipidemia on vascular wall and plaque structure.

5.6.2. Coronary Artery Pressure and Flow: Use of Fractional Flow Reserve and Coronary Vasodilatory Reserve

Class IIa

It is reasonable to use intracoronary physiologic measurements (Doppler ultrasound, fractional flow reserve) in the assessment of the effects of intermediate coronary stenoses (30% to 70% luminal narrowing) in patients with anginal symptoms. Coronary pressure or Doppler velocimetry may also be useful as an alternative to performing noninvasive functional testing (e.g., when the functional study is absent or ambiguous) to determine whether an intervention is warranted. *(Level of Evidence: B)*

Class IIb

1. **Intracoronary physiologic measurements may be considered for the evaluation of the success of PCI in restoring flow reserve and to predict the risk of restenosis. *(Level of Evidence: C)***
2. **Intracoronary physiologic measurements may be considered for the evaluation of patients with anginal symptoms without an apparent angiographic culprit lesion. *(Level of Evidence: C)***

Class III

Routine assessment with intracoronary physiologic measurements such as Doppler ultrasound or fractional flow reserve to assess the severity of angiographic disease in patients with a positive, unequivocal noninvasive functional study is not recommended. *(Level of Evidence: C)*

Historically, translesional pressure gradients were used as end points for early interventional cardiology procedures. The use of a translesional pressure gradient measured at rest was abandoned because of difficult technique and improved angiographic imaging. Pijls et al. (545) introduced the concept of fractional flow reserve (FFR) of the myocardium, the ratio of distal coronary pressure to aortic pressure measured during maximal hyperemia, which correlates with the fraction of normal blood flow through the stenotic artery (629,630). The coronary pressure measuring technique is relatively simple, especially with pressure guidewires, a method superior to small catheters. The normal FFR value for all vessels under all hemodynamic conditions, regardless of the status of microcirculation, is 1.0. FFR values less than 0.75 are associated with abnormal stress tests (631). Unlike coronary flow velocity reserve (CVR), the FFR is relatively independent of microcirculatory disturbances. FFR does not use measurements in a reference vessel and is thought to be epicardial lesion-specific. FFR provides no information on the microcirculation or on the absolute magnitude of the change in coronary flow.

On the other hand, CVR is the ratio of hyperemic to basal flow and reflects flow resistance through the epicardial artery and the microvascular bed. CVR less than 2.0 is positively correlated to abnormal stress perfusion imaging (632-634). In some cases, the uncertainty as to whether the impaired flow reserve is due to the target stenosis or to an abnormal microcirculation may be reduced by use of relative coronary flow reserve (rCVR, which is equal to CVR of the target vessel divided by CVR of the reference vessel). From preliminary studies, rCVR greater than 0.8 may have prognostic values similar to those of negative stress testing (635). There is a correlation between rCVR and pressure-derived FFR (629,635). An abnormal CVR indicates that the stenosis in the epicardial artery is significant when the microcirculation is normal. For coronary lesion assessment, the best measurement appears to be FFR.

CVR measurement of less than 2 after stent placement was an independent predictor of target-vessel revascularization. CVR after PCI in DEBATE-2 (Doppler Endpoints Balloon Angioplasty Trial Europe) also predicted early MACE due to microcirculatory disturbances (636). However, because of the complexity in the interpretation of CVR, pressure-derived FFR is the preferred measurement for lesion assessment and outcome of PCI. Coronary physiologic measurements associated with major clinical outcomes are supported by numerous studies (Table 23) (632,637).

Strong correlations exist between myocardial stress testing and FFR or CVR (633,638-649). An FFR of less than 0.75 identified physiologically significant stenoses associated with inducible myocardial ischemia with high sensitivity (88%), specificity (100%), positive predicted value (100%), and overall accuracy (93%). An abnormal CVR (less than 2.0) corresponded to reversible myocardial perfusion imaging defects with high sensitivity (86% to 92%), specificity (89% to 100%), predictive accuracy (89% to 96%), and positive and negative predictive values (84% to 100% and 77% to 95%, respectively).

The clinical outcomes of deferring coronary intervention for intermediate stenoses with normal physiology are remarkably consistent, with clinical event rates of less than 10% over a 2-year follow-up period (639,647-651). Bech et al. (649) studied 325 patients with intermediate coronary stenosis without documented myocardial ischemia and randomly assigned those with FFR greater than 0.75 to a deferral group of 91 patients or a performance group of 90 patients. PTCA was performed as planned in 144 patients with FFR less than 0.75. At clinical follow-up of 1, 3, 6, 12, and 24 months, event-free survival was similar between the deferral and performance groups (92% vs 89% at 12 months and 89% vs 83% at 24 months). However, these rates were significantly lower in the reference (PTCA) group (80% at 12 months and 78% at 24 months). The percentage of patients free from angina was similar between the deferral and the performance group at 12 and 24 months, but there was a significantly higher incidence of angina in the refer-

Table 23. Catheter-Based Anatomic and Physiological Criteria Associated With Clinical Outcomes

Application	IVUS	CVR	rCVR	FFR
Ischemia detection	Less than 3 to 4 mm^2	Less than 2.0	Less than 0.8	Less than 0.75
Deferred angioplasty	NA	Greater than 2.0	NA	Greater than 0.75
End point of stenting	Greater than 9 mm^2 Greater than 80% reference area, full apposition (depending on vessel size and volume plus morphology of plaque in target-vessel segment)			Greater than 0.94 (depending on diffuse disease in persistent segment)

CVR indicates coronary flow velocity reserve; FFR, fractional flow reserve; IVUS, intravascular ultrasound; NA, not applicable; and rCVR, relative coronary flow velocity.
Modified with permission from Kern. Circulation 2000;101:1344-51 (637).

ence group (67% vs 50% at 12 months and 80% vs 50% at 24 months). These data indicated that in patients with coronary stenosis without evidence of ischemia, coronary pressure–derived FFR identifies those patients who will benefit from PCI as well as those who will not.

FFR after stenting predicts adverse cardiac events at follow-up. Pijls et al. (648) examined 750 patients with postprocedural FFR and related these findings to MACE at 6 months. In 76 patients (10.2%), 1 adverse event occurred. Five patients died, 19 experienced MI, and 52 underwent at least 1 repeat target-vessel revascularization. Fractional flow reserve immediately after stenting was an independent variable related to all types of events. In 36% of patients, FFR normalized (greater than 0.95) with an event rate of 5%. In 32% of patients with poststenting FFR between 0.90 and 0.95, the event rate was 6%. In the remaining 32% with FFR less than 0.90, event rates were 20%. In 6% of patients with FFR less than 0.80, the event rate was 30% (Table 23) (637). FFR after stenting is a strong predictor of outcome at 6 months. These data suggest that both edge stent subnormalization and diffuse disease are associated with worse long-term outcome.

6. MANAGEMENT OF PATIENTS UNDERGOING PCI

6.1. Evolution of Technologies

The introduction of coronary stents and other devices has broadened the scope of patients who can be approached by PCI beyond those who could be safely treated by PTCA alone. Coronary stenting has become the dominant final therapy in patients undergoing PCI. The NHLBI registry, which collects sampling of unselected patients from 15 medium- to large-volume institutions, shows increasing use of stenting over the past 5 years. In the most recent wave of this registry, 83.6% of PCI patients received stents, and stents were placed in 79.4% of all lesions treated. Stenting has been more successful than balloon angioplasty in mid-sized coronary lesions, chronic total occlusions (652,653), and SVGs (562). Directional coronary atherectomy has been used successfully in proximal anterior descending lesions and bifurcation lesions (638). Rotational atherectomy successfully treats calcific and diffusely diseased coronary vessels (654) and ostial stenoses (655,656). Excimer laser has been used to treat diffuse disease (657). Vascular brachytherapy has been successful in treating restenosis occurring within stents (92,658,659). Other adjunctive therapies for ISR have shown mixed results. The cutting balloon has been used successfully; however, a recent trial did not show superiority for the cutting balloon compared with the normal balloon (95). Rotary ablation, excimer laser, and restenting have also been used for ISR; however, there are no data to indicate that these methods are better than balloon angioplasty.

Intracoronary brachytherapy with both gamma and beta radiation sources has been effective in treatment of ISR, and both radiation sources were approved by the FDA as therapy approved specifically for ISR (92,658-660).

Beta-radiation systems have been used most widely, resulting in an approximately 50% reduction in the need for reintervention over the 9 months after the procedure (92,659). In-stent restenosis is now significantly less than in prior years, but even with drug-eluting stenting, the problem still exists. Early observation of the use of DES to treat ISR has shown mixed results. Studies are currently under way comparing placement of DES to brachytherapy for ISR. Results of those trials are not available at this time.

6.1.1. Acute Results

Class I

It is recommended that distal embolic protection devices be used when technically feasible in patients undergoing PCI to saphenous vein grafts. ***(Level of Evidence: B)***

Historically, one of the important limitations of balloon angioplasty has been its high rate of abrupt closure (4% to 7%) and less than optimal acute angiographic result (30% residual diameter stenosis, with frequent evidence of dissections). Significant reductions in acute complication rates for PTCA have resulted from the wide use of stenting, which has been shown to reduce abrupt closure and periprocedural emergency surgery rates. Improved acute outcomes in terms of reduced target-lesion residual diameter stenosis have also been seen with the use of coronary stents, directional coronary atherectomy, and other adjunctive therapies. The GuardWire distal protection device, as studied in the SAFER (Saphenous vein graft Angioplasty Free of Emboli Randomized) trial, has reduced the incidence of MI in patients treated for SVG lesions (255), and the FilterWire was shown not to be inferior to the GuardWire in the FIRE (FilterWire EX Randomized Evaluation) trial (254) (see Section 5.5.2.). However, "embolic" protection devices have not shown a similar benefit in the setting of primary PCI for STEMI, as noted in the EMERALD (Enhanced Myocardial Efficacy and Recovery by Aspiration of Liberated Debris) trial (GuardWire), in which distal protection did not convey significant benefit (661). Thus, the use of distal embolic protection devices for STEMI patients undergoing PCI requires further evaluation (253,661).

6.1.2. Late-Term Results

PCI devices, especially coronary stents, offer the possibility of lower restenosis than with PTCA in the native coronary circulation. Lower restenosis rates have been demonstrated for balloon-expandable stents in large (3 mm) native coronary arteries (80,83) and in saphenous vein lesions (562).

The use of stents in smaller arteries has shown mixed results. Use of stenting in the treatment of chronic total occlusions has been superior to balloon angioplasty alone (652,653). The use of vascular brachytherapy has been shown to reduce restenosis rates and improve clinical outcomes in patients with ISR (92,658,660).

Directional coronary atherectomy, when applied aggressively, produces a larger lumen and has been associated with a lower angiographic restenosis rate (85). Despite the improvement in acute results seen for rotational atherectomy and excimer laser, there is no evidence that these devices improve late outcomes in lesions that can be safely treated with balloon angioplasty or stenting alone (662-664).

6.2. Antiplatelet and Antithrombotic Adjunctive Therapies for PCI

6.2.1. Oral Antiplatelet Therapy

Class I

1. **Patients already taking daily chronic aspirin therapy should take 75 to 325 mg of aspirin before the PCI procedure is performed.** ***(Level of Evidence: A)***
2. **Patients not already taking daily chronic aspirin therapy should be given 300 to 325 mg of aspirin at least 2 hours and preferably 24 hours before the PCI procedure is performed.** ***(Level of Evidence: C)***
3. **After the PCI procedure, in patients with neither aspirin resistance, allergy, nor increased risk of bleeding, aspirin 325 mg daily should be given for at least 1 month after bare-metal stent implantation, 3 months after sirolimus-eluting stent implantation, and 6 months after paclitaxel-eluting stent implantation, after which daily chronic aspirin use should be continued indefinitely at a dose of 75 to 162 mg.** ***(Level of Evidence: B)***
4. **A loading dose of clopidogrel should be administered before PCI is performed.** ***(Level of Evidence: A)*** **An oral loading dose of 300 mg, administered at least 6 hours before the procedure, has the best established evidence of efficacy.** ***(Level of Evidence: B)***
5. **In patients who have undergone PCI, clopidogrel 75 mg daily should be given for at least 1 month after bare-metal stent implantation (unless the patient is at increased risk of bleeding; then it should be given for a minimum of 2 weeks), 3 months after sirolimus stent implantation, and 6 months after paclitaxel stent implantation, and ideally up to 12 months in patients who are not at high risk of bleeding.** ***(Level of Evidence: B)***

Class IIa

1. **If clopidogrel is given at the time of procedure, supplementation with GP IIb/IIIa receptor antagonists can be beneficial to facilitate earlier platelet inhibition than with clopidogrel alone.** ***(Level of Evidence: B)***
2. **For patients with an absolute contraindication to aspirin, it is reasonable to give a 300-mg loading dose of clopidogrel, administered at least 6 hours before PCI, and/or GP IIb/IIIa antagonists, administered at the time of PCI.** ***(Level of Evidence: C)***
3. **When a loading dose of clopidogrel is administered, a regimen of greater than 300 mg is reasonable to achieve higher levels of antiplatelet activity more rapidly, but the efficacy and safety compared with a 300-mg loading dose are less established.** ***(Level of Evidence: C)***
4. **It is reasonable that patients undergoing brachytherapy be given daily clopidogrel 75 mg indefinitely and daily aspirin 75 to 325 mg indefinitely unless there is significant risk for bleeding.** ***(Level of Evidence: C)***

Class IIb

In patients in whom subacute thrombosis may be catastrophic or lethal (unprotected left main, bifurcating left main, or last patent coronary vessel), platelet aggregation studies may be considered and the dose of clopidogrel increased to 150 mg per day if less than 50% inhibition of platelet aggregation is demonstrated. ***(Level of Evidence: C)***

Aspirin reduces the frequency of ischemic complications after PCI. Although the minimum effective aspirin dosage in the setting of PCI has not been established, for those patients not already taking chronic aspirin therapy (75 to 162 mg per day), an empiric dose of aspirin (300 to 325 mg) given at least 2 h and preferably 24 h before the PCI procedure is generally recommended (665-668). Although other antiplatelet agents have antiplatelet effects similar to aspirin (669), only the thienopyridine derivatives (670) ticlopidine and clopidogrel have been used routinely as alternative antiplatelet agents in aspirin-sensitive patients during coronary angioplasty. Glycoprotein IIb/IIIa antagonists might also be substituted for aspirin before PCI. However, aspirin desensitization can be performed safely in selected patients (671,672). A strategy of pretreatment with clopidogrel in patients who have not already had their coronary anatomy defined is controversial, because patients who undergo CABG within 5 to 7 days of clopidogrel treatment have an increased risk of bleeding (665,673).

Clopidogrel and ticlopidine have similar side effects, which include gastrointestinal distress (20%), cutaneous rashes (4.8% to 15%), and abnormal liver function tests (674). Severe neutropenia has been reported to occur in approximately 1% of patients taking ticlopidine (674,675). Rare (less than 1:1000) but fatal episodes of thrombotic thrombocytopenic purpura have also been reported (676-678). Patients receiving ticlopidine should be monitored for the occurrence of this untoward sequela. A shorter duration (10 to 14 days) of ticlopidine therapy may reduce untoward side effects of therapy while maintaining therapeutic efficacy (679). For these reasons, clopidogrel has become the preferred thienopyridine for patients undergoing PCI. Available data show that approximately 4% to 30% of patients treated with conventional doses of clopidogrel do not display adequate platelet response (680). Preliminary data suggests that clopidogrel "nonresponders" may be at higher risk for thrombotic events. Thus, in patients in whom stent thrombosis may be catastrophic or lethal (ULM, bifurcating left main, and last patent coronary vessel), platelet aggregation studies may be considered and the dose of clopidogrel increased to 150 mg per day if less than 50% inhibition of platelet aggregation is demonstrated.

Before the advent of potent combination antiplatelet therapy in recent years, enthusiasm for stenting during MI (with or without ST elevation) or UA was tempered by the sudden and often unpredictable occurrence of subacute stent thrombosis, which developed in 3.5% to 8.6% of stent-treated patients (80,83,681,682). Anatomic factors (e.g., underdilation of the stent, proximal and distal dissections, poor inflow or outflow obstruction, less than 3-mm vessel diameter) were believed to predispose some patients to the occurrence of subacute stent thrombosis (612,683,684). With the advancements in PCI technology and adjunctive antiplatelet therapy (aspirin plus thienopyridine) after PCI, the incidence of stent thrombosis is now approximately 1% (685,686). The potential risk of stent occlusion should be considered when discontinuation of antiplatelet therapy is contemplated in patients undergoing stent implantation (687,688).

The efficacy of combination antiplatelet therapy in patients undergoing urgent and elective stent implantation has been shown by the Intracoronary Stenting and Antithrombotic Regimen (ISAR) trial of 517 patients treated with BMS for MI, suboptimal angioplasty, or other high-risk clinical and anatomic features. Patients were randomly assigned to treatment with aspirin plus ticlopidine or aspirin, intravenous heparin, and phenprocoumon after successful stent placement (689). The primary end point of cardiac death, MI, coronary bypass surgery, or repeat angioplasty occurred in 1.5% of patients assigned to antiplatelet therapy and 6.2% of those assigned to anticoagulant therapy (relative risk 0.25; 95% CI 0.06 to 0.77) (689).

In the STARS trial (619), the efficacy of aspirin (325 mg daily), the combination of aspirin (325 mg daily) plus ticlopidine (500 mg daily for 1 month), and aspirin (325 mg daily) plus warfarin on ischemic end points at 30 days in 1653 in low-risk patients after optimal BMS placement demonstrated more adverse events in patients not receiving ticlopidine as part of the therapeutic regimen. The primary 30-day composite end point of death, target-lesion revascularization, subacute thrombosis, or MI was 3.6% in patients assigned to aspirin only, 2.7% in those assigned to aspirin plus warfarin, and 0.5% in those assigned to aspirin plus ticlopidine (aspirin plus ticlopidine vs aspirin alone, *P* less than 0.001; aspirin plus ticlopidine vs aspirin plus warfarin, *P* equals 0.014) (619). Pretreatment with ticlopidine without a loading dose for more than 72 h may allow more effective inhibition of platelet activation than shorter durations of therapy (691,692).

In the CURE (Clopidogrel in Unstable angina to prevent Recurrent Events) trial, the effects of clopidogrel in addition to aspirin were tested in 12 562 patients with non–ST-elevation acute coronary syndromes with either positive biomarkers of myocardial injury or new ECG changes (665). The patients were randomized to receive an immediate 300-mg loading dose of clopidogrel in the emergency room followed by 75 mg a day for 1 year or to a matching placebo.

The primary end points of MI, stroke, and cardiovascular death from randomization to 1 year were reported. There was a 20% RRR in the primary outcome of MI, stroke, or cardiovascular death, a highly significant result at 12 months in patients treated with clopidogrel. The most pronounced benefit was observed in the reduction of MIs, with the largest reductions of 40% in Q-wave or ST-elevation MI, also statistically significant. In parallel with the reduction in large MI was a 43% reduction in the use of fibrinolytic therapy after randomization and an 18% reduction in radiologically confirmed HF, both of which reached statistical significance. In PCI CLARITY, patients treated with fibrinolysis for STEMI who underwent PCI 2 to 8 days after receiving a 300 mg loading dose of clopidogrel, had reduced incidence of CV death or ischemic complications when compared to those receiving 300 mg clopidogrel immediately prior to PCI (665a). In another trial (ISAR-REACT [Intracoronary Stenting and Antithrombotic Regimen-Rapid Early Action for Coronary Treatment]), a higher loading dose of clopidogrel (600 mg) was used before elective, low-risk stent procedures with favorable results compared with routine abciximab administration (693). However, the sample size was such that it may have been underpowered to show a benefit of abciximab administration in low-risk populations.

After PCI with BMS implantation, short term (at least 1 month) clopidogrel therapy in addition to aspirin leads to greater protection from thrombotic complications than aspirin alone. The benefits of long-term treatment with clopidogrel after PCI and the benefit of initiating pretreatment with clopidogrel with a preprocedural loading dose in addition to aspirin therapy were tested in CREDO (Clopidogrel for the Reduction of Events During Observation), a randomized, double-blind, controlled trial of early and sustained dual oral antiplatelet therapy after PCI (666). In this trial of 2116 patients undergoing PCI from 99 North American centers, the patients received either a 300-mg loading dose of clopidogrel (n equals 1053) or placebo (no loading dose; n equals 1063) 3 to 24 h before PCI. All patients thereafter received clopidogrel 75 mg daily through day 28. For the following 12 months, patients in the loading dose group received clopidogrel and those in the control group received placebo. All patients received aspirin (325 mg per day through day 28, 81 to 325 mg daily thereafter) throughout the study. At 1 year, long-term clopidogrel therapy was associated with a 27% RRR in the combined risk of death, MI, or stroke for an absolute reduction of 3% (*P* equals 0.02). Clopidogrel pretreatment did not significantly reduce MACE at 28 days. However, in a prespecified subgroup analysis, the patients who received clopidogrel at least 6 h before PCI had a RRR of 39% (*P* equals 0.051) for the combined end point compared with no reduction with treatment less than 6 h before PCI. Major bleeding risk at 1 year increased but not significantly (8.8% with clopidogrel vs 6.7% with placebo, *P* equals 0.07). These data suggest that after PCI, long-term clopidogrel therapy (1 year) significantly reduced the risk of adverse ischemic events. A 300-mg loading dose of clopidogrel given at least 3 h before the procedure did not reduce events at 28 days, but longer intervals between the loading dose and PCI appeared to be associated with a highly favorable trend toward reduced events.

Importantly, the CREDO trial did not have a control group that was given a loading dose at the time of the procedure.

The effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing PCI was also evaluated in the PCI CURE study (667). The PCI CURE study examined 2658 patients with non–ST-elevation acute coronary syndromes undergoing PCI assigned randomly to double-blind treatment with clopidogrel (n equals 1313) or placebo (n equals 1345). The patients were pretreated with aspirin and the study drug for 6 days before PCI during initial hospital admission and for 10 days overall. After PCI, 80% of patients in both groups received open-label clopidogrel for 4 weeks, after which the study drug was restarted for a mean of 8 months. Fifty-nine patients (4.5% in the clopidogrel group) experienced the primary end point of cardiovascular death, MI, or urgent target-lesion revascularization within 30 days compared with 6.4% in the placebo group (*P* equals 0.03). Long-term clopidogrel administration after PCI conferred a lower rate of cardiovascular death, MI, or any revascularization (*P* equals 0.03) and cardiovascular death or MI (*P* equals 0.047). Including events before and after PCI, there was an overall reduction of 31% in cardiovascular death and MI (*P* equals 0.002).

The use of clopidogrel in patients with diabetes had especially favorable results. The CAPRIE (Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events) trial showed a 9% RRR that favored clopidogrel versus aspirin for cardiovascular events. A subgroup analysis in patients who had prior cardiac surgery and who had been randomized to clopidogrel revealed a significant reduction in risk of MI, stroke, and cardiovascular death compared with those taking aspirin. In patients with diabetes in the CAPRIE substudy, the benefit of clopidogrel appeared larger compared with aspirin alone, especially in those who required insulin (694). Tabulation of the number of adverse events prevented per 1000 patients treated for 1 year with clopidogrel compared with aspirin revealed 9 events prevented in the patients without diabetes, with 21 events in all patients with diabetes and 38 in insulin-requiring patients with diabetes.

Further trials are needed to identify the optimum loading dose and timing of clopidogrel administration before PCI. A strategy of administering a 300-mg loading dose 6 h before PCI has the best established evidence of efficacy (666). Higher loading doses increase the magnitude and speed of inhibition of platelet aggregation; however, no large-scale randomized trials have been conducted to date comparing the efficacy and safety of different loading doses of clopidogrel. Furthermore, an important consideration in the decision for pretreatment is the increased risk of bleeding in patients managed with CABG. The ARMYDA-2 trial (Antiplatelet therapy for the Reduction of MYocardial Damage during Angioplasty) is a randomized, prospective, double-blind study of patients with stable angina or UA/NSTEMI and indications for coronary angiography. In this trial, 126 patients were randomized to a 600-mg loading dose and 129 patients to a 300-mg loading dose 4 to 8 h before PCI. The primary end point of death, MI (defined as CK-MB greater than 3 times the upper limit of normal), or target-vessel revascularization up to 30 days after the procedure occurred in 4% of patients in the 600-mg loading dose group and 12% in the 300-mg loading dose group (*P* equals 0.041) owing to a reduction in periprocedural MI. This was a small study of relatively low-risk patients, with only a few patients receiving IIb/IIIa inhibitors. Thus, whether the results would also apply to higher-risk patients taking IIb/IIIa blockers is unknown (695). Some insights may be derived from the CLEAR PLATELETS study (Clopidogrel Loading With Eptifibatide to Arrest the Reactivity of Platelets), which evaluated a 300-mg and 600-mg clopidogrel loading dose with or without eptifibatide in 120 patients undergoing elective stenting procedures. Clopidogrel was administered immediately after stenting. Aggregometry and flow cytometry were used to assess platelet reactivity. The authors concluded that a strategy of eptifibatide administration was associated with superior platelet inhibition and lower cardiac biomarker release than high-dose (600 mg) or standard-dose (300 mg) clopidogrel at the time of PCI (696). Further study is needed to determine the relationship of platelet reactivity to clinical outcomes such as bleeding, myocardial necrosis, and stent thrombosis, which could not be derived from this small, pharmacodynamic study.

Continuation of combination treatment with aspirin and clopidogrel after PCI appears to reduce rates of cardiovascular ischemic events (666,667,697,698). On the basis of randomized clinical trial protocols, aspirin 325 mg daily should be given for at least 1 month after BMS implantation (unless there is a risk of bleeding, in which case it should be given for 2 weeks), 3 months after SES implantation, and 6 months after paclitaxel-eluting stent (PES) implantation, after which daily chronic aspirin should be continued indefinitely at a dose of 75 to 162 mg. Likewise, clopidogrel 75 mg daily should be given for at least 1 month after BMS implantation, 3 months after SES implantation, and 6 months after PES implantation and ideally up to 12 months in patients who are not at high risk of bleeding. To reduce the incidence of bleeding complications associated with dual antiplatelet therapy, lower-dose aspirin (75 to 162 mg daily) is recommended for long-term therapy (665).

6.2.2. Glycoprotein IIb/IIIa Inhibitors

Class I

In patients with UA/NSTEMI undergoing PCI without clopidogrel administration, a GP IIb/IIIa inhibitor (abciximab, eptifibatide, or tirofiban) should be administered. ***(Level of Evidence: A)****

Class IIa

1. **In patients with UA/NSTEMI undergoing PCI with clopidogrel administration, it is reasonable to administer a GP IIb/IIIa inhibitor (abciximab, eptifibatide, or tirofiban).** ***(Level of Evidence: B)****
2. **In patients with STEMI undergoing PCI, it is reasonable to administer abciximab as early as possible.**

(Level of Evidence: B)

3. **In patients undergoing elective PCI with stent placement, it is reasonable to administer a GP IIb/IIIa inhibitor (abciximab, eptifibatide, or tirofiban).** ***(Level of Evidence: B)***

Class IIb

In patients with STEMI undergoing PCI, treatment with eptifibatide or tirofiban may be considered. ***(Level of Evidence: C)***

*It is acceptable to administer the GP IIb/IIIa inhibitor before performance of the diagnostic angiogram ("upstream treatment") or just before PCI ("in-lab treatment").

Aspirin is only a partial inhibitor of platelet aggregation (699,700), because it affects only cyclooxygenase, thereby preventing the formation of thromboxane A_2. Functionally active GP IIb/IIIa receptors aggregate platelets through fibrin bound at the receptor sites. These receptors are activated by a variety of agonists, including thromboxane A_2, serotonin, adenosine diphosphate, and collagen, among others. The binding of fibrinogen and other adhesive proteins to adjacent platelets by means of the GP IIb/IIIa receptor serves as the "final common pathway" of platelet-thrombus formation and can be effectively attenuated by GP IIb/IIIa antagonists. These agents have reduced the frequency of ischemic complications after coronary angioplasty. Individual studies evaluating the impact of intravenous GP IIb/IIIa receptor antagonists on survival for patients undergoing PCI have not had adequate power to examine a difference in mortality. Two meta-analyses of GP IIb/IIIa trials (abciximab, eptifibatide, and tirofiban) have been performed to examine this potential benefit. In 1 meta-analysis involving 12 trials of 20 186 patients, overall 30-day mortality was significantly reduced by GP IIb/IIIa inhibition, although no individual trial showed a mortality benefit. At 6 months, the survival benefit was not significant. The trials included in this analysis encompassed a range of patient characteristics (e.g., UA, NSTEMI, and STEMI), therapeutic regimens (e.g., elective PCI, primary PCI), and adjunctive drugs. In another meta-analysis, which involved 19 trials of 20 137 patients, 30-day and 6-month mortality were both significantly reduced for those receiving IIb/IIIa receptor antagonists (Tables 24a and 24b) (64,111,112,191,195,198,200,201,442,443,701-717). Thus, patients undergoing PCI can expect a lower 30-day mortality when GP IIb/IIIa therapy is utilized. The RRR appears to be similar in trials of patients with or without acute MI and for trials using stents or another PCI as the intended primary procedure. Similar reductions in nonfatal MI are seen in association with the use of GP IIb/IIIa receptor antagonists.

There is no consistent evidence that the GP IIb/IIIa inhibitors reduce the frequency of late restenosis in patients without diabetes. In EPISTENT, patients with diabetes who received abciximab therapy in conjunction with stent deployment had a 51% reduction in target-vessel revascularization at 6 months (230,718). This trial is the only one that has shown a reduction in target-vessel revascularization in the diabetic group.

A long-term mortality benefit of abciximab in patients with diabetes undergoing PCI was demonstrated in a pooled analysis of 3 trials (EPIC, EPILOG, and EPISTENT; 4.5% vs 2.5%, *P* equals 0.03) (718). A meta-analysis showed that the 30-day mortality benefit in patients with diabetes in the setting of UA/NSTEMI was greater in patients undergoing PCI (719).

In a meta-analysis of invasive versus conservative therapy of patients with UA/NSTEMI, men demonstrated a clear survival advantage with routine invasive therapy with GP IIb/IIIa inhibitors and intracoronary stents; however, with similar therapy, the results for women were not improved significantly (205).

On the basis of the numerous trials to date, intravenous GP IIb/IIIa receptor inhibitors should be considered in patients undergoing PCI, particularly those with UA/NSTEMI or with other clinical characteristics of high risk (Table 25). Detailed discussion of the trials applicable to UA/NSTEMI and STEMI patients can be found in the respective ACC/AHA guidelines (332,493).

6.2.2.1. Abciximab

Trials of GP IIb/IIIa inhibitors have utilized different definitions for adjuncting end points. These should be considered when the results are evaluated.

The clinical safety and efficacy of abciximab have been evaluated extensively in many randomized trials of patients with acute coronary syndromes with and without high-risk clinical features. These studies include EPIC (Evaluation of 7E3 for the Prevention of Ischemic Complications) (704), EPILOG (Evaluation of Percutaneous transluminal coronary angioplasty to Improve Long-term Outcome with abciximab GP IIb/IIIA blockade) (705), and EPISTENT (Evaluation of Platelet IIb/IIIa Inhibition in STENTing) (111). Despite early problems with excessive bleeding when weight-adjusted heparin dosing was not employed, abciximab was superior to placebo in all settings for reducing MACE.

ISAR-REACT randomly compared abciximab (n equals 1079) versus placebo (n equals 1080) in low-risk PCI patients pretreated with high-dose clopidogrel (600 mg orally) 2 h before the procedure, then with 75 mg BID for 3 days followed by 75 mg per day for 3 months (693). At 30 days, there was no difference between the groups. Thus, in that trial of low-risk patients having elective PCI, there was no benefit to the use of abciximab in patients receiving high-dose pretreatment with clopidogrel. The sample size was such that it may have been underpowered to show a benefit in low-risk populations (693).

Heeschen et al. (192), for the CAPTURE (Chimeric c7E3 AntiPlatelet Therapy in Unstable angina REfractory to standard treatment) investigators, demonstrated that troponin T, but not C-reactive protein, was predictive of cardiac risk during the initial 72-h period in the treatment of UA patients with standard therapy or with abciximab. Hamm et al. (193),

Table 24a. Eligible Trials of Intravenous Glycoprotein IIb/IIIa Inhibitors Used in Evaluation of Mortality After PCI

Trial (Reference)	n	PCI	AMI, % (Time)	Post-PCI Heparin	Male, %	Mean Age, y	Past Medical History, % DM	HTN	MI	PCI	CABG
Abciximab											
RAPPORT (443)	483	PTCA or DCA	100 (less than 12 h)	Yes	72	61	22	48	19	14	
ADMIRAL (442)	300	Stenting	100 (less than 12 h)	Yes	82	61	18	38	11	14	12
CADILLAC (64)	2082	PTCA/stenting	100 (less than 12 h)	No	73	60	17	48	14	11	2
EPIC (702-704)	2099	PTCA or DCA	30 (less than 12 h)	Yes	72	61	24	55	38	22	15
EPILOG (705,706)	2792	PTCA or DCA	0	No	72	60	23	ND	27	ND	13
EPISTENT (111,112,191)	1603	Stenting	0	No	75	59	20	53	51	ND	9
CAPTURE (195)	1266	PTCA	0	Yes	73	61	14	42	40	13	3
ERASER (280)	225	Stenting	Negligible*	No	79	59	14	50	ND	14	ND
Petronio et al. (708)	89	PTCA	100 (less than 24 h)	No	65	60	18	ND	10	ND	1
Simoons et al. (710)	60	PTCA	0	No	73	61	ND	ND	42	15	4
Kini et al. (711)	100	HSRA	0	No	75	64	26	44	18	ND	15
Tamburino et al. (712)	107	Stenting	0	No	87	62	27	34	67	ND	ND
ISAR-2 (707)	401	Stenting	100	Yes	76	60	15	64	ND	7	4
Eptifibatide											
IMPACT (713)	150	PTCA or DCA	0	Yes	75	61	21	53	43	39	17
IMPACT-II (198)	4010	Various†	3 (less than 24 h)	No	75	61	23	54	41	30	16
ESPRIT (200,201)	2064	Stenting	0	No	73	62	20	59	32	23	10
Harrington et al. 73 (714)		Various†	0	No	75	60	29	68	45	ND	26
Tirofiban											
RESTORE (715,716)	2141	PTCA or DCA	32 (less than 72 h)	No	72	59	20	55	34	21	7
Kereiakis et al. (717)	93	PTCA	0	Yes	82	59	24	53	47	23	15

AMI indicates acute MI; CABG, coronary artery bypass graft surgery; DCA, directional coronary atherectomy; DM, diabetes mellitus; h, hour; HSRA, high-speed rotational atherectomy; HTN, hypertension; MI, myocardial infarction; n, number of patients; ND, no data; PCI, percutaneous coronary intervention (originally intended procedure[s] in each trial); PTCA, percutaneous transluminal coronary angioplasty; and y, year. For expansion of study names, see corresponding reference.

*14% of patients had unstable angina or AMI within less than 48 h.

†PTCA, DCA, and HSRA (also excimer laser in IMPACT-II).

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Table 24b. Subgroup Analyses for Mortality After PCI in Trials of Glycoprotein IIb/IIIa Inhibitors (See Table 24a for eligible trials)

	30 Days		**6 Months**	
	No. of Studies 20 (20 137)*	**RR (95% CI) 0.69 (0.53 to 0.90)***	**No. of Studies 14 (15 651)***	**RR (95% CI) 0.79 (0.64 to 0.97)***
Population				
AMI	6 (3355)	0.69 (0.45 to 1.05)	6 (3355)	0.76 (0.55 to 1.05)
Mixed	2 (4240)	0.95 (0.54 to 1.68)	2 (4240)	0.97 (0.65 to 1.44)
Non-AMI	12 (12 542)	0.59 (0.39 to 0.89)	6 (8056)	0.71 (0.49 to 1.03)
Procedure				
Stent	7 (5736)	0.69 (0.43 to 1.09)	7 (5736)	0.70 (0.49 to 1.01)
Other	13 (14 401)	0.70 (0.51 to 0.96)	7 (9915)	0.84 (0.65 to 1.09)
Postprocedure				
Heparin	7 (4791)	0.72 (0.47 to 1.09)	5 (4548)	0.83 (0.60 to 1.13)
No heparin	13 (15 346)	0.68 (0.49 to 0.95)	9 (11 103)	0.77 (0.58 to 1.01)
Agent				
Abciximab	14 (11 606)	0.69 (0.51 to 0.94)	12 (11 446)	0.77 (0.61 to 0.96)
Tirofiban	2 (2234)	1.05 (0.42 to 2.61)	1 (2141)	1.27 (0.65 to 2.48)
Eptifibatide	4 (6297)	0.60 (0.33 to 1.06)	1 (2064)	0.56 (0.24 to 1.34)

AMI indicates acute myocardial infarction; CI, confidence interval; No., number; and RR, risk ratio (fixed effects).
There was no statistically significant heterogeneity in any case, and random effects estimates were similar (data not shown).
*Refers to all patients.
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for the CAPTURE investigators, also reported that among the 1265 patients with UA enrolled in the CAPTURE trial, troponin T and CK-MB from 890 patients correlated with subsequent 6-month adverse cardiac risk. In patients without elevated troponin T levels, there was no benefit of treatment with respect to the relative risk of death or MI at 6 months (OR 1.26, CI 95% 0.74 to 2.31; *P* equals 0.47). Serum troponin T level, which is considered to be a surrogate marker for thrombus formation, identified a high-risk subgroup of patients with refractory UA suitable for coronary intervention who would particularly benefit from antiplatelet treatment with abciximab (192).

One putative limitation of abciximab is the potential for immune-mediated hypersensitivity reactions after subsequent readministration. Thrombocytopenia after readministration occurs in 3.5% to 6.3% of patients, which is similar to the rate of occurrence in patients receiving abciximab for the first time. Therefore, the absence of thrombocytopenia after a first abciximab exposure does not guarantee protection against its occurrence upon re-exposure. Moreover, the prevalence of severe thrombocytopenia (2.8%) and profound thrombocytopenia (2.0%) is greater with readministration than the incidence observed after first-time administration (1.0% and 0.4% for severe and profound thrombocytopenia, respectively) (202). With the first administration, human antichimeric antibodies (HACA) form in approximately 6% of patients (702). The implications of HACA, however, are unclear. Among 500 patients enrolled in the ReoPro Readministration Registry (R3), there were no cases of anaphylaxis or other allergic manifestations whether or not HACA was present, and HACA was not predictive of any other measure of complication or success. From the R3 study, HACA has been shown to be an IgG (not IgE) immunoglobulin that does not neutralize abciximab. The more worrisome clinical phenomenon associated with readministration is the potential for increased rates of thrombocytopenia. In the 500-patient R3, a 4.4% incidence in thrombocytopenia (to a platelet count of less than 100 × 109 per liter) was observed, with half of the patients developing acute profound thrombocytopenia (to a platelet count of less than 20 × 109 per liter). This potential complication should always be monitored when treating a patient with abciximab (194-197). Abciximab readministration poses greater risk within 2 weeks of original abciximab dose.

6.2.2.2. Eptifibatide

The clinical utility of eptifibatide, a short-acting cyclic heptapeptide that also inhibits the GP IIb/IIIa receptor, was evaluated in the Integrilin to Manage Platelet Aggregation to prevent Coronary Thrombosis-II (IMPACT-II) trial, a double-blind, randomized, placebo-controlled multicenter trial that enrolled 4010 patients undergoing coronary angioplasty (198). Patients were assigned to treatment with aspirin, heparin and placebo, aspirin, heparin, and eptifibatide bolus (135 mcg per kg) followed by a low-dose eptifibatide infu-

Table 25. Recommendations for Use of GP IIb/IIIa Inhibitors in Patients Undergoing PCI

UA/NSTEMI and Clopidogrel Used	UA/NSTEMI and Clopidogrel Not Used	STEMI	Elective PCI
Abciximab, eptifibatide, or tirofiban	Abciximab, eptifibatide, or or tirofiban	Abciximab	Abciximab, eptifibatide, or tirofiban
Class IIa; LOE: B	*Class I; LOE: A*	*Class IIa; LOE: B*	*Class IIa; LOE: B*
		Eptifibatide or tirofiban	
		Class IIb; LOE: C	

LOE indicates level of evidence; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; and UA/NSTEMI, unstable angina/non–ST-elevation myocardial infarction.

sion (0.5 mcg per kg per min for 20 to 24 h), or aspirin, heparin, and eptifibatide bolus (135 mcg per kg) and higher-dose infusion (0.75 mcg per kg per min for 20 to 24 h) (198). The 30-day composite primary end point of death, MI, unplanned surgical or repeat percutaneous revascularization, or coronary stent implantation for abrupt closure occurred in 11.4% of placebo-treated patients compared with 9.2% in the 135/0.5-mcg eptifibatide group (*P* equals 0.063) and 9.9% in the 135/0.75-mcg eptifibatide group (*P* equals 0.22) (198). The frequency of major bleeding events and transfusions was similar among the 3 groups.

A higher bolus and infusion of eptifibatide was evaluated in 10 948 patients with UA/NSTEMI who were assigned to treatment with placebo or 1 of 2 doses of eptifibatide: 180 mcg per kg bolus plus 1.3 mcg per kg per min infusion (180/1.3) or 180 mcg per kg bolus plus 2.0 mcg per kg per min infusion (180/2.0) (199). Compared with placebo, patients receiving 180/2.0-mcg eptifibatide had a lower frequency of 30-day death or MI (15.7% vs 14.2%; *P* equals 0.042). In patients undergoing early (less than 72 h) coronary intervention, 30-day composite events occurred less often in patients receiving 180/2.0-mcg eptifibatide (11.6% and 16.7% in placebo-treated patients; *P* equals 0.01) (200, 201).

The ESPRIT (Enhanced Suppression of the Platelet IIb/IIIa Receptor with Integrilin Therapy) trial evaluated the efficacy and safety of eptifibatide treatment as adjunctive therapy during nonemergency coronary stent implantation. A total of 2064 patients were enrolled from June 1999 to February 2000 in this multicenter, randomized, double-blind, parallel-group, placebo-controlled (crossover-permitted) clinical trial. A double-bolus regimen of eptifibatide (180 mcg per kg bolus followed by a 2.0 mcg per kg per min infusion, with a second 180 mcg per kg bolus given 10 min after the first bolus) was compared with placebo treatment. The 48-h primary composite end point of death, MI, urgent target-vessel revascularization, or bailout treatment with open-label GP IIb/IIIa inhibitor therapy was reduced 37% from 10.5% to 6.6% (*P* equals 0.0015). There was a consistent treatment benefit across all components of the end point and across all subgroups of patients. At 30 days, the key secondary composite end point of death, MI, and urgent target-vessel revascularization was also improved 35% from 10.4% to 6.8% (*P* equals 0.0034) (200,201).

6.2.2.3. Tirofiban

Tirofiban is a nonpeptidyl tyrosine derivative that produces a dose-dependent inhibition of GP IIb/IIIa–mediated platelet aggregation (720). The clinical effect of tirofiban during coronary angioplasty was evaluated in the Randomized Efficacy Study of Tirofiban for Outcomes and Restenosis (RESTORE) trial, a double-blind, placebo-controlled trial of 2139 patients with UA or acute MI defined by CK measured at the end of 36 h or at the time of discharge (715). Patients were randomly assigned to aspirin, heparin, and a tirofiban bolus (10 mcg per kg over 3 min) plus infusion (0.15 mcg per kg per minute), or to aspirin, heparin, and a placebo bolus plus infusion for 36 h. The primary end point of the trial was the occurrence of major events at 30-day, including death due to any cause, MI, coronary bypass surgery due to angioplasty failure or recurrent ischemia, repeat target-vessel angioplasty for recurrent ischemia, or insertion of a stent due to threatened abrupt closure (715). The rate of primary 30-day end point was reduced from 12.2% in the placebo group to 10.3% in the tirofiban group (*P* equals 0.160). Patients treated with tirofiban had a 38% relative reduction in the composite end point at 48 h (*P* less than 0.005) and a 27% relative reduction at 7 days (*P* equals 0.022). The incidence of major bleeding was similar in the 2 groups with the TIMI criteria (2.4% in tirofiban-treated patients and 2.1% in placebo-treated patients; *P* equals 0.662) (715), although major bleeding tended to be higher in tirofiban-treated patients (5.3% vs 3.7% in placebo-treated patients; *P* equals 0.096). Thrombocytopenia was similar in both groups (0.9% for the placebo group vs 1.1% for the tirofiban group; *P* equals 0.709) (721). A larger clinical benefit with tirofiban was seen in patients with UA undergoing coronary angioplasty in the PRISM-PLUS study, a randomized trial of 1570 patients with UA or non–Q-wave MI assigned to 48- to 108-h treatment with heparin plus tirofiban or heparin alone (722). Coronary angioplasty was performed in 30.5% of patients between 49 to 96 h after randomization (722). The composite end point of death, MI, or refractory ischemia was reduced significantly in the heparin plus tirofiban group compared with the heparin alone group (10.0% vs 15.7%; *P* less than 0.01) (722).

6.2.3. Antithrombotic Therapy

6.2.3.1. Unfractionated Heparin, Low-Molecular-Weight Heparin, and Bivalirudin

Class I

1. **Unfractionated heparin should be administered to patients undergoing PCI.** ***(Level of Evidence: C)***
2. **For patients with heparin-induced thrombocytopenia, it is recommended that bivalirudin or argatroban be used to replace heparin.** ***(Level of Evidence: B)***

Class IIa

1. **It is reasonable to use bivalirudin as an alternative to unfractionated heparin and glycoprotein IIb/IIIa antagonists in low-risk patients undergoing elective PCI.** ***(Level of Evidence: B)***
2. **Low-molecular-weight heparin is a reasonable alternative to unfractionated heparin in patients with UA/NSTEMI undergoing PCI.** ***(Level of Evidence: B)***

Class IIb

Low-molecular-weight heparin may be considered as an alternative to unfractionated heparin in patients with STEMI undergoing PCI. ***(Level of Evidence: B)***

Intravenous unfractionated heparin prevents clot formation at the site of arterial injury (723) and on coronary guidewires and catheters used for coronary angioplasty (724). Although the intensity of anticoagulation with unfractionated heparin is generally determined with activated partial thromboplastin times, these values are less useful for monitoring anticoagulation during coronary angioplasty, because higher levels of anticoagulation are needed than can be discriminated with the activated partial thromboplastin time alone. Instead, the activated clotting time (ACT) has been more useful to follow heparin therapy during coronary angioplasty (725). The Hemochron and HemoTec devices are commonly used to measure ACT values during coronary angioplasty (725-727). The Hemochron ACT generally exceeds the HemoTec ACT by 30 to 50 s, although considerable measurement variability exists.

Empiric recommendations regarding heparin dosage during coronary angioplasty have been proposed (728,729), but ACT levels after a fixed dose of unfractionated heparin may vary substantially due to differences in body size (730), concomitant use of other medications, including intravenous nitroglycerin (731,732), and in the presence of acute coronary syndromes that increase heparin resistance.

The relationship between the level of the ACT and development of ischemic complications during coronary angioplasty has been controversial. Whereas some studies have identified an inverse relationship between the initial ACT and the risk of ischemic events (733,734), others found either no relationship or a direct relationship between the degree of anticoagulation and occurrence of complications (735). It is generally believed that very high levels (ACTs greater than 400 to 600 s) of periprocedural anticoagulation are associated with an increased risk for bleeding complications (736).

The safety of low-dose heparin during coronary angioplasty has also been shown in a recent study. Fatal complications (0.3%), emergency bypass surgery (1.7%), MI (3.3%), or repeat angioplasty within 48 h (0.7%) were uncommon after an empiric bolus of heparin 5000 U at the beginning of the procedure (618). In a smaller randomized study of 400 patients assigned to fixed-dose heparin (15 000 international units [IU]) or weight-adjusted heparin (100 IU per kg), there were no differences in procedural success or bleeding complications between the 2 groups (737), although use of the weight-adjusted heparin resulted in earlier sheath removal and more rapid transfer to a step-down unit (737). Another advantage of weight-adjusted heparin dosing is that "overshooting" of the ACT value can be avoided.

Two analyses of ACT and PCI-related complications have not detected any relationship between ACT level and ischemic complications, which suggests that the degree of anticoagulation during PCI may be less of a factor in determining complications than in the earlier era of balloon angioplasty (738,739). The results of these limited studies suggest that heparin is an intraprocedural component for PCI, despite dosing uncertainties and an unpredictable therapeutic response with the unfractionated preparation. It appears that weight-adjusted heparin dosing may provide a clinically superior anticoagulation method to fixed heparin dosing, although definitive studies are lacking.

Routine use of unfractionated heparin after an uncomplicated coronary angioplasty is no longer recommended (72,740-743) and may be associated with more frequent bleeding events (72,740), particularly when platelet GP IIb/IIIa inhibitors are used (72,740). Subcutaneous administration of unfractionated heparin (741) may provide a safer and less costly means of extending antithrombin therapy than intravenous unfractionated heparin if there are clinical reasons to continue anticoagulation, such as residual thrombus or significant residual dissections.

In the SYNERGY (Superior Yield of the New strategy of Enoxaparin, Revascularization and Glycoprotein IIb/IIIa Inhibitors) study, patients with NSTEMI were randomized to treatment with either unfractionated heparin or subcutaneously administered enoxaparin. In patients who underwent PCI within 8 h of the last subcutaneous dose, no additional anticoagulation was administered. In those patients who underwent PCI 8 to 12 h after the last subcutaneous dose, an additional intravenous dose of enoxaparin 0.3 mg per kg was administered at the time of PCI. The rates of major ischemic complications in those patients undergoing PCI were similar between those treated with unfractionated heparin and those treated with enoxaparin (744). Bleeding was observed to be higher in those patients who "crossed over" from one anticoagulant to the other. Some of these crossover patients were those who received a different anticoagulant than what they had been randomized to and had received before. On the basis of this observation, it appears prudent to not give an additional anticoagulant to patients who are receiving one form of anticoagulant (e.g., not to give unfractionated heparin to those who have received subcutaneous enoxaparin within the last 12 h and not to give intravenous enoxaparin to those receiving intravenous heparin).

The safety and efficacy of low-molecular-weight heparin therapy in patients undergoing PCI has been evaluated. In all but 1 of these studies, the agent studied has been enoxaparin. These studies have found bleeding and ischemic complication rates to be low and comparable to those observed in PCI patients who had been treated with unfractionated heparin.

In those patients who have received subcutaneous enoxaparin for the treatment of NSTEMI and are to undergo PCI within 8 h of the last subcutaneous dose, no additional anticoagulant should be administered. In those who undergo PCI 8 to 12 h after the last subcutaneous dose, an additional intravenous dose of 0.3 mg per kg should be administered immediately before device activation.

Bivalirudin, a hirudin analog, is a direct thrombin inhibitor. It has been tested against heparin and a GP IIb/IIIa inhibitor in the REPLACE-2 trial of patients undergoing PCI without high-risk features. The primary end point at 30 days included major bleeding plus the usual end points of death, MI, and urgent revascularization. These events occurred in 9.2% of the bivalirudin group and 10% of the group given unfractionated heparin plus GP IIb/IIIa inhibitors (nonsignificant). The secondary end point was freedom from death, MI, and urgent revascularization and occurred in 7.6% of the bivalirudin group and 7.1% of the group given unfractionated heparin plus GP IIb/IIIa inhibitors (also nonsignificant), but bleeding (combined major and moderate bleeding) was significantly reduced in the bivalirudin group (from 7.1% to 2.4%, *P* less than 0.001). Although a small, nonsignificant increase in periprocedural NSTEMI was seen in the bivalirudin-treated patients, by 1 year mortality was not significantly increased in the bivalirudin group (1.89% vs 2.46 %) (744a). These results established that bivalirudin is not superior to standard therapy, but it appears to be a reasonable alternative in non-high-risk patients (745). Bivalirudin is a good anticoagulant for use in patients with heparin-induced thrombocytopenia and those with renal failure (746). Argatroban is also an effective therapy for heparin-induced thrombocytopenia (747). More data are needed to establish its use for patients with STEMI, NSTEMI, and diabetes.

6.2.3.2. Heparin Dosing Guidelines

In those patients who do not receive GP IIb/IIIa inhibitors, sufficient unfractionated heparin should be given during coronary angioplasty to achieve an ACT of 250 to 300 s with the HemoTec device and 300 to 350 s (200,201) with the Hemochron device. A weight-adjusted bolus heparin (70 to 100 IU per kg) can be used to avoid excess anticoagulation. If the target values for ACT are not achieved after a bolus of heparin, additional heparin boluses (2000 to 5000 IU) can be given. Early sheath removal should be performed when the ACT falls to less than 150 to 180 s.

The unfractionated heparin bolus should be reduced to 50 to 70 IU per kg when GP IIb/IIIa inhibitors are given in order to achieve a target ACT of 200 s with either the HemoTec or Hemochron device. The currently recommended target ACT for eptifibatide and tirofiban is less than 300 s during coronary angioplasty. Postprocedural heparin infusions are not recommended during GP IIb/IIIa therapy (748-750).

Transitioning of patients with acute coronary syndromes who have been treated with enoxaparin from the medical floor to the cardiac catheterization laboratory is based on pharmacokinetic data, clinical experience, and expert opinion. In patients who received the last subcutaneously administered dose of enoxaparin within 8 h, no additional anticoagulant therapy is needed before PCI is performed. In patients who received the last subcutaneously administered dose of enoxaparin between 8 and 12 h before PCI, an additional 0.3 mg per kg dose of enoxaparin should be administered intravenously before PCI (whether or not the patient is to be treated with a GP IIb/IIIa inhibitor). Alternatively, in the latter group of patients, supplemental anticoagulation with unfractionated heparin can be used. Unfractionated heparin 50 U per kg (with a target ACT of 200 to 250 s) may be administered in those patients to be treated with a GP IIb/IIIa inhibitor; 60 U per kg unfractionated heparin (with a target ACT of 250 to 300 s) may be administered in those patients who are not concomitantly treated with a GP IIb/IIIa inhibitor. A higher risk of bleeding may result if patients cross over between different anticoagulant therapies during the index admission.

Low-molecular-weight heparins have little effect on measurements of ACT. Therefore, the ACT should not be used as a guide to anticoagulation therapy in patients currently being treated with a low-molecular-weight heparin. Sheath removal when followed by manual groin compression may be performed 4 h after the last intravenous dose of enoxaparin or 6 to 8 h after the last subcutaneous dose of enoxaparin (751,752).

6.3. Post-PCI Management

After PCI, in-hospital care should focus on monitoring the patient for recurrent myocardial ischemia, achieving hemostasis at the catheter insertion site, detecting and preventing contrast-induced renal failure, and monitoring results of the vascular closure device, if used (753). Attention should also be directed toward implementing appropriate secondary atherosclerosis prevention programs. The patient should understand and adhere to recommended medical therapies and behavior modifications known to reduce subsequent morbidity and mortality from coronary heart disease.

Most patients can be safely discharged from the hospital within the next calendar day after an uncomplicated elective PCI. Special skilled nursing units have been developed by many institutions to facilitate post-PCI management. Specific protocols for sheath removal, continuation of anticoagulation or antiplatelet therapies, and observation for recurrent myocardial ischemia/infarction and contrast-induced renal failure are of particular assistance in ensuring appropriate outcomes during this period. Pilot studies suggest that selected patients may be discharged on the same day after PCI (754,755) especially when the procedure is performed by the percutaneous radial or brachial approach (756). However, confirmation by larger studies is necessary before widespread endorsement of this strategy.

In the prior setting of aggressive systemic anticoagulation, vascular complications may occur in as many as 14% of patients after PCI, but those requiring surgical repair occur in 3.5% (736) of patients, although lower rates of vascular complications can now be expected with reduced anticoagulation and smaller sheath sizes (757-762). Major factors associated with vascular complications include use of fibrinolytic or platelet inhibitor therapy, coexisting peripheral vascular disease, female gender, prolonged heparin use with delayed sheath removal, and older age (736,758,760-764). Although most bleeding complications at the vascular access site are obvious and readily managed, physicians and nurses should remain alert for retroperitoneal hematoma, the signs and symptoms of which may include hypotension, marked suprainguinal tenderness, and severe back or lower-quadrant abdominal pain (765). Post-PCI hematocrit should be monitored for a decrease greater than absolute 5% to 6%. Computed tomography can confirm the diagnosis of retroperitoneal hematoma, and more than 80% of patients can be treated conservatively with transfusions without surgery (764). Pseudoaneurysms may be treated effectively with ultrasound-directed compression in the majority of patients who are not bleeding and do not require continued anticoagulation (763,766,767). Arteriovenous fistulas, generally occurring late after a procedure, are detected by a continuous murmur over the puncture site and, in rare cases, may be associated with high-output failure. In general, repeat use of the access site should be avoided because of the possibility of making the fistula larger, accessing the vein when attempting to access the artery, and increasing potential issues with hemostasis. Both pseudoaneurysm and arteriovenous fistula can occur secondary to cannulation of the superficial rather than the common femoral artery (768). Arterial compression systems and percutaneous vascular closure devices reduce the incidence of vascular complications (753,756). A meta-analysis involving 37 000 patients undergoing diagnostic coronary arteriography and PCI compared manual compression with 3 closure devices (VasoSeal™, AngioSeal™, and PerClose™). No difference was seen in access-related complications between manual compression, PerClose™, and AngioSeal™; however, there were more complications associated with VasoSeal™ than with manual compression. The complications evaluated included pseudoaneurysm requiring ultrasound-guided compression or surgical repair; arteriovenous fistula; retroperitoneal hematoma causing hemodynamic compromise and necessitating surgery, blood transfusion, prolonged hospitalization, and/or death; femoral artery thrombosis (vessel occlusion requiring surgery or thrombolysis); surgical vascular repair; access-site infection necessitating treatment with antibiotics or surgical drainage; and blood transfusion. The study was performed with early generations of devices. Potential benefits of newer adjunctive therapies are not well established (753,769). However, the degree to which these technologies reduce length of hospital stay and cost remains to be determined (764,770-772).

Patients with pre-existing renal insufficiency, diabetes, and dehydration are at higher risk and should be monitored for contrast-induced nephropathy, generally defined as an increase of greater than 25% or greater than 0.5 mg per dL in serum creatinine that occurs within 48 h after PCI. In addition, those patients receiving higher contrast loads or a second contrast load within 72 h and those undergoing IABP placement should have renal function assessed. A risk score based on 8 variables (hypotension, IABP, HF, chronic renal insufficiency, diabetes, age more than 75 years, anemia, and contrast volume) has been developed to assist in the identification of patients at risk for contrast-induced nephropathy after PCI (773). Whenever possible, nephrotoxic drugs (certain antibiotics, nonsteroidal anti-inflammatory agents, and cyclosporine) and metformin (especially in those with pre-existing renal dysfunction) should be withheld for 24 h before PCI is performed, and consideration should be given to withholding angiotensin converting enzyme inhibitors and angiotensin receptor blockers on the day of the procedure (774-776). Although data on the prevention of contrast-induced nephropathy are inconclusive, several measures including preprocedural and postprocedural hydration, use of low and iso-osmolar contrast agents, and pretreatment with acetylcysteine or sodium bicarbonate may be helpful in reducing the incidence of contrast-induced nephropathy among higher-risk patients (774,775,777).

6.3.1. Postprocedure Evaluation of Ischemia

After PCI, chest pain may occur in as many as 50% of patients. ECG evidence of ischemia identifies those with significant risk for acute vessel closure (6,118,119,778-780). When angina pectoris or ischemic ECG changes occur after PCI, the decision to proceed with further interventional procedures, CABG surgery, or medical therapy should be individualized on the basis of factors such as hemodynamic stability, amount of myocardium at risk, and the likelihood that the treatment will be successful.

A 12-lead ECG should be obtained before and soon after PCI and again if symptoms should occur. Angina-like symptoms with ECG changes will assist in determining the need for repeat angiography and for additional therapy.

As discussed in Section 6.2.2, coronary stents and platelet GP receptor inhibitors have reduced the incidence of acute closure significantly. Factors that correlate with a poor outcome after acute coronary closure include age greater than 70 years, large ischemic burden, presentation with acute coronary syndromes, and LV ejection fraction less than 30% (778-780).

Elevated levels of CK or the MB subfraction (CK-MB) or ECG abnormalities are reported to occur in 5% to 30% of patients after PCI (23). The mechanisms associated with CK release include side-branch occlusion, distal embolization, intimal dissection, and coronary spasm (781). A more frequent requirement for revascularization procedures and a higher risk of death or subsequent MI are associated with elevated cardiac biomarkers, increasing as a continuous function with no obvious threshold effect. Both acute and chronic complications are more common among patients with elevated cardiac biomarkers. Even in patients with low-level elevations of CK-MB in whom the in-hospital risk is low, the intermediate- and long-term risks are also increased. Postprocedural increases in CK and CK-MB are not specific for a particular technique and have been reported after balloon angioplasty, directional and rotablator atherectomy, excimer laser angioplasty, and stent placement. Kong et al. (782) found that increased levels of CK are a significant independent predictor of cardiac mortality and subsequent MI (56). Cardiac mortality after elective PCI was significantly higher for patients with high (more than 3.0 times normal) and intermediate (1.5 to 3.0 times normal) CK compared with those with low CK (more than 1.0 but less than 1.5 times normal) elevations and control patients (*P* equals 0.007). (See Section 3.2, Acute Outcome: Procedural Complications.)

CK and CK-MB measurements should be obtained in patients with suspected ischemia (prolonged chest pain, side-branch occlusion, recurrent ischemia, or hemodynamic instability) during PCI. Ideally, the European Society of Cardiology and the ACC recommend that small infarcts may and should be detected by serial blood sampling and analysis before and after the procedure (6 to 8 h before and 24 h after, respectively) (21). In patients in whom a clinically driven CK-MB determination is made, a CK-MB index increase of more than 5 times the upper limit of normal should be treated as signifying an MI, and the patient should be referred for further observation. The results of CK-MB should be considered for the discharge management strategies for these patients.

The troponin isoforms I and T have a high level of sensitivity and specificity for the diagnosis of acute MI. Troponin T or I elevation occurs frequently after PCI. The timing of the peak elevation after PCI is unclear (25). Minor elevations do not appear to have prognostic value, whereas marked (more than 5 times) elevations are associated with worsened 1-year outcome (26,27).

6.3.2. Risk Factor Modifications

All patients should be instructed about necessary behavior and risk factor modification, and the appropriate medical therapies should be initiated for the secondary prevention of atherosclerosis before the patient leaves the hospital. The interventional cardiologist should emphasize the importance of these measures directly to the patient, because failure to do so may suggest that secondary prevention therapies are not necessary. The interventional cardiologist should interact with the primary care physician to ensure that the necessary secondary prevention therapies initiated during hospitalization are maintained by patients after discharge from the hospital. Secondary prevention measures are an essential part of long-term therapy because they can reduce future morbidity and mortality associated with the atherosclerotic process.

Depending on the risk factors and contraindications present, advice should include antithrombotic therapy (aspirin and/or clopidogrel or ticlopidine), control of hypertension, diabetic management, aggressive control of serum lipids, maintenance of a low-density lipoprotein cholesterol level substantially below 100 mg per dL (optional therapeutic target less than 70 mg per dL in very-high-risk patients [611]), abstinence from tobacco use, weight control, regular exercise, beta-blocker use, and inhibition of the renin-angiotensin-aldosterone system as recommended in the ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (Table 26) (332,783). Given the natural history and pathophysiology of CAD among patients undergoing PCI, the clinically indicated secondary prevention measures (Table 26) (332,783), which usually include aspirin, statin therapy, beta-blockers, and inhibitors of the renin-angiotensin-aldosterone system, should be continued indefinitely except in those patients intolerant to these agents (242,783-792). Patients should receive instructions on participation in cardiac rehabilitation and the timing of return to full activities, be informed to contact their physician or seek immediate medical attention if symptoms recur, and have made plans for a follow-up visit to assess compliance with secondary prevention therapies.

6.3.3. Exercise Testing After PCI

The published ACC/AHA practice guidelines for exercise testing (793) provide an excellent summary of the available information on exercise testing after PTCA. Although restenosis remains the major limitation of PCI, symptom status is an unreliable index to development of restenosis, with 25% of asymptomatic patients documented as having ischemia on exercise testing (794). (See Section 5.1, Patients With Asymptomatic Ischemia or CCS Class I or II Angina for further information.)

To identify restenosis rather than predict the probability of its occurrence, patients may be tested later (3 to 6 months after PCI). Table 27 reviews the predictive value of exercise testing for restenosis (794-802). Variability is attributed predominantly to differences in the populations studied and criteria for restenosis.

Because myocardial ischemia, whether painful or silent, worsens prognosis (803), some authorities have advocated routine testing. However, the ACC/AHA practice guidelines for exercise testing favor selective evaluation in patients considered to be at particularly high risk (e.g., patients with decreased LV function, multivessel CAD, proximal LAD disease, previous sudden death, diabetes mellitus, left main disease, hazardous occupations, and suboptimal PCI results) (793). The exercise ECG is an insensitive predictor of restenosis, with sensitivities ranging from 40% to 55%, significantly less than those obtainable with single photon emission computed tomography (SPECT) (804,805) or exercise echocardiography (806-808). This lower sensitivity of the exercise ECG and its inability to localize disease limit its usefulness in patient management both before and after PCI (797,804,809). For these reasons, stress imaging is preferred

Table 26. Comprehensive Risk Reduction for Patients With Coronary and Other Vascular Disease After PCI

Goals	Intervention Recommendations
Smoking: Goal Complete cessation. No exposure to environmental tobacco smoke	Ask about tobacco status at every visit. Strongly encourage patient and family to stop smoking and to avoid environmental tobacco smoke. Assess the tobacco user's willingness to quit. Assist by counseling and developing a plan for quitting. Arrange follow-up, referral to special programs, orpharmacological therapy (including nicotine replacement and buproprion). Urge avoidance of exposure to environmental tobacco smoke at work and home.
Blood pressure control: Goal Less than 140 over 90 mm Hg or less than 130 over 80 mm Hg if chronic kidney disease or diabetes is present	*If blood pressure is 120 over 80 mm Hg or greater:·* • Initiate or maintain lifestyle modification (weight control, increased physical activity, alcohol moderation, moderate sodium restriction, and emphasis on fruits, vegetables, and low-fat dairy products) in all patients. *If blood pressure is 140 over 90 mm Hg or greater (or 130 over 80 mm Hg or greater for individuals with chronic kidney disease or diabetes):* • Add blood pressure medication, emphasizing the use of beta-blockers and inhibitors of the renin-angiotensin-aldosterone system.
Lipid management: (TG less than 200 mg per dL)	Start dietary therapy in all patients (less than 7% of total calories as saturated fat and less than 200 mg of cholesterol per day). Promote physical activity and weight management. Encourage increased consumption of omega-3 fatty acids in fish# or 1 g per day omega-3 fatty acids from supplements for risk reduction (for treatment of elevated TG, higher doses are usually necessary for risk reduction).
Primary goal LDL-C substantially less than 100 mg per dL (optional target less than 70 mg per dL for very-high-risk patients)¶	Assess fasting lipid profile in all patients, preferably within 24 h of an acute event. For patients hospitalized, initiate lipid-lowering medication as recommended below before discharge according to the following guide: LDL-C less than 100 mg per dL (baseline or on-treatment): • Statins preferred to lower LDL-C. LDL-C greater than or equal to 100 mg per dL (baseline or on-treatment): • Initiate or intensify LDL-C–lowering therapy with drug treatment. May require combination therapy with standard-dose ezetimide, bile acid sequestrant, or niacin‡.
Lipid management: (TG 200 mg per dL or greater)	If TG is greater than or equal to 150 mg per dL or HDL-C is less than 40 mg per dL: • Emphasize weight management and physical activity. Advise smoking cessation.
Primary goal Non–HDL-C* substantially less than 130 mg per dL	If TG is 200-499 mg per dL: • After LDL-C–lowering therapy†**, consider adding fibrate or niacin‡. If TG is greater than or equal to 500 mg per dL: • Consider fibrate or niacin‡ before LDL-C–lowering therapy.†** • Consider omega-3 fatty acids as adjunct for high TG.
Physical activity: Minimum goal 30 minutes 5 days per week; optimal daily	Assess risk, preferably with exercise test, to guide prescription. Encourage minimum of 30 to 60 minutes of activity, preferably daily or at least 5 times weekly (brisk walking, jogging, cycling, or other aerobic activity) supplemented by an increase in daily lifestyle activities (e.g., walking breaks at work, gardening, household work). Encourage resistance training 2 days per week. Cardiac rehabilitation programs are recommended, particularly for those patients with multiple modifiable risk factors and/or those moderate- to high-risk patients in whom supervised exercise training is warranted.

Continued on next page

Table 26. *Continued*

Goals	Intervention Recommendations
Weight management: Goal BMI 18.5 to 24.9 kg per m^2 Waist circumference: Women: Less than 35 inches Men: Less than 40 inches	Calculate BMI and measure waist circumference as part of evaluation. Monitor response of BMI and waist circumference to therapy. Start weight management and physical activity as appropriate. Desirable BMI range: 18.5 to 24.9 kg per m^2. If waist circumference is 35 inches or greater in women or 40 inches or greater in men, initiate lifestyle changes and consider treatment strategies for metabolic syndrome.
Diabetes management: Goal HbA1c less than 7%	Appropriate glucose-lowering therapy to achieve near-normal fasting plasma glucose as indicated by HbA1c. Treatment of other risk factors (e.g., physical activity, weight management, blood pressure cholesterol management).
Antiplatelet agents/ anticoagulants:	For all post-PCI stented patients, aspirin 325 mg daily should be given for at least 1 month after bare metal stent implantation, 3 months after sirolimus stent, and 6 months after paclitaxel stent, after which daily chronic aspirin†† (75 to 162 mg per day) should be continued indefinitely in all patients if not contraindicated. For post-PCI stented patients, clopidogrel 75 mg per day should be given for at least 1 month after bare metal stent implantation, 3 months after sirolimus stent, and 6 months after paclitaxel stent, after which clopidogrel should ideally be continued up to 12 months in all stented patients who are not at high risk of bleeding. Use warfarin in combination with clopidogrel and low-dose aspirin with great caution and when INR is carefully regulated (2.0 to 3.0). Manage warfarin to INR 2.5 to 3.5 for post-MI patients when clinically indicated or for those not able to take aspirin or clopidogrel.
Renin-angiotensin-aldosterone system blockers:	Consider ACE inhibitors for all CHD patients indefinitely; start early after MI in stable high-risk patients (anterior MI, previous MI, Killip class greater than or equal to II [S_3 gallop, rales, radiographic HF]). Continue indefinitely in for all patients with LV dysfunction (ejection fraction less than or equal to 0.40) or symptoms of heart failure. Use as needed to manage blood pressure or consider for chronic therapy in all other patients. Use angiotensin receptor blockers in post-STEMI patients who are intolerant of ACE inhibitors and who have either clinical or radiological signs of heart failure or LVEF less than 0.40. Aldosterone blockade in post-STEMI patients without significant renal dysfunction§ or hyperkalemia‖ who are already receiving therapeutic doses of an ACE inhibitor, have an LVEF less than or equal to 0.40, and have either diabetes or heart failure.
Beta-blockers:	Start in all post-MI and acute patients (arrhythmia, LV dysfunction, inducible ischemia). Continue for a minimum of 6 months; continue indefinitely in patients with STEMI. Observe usual contraindications. Use as needed to manage angina, rhythm, or blood pressure in all other patients.

ACE indicates angiotensin-converting enzyme; BMI, body mass index; HF, congestive heart failure; CHD, coronary heart disease; HDL-C, high-density lipoprotein cholesterol; INR, international normalized ratio; LDL-C, low-density lipoprotein cholesterol; LV, left ventricular; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; and TG, triglyceride.

*Non–HDL-C equals total cholesterol minus HDL cholesterol.

†Treat to a goal of non–HDL-C substantially less than 130 mg per dL.

‡Dietary supplement niacin must not be used as a substitute for prescription niacin.

§Creatinine should be less than or equal to 2.5 mg per dL in men and less than or equal to 2.0 mg per dL in women.

‖Potassium should be less than or equal to 5.0 mEq per liter.

¶Patients with acute coronary syndromes and other very-high-risk patients (e.g., established CHD plus multiple major risk factors [especially diabetes] or severe and poorly controlled risk factors [especially continued cigarette smoking and/or metabolic syndrome]) should be considered for optional LDL-C goal less than 70 mg per dL.

#Pregnant and lactating women should limit their intake of fish to minimize exposure to methylmercury.

**The use of resin is relatively contraindicated when TGs are greater than 200 mg per dL.

††Some recommend avoiding regular use of ibuprofen, which may limit the cardioprotective effects of aspirin. Use of cyclo-oxygenase-2 inhibitors may be associated with increased incidence of cardiovascular events.

Modified with permission from Smith et al. Circulation 2001;104:1577-9 (810) (undergoing update with anticipated release in 2005) and Antman et al. J Am Coll Cardiol 2004;44:e1-e211 (362).

Table 27. Predictive Value of Exercise ECG Testing for Identification of Restenosis After PCI

Author	Year	Ref	n	Clinical	Post-PCI, mo	Restenosis, %	Positive PV, %	Negative PV, %	Definition of Restenosis
Kadel	1989	(795)	398	Consecutive	Up to 6	33	66	75	Greater than 70% luminal diameter stenosis
Honan	1989	(796)	144	Post-MI	6	40	57	64	Greater than 75% luminal diameter stenosis
Schroeder	1989	(797)	111	Asymptomatic	6	12	53	63	Greater than 70% luminal diameter stenosis
Laarman	1990	(798)	141	Asymptomatic	1 to 6	12	15	87	Greater than 50% luminal diameter stenosis
el-Tamimi	1990	(799)	31	Consecutive	6	45	100	94	Loss of more than 50% initial gain of lumen diameter
Bengston	1990	(794)	200	Asymptomatic (n=127)	6	44	46	63	Greater than 75% luminal diameter stenosis
			200	Symptomatic (n=66)	6	59	76	47	Greater than 75% luminal diameter stenosis
Roth	1994	(800)	78	1-vessel CAD	6	28	37	77	Greater than 50% luminal diameter stenosis
Desmet	1995	(801)	191	Asymptomatic	6	33	52	70	Greater than 50% luminal diameter stenosis

CAD indicates coronary artery disease; MI, myocardial infarction; mo, month; n, number of patients; PCI, percutaneous coronary intervention; PV, predictive value; and Ref, reference.

to evaluate symptomatic patients after PCI. If the patient's exertional capacity is significantly limited, coronary angiography may be more efficacious to evaluate symptoms of typical angina. Exercise testing after discharge is helpful for activity counseling and exercise training as part of cardiac rehabilitation. Neither exercise testing nor radionuclide imaging is indicated for the routine, periodic monitoring of asymptomatic patients after PCI without specific indications.

6.3.4. Left Main CAD

Class IIa

It is reasonable that patients undergoing PCI to unprotected left main coronary obstructions be followed up with coronary angiography between 2 and 6 months after PCI. *(Level of Evidence: C)*

Careful postprocedure surveillance with coronary angiography is needed to prevent fatal MI or sudden death that may be associated with ISR with a large area of myocardium in jeopardy; however, the frequency and best method of follow-up is unknown (162). Early experience in the ULTIMA registry using BMS for ULM lesions suggested a high early mortality (2% per month) after PCI, which led the study's authors to suggest routine surveillance angiography at 2 and 4 months after PCI (153). Others advocate routine stress testing or cardiac catheterization at 3 and 6 months even in asymptomatic patients (148,150). In view of these observations and suggestions, the Committee recommends routine surveillance angiography at 2 to 3 months for all patients after ULM PCI. Studies from the DES era have reported the performance of routine angiography 4 to 8 months after PCI or earlier if clinically indicated by symptoms or documented myocardial ischemia (159,160).

7. SPECIAL CONSIDERATIONS

7.1. Ad Hoc Angioplasty—PCI at the Time of Initial Cardiac Catheterization

Ad hoc coronary intervention is defined as PCI performed at the same time as diagnostic cardiac catheterization. During the past several years, in an effort to reduce hospital length of stay and potentially reduce costs, PCI has increasingly been performed immediately after the diagnostic coronary angiographic procedure (811), with reported incidence ranging from 52% to 83% (812-814). The indications for diagnostic catheterization and coronary angiography in different catheterization laboratory settings are discussed in the ACC/SCAI Expert Consensus Document on Catheterization Laboratory Standards (Table 28) (309,815).

Ad hoc angioplasty has several inherent advantages. It expedites patient care, avoids a second invasive procedure with its associated risks and recognized morbidity, and reduces total X-ray exposure and therefore cost, but only in settings in which intrinsic risks are low (813). However, ad hoc intervention is associated with a higher procedural contrast use and should be avoided in situations where excessive

Table 28. Exclusion Criteria for Invasive Cardiac Procedures in Settings Without Full-Support Services

Location	Type of Patient	Diagnostic Procedures	Therapeutic Procedures
Hospitals	Adult	Age greater than 75 years NYHA class III or IV heart failure Acute, intermediate, or high-risk ischemic syndromes Recent MI with postinfarction ischemia Pulmonary edema thought to be caused by ischemia Markedly abnormal noninvasive test indicating a high likelihood of left main or severe multivessel coronary disease Known left main coronary artery disease Severe valvular dysfunction, especially in the setting of depressed LV performance	All valvuloplasty procedures, complex adult congenital heart disease diagnostic or therapeutic procedures Diagnostic pericardiocentesis when the effusion is small or moderate in size and there is no tamponade Elective coronary intervention
	Pediatric	No procedures approved	No procedures approved
Freestanding laboratories	Adult	All of the above plus high-risk patients by virtue of comorbid conditions, including need for anticoagulation, poorly controlled hypertension or diabetes, contrast allergy, or renal insufficiency	
	Pediatric	No procedures approved	No procedures approved

LV indicates left ventricular, MI, myocardial infarction; and NYHA, New York Heart Association.
Modified from Bashore et al. J Am Coll Cardiol 2001;37:2170-214.

contrast has been used and when adequate pretreatment with aspirin or antiplatelet agents has not been achieved (814).

In contrast to ad hoc angioplasty, a staged approach also has several advantages. It allows ample time to review the angiogram and plan the procedural strategy; discuss the risks, benefits, and alternatives with the patient and family; and obtain consultation from cardiothoracic surgical colleagues. It is far more difficult to adequately inform the patient of risks, benefits, and alternatives without knowledge of the anatomy and the extent of coronary disease. A staged approach also allows for optimal hydration and pretreatment with oral antiplatelet agents. Explicit and clear informed consent, especially for ad hoc PCI, should be discussed by the interventional cardiologist with the patient and family.

Studies evaluating the outcome of patients undergoing ad hoc coronary intervention have reported that informed patients with suitable anatomy have a shorter hospital stay, less radiation exposure, and lower costs without an increase in procedural complications compared with patients undergoing a staged approach (812,813,816,817). In a multicenter cohort study of 35 700 patients undergoing elective coronary angioplasty between 1992 and 1995, the risk of a major complication (MI, emergency CABG, or death) from combined ("ad hoc") versus staged procedures was 2% and 1.6%, respectively. After adjustment for clinical and angiographic differences between groups, the risk from combined procedures was not significantly different. However, patients with multivessel disease, women, patients older than 65 years, and patients undergoing multilesion coronary angioplasty were at increased risk of an adverse outcome (818). In an analysis of patients in the New York State PCI Registry, in-hospital mortality was similar in patients undergoing ad hoc and staged procedures, although patients with HF had a significantly lower mortality when undergoing staged procedures. These studies suggest that it is safe to perform PCI after diagnostic catheterization in selected patients (819).

Ad hoc coronary intervention is particularly suitable for patients with clinical evidence of restenosis 6 to 12 months after the initial procedure (820), patients undergoing primary angioplasty for MI, and patients with refractory UA in need of urgent revascularization (821). Before the procedure, these patients should be treated with aspirin and clopidogrel (822) only when PCI with stent placement is highly likely, and they should give appropriate informed consent for anticipated PCI. Ad hoc PCI should be performed only in a well-informed patient, particularly in the setting of single-vessel disease without morphologic features predictive of an adverse outcome, when it is clear that this treatment strategy is the best alternative. However, ad hoc percutaneous revascularization should not be performed in patients in whom the angiographic findings are unanticipated or in whom the indication, suitability, or preference for percutaneous revascularization is unclear (823). Patient safety should be the paramount consideration when ad hoc intervention is being considered. This Committee endorses the recommendations from the SCAI that ad hoc PCI be individualized and not be a standard or required strategy for all patients (824). The Writing Committee encourages future studies to further evaluate the outcomes associated with ad hoc angioplasty and its cost effectiveness.

7.2. PCI in Cardiac Transplant Patients

Allograft atherosclerosis and vasculopathy are the main cause of death in cardiac transplant recipients. Because no medical therapy is known to prevent graft atherosclerosis, and retransplantation is associated with decreased survival, palliative therapy with PCI has been proposed and performed (825). No single medical center has performed PCI in many patients, and thus, the responses and outcomes of a large cohort are unavailable for review. However, pooled information from 11 medical centers retrospectively analyzing results of coronary angioplasty in cardiac transplant patients has been reported (826). These investigators concluded that although high procedural success can be achieved and PCI may be applied in a selected cardiac transplant population with success and complication rates comparable to the routine patient population, it remains unknown whether PCI prolongs allograft survival.

Coronary stenting in cardiac allograft vascular disease has been performed in small numbers of patients with favorable results (827). Heublein et al. (828) compared angioplasty and stenting in 27 patients who received 48 stents, 5.7 plus or minus 2.9 years after heart transplantation. Coronary angioplasty resulted in a minimal increase in luminal dimensions compared with stenting (2.04 plus or minus 0.36 mm for angioplasty vs 2.53 plus or minus 0.38 mm for stenting). There were no stent thromboses or bleeding complications. At a mean follow-up period of 8 plus or minus 5 months (range 2 weeks to 23 months), all patients were clinically event-free. Six of 24 stented vessels in 16 patients had restenosis greater than 50% by ultrasound or angiography 6 months after the procedure. These somewhat disappointing results highlight the need for a better understanding of the mechanism of graft vasculopathy and the development of refined, specific PCI-related therapies with better outcomes. The largest reported experience of PCI in cardiac transplant recipients to date showed that PCI with stents is effective in relieving focal stenoses in patients with allograft coronary disease (829). Between 1990 and 2000, 62 patients (1.5 to 15 years after transplant) underwent 151 procedures that resulted in PCI of 219 lesions. Periprocedural mortality was low at 2% (4 of 151 procedures). Two-year freedom from allograft coronary disease death or graft loss was 74% for 1-vessel disease at first PCI, 75% for 2-vessel disease, and 27% for 3-vessel disease (*P* equals 0.009). There were no incidences of acute stent thrombosis. Freedom from repeat PCI of the same vessel ranged from 75% at 6 months to 57% at 4 years. Freedom from restenosis ranged from 95% at 1 month to 57% at 6 months. Multivariate predictors of freedom from restenosis were the use of stents, higher antiproliferative immunosuppressant dose, and an era effect (e.g., procedural advances and widespread use of periprocedural GP IIb/IIIa inhibitors and thienopyridines, among others). Long-term survival effects remain under examination (Table 29) (826,830-833).

7.3. Clinical Restenosis: Background and Management

7.3.1. Background on Restenosis After PTCA

Angiographic restenosis after PTCA has been reported to occur in 32% to 40% of patients within 6 months after the procedure (80,85). Initial procedural success rates after PTCA of restenotic lesions appear similar to those after PTCA for de novo lesions. The risk for repeat angiographic restenosis after repeat PTCA for a single episode of restenosis also appears similar to the restenosis risk for de novo lesions (834,835). The risk of recurrent symptoms progressively increases with the number of restenosis episodes, approaching 50% to 53% for patients undergoing a fourth PTCA for a third episode of restenosis (836,837).

7.3.2. Clinical and Angiographic Factors for Restenosis After PTCA

A number of factors are associated with lesion recurrence among patients undergoing a second PTCA for restenosis. These factors include an interval less than 60 to 90 days between the initial angioplasty and the treatment of restenosis (834-838), LAD lesion location (837), multivessel versus single-vessel redilations (838), the presence of diabetes mellitus (834,838), hypertension (834), UA (834), need for higher (7 atm) balloon inflation pressures (835), and multiple (3) balloon inflations (835,836). Of these, the most important factor is the time between the initial and subsequent PTCA (839). In a series of 423 patients, restenosis was more common in those having repeat angioplasty less than 3 months after a first angioplasty than in patients undergoing later redilation (56% vs 37%, *P* equals 0.007) (839).

Some studies have suggested that lesions become longer and more severe after repeat PTCA of restenotic lesions (840,841). In a serial angiographic study, the mean stenosis length before the initial angioplasty was 7.0 mm but increased to 8.7 mm at the time of the repeat procedure (an increase of more than 1.7 mm, 95% CI 0.6 to 2.8 mm, *P* less than 0.01) (841). A history of restenosis may also predict the risk for subsequent restenosis after PTCA of a new lesion (104). Multivariate analysis identified that prior restenosis (*P* less than 0.02, OR equals 3.4), LAD location of stenosis (*P* less than 0.04, OR equals 3.0), and severity of stenosis before PTCA (*P* less than 0.02, OR equals 1.8) were independently associated with restenosis after PTCA (104).

7.3.3. Management Strategies for Restenosis After PTCA

Class IIa

It is reasonable to consider that patients who develop restenosis after PTCA or PTCA with atheroablative devices are candidates for repeat coronary intervention with intracoronary stents if anatomic factors are appropriate. ***(Level of Evidence: B)***

Long-term patency of the initial target lesion may be achieved with repeated balloon dilatations. In a series of 1455 de novo lesions treated with PTCA, angiographic restenosis requiring repeat PTCA developed in 32% (842). Late patency was achieved in 93% of lesions with up to 3 PTCA procedures. Only 23 lesions (1.6%) required 4 or more procedures (842).

Although atheroablation devices have been developed in an attempt to lower the second restenosis risk in patients, none has shown an incremental benefit over PTCA. In a study of 1569 patients who underwent excimer laser coronary angioplasty for restenotic (n equals 620 patients) or de novo (n equals 949) lesions (843), procedural success was higher in restenotic patients (92% vs 88% in de novo patients; *P* less than 0.001), although clinical recurrence was high in both groups (49% in restenotic patients and 44% in de novo patients, *P* equals NS) (843).

Stent placement is superior to PTCA for the treatment of restenotic lesions. In the REstenosis STent (REST) Study (844), a randomized clinical trial, late clinical and angiographic outcomes were compared in 351 patients undergoing either PTCA or Palmaz-Schatz stent placement for restenotic lesions. Stent-treated patients had lower rates of target-lesion revascularization (10% vs 32% in balloon-treated patients) and restenosis (18% vs 32% in balloon-treated patients; *P* equals 0.03) (844).

Given these findings, it is recommended that patients who develop restenosis after an initially successful PTCA be considered for repeat PCI with stent placement. Factors that may influence this decision include the technical difficulty of the initial procedure, the potential for the lesion to be treated successfully with a stent, and the severity and extent of the restenotic process. If restenosis presents as a much longer lesion than was originally present, additional procedures may aggravate rather than relieve coronary narrowing. If repeat intervention is performed, treatment with a stent appears to be preferred. Each time restenosis recurs, consideration should be given to alternate methods of revascularization, particularly CABG surgery, as well as continued medical therapy. Patients who have angiographic evidence of restenosis but no symptoms or evidence for ischemia may be able to continue with medical therapy alone. It is recommended that patients who develop restenosis after PTCA or atheroablative device therapy plus PTCA be candidates for repeat coronary intervention with intracoronary stents if anatomy is appropriate. Patients who have no signs or symptoms of ischemia and who have intermediate (50%) stenoses at the time of clinical follow-up may not require PCI and, especially where the anatomy is complex, may be followed up for evidence of ischemia rather than subjected to PCI.

7.3.4. Background on Restenosis After BMS Implantation

Although coronary stents have been shown to reduce the frequency of restenosis compared with conventional balloon angioplasty, lumen renarrowing due to intimal hyperplasia within the stent may develop in 17% to 32% of patients

Table 29. Coronary Angioplasty Studies in Heart Transplant Patients

First Author	Year	Ref.	n	Procedures	Lesions	Time After Tx, mo	Success Rate, %	Major Complex	Minor Complex	Restenosis Rate at More Than 6 mo, %	1-Year Event-Free Rate, %	Late Death or reTx at More Than 6 mo, n
Halle	1992	(826)	35	51	95	45 plus or minus 5	93	3	3	NA	60	7
Sandhu	1992	(830)	8	11	13	43 plus or minus 19	85	NA	1	NA	38	4
Swan	1993	(831)	13	31	NA	NA	NA	NA	NA	100	NA	NA
Von Scheidt	1995	(832)	14	38	62	41 plus or minus 25	97	1	NA	61	60	5
Pande	1996	(833)	8	NA	11	NA	91	1	1	NA	50	3

mo indicates month; n, number of patients; NA, not applicable; Ref, reference; reTX, retreatment; and Tx, treatment.

(80,83,845). A number of factors have been associated with the propensity to develop stent restenosis, including small vessel size (846), smaller postprocedure minimum lumen diameter (847), higher residual percent diameter stenosis (848), lesions located in the LAD (83), stent length, and the presence of diabetes mellitus (721,841,842,844,846-848).

Stent restenosis may occur within the stent, due to intimal hyperplasia, or at the stent margins, due to both intimal hyperplasia and arterial remodeling (849). A serial IVUS study performed in 115 lesions treated with the Palmaz-Schatz stent demonstrated that tissue growth was uniformly distributed throughout the stent at follow-up study, with a slightly higher tendency for neointimal tissue accumulation at the central articulation (850). The stent lumen tended to be smallest at the articulation site, presumably owing to tissue prolapse between the stent struts. For multiple stents, there was no difference in the postintervention or follow-up lumen when overlapped stents were compared with nonoverlapped stents (850). In another series of patients treated with the Palmaz-Schatz stent, 77 (26%) of 301 stent margins were restenotic at follow-up (more than 50% late lumen loss) (849). The dominant periprocedural predictor of stent margin restenosis was the plaque burden of the contiguous reference segment (849).

Balloon angioplasty has been used frequently to treat patients with stent restenosis (851-853). The mechanism of lumen improvement after balloon angioplasty for stent restenosis relates to further stent expansion (851) and extrusion of the tissue through the stent struts (851-854). In an IVUS study of 64 restenotic Palmaz-Schatz stents, 56% plus or minus 28% of the lumen enlargement was the result of additional stent expansion and 44% plus or minus 28% was the result of a decrease in neointimal tissue (851). Despite the use of high-pressure balloon dilation, a relatively high residual stenosis (18% plus or minus 12%) remained after treatment with balloon angioplasty.

The outcome after balloon angioplasty has been variable, depending, in part, on the size of the stented segment and length of the stent restenosis (855). In a consecutive series of 124 patients presenting with stent restenosis successfully treated with repeat percutaneous intervention, clinical follow-up was obtained at 27.4 plus or minus 14.7 months (855). Recurrent clinical events occurred in 25 patients (20%), including death (2%), MI (1%), and target-vessel revascularization (11%) (855). Cumulative event-free survival at 12 and 24 months was 86.2% and 80.7%, respectively (855).

A number of factors have been related to the frequency of clinical recurrence after balloon angioplasty for stent restenosis (855), which include repeat intervention in SVGs, multivessel disease, low ejection fraction, and a 3-month interval between stent implantation and repeat intervention. One preliminary report has shown target-lesion revascularization was related to the length of the stent restenosis, ranging from 10% for focal stent stenosis to 25% for intrastent restenosis, 50% for diffuse stent restenosis, and 80% for stent total occlusions (856).

New coronary devices, including directional (857,858), rotational (859,860), extraction (861-865), and pullback (866) atherectomy, a cutting balloon, and excimer laser-assisted angioplasty, have also been used for stent restenosis before balloon dilation. Although some comparative registry series have suggested an improved angiographic outcome associated with the use of these ablative devices, no long-term studies demonstrating clinical advantage have been completed.

When a significant residual stenosis exists after conventional PTCA of stent restenosis fails to achieve an optimal lumen diameter, additional stents have been used to improve the initial angiographic result (867-869). Although preliminary results of clinical trials failed to demonstrate a benefit using routine BMS placement for the treatment of stent restenosis, favorable results have been shown with DES (see Section 7.3.5 for further discussion) (116,870,871).

Acute platelet inhibition with abciximab does not reduce ISR, as demonstrated in the ERASER (Evaluation of ReoPro And Stenting to Eliminate Restenosis) study (280). In a study of 225 patients randomly allocated to placebo or abciximab before intervention, 215 patients received a stent and the study drug. Of the 191 patients who returned for follow-up more than 4 months after evaluation, there was no difference between tissue volume as measured by IVUS between the placebo and treatment groups. Lack of abciximab benefit was confirmed by quantitative angiography. The investigators concluded that potent platelet inhibition with abciximab as administered in the ERASER study did not reduce ISR.

Since the last (2001) revision of the ACC/AHA PCI guideline, the proportional use of stents in percutaneous interventions has continued to increase. In part, this derives from randomized trial data suggesting that routine stenting is more effective than provisional stenting (636,872-874). In addition, stents are being used in a much wider spectrum of coronary and even graft anatomies (875). Accordingly, ISR has become increasingly important. Because stents prevent elastic recoil and late negative remodeling, the predominant mechanism of ISR is neointimal hyperplasia due to smooth muscle cell proliferation and extracellular matrix production. Two of the biggest changes since the 2001 revision have been the expanding databases of 1) brachytherapy to treat ISR and 2) DES to try to prevent ISR.

7.3.5. Drug-Eluting Stents

Class I

A drug-eluting stent (DES) should be considered as an alternative to the bare-metal stent in subsets of patients in whom trial data suggest efficacy. ***(Level of Evidence: A)***

Class IIb

A DES may be considered for use in anatomic settings in which the usefulness, effectiveness, and safety have not been fully documented in published trials. ***(Level of Evidence: C)***

All PCI creates injury to the vessel wall, specifically tears or dissection. Larger devices and higher pressures are associated with tears at deeper levels of the vessel wall (media or even adventitia, as opposed to intima and plaque boundary only). All injuries tend to heal; specifically, injury to the vessel wall is associated with re-establishment of an intact endothelial layer. Failure to re-establish an intact, functional endothelial layer is likely to be associated with continued risk of arterial thrombosis and an abnormal balance between vasoconstrictive and vasodilatory mechanisms. In general, deeper injury is associated with more proliferative healing (876-878). The demonstration, by quantitative angiography, that late lumen diameter after balloon angioplasty follows a "normal" or Gaussian distribution supports the concept that restenosis is an exaggerated healing response rather than a distinct biologic process, which occurs in a minority of individuals.

For balloon angioplasty, the healing response includes, on the macroscopic level, negative (narrowing) and positive (dilatation) remodeling, elastic recoil, and neointimal hyperplasia. Because stents block elastic recoil and negative remodeling, ISR is predominantly due to neointimal hyperplasia. Neointimal hyperplasia is the name given to a complex process of multifactorial causation, which leads to vessel lumen encroachment. The causes of neointimal hyperplasia appear to include, but are not limited to, the following inflammatory response involving cells and molecular mediators; growth factors and cytokines; release of mediators and upregulation of signaling systems that stimulate cellular migration and proliferation; activation, adherence, and aggregation of platelets; and thrombosis with release of clotting factors. Neointimal hyperplasia may be distinct from atherosclerosis and negative remodeling, but it shares many of the same causative factors. Accordingly, investigators and clinicians are inclined to try many of the same antithrombotic, antiplatelet, anti-inflammatory, and antiproliferative agents to try to modify atherosclerosis, neointimal hyperplasia, and negative remodeling. Additionally, many therapeutic agents affect multiple mechanisms.

To date, no systemically administered therapeutic agent has consistently reduced restenosis after balloon angioplasty or placement of BMS. Stents have reduced restenosis relative to balloon angioplasty (albeit with increased late loss due to increased neointimal proliferation), and locally delivered radiation (brachytherapy) has reduced ISR. Taken together, these observations and the early success of sirolimus- and paclitaxel-eluting stents have supported the paradigm of blocking elastic recoil and negative remodeling with a mechanical stent and inhibiting neointimal hyperplasia with a locally delivered (higher concentration than can be achieved systemically) antiproliferative and anti-inflammatory agent.

Local delivery of a therapeutic agent with stents has taken 2 forms: simple coating of the stent and adherence of the therapeutic agent to a polymer, which allows for sustained release over time. Diffusion of the therapeutic agent into the tissues and into blood is an additional complexity. For coated stents, the long-term outcome depends on the response to both stent and coating. For DES, the long-term healing response depends on the response to the polymer and the therapeutic agent, as well as the stent. As evidenced by the trials of gold coating and the preliminary experiences (registry) with the QuaDS stent, actinomycin, and batimastat, some combinations are potentially even more proliferative, inflammatory, or thrombogenic than BMS.

Peer-reviewed publications of human DES implantation, including consecutive case series and randomized trials, are available for 3 polymer-based, drug-eluting, balloon-expandable stent systems (Table 30) (236,441,624,628,697,698, 879-888): the antiproliferative, antimigratory, anti-inflammatory macrolide antibiotic rapamycin (sirolimus) affixed to a stent (Bx Velocity); the 7-hexanoyltaxol (QP2)-eluting polymer stent system (QuaDS); and the microtubule inhibitor paclitaxel (TAXUS) affixed to a stent. Each of these systems had undergone rigorous testing in animal models that demonstrated an intact endothelial layer and significant reductions in neointimal hyperplasia and inflammation.

The first reported series of 45 patients who underwent SES implantation in either Sao Paulo, Brazil, or Rotterdam, Holland, demonstrated the virtual absence of intimal hyperplasia at 4 months (889). Subsequent studies of the same cohort at 1 and 2 years continued to document sustained suppression of neointimal hyperplasia as detected with both IVUS and quantitative angiography (628,879). In the Randomized Study With the Sirolimus-Eluting Bx Velocity Balloon-Expandable Stent (RAVEL) trial, 238 patients were randomly allocated between BMS and SES (624). At 6 months the binary restenosis rate was 26% for the bare metal group versus 0% for the DES group, and there were no subacute stent thromboses with a 2-month dual antiplatelet regimen. In 1 year of follow-up, the bare metal group had a 29% rate of MACE versus 5.8% for the sirolimus-eluting group; this difference was driven entirely by target-vessel revascularization.

A 3-year follow-up of the RAVEL trial (890), involving 114 patients from the SES arm and 113 in the BMS arm, documented target-vessel revascularization in 11.4% of the SES group compared with 33.6% of the BMS group. These data support the long-term durability of SES in reducing repeat revascularization compared with BMS.

The SIRIUS (Sirolimus-Eluting Balloon Expandable Stent in the Treatment of Patients With De Novo Native Coronary Artery Lesions) investigators reported 1058 patients randomly allocated at 1 of 53 centers between BMS and SES (93). This cohort included diabetic patients (26%) and somewhat longer lesions (mean 14.4 mm) and smaller-diameter vessels (mean 2.8 mm) than the RAVEL population. Again, the sirolimus-eluting group had lower MACE at 270 days than the BMS group (7.1% vs 18.9%), which was driven by lower rates of target-vessel revascularization (4.1% vs 16.6%). Both quantitative angiography and IVUS were used to document that the mechanism for this salutary effect was decreased neointimal hyperplasia. SIRIUS was the pivotal

Table 30. Published Randomized Trials and Selected Registry Experiences of Drug-Eluting Stents Compared With Bare Metal Stents

Eluting Drug	Trial (Ref.)	Year	n, Active/Control	Stent	Eluting Drug Dosage	Deaths Active/Control, %	MI, Active/Control, %	Restenosis, Active/Control, %	TLR, Active/Control, %
Sirolimus	FIM (628)	2001	30 in Sao Paulo; 15 in Rotterdam	BxVelocity	140 mcg/cm²	NA	NA	0% at 1 year	Minimal neointimal proliferation at 1 year
	FIM (879)	2002	15 from Rotterdam	BxVelocity	140 mcg/cm²	NA	NA	0% at 2 years	Minimal neointimal proliferation at 2 years
	RAVEL (624)	2002	120/118	BxVelocity	140 mcg/cm²	1.7/1.7	3.3/4.2	0/26.6 at 6 months (*P* less than 0.001)	0/22.9 at 1 year (*P* equals 0.001)
	SIRIUS (698)	2004	533/525	BxVelocity	140 mcg/cm²	0.9/0.6	2.8/3.2	8.9/36.3 at 8 months (*P* less than 0.001)	4.9/20 at 1 year (*P* less than 0.001)
	C-SIRIUS (880)	2004	50/50	BxVelocity	140 mcg/cm²	0/0	2.0/4.0	2.3/51.1	4.0/18.0 at 9 months (*P* less than 0.001)
	E-SIRIUS (881)	2003	175/177	BxVelocity	140 mcg/cm²	1.1/0.6	4.6/2.3	5.9/42.3	4.0/20.9 at 9 months (*P* less than 0.001)
	RESEARCH Registry Overall (236)	2004	508/450	BxVelocity	140 mcg/cm²	1.6/2.0 at 30 days	0.8/1.6 at 30 days	NA	1.0/1.8 at 30 days
	RESEARCH Registry ACS (882)	2003	198/301	BxVelocity	140 mcg/cm²	3.0/3.0 at 30 days	3.0/1.0 at 30 days	NA	1.0/2.7 at 30 days
	RESEARCH Registry STEMI (441)	2004	186/183	BxVelocity	140 mcg/cm²	8.3/8.2 at 300 days	0.5/2.2 at 300 days	NA	1.1/8.2 at 300 days (*P* less than 0.01)
	RESEARCH Registry Chronic Totals (883)	2004	56/28	BxVelocity	140 mcg/cm²	0/0 in hospital	NA	NA	12-month MACE: 5.6/17.2 (*P* less than 0.05)

Continued on next page

Table 30. *Continued*

Eluting Drug	Trial (Ref.)	Year	n, Active/Control	Stent	Eluting Drug Dosage	Deaths Active/Control, %	MI, Active/Control, %	Restenosis, Active/Control, %	TLR, Active/Control, %
Paclitaxel	QuaDS-QP2 (884)	2002	15	QuaDS-QP2	2400 to 3200 mcg total dose	NA	NA	13.3 at 6 months 61.5 at 1 year	20 at 6 months 60 at 1 year
	ASPECT (885)	2003	59 High dose 58 low dose/ 59 control	Supra-G	3.1 mcg/mm^2 1.3 mcg/mm^2	0.9/0	2.6/1.7	4/12/27 at 4 to 6 months (high dose vs control, *P* less than 0.001)	2/2/2 at 1 to 6 months
	TAXUS I (886)	2003	31/30	NIR	1.0 mcg/mm^2	0/0	0/0	0/10 at 6 months (*P* equals 0.012)	0/10 at 1 year (*P* equals 0.237)
	TAXUS II (887)	2003	266/279	NIR	1.0 mcg/mm^2	0/0.8	3.1/5.3	7.1/21.9 at 6 months	10.4/21.7 at 12 months
	TAXUS III (888)	2003	28 ISR	NIR	1.0 mcg/mm^2	NA	NA	NA	21.4 at 1 year
	TAXUS IV (697)	2004	662/652	EXPRESS	1.0 mcg/mm^2	1.4/1.1	3.5/3.7	7.9/26.6 at 9 months (*P* less than 0.0001)	4.4/15.1 at 1 year (*P* less than 0.0001)

ACS indicates cute coronary syndromes; ASPECT, Asian Paclitaxel-Eluting Stent Clinical Trial; FIM, First in Man; ISR, in-stent restenosis; NA, not applicable; RESEARCH, Rapamycin-Eluting and Taxus Stent Evaluated At Rotterdam Cardiology Hospital; SIRIUS, Sirolimus-Eluting Balloon Expandable Stent in the Treatment of Patients With De Novo Native Coronary Artery Lesions (C-SIRIUS indicates Canadian study; E-SIRIUS, European study); and TLR, target-lesion revascularization.

trial for FDA release of the rapamycin, polymer, Bx Velocity system.

Subsequent studies from the RESEARCH (Rapamycin-Eluting and TAXUS Stent Evaluated At Rotterdam Cardiology Hospital) registry experience at Thoraxcenter, Rotterdam, Netherlands, have documented the short-term safety of using these SES systems in patients with acute coronary syndromes, including STEMI (882,891). An additional small registry experience from the Rotterdam group suggests the potential applicability of the sirolimus DES system to ISR. A consecutive case series of 368 patients with 735 lesions for which 841 SES were implanted documented only 11 cases of restenosis (greater than 50% diameter), and all of those occurred in a focal pattern (892). The operators in that series, which included longer lesions (mean length of lesion 17.48 plus or minus 12.19 mm) and more complex anatomic subsets, learned from earlier studies of DES edge lesions to fully cover diseased segments (mean stent length 27.59 plus or minus 14.02 mm) (892).

TAXUS-I was the first feasibility and safety study of the paclitaxel, polymer, NIR stent system. There were 61 patients randomly allocated between a BMS and DES. At 12 months, the MACE rate was 3% (1 event) in the TAXUS group and 10% in the BMS group (4 events in 3 patients), and there were no subacute stent thromboses. Although these differences were not statistically significantly different, the continuous outcome of minimal lumen diameter was significantly better in the TAXUS group (886).

The ASPECT trial was a 3-center prospective, randomized trial of 177 patients with short (less than 15 mm), favorable (2.25 to 3.5 mm diameter) native vessel lesions who were randomly allocated between bare-metal Cook Supra-G stents and stents bonded with 1 of 2 doses of paclitaxel (885). Interpretation of this trial was complicated by the use of 3 different antiplatelet regimens. Binary restenosis was 4% in the high dose of paclitaxel, 12% in the low dose of paclitaxel, and 27% in the BMS arm. Subsequent mechanistic studies with IVUS documented that the paclitaxel-coated stents reduced neointimal hyperplasia (893).

TAXUS-IV was a prospective, randomized clinical trial of the slow-release; polymer-based paclitaxel-NIR stent system conducted at 73 US centers (94). A total of 1314 patients with native coronary lesions 10 to 28 mm in length and 2.5 to 3.75 mm in diameter were randomly allocated between BMS and the paclitaxel polymer system. At 9 months, angiographic restenosis was reduced from 26.6% to 7.9% with DES, albeit there were no differences in death, MI, or subacute stent thrombosis (0.6% and 0.8%, respectively). It is primarily on the basis of TAXUS-IV that the FDA released the paclitaxel, polymer NIR stent system. TAXUS-III was a registry study that demonstrated the potential efficacy of this DES system for ISR (888).

There is considerable promise and excitement surrounding the release of DES; nevertheless, important reservations remain, including the following:

- Most of the follow-up is still relatively short-term (1 year or less)
- Comparison of the 2 FDA-released systems is needed and should provide clinically useful information. One such trial that supplies information in this regard is ISAR-DESIRE (Intracoronary Stenting and Angiographic Results: Drug-Eluting Stents for In-Stent Restenosis), which is discussed in Section 7.3.6.2.
- Preliminary results from randomized trials (REALITY, SIRTAX) comparing SES and PES (CYPHER versus TAXUS) have not shown large differences in clinical outcomes [M.C. Morice, oral presentation, American College of Cardiology Scientific Session, Orlando, Fla, March 2005; S. Windecker, oral presentation, American College of Cardiology Scientific Session, Orlando, Fla, March 2005].
- Mandated angiographic follow-up applied in trials has increased the reintervention rate, and therefore, the difference between DES and BMS in clinical practice may be less.

The major trials of SES and PES, which were the basis for FDA approval, involved patients with stable or unstable ischemia with documented coronary artery narrowing of 51% to 99%, which stenoses were, for the most part, between 2.75 and 3.5 mm in diameter and 15 to 30 mm in length. Specific clinical exclusions from these landmark trials included the following: MI within 48 h; LV ejection fraction less than 0.25; previous or planned use of brachytherapy; previous PCI of the same lesion; coexisting medical conditions likely to limit life expectancy; contraindications to aspirin, thienopyridines, or stent substances; and severe renal or hematologic comorbidity. Specific angiographic exclusions from these landmark trials included the following: ostial lesions; bifurcation lesions; ULM lesion; SVG lesion; severe calcification; angiographic thrombus; severe tortuosity; and occluded vessel. Babapulle and coworkers have performed a Bayesian meta-analysis of randomized clinical trials of DES that incorporates the results of RAVEL, SIRIUS, C-SIRIUS, and E-SIRIUS regarding rapamycin-eluting stents and TAXUS, I, II, and IV regarding PES (234, 880, 881). These authors also included 4 trials of a nonpolymeric formulation of paclitaxel, which has not been shown to be effective in reducing restenosis or target-lesion or target-vessel revascularization and which has not been released for commercial use (234).

In an effort to extend the application of DES to most of the other clinical angiographic subsets, unstudied in these landmark trials, Serruys and coworkers at Thoraxcenter Rotterdam, the Netherlands, established the RESEARCH Registry (882). In this experience, the rapamycin-eluting stent has been used as the default strategy since it became available, and consecutive prospective cases of particular clinical and angiographic subsets have been compared with the immediately prior experience at the same institution with the particular subset (882).

Patients with acute coronary syndromes were considered for SES in a RESEARCH registry comparison of 198 consecutive patients receiving the SES versus a prior consecutive case series of 301 patients with acute coronary syndromes treated with BMS (882). Major adverse cardiac events including death (3.0% vs 3.0%), nonfatal MI (3.0% vs 1.0%), and target-vessel revascularization (1.0% vs 2.7%) were comparable for SES and BMS (total 6.1% vs 6.6%). Lemos and colleagues reported a series of 186 consecutive STEMI patients treated with an SES and compared that group with 183 patients treated with a BMS in terms of both short- and long-term outcomes (441). MACE at 30 days (7.5% vs 10.4%) and stent thrombosis (0% vs 1.6%) were not significantly different for SES compared with BMS patients. By 300 days, both target-vessel revascularization (1.1% vs 8.2%) and MACE (9.4% vs 17.0%) were reduced with SES versus BMS (441). A quantitative study reported by Saia et al demonstrated a binary restenosis rate of 0% at 6 months in a subset of 96 STEMI patients, which documented reduced late loss to a degree comparable to what was seen in the landmark trials of more stable patients with less complex anatomy (891).

Hoye and coauthors compared the outcomes of a consecutive case cohort of 56 patients with chronic total occlusions treated with SES and compared them with a prior consecutive case series of 28 patients with chronic total occlusions treated with BMS (883). By 12 months, MACE was 96.4% with SES and 82.1% with BMS (*P* less than 0.05 by log-rank testing) (883). A consecutive case series of 19 patients with 21 lesions of old SVGs treated with SES had 0% early revascularization and a 1-year (average) MACE of 84% (894). Unlike the other RESEARCH Registry series, this report included no historic control group.

7.3.6. Management Strategies for ISR

Since the last (2001) revision of the ACC/AHA PCI guideline, the proportional use of stents in percutaneous interventions has continued to increase. In part, this derives from randomized trial data suggesting that routine stenting is more effective than provisional stenting (636,872-874). In addition, stents are being used in a much wider spectrum of coronary and even graft anatomies (875). Accordingly, ISR has become increasingly important. Because stents prevent elastic recoil and late negative remodeling, the predominant mechanism of ISR is neointimal hyperplasia due to smooth muscle cell proliferation and extracellular matrix production. Two of the biggest changes since the 2001 revision have been the expanding databases evaluating the use of 1) DES to prevent ISR and 2) brachytherapy to treat ISR (discussed in Sections 7.3.6.2 and 7.3.6.3, respectively).

7.3.6.1. PTCA

PTCA has been used to treat patients with ISR (851-853). The mechanism of lumen improvement after PTCA for ISR relates to further stent expansion (851) and extrusion of the tissue through the stent struts (851-854). In an IVUS study of 64 restenotic Palmaz-Schatz stents, 56% plus or minus 28% of the lumen enlargement was the result of additional stent expansion, and 44% plus or minus 28% was the result of a decrease in neointimal tissue (851). Despite the use of high-pressure balloon dilation, a relatively high residual stenosis (18% plus or minus 12%) remained after treatment with PTCA.

The outcome after PTCA has been variable, depending in part on the size of the stented segment and length of the stent restenosis (855). In a consecutive series of 124 patients presenting with stent restenosis successfully treated with repeat PTCA, clinical follow-up was obtained at 27.4 plus or minus 14.7 months (855). Recurrent clinical events occurred in 25 patients (20%), including death (2%), MI (1%), and target-vessel revascularization (11%) (855). Cumulative event-free survival at 12 and 24 months was 86.2% and 80.7%, respectively (855).

A number of factors have been related to the frequency of clinical recurrence after PTCA for ISR (855), which include repeat intervention in SVGs, multivessel disease, low ejection fraction, and a 3-month interval between stent implantation and repeat intervention. One report involving 245 patients receiving BMS in the pre-DES era has categorized ISR into 4 classifications: focal, diffuse intrastent, diffuse proliferative, and total occlusion. Pattern I contains 4 types (A-D). Patterns II through IV are defined according to geographic position of ISR in relation to the previously implanted stent. Target-lesion revascularization was related to the length of the ISR, ranging from 10% for focal in-stent stenosis (class I) to 25% for intrastent restenosis (class II), 50% for diffuse proliferative ISR (class III), and 80% for ISR with total occlusion (class IV) (856).

A broad array of catheter-based technologies, including directional (857,858), rotational (859,860), extraction (861-865), and pullback (866) atherectomy, a cutting balloon, and excimer laser-assisted angioplasty, have been used to treat ISR in association with PTCA. Although some comparative registry series have suggested an improved angiographic outcome associated with the use of these ablative devices, no long-term studies demonstrating clinical advantage have been completed.

When a significant residual stenosis exists after conventional PTCA for ISR, PCI with stenting has been used to improve the initial angiographic result (867-869). Although preliminary results of clinical trials failed to demonstrate a benefit using routine BMS placement for the treatment of ISR, favorable results have been shown with DES, as summarized in the following section (116,870,871).

7.3.6.2. Drug-Eluting Stents

Class IIa

It is reasonable to perform repeat PCI for ISR with a DES or a new DES for patients who develop ISR if anatomic factors are appropriate. ***(Level of Evidence: B)***

In-stent restenosis represents a clinical challenge of great interest for DES technology. Sousa and coworkers treated 25 consecutive cases of ISR with SES (870). They demonstrated minimal intimal hyperplasia and no delayed malapposition by intracoronary ultrasound (870). Clinically, they reported a remarkable 0 repeat revascularizations, stent thromboses, or deaths (870). Degertekin and colleagues reported a group of 26 consecutive ISR patients treated with SES (871). They also used 3-dimensional ultrasound to document minimal neointimal formation by 4 months (871). This more complex cohort included 1 patient with transplant vasculopathy and 4 with prior brachytherapy, which provided support not only for the effectiveness of SES but also of the need for prolonged antiplatelet therapy and risk factor modification in patients with diffuse coronary disease (871). Saia and coworkers reported a series of 12 patients with ISR refractory to brachytherapy who received SES; 4 of 10 patients who were followed up long-term developed restenosis (895).

The ISAR-DESIRE trial compared the use of balloon angioplasty SES and PES treatment of ISR in 300 patients (896). Angiography at 6 months in 92% of the patients (n equals 275) demonstrated angiographic restenosis in 44.6% (41 of 92) of the balloon-alone group; 14.3% (13 of 91) of the SES group; and 21.7% (20 of 92) of the PES group. Both DES were superior to balloon alone, reducing the incidence of target-vessel revascularization (33% for balloon alone vs 8% for SES and 19% for PES). There was a trend toward superiority of SES over PES in angiographic restenosis that was marginally significant (*P* equals 0.19) and significance for target-vessel revascularization (*P* equals 0.02). These data support the use of either approved DES for the treatment of ISR over a BMS. Additional data for DES and ISR have been reported in the TReatment Of Patients with an In-STENT REstenotic Coronary Artery Lesion (TROPICAL) Study, which assessed outcomes in 155 patients with ISR receiving an SES. In-lesion late loss of 0.08 plus or minus 0.49 and a binary restenosis rate of 9.7% was reported at 6-month follow-up, with a reintervention rate of 7.4% (897). Furthermore, preliminary data suggest that in patients receiving SES for ISR (TROPICAL group), late lesion loss and binary restenosis at 6 months were significantly reduced compared with a historical group receiving brachytherapy for ISR in the GAMMA I and II studies [F.J. Neumann, oral presentation, EuroPCR, Paris, France, May 2004]. The potential benefit of SES compared with brachytherapy remains to be delineated in ongoing randomized trials.

7.3.6.3. Radiation

Class IIa

Brachytherapy can be useful as a safe and effective treatment for ISR. ***(Level of Evidence: A)***

Both gamma energy (photons), and beta energy (electrons) have been used in randomized clinical trials and prospective registries to reduce the neointimal proliferation associated with ISR (898-900). In the 2001 revision of the guideline, the initial results of the SCRIPPS trial (Scripps Coronary Radiation to Inhibit Proliferation Post Stenting) were summarized (117). Since then, the 5-year results of the SCRIPPS cohort have been published (901). The Ir-192–treated patients continued to demonstrate improved event-free survival (freedom from death, MI, or target-lesion revascularization) compared with placebo (61.5% vs 34.5%; *P* equals 0.02) (900). As shown in Table 31, this composite end point derived from improvements in each of the 3 component end points (92,116,117,658-660,901-903).

A number of reports of the GAMMA-1 trial have been published since the 2001 revision (622,658,904,905). The initial report of 9 months of follow-up demonstrated a statistically significant reduction in target-lesion revascularization with Ir-192 (42% vs 24 %; *P* less than 0.01). Death and MI were insignificantly higher with radiation.

The WRIST (Washington Radiation for In-Stent Restenosis Trial) investigators randomized 130 patients (65/65) with ISR between placebo and 15 Gy Ir-192 (116). The SVG-WRIST investigators randomized 120 patients (60/60) between placebo and Ir-192 for the treatment of ISR in SVGs (902). Again, the brachytherapy-treated cohort had lower rates of binary restenosis (21% vs 44%; *P* equals 0.005) and target-lesion revascularization (17% vs 57%; *P* less than 0.001).

Among the specific limitations of gamma radiation are the need for long treatment times and the high radiation exposure, which necessitate special shielding and removal of staff from the treatment room during dwell times (906). Beta radiation, in the form of electrons or particulate energy, has also demonstrated effectiveness in randomized trials of ISR, despite its more limited tissue penetration (92,659,660). Taken together, these data support the effectiveness of radiation in reducing restenosis after treatment of ISR. Further investigation into the causes of late stent thrombosis (907) have led to recommendations that 1) new stents not be implanted at the time of brachytherapy unless necessary and 2) antiplatelet therapy with both aspirin and a thienopyridine be continued for at least 6 to 12 months after brachytherapy (898-900,906).

Brachytherapy dosing for ISR is prescribed so as to achieve adequate radiation in the vessel wall to block cellular proliferation. The manufacturer's recommended dosing for the beta radiation source is 18.4 Gy at 2 mm from the source center for vessels from 2.7 to 3.35 mm in diameter and 23 Gy for vessels 3.35 to 4.0 mm in diameter. It is also recommended that radiation be delivered over the entire segment injured by balloon dilation and that at least a 5-mm margin be allowed on each side of the injured segment (908).

To date, the following potential limitations have been observed with the use of brachytherapy to treat ISR: edge stenoses or geographic miss; acute thrombosis; late thrombosis and occlusion (up to 14%); persistent dissections; late stent malapposition; increased plaque burden outside the stent; IVUS echolucent areas or black holes (898-900,906);

Table 31. Randomized Clinical Trials of Brachytherapy for In-Stent Restenosis

Trial (Ref.)	Year	n XRT/Placebo	Follow-Up, Angiographic/ Clinical	Source	Restenosis, XRT/Placebo	TLR, % XRT/Placebo	MI, XRT/Placebo	Death, XRT/Placebo
SCRIPPS (117)	1997	26/29	6 mo 12 mo	Gamma IR-192	17%/54% (*P* equals 0.01)	12%/45% (*P* equals 0.01)	4%/0% (*P* equals NS)	0%/3 % (*P* equals NS)
PREVENT (660)	2000	80/25	6 mo 12 mo	Beta P-32	22%/50% (*P* equals 0.018)	6%/24% (*P* less than 0.05)	10%/4% (*P* equals NS)	1%/0% (*P* equals NS)
WRIST (116)	2000	65/65	6 mo 12 mo	Gamma IR-192	22%/60% (*P* equals 0.0001)	3%/63% (*P* less than 0.001)	9%/9% (*P* equals NS)	6%/6% (*P* equals NS)
GAMMA-ONE (658)	2001	131/121	6 mo 9 mo	Gamma IR-192	32%/55% (*P* equals 0.01)	24%/42% (*P* less than 0.01)	9.9%/4.1% (*P* equals 0.09)	3.1%/0.8% (*P* equals 0.17)
INHIBIT (659)	2002	166/166	9 mo 290 d	Beta P-32	26%/52% (*P* less than 0.0001)	8%/26% (*P* less than 0.0001)	3%/3% (*P* equals NS)	3%/2% (*P* equals NS)
SCRIPPS (901)	2002	26/29	5 y	Gamma IR-192	NA	23%/48% (*P* equals 0.05)	4%/10% (*P* equals NS)	19%/31% (*P* equals NS)
START (92)	2002	244/232	8 mo	Beta Sr-90/Y-90	29%/45% (*P* equals 0.001)	14%/25% (*P* less than 0.001)	1.7%/3.3% (*P* equals 0.364)	1.3%/0.5% (*P* equals 0.625)
SVG-WRIST (902)	2002	60/60	6 mo 12 mo	Gamma IR-192	21%/44% (*P* equals 0.005)	17%/57% (*P* less than 0.001)	2%/3% (*P* equals NS)	7%/7% (*P* equals NS)
Long WRIST (903)	2003	60/60	6 mo 12 mo	Gamma IR-192	45%/73% (*P* less than 0.05)	39%/62% (*P* less than 0.05)	16.9%/18.3% (*P* equals NS)	6.8%/1.7% (*P* equals NS)

n indicates number of patients; NA, not applicable; NS, not significant; MI, myocardial infarction; TLR, target-lesion revascularization; and XRT, radiation therapy.

and very late catch-up phenomenon (in studies with more than 1 year of follow-up).

7.3.6.4. Medical Therapy

Acute platelet inhibition with abciximab does not reduce ISR, as demonstrated in the ERASER study (280). In a study of 225 patients randomly allocated to placebo or abciximab before intervention, 215 patients received a stent and the study drug. Of the 191 patients who returned for follow-up more than 4 months after evaluation, there was no difference between tissue volume, as measured by IVUS, between the placebo and treatment groups. Lack of abciximab benefit was confirmed by quantitative angiography. The investigators concluded that potent platelet inhibition with abciximab as administered in the ERASER study did not reduce ISR. In the Oral Sirolimus to Inhibit Recurrent In-Stent Restenosis (OSIRUS) trial, 300 patients were randomly assigned to receive a cumulative loading dose of either placebo (0 mg), usual-dose (8 mg) oral sirolimus, or high-dose (24 mg) oral sirolimus 2 days before and the day of repeat PCI, followed by maintenance therapy of 2 mg per day for 7 days (909). Restenosis was significantly reduced from 42.2% to 36.8% and 22.1% in the placebo, usual-dose, and high-dose groups, respectively (*P* equals 0.005). The need for target-vessel revascularization was reduced from 25.5% to 24.2% and 15.2%, respectively, although this was not statistically significant (*P* equals 0.08). Blood concentration of oral sirolimus was significantly correlated with late lumen loss at follow-up (*P* less than 0.001). The investigators concluded that oral adjunctive sirolimus treatment for treatment of ISR resulted in significant improvement in the angiographic parameters of restenosis. Further elucidation of optimal dosing, need for pretreatment, and duration of oral sirolimus, as well as long-term follow-up, are needed.

7.3.7. Subacute Stent Thrombosis

The issues of subacute stent thrombosis and technical issues with the PES balloon-delivery system were early causes for concern (910). After many more data have been accumulated, as exemplified by the above-cited registry data, there does not appear to be an increased incidence of early thrombosis with either SES or PES. As reported in the FDA editorial (910), Boston Scientific has recalled a number of TAXUS stent systems because of reports of balloon deflation or retrieval problems and is working closely with the FDA to monitor the situation.

7.3.8. Drug-Eluting Stents: Areas Requiring Further Investigation

Both small vessels (less than 2.75 mm) and long lesions (greater than 18 mm) have been included in the C-SIRIUS and E-SIRIUS trials (880,881). In addition, there are increasing numbers of patients entered into prospective registries and compared retrospectively with the following clinical and angiographic subsets, which were not included in randomized comparative trials of DES versus BMS: acute coronary syndromes; STEMI, chronic total occlusions; SVGs; and ISR. Most of the data currently available regarding the use of DES for ostial lesions, bifurcation lesions, ULM arteries, and extremely long segments are in the form of uncontrolled case reports or series. Nonetheless, given the promising results in reducing late target-lesion and target-vessel revascularization in nearly every group, it is to be expected that registry and randomized trial data will continue to accumulate at a rapid pace.

7.4. Cost-Effectiveness Analysis for PCI

Among all diseases worldwide, ischemic heart disease currently ranks fifth in disability burden and is projected to rank first by the year 2020 (911). As healthcare delivery systems in countries with established economic markets continue to incorporate new and expensive technologies, the costs of medical care have seemingly escalated beyond the revenue historically allotted to health care. Given limited healthcare resources, a cost-effectiveness analysis is appropriate to evaluate percutaneous coronary revascularization strategies (912). The results of cost-effectiveness analyses for any comparable treatment are reported in terms of the incremental cost per unit of health gained, such as 1 year of life adjusted to perfect health (quality-adjusted life year, QALY) compared with the standard of care (913). By modeling different treatments, different patient subsets, and different levels of disease, a series of cost-effectiveness ratios may be constructed to show the tradeoffs associated with choosing among competing interventions.

Although there is no established cost-effectiveness ratio threshold, cost-effectiveness ratios of less than $20 000 per QALY (such as seen in the treatment of severe diastolic hypertension or with cholesterol lowering in patients with ischemic heart disease) are considered highly favorable and consistent with well-accepted therapies. Incremental cost-effectiveness ratios that range between $20 000 and $60 000 per QALY may be viewed as reasonably cost-effective and thus acceptable in most countries, whereas ratios greater than $60 000 to $80 000 may be considered too expensive for most healthcare systems. The Committee defines useful and efficacious treatments, in terms of cost-effectiveness, as treatments with acceptable or favorable cost-effectiveness ratios. Cost-effectiveness analysis is not by itself sufficient to incorporate all factors necessary for medical decision making on an individual patient basis, nor is it sufficient to dictate the broad allocation of societal resources for health care. Rather, cost-effectiveness analysis aims to serve mainly as an aid to medical decision making on the basis of comparison with other evaluated therapies.

The results of cost-effectiveness analysis in the field of percutaneous revascularization for ischemic heart disease have been derived from decision models that incorporate literature-based procedure-related morbidity and mortality, coronary disease–related mortality, and estimates of the benefit of selected revascularization procedures. When available, results from randomized trials (levels of evidence A and B) are used to estimate the outcomes of each decision tree branch within the decision-analytical model, for example, using data estimating the restenosis rate after uncomplicated coronary stenting of a single, simple lesion. Cost-effectiveness analyses have been used to compare medical therapy with PTCA with CABG (914), balloon angioplasty with coronary stenting (915,916), and routine coronary angiography after acute MI with symptom-driven coronary angiography (917).

In patients with severe angina, normal LV function, and single-vessel disease of the LAD, the cost-effectiveness ratio for PTCA, directional coronary atherectomy, or coronary stenting that can be expected to provide a more than 90% success rate with a less than 3% major acute complication rate is very favorable (less than $20 000 per QALY) compared with medical therapy (914). The rating also applies to patients with symptomatic angina or documented ischemia and 2-vessel coronary disease, in whom percutaneous coronary revascularization can be expected to provide a more than 90% success rate with a less than 3% major acute complication rate. In patients with 3-vessel coronary disease who have comorbidities that increase the operative risk for CABG surgery, PCI that is believed to be safe and feasible is reasonably acceptable ($20 000 to $60 000 per QALY). In patients in the post-MI setting, a strategy of routine, non–symptom-driven coronary angiography and PCI performed for critical (greater than 70% diameter stenosis) culprit coronary lesions amenable to balloon angioplasty or stenting has been proposed to be reasonably cost-effective in many subgroups (917).

In patients with symptomatic angina or documented ischemia and 3-vessel coronary disease, for which bypass surgery can be expected to provide full revascularization and an acute complication rate of less than 5%, the cost-effectiveness of PCI is not well established. Although PTCA for 2- and 3-vessel coronary disease appears to be as safe as but initially less expensive than CABG surgery, the costs of PTCA converge toward the higher costs of bypass surgery after 3 to 5 years (918,919). Thus, whereas PTCA or CABG surgery has been shown to be cost-effective compared with medical therapy, there is no evidence for incremental cost-effectiveness of PTCA over bypass surgery for 2- or 3-vessel coronary disease in patients who are considered good candidates for both procedures. For patients with 1- or 2-vessel coronary disease who are asymptomatic or have only mild angina, without documented left main disease, the estimated cost-effectiveness ratios for PCI are greater than $80 000 per QALY compared with medical therapy and are thus considered less favorable.

The initial mean cost of angioplasty was 65% that of surgery, but the need for repeat interventions increased medical expenses so that after 5 years, the total medical cost of PTCA was 95% that of surgery ($56 225 vs $58 889), a significant difference of $2664 (*P* equals 0.047). Compared with CABG, PTCA appeared less costly for patients with 2-vessel disease but not for patients with 3-vessel disease.

The use of DES is affecting the cost-effectiveness of PCI. In the SIRIUS trial (93), there were 21 fewer repeat revascularization procedures per 100 patients treated with the sirolimus stent. Although the DES group's hospital costs were $2800 more, much of that was negated in follow-up by the high reintervention rate in the BMS group (920). However, the number of repeat procedures in such trials with routine angiographic follow-up is inflated compared with registries of BMS, which suggests only 6 to 7 repeat procedures are avoided by routinely using DES (882). The ultimate cost effectiveness of drug-eluting stenting will depend on the cost of the stents, how many are implanted per patient, and how many repeat procedures are avoided.

Because cost-effectiveness analysis research is new in the field of PCI, its results are limited. The Committee underscores the need for cost containment and careful decision making regarding the use of PCI strategies.

8. FUTURE DIRECTIONS

The field of coronary intervention has expanded dramatically over the past decade and will continue to evolve over the next several years. New directions will focus on strategies that will further improve procedural safety, reduce the recurrence rate after PCI, and expand the procedure to more complex anatomic subsets. Clinical acceptance of these technologies will be based on demonstration of safety and efficacy over conventional therapies in randomized clinical studies. Several novel strategies are summarized below.

Because the widespread use of stent implantation has lessened the risk of need for emergency bypass, future clinical research will focus on remaining obstacles that decrease procedural success or increase risk. Chronic total occlusion remains a stubborn problem. New devices such as the Frontrunner catheter and new ultrastiff guidewires show some promise in improving procedural success; however, new approaches are needed.

Degenerated vein graft disease remains a high-risk subset. The SAFER trial (255) has demonstrated that distal protection with a balloon occlusive device with intraprocedural aspiration decreases procedural risk. Similarly, a number of distal filter devices are undergoing active testing (254). The results of one such multicenter trial comparing a filter-based catheter with a balloon occlusive and aspiration device showed similar results for MACE at 30 days (254). In spite of these approaches, these procedures are still associated with MACE event rates of 8% to10%. More research is still needed in this area. The use of distal protection devices in settings other than degenerative vein graft disease requires further study. For example, initial studies in primary PCI suggested a benefit with the FilterWire™; however, subsequent trials with the GuideWire have failed to show any benefit, instead showing poor outcomes in this setting. Thus, further research is needed before this technology is adopted for use beyond degenerative vein graft disease.

Dramatic advances have been made in the treatment of restenosis. Although the oral agents tranilast (921) and folic acid have proven unsuccessful, other catheter-based strategies have dramatically decreased restenosis risk. Brachytherapy (for ISR), rapamycin-eluting stents, and PES have been extremely effective. Subgroups such as diffuse ISR and insulin-dependent diabetes mellitus will require further study. Other therapies, such as photodynamic therapy, cryotherapy, and therapeutic ultrasound, remain interesting but unproven approaches to treat restenosis.

In patients with refractory angina who have no vessels suited for revascularization, a number of new therapies are being tested. Enhanced external counterpulsation appears to decrease symptoms (922). Treatment with fibroblast growth factor by an intracoronary approach also shows promise (923). Percutaneous laser transmyocardial revascularization has shown mixed results. The PACIFIC trial (Potential Class Improvement From Intramyocardial Channels) putatively demonstrated some benefit of percutaneous laser transmyocardial revascularization, but the major limitation of that study was that it was not placebo-controlled; thus, after its failure to address potential concerns, general consensus attributes the results in PACIFIC to a placebo effect. Also, in PACIFIC, diverse outcomes tended to be higher with laser therapy (924). Although the randomized, double-blind BELIEF trial (Blinded Evaluation of Laser PMR Intervention Electively For angina pectoris) of 82 patients appeared to show some benefit of percutaneous laser transmyocardial revascularization versus sham procedure on angina class and quality-of-life measures, the results were inconclusive given the small size of the study (925). To date, data are insufficient for FDA approval of percutaneous laser therapy. A new frontier has been opened with the intra-arterial infusion of marrow-derived stem cells (926) and direct injection of skeletal muscle–derived myoblasts (927) for myogenesis. Studies to date were performed in patients with severe angina; thus, it is uncertain how this technology might apply to other subsets of patients with coronary disease (e.g., acute coronary syndromes, ischemic cardiomyopathy), and rigorous, blinded evaluation of these approaches must occur.

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APPENDIX 1. ACC/AHA/SCAI Committee to Update 2002 Guidelines for Percutaneous Coronary Intervention—Relationships with Industry

Committee Member	Research Grant	Speakers Bureau/ Honoraria	Stock Ownership	Consultant
Dr. Ted E. Feldman	Abbot Boston Scientific Cardia EV3 Evalve Guidant	Boston Scientific	None	None
Dr. John W. Hirshfeld, Jr	None	None	None	None
Dr. Alice K. Jacobs	None	None	None	Wyeth
Dr. Morton J. Kern	None	None	None	None
Dr. Spencer B. King, III	Guidant	BMS-Sanofi Guidant	None	Medtronic Novoste
Dr. Douglass A. Morrison	None	None	None	None
Dr. William W. O'Neill	None	None	None	None
Dr. Hartzell V. Schaff	None	None	None	None
Dr. Sidney C. Smith, Jr	Merck	Bayer	Johnson & Johnson Medtronic	Bristol-Myers Squibb Eli Lilly Pfizer Sanofi-Aventis
Dr. Patrick L. Whitlow	Abbot Cordis, Inc Fox Hollow Technologies Lumend, Inc	None	Medtronic	None
Dr. David O. Williams	None	None	None	None

This table represents the relevant relationships of authors with industry that were reported orally at the initial writing committee meeting in July 2002 and updated in conjunction with all meetings and conference calls of the writing committee. It does not reflect any actual or potential relationships at the time of publication.

Attachment D

APPENDIX 2. External Peer Reviewers for the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention*

Peer Reviewer Name†	Representation	Research Grant	Speakers Bureau/ Honoraria	Stock Ownership	Consultant/ Advisory Board
Dr. Michael Cowley	Official Reviewer – SCAI	None	None	None	None
Dr. David Faxon	Offical Reviewer – ACC/AHA Task Force on Practice Guidelines	None	None	None	None
Dr. Roxana Mehran	Official Reviewer – SCAI	None	The Medicines Co.	None	None
Dr. E. Magnus Ohman	Official Reviewer – AHA	Berlex Bristol-Myers Squibb Millennium Schering-Plough	None	Inovise Medical Medtronic Response Medical	None
Dr. Richard Pomerantz	Official Reviewer – ACCF Board of Governors		Aventis	Amgen Johnson & Johnson Pfizer Schering-Plough	Medacorp
Dr. Robert D. Safian	Official Reviewer – AHA	None	None	None	None
Dr. W. Douglas Weaver	Official Reviewer – ACCF Board of Trustees	None	None	None	None
Dr. Jeffrey L. Anderson	Content Reviewer – Individual Review	Sanofi/Bristol-Myers Squibb Novartis	Merck Sanofi/Bristol-Myers Squibb	None	Merck
Dr. Elliott M. Antman	Content Reviewer – Individual Review	Aventis Bayer Biosite Boehringer-Mannheim Bristol-Myers Squibb British Biotech Centor Cor/Millennium Corvas Dade Genentech Lilly Merck Pfizer Sunol	None	None	Aventis
Dr. Larry S. Dean	Content Reviewer – ACCF Cardiac Catheterization and Intervention Committee	None	None	None	None
Dr. Tommaso Gori	Content Reviewer – AHA Diagnostic and Interventional Cardiac Catheterization Committee	None	None	None	None
Dr. Sharon A. Hunt	Content Reviewer – Individual Review	None	None	None	None
Dr. Lloyd Klein	Content Reviewer – AHA Diagnostic and Interventional Cardiac Catheterization Committee	None	None	None	None
Dr. Glenn Levine	Content Reviewer AHA Diagnostic and Interventional Cardiac Catheterization Committee	None	Aventis	None	None
Dr. Joseph P. Ornato	Content Reviewer – Individual Review	Genentech	None	None	Bristol-Myers Squibb Genentech

This table represents the relevant relationships of peer reviewers with industry to this topic that were disclosed at the time of peer review of this guideline. It does not necessarily reflect relationships with industry at the time of publication.
*Participation in the peer review process does not imply endorsement of the document.
†Names are listed in alphabetical order within each category of review.

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Attachment E

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JOURNAL of the AMERICAN COLLEGE of CARDIOLOGY

ACCF/AHA/SCAI 2007 Update of the Clinical Competence Statement on Cardiac Interventional Procedures: A Report of the American College of Cardiology Foundation/American Heart Association/American College of Physicians Task Force on Clinical Competence and Training (Writing Committee to Update the 1998 Clinical Competence Statement on Recommendations for the Assessment and Maintenance of Proficiency in Coronary Interventional Procedures)

Spencer B. King, III, Thomas Aversano, William L. Ballard, Robert H. Beekman, III, Michael J. Cowley, Stephen G. Ellis, David P. Faxon, Edward L. Hannan, John W. Hirshfeld, Jr, Alice K. Jacobs, Mirle A. Kellett, Jr, Stephen E. Kimmel, Joel S. Landzberg, Louis S. McKeever, Mauro Moscucci, Richard M. Pomerantz, Karen M. Smith, George W. Vetrovec, Mark A. Creager, John W. Hirshfeld, Jr, David R. Holmes, Jr, L. Kristin Newby, Howard H. Weitz, Geno Merli, Ileana Piña, George P. Rodgers, and Cynthia M. Tracy

J. Am. Coll. Cardiol. 2007;50;82-108; originally published online Jun 25, 2007;
doi:10.1016/j.jacc.2007.05.006

Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 50, No. 1, 2007
ISSN 0735-1097/07/$32.00
doi:10.1016/j.jacc.2007.05.006

ACCF/AHA/SCAI CLINICAL COMPETENCE STATEMENT

ACCF/AHA/SCAI 2007 Update of the Clinical Competence Statement on Cardiac Interventional Procedures

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TABLE OF CONTENTS

This document was approved by the American College of Cardiology Board of Trustees in May 2007, the American Heart Association Science Advisory and Coordinating Committee in May 2007, and the Society for Cardiovascular Angiography and Interventions in May 2007.

When citing this document, the American College of Cardiology, American Heart Association, and Society for Cardiovascular Angiography and Interventions would appreciate the following citation format: King SB III, Aversano T, Ballard WL, Beekman RH III, Cowley MJ, Ellis SG, Faxon DP, Hannan EL, Hirshfeld JW Jr., Jacobs AK, Kellett MA Jr., Kimmel SE, Landzberg JS, McKeever LS, Moscucci M, Pomerantz RM, Smith KM, Vetrovec GW. ACCF/AHA/SCAI 2007 update of the clinical competence statement on cardiac interventional procedures: a report of the American College of Cardiology Foundation/American Heart Association/American College of Physicians Task Force on Clinical Competence and Training (Writing Committee to Update the 1998 Clinical Competence Statement on Recommendations for the Assessment and Maintenance of Proficiency in Coronary Interventional Procedures). J Am Coll Cardiol 2007;50:82–108.

This article has been copublished in the July 3, 2007, issue of *Circulation*.

Copies: This document is available on the World Wide Web sites of the American College of Cardiology (www.acc.org), the American Heart Association (www.americanheart.org), and the Society for Cardiovascular Angiography and Interventions (www.scai.org). For copies of this document, please contact Elsevier Inc. Reprint Department, fax (212) 633-3820, e-mail reprints@elsevier.com.

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Preamble

The granting of clinical staff privileges to physicians is a primary mechanism used by institutions to uphold the quality of care. The Joint Commission on Accreditation of Health Care Organizations requires that the granting of continuing medical staff privileges be based on the criteria specified in the medical staff bylaws. Physicians themselves are thus charged with identifying the criteria that constitute professional competence and with evaluating their peers accordingly. Yet, the process of evaluating physicians' knowledge and competence is often constrained by the evaluator's own knowledge and ability to elicit the appropriate information, problems compounded by the growing number of highly specialized procedures for which privileges are requested.

The American College of Cardiology Foundation/American Heart Association/American College of Physicians (ACCF/AHA/ACP) Task Force on Clinical Competence and Training was formed in 1998 to develop recommendations for attaining and maintaining the cognitive and technical skills necessary for the competent performance of a specific cardiovascular service, procedure, or technology. These documents are evidence based and, where evidence is not available, expert opinion is utilized to formulate recommendations. Indications and contraindications for specific services or procedures are not included in the scope of these documents. Recommendations are intended to assist those who must judge the competence of cardiovascular health care providers entering practice for the first time and/or those who are in practice and undergo periodic review of their practice expertise or who apply for privileges at a new institution. The assessment of competence is complex and multidimensional, therefore, isolated recommendations contained herein may not necessarily be sufficient or appropriate for judging overall competence. The current document addresses competence in cardiac interventional procedures and is authored by representatives of the ACCF, the AHA, and the Society for Cardiovascular Angiography and Interventions (SCAI). This document applies to specialists trained in internal medicine and/or adult cardiology and is not meant to be a clinical competence statement on procedures for congenital heart disease in the child or young adult.

The ACCF/AHA/ACP Task Force makes every effort to avoid any actual or potential conflicts of interest that might arise as a result of an outside relationship or personal interest of a member of the ACCF/AHA/ACP Writing Committee. Specifically, all members of the Writing Committee were asked to provide disclosure statements of all such relationships that might be perceived as real or potential conflicts of interest relevant to the document topic. These statements were reviewed by the Writing Committee and updated as changes occurred. The relationships with industry for authors and peer reviewers are published in the appendices of the document.

Mark A. Creager, MD, FACC, FAHA
Chair, ACCF/AHA/ACP Task Force on
Clinical Competence and Training

Introduction

Coronary intervention has evolved from an investigational procedure to a widely practiced, mature mainstream clinical therapy (1). Conventional balloon angioplasty, while still a core procedure in interventional cardiology, has been augmented by adjunctive stenting, which greatly improves procedure efficacy and modestly reduces the risk of restenosis (2). Bare-metal stents have been replaced by drug-eluting stents in the majority of cases, which further reduce the risk of restenosis (3). Because stents or other interventional devices are commonly used, the coronary angioplasty procedure is more aptly termed "percutaneous coronary intervention" (PCI).

The AHA estimated that more than 1,000,000 PCIs were performed in the United States in 2003 (4). Physicians performing these procedures represent approximately 25% of board-certified cardiologists in the United States (5).

As a result of the maturation of PCI as a discipline and the ongoing clarification of its role in the management of coronary heart disease, the public can and should appropriately expect consistent access to high-quality PCI capability. However, there is potential for substantial variation in the quality of PCI services. PCI is often a complex, demanding procedure. To perform PCI optimally, an operator must possess a substantial cognitive knowledge base as well as considerable technical skill. In addition, the technical difficulty of a particular procedure can vary greatly from one patient to another. Furthermore, serious complications of coronary interventional procedures may occur unpredictably in procedures that initially appear to be straightforward. Recognition and management of complications are critical components of PCI procedures that require skill, knowledge, experience, and judgment. Since there can be variation among operators in cognitive knowledge and skill and among procedures in technical difficulty, there is a potential for substantial variation in procedure safety and efficacy.

Credentialing physicians to perform procedures is the responsibility of the governance of the local health care facility. The Joint Commission on the Accreditation of Health Care Organizations requires that medical staff privileges be granted to applicants only after assessment based on professional criteria. Physicians are charged with the responsibility to establish the criteria that constitute professional competence and to evaluate their peers on the basis of such criteria. The U.S. health care system relies, in part, on this process of granting and renewing clinical privileges to maintain quality.

The issue of determining quality standards and credentialing criteria has presented a major challenge to the medical profession. Developing standards has been difficult because, until recently, there were few data available on which to base them and because PCI techniques, indications, and capability have evolved rapidly. During the past several years, documents have been published that have offered guidelines and standards for the training and maintenance of competence (6–15). Because of the paucity of clinical data, the earlier standards were developed principally through observation, experience, and intuition. These standards relied heavily on operator activity level as a surrogate for skill and quality.

The most recent document published by the ACC was based on the information available in 1998 (16). The recommendations of this and other similar documents require updating as technology and training evolve (17).

Percutaneous noncoronary cardiac interventions, such as aortic and mitral valvuloplasty, atrial septal defect (ASD) and patent foramen ovale (PFO) closure, and alcohol septal ablation therapy, were not addressed in the previous document (16). These procedures, although constituting a small minority of interventional activity, are performed by interventional cardiologists and are included in the Accreditation Council on Graduate Medical Education (ACGME) curriculum and the American Board of Internal Medicine (ABIM) certifying exam. There have been no statements addressing clinical competence in noncoronary interventions.

The ACC, the ACP, the SCAI, the Society for Vascular Medicine and Biology (SVMB), and the Society for Vascular Surgery (SVS) have jointly developed a document on acquisition and maintenance of competence in vascular medicine and catheter-based vascular interventions (18); however, PCI and other percutaneous cardiac procedures are not addressed by the current document. This document is divided into 2 sections: PCI and percutaneous noncoronary cardiac interventions.

Purpose

This document was developed to review the currently available scientific data with the following purposes:

1. To characterize the expected success and complication rates for coronary interventional procedures when performed by highly skilled operators.
2. To identify comorbidities and other risk factors that may be used for risk adjustment when assessing procedure-specific expected success and complication rates.
3. To assess the relationship between operator activity level and success rates in PCI procedures as assessed by risk-adjusted outcome statistics.
4. To assess the relationship between institutional activity level and success rates in PCI procedures as assessed by risk-adjusted outcome statistics.
5. To develop recommendations for standards to assess operator proficiency and institutional program quality. These include standards for data collection to permit monitoring of appropriateness and effectiveness of PCI procedures both at the level of the operator and the institution.
6. To expand the scope of this competency document, previously limited to coronary procedures, to also include noncoronary cardiac interventions.

Writing Group Composition

The Writing Group was selected to represent a broad range of experience and expertise to bear on this issue. The members of the Writing Group were identified on the basis of 1 or more of the following attributes: PCI operators with a broad range of experience (in practice and in academic settings); individuals who have performed clinical research studying the outcome of PCI procedures; individuals who direct catheterization laboratories with a broad cross section of interventional operators; and individuals with broad clinical experience who have had considerable previous involvement with PCI.

Literature Review

A literature search was conducted with 5 goals:

1. To identify published coronary and other cardiac interventional outcomes data that could be used as benchmarks for quality assessment. In addition, the process sought to identify those risk adjustment variables that affect the likelihood of success and complications. This review focused on outcomes of coronary interventions, including the latest interventional devices as of the date of this revision.
2. To identify data that examines the relationships between operator and institutional experience, and activity levels, and their impact on procedural success and complication rates.
3. To assess the issues and problems associated with judging operator and institutional proficiency based on outcome statistics—in particular, the challenge of accurately assessing the performance of low-volume operators and institutions.
4. To expand the recommendations beyond coronary interventions to other cardiac interventional procedures.
5. To identify methods for monitoring appropriateness of performance of PCI.

Percutaneous Coronary Intervention

Evolution of Competence and Training Standards

Initially, because experience was limited, the coronary angioplasty technique was disseminated informally among physicians who were highly experienced at diagnostic cardiac catheterization. During this period, physicians acquired angioplasty skills through "on-the-job" experience, and no standards existed for either training requirements or for demonstration of competence.

As the coronary angioplasty knowledge base grew and techniques evolved, standards were developed for training (19). Formal angioplasty training programs were first organized in the early 1980s. The most recent recommendations were published by the ACC in 1999 (20). The ABIM developed an Examination in Interventional Cardiology that was first administered in 1999. As of 2005, 5,020 physicians had successfully passed the examination and become board certified in interventional cardiology. Currently, eligibility to sit for the ABIM interventional cardiology examination requires completion of a fourth-year fellowship in interventional cardiology in an ACGME-accredited program. During academic year 2004 to 2005, there were 122 accredited interventional cardiology programs in the United States that had 240 filled training positions.

Professional organizations have addressed the issue of standards and criteria for proficiency in PCI procedures since 1986, with an increasing focus on the issue of

JACC Vol. 50, No. 1, 2007
July 3, 2007:82–108

maintenance of proficiency and skills (6–15). These documents have universally endorsed an annual caseload goal for maintenance of proficiency. The most commonly endorsed activity level has been 75 procedures per year per operator. This standard was initially based on general consensus of experts. In recent years, considerable research has examined the volume–outcome relationship and, in general, has affirmed it (21,22).

Since the previous guidelines were published, there has been debate over the relationship between volume and quality. While a relationship between volume and outcomes exists, volume alone does not determine quality. Also, the ABIM interventional cardiology board exam has been established to certify a level of knowledge and experience in the field. This competency document addresses these factors as they relate to determinations of overall operator and institutional quality.

Evolution of Coronary Interventional Capabilities

The cognitive and technical knowledge base required for proficiency in PCI has expanded. The fundamental concepts of coronary angioplasty technique, namely the coaxial guide catheter and the dilation catheter with a minimally compliant cylindrical balloon, were formulated by Andreas Gruntzig (23). Because of the initial comparatively primitive equipment design and capability, coronary angioplasty was only applicable to readily accessible discrete proximal coronary stenoses. Subsequent refinement in instrumentation has greatly enhanced procedural success and extended the indications for the performance of PCI. Complex anatomic situations now considered technically suitable for PCI procedures include multivessel disease (24–30), distal and bifurcation stenoses, total occlusions (31), saphenous vein graft stenoses (32), and complex stenoses. Challenging clinical situations now considered appropriate for coronary intervention include patients with unstable angina (33,34) and myocardial infarction (MI) (35,36) and those who are not considered candidates for coronary bypass surgery.

Nonballoon devices, including coronary stents, and directional, rotational, and laser atherectomy devices, have been introduced. These devices augment conventional balloon angioplasty and extend its capability; however, they all require specific training and mentoring by a previously experienced operator. To become competent in the use of any of these newer interventional devices, an operator must acquire the additional knowledge and technical skills specific to each device.

A number of adjunctive antithrombotic and antiplatelet medications have been introduced for the purpose of reducing acute thrombus-related treatment site complications. Understanding the appropriate indications for and complications associated with the use of these medications, which are powerful anticoagulants, requires knowledge of hemostatic mechanisms.

Procedural Success and Complications of Coronary Interventional Procedures

Recent clinical studies have demonstrated that despite a continuing increase in clinical and angiographic complexity, procedural and clinical success rates have remained high and complication rates have remained low (37–45) (Table 1). Angiographic success occurs in over 95% of patients. Among patients without ST-segment elevation myocardial infarction (STEMI), PCI is associated with an average mortality rate of less than 1%, a Q-wave MI rate of less than 1%, and an emergency coronary artery bypass surgery (CABG) rate of less than 1%. Table 1 contains data from 5 large contemporary registries of PCI procedures and the first 2 National Heart, Lung, and Blood Institute (NHLBI) registries for historical comparison. These data constitute a point of departure for developing benchmarking standards.

Adverse events related to PCI procedures are categorized either by the mechanism of the complication or by the adverse event caused by the procedure. A given adverse event, such as death, may be caused by a variety of complications.

Complications can be divided into 3 mechanistic categories:

1. **Coronary vascular injury.** Coronary arterial injury can occur when devices are introduced into coronary vessels or result from embolization of thrombotic or atherosclerotic material from devices or vessel walls. Examples include coronary dissection, thrombosis, perforation, and embolization.
2. **Other vascular events.** Other vascular events are caused either by injury to a peripheral vessel by catheter insertion, manipulation, or removal, or by embolization of thrombotic or atherosclerotic material. Examples include pseudoaneurysm, retroperitoneal hemorrhage, arteriovenous fistula, and stroke.
3. **Systemic nonvascular events.** Systemic nonvascular adverse events are caused by the procedure but are not due to vascular injury. They include all the systemic hazards of cardiovascular radiographic angiography procedures. Examples include contrast agent-induced nephropathy and acute pulmonary vascular congestion.

For the purpose of assessing clinical competence, complications may be divided into 8 basic outcome categories:

1. **Death**: related to the procedure, regardless of mechanism
2. **Stroke**
3. **MI**: related to the procedure, regardless of mechanism
4. **Ischemia requiring emergency CABG**: either as a result of procedure failure or a procedure complication
5. **Vascular access site complications**
6. **Contrast agent nephropathy**
7. **Excessive bleeding, requiring treatment**
8. **Other (such as coronary perforation and tamponade)**

The first 4 of these categories are generally considered major adverse cardiac and cerebral events (MACCE). Be-

Table 1. Changes in Coronary Interventional Practice and Outcome From Registry Data

Variable	NHLBI-1 (40)	NHLBI-2 (38,39)	NHLBI Dynamic Registry (41)	ACC National Cardiovascular Data Registry (42)	Northern New England Consortium (43)	Michigan Blue Cross Consortium (44)	New York State Registry (45) Nonemergent	New York State Registry (45) Emergent
Clinical Characteristics								
Years of entry	1977–1981	1985–1986	1997–2002	1998–2005	2000–2004	2002	2001–2003	
No. of patients	1,155	1,802	6,183	1,082,690	36,831	5,901	124,096	14,946
Stent use (%)	0	0	78	91.6	86	84.0	87.5	92.7
Mean patient age (yrs)	54	58	63	61	62	63	65	60
Unstable angina (%)	37	49	44	35	43	32.0	27.8	83.6
ST-segment elevation MI (%)	0	0	25	13	12	18.9	0	53
Success and Complication Indicators								
Angiographic success (%)	68	91	93	2005: stented lesions: 99; nonstented lesions: 86	94	NA	97.5	97.5
Emergency CABG (%)	5.80	3.40	1.00	0.4	0.4	0.51	0.20	0.54
Mortality (%)	1.2	1.0	1.33	1.2 unadjusted rate	1.17	1.27	0.36	3.25

Reprinted with permission from Smith SC Jr., Feldman TE, Hirshfeld JW Jr., et al. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). J Am Coll Cardiol 2006;47:216–35 (15).

ACC = American College of Cardiology; CABG = coronary artery bypass graft surgery; MCD = multicenter database; MI = myocardial infarction; NA = not available; NHLBI = National Heart, Lung, and Blood Institute.

cause adverse events are definite end points, they are easily recognized and captured for statistical summary purposes. The ACC-National Cardiovascular Data Registry (NCDR)® has developed a comprehensive data dictionary with rigorous definitions of recognized adverse events (46). It may be impossible to determine conclusively whether death or a complication was caused by a procedure. Nonetheless, for the purposes of monitoring performance, rate of complications or deaths substantially above that expected, after adjustment for patient risk factors, is a cause for concern.

Patient, Lesion, and Institutional Variables Influencing Success and Complication Rates

A number of factors have improved the overall success and complication rates of PCI procedures. These include increased operator experience, modifications in conventional instrumentation (balloon catheters, guide catheters, guide wires), newer interventional devices (stents and embolization protection devices), and advances in adjunctive pharmacologic therapy. Concurrently, these improvements have led to the extension of interventional treatment to higher-risk patients with more complex coronary anatomy and comorbid disease. These factors have influenced overall acute and long-term outcome associated with PCI procedures.

Measures/Definitions of Success

Anatomic success. The definition of anatomic success focuses exclusively on the enlargement of the lumen at the target site and blood flow through the epicardial coronary artery. Although there has been disagreement, the current definition of success of PCI with stenting is the achievement of a minimal diameter stenosis of less than 20% as visually assessed by angiography and maintenance of Thrombolysis In Myocardial Infarction (TIMI) flow grade 3 (15). Anatomic success of PCI without stenting is defined as stenosis diameter reduction greater than 20% with residual stenosis less than 50%. Notably, there is frequently a disparity between the visual estimate of lumen diameter and quantitative measurements (47,48).

Procedural success. Procedural success has been defined as the achievement of anatomic success of all treated lesions without the major complications of death, MI, or emergency CABG (14,40). Although emergency CABG during hospitalization and death are easily identified end points, the definition of periprocedural MI has been more problematic. Some definitions require the development of Q waves in addition to a threshold value for creatine kinase (CK) elevation. However, more recent reports have included non-STEMIs with CK elevations greater than 3 or 5 times the upper limit of normal as clinically significant, since they have been shown to correlate with long-term mortality (49). Although major adverse cardiac events (MACE) have been

JACC Vol. 50, No. 1, 2007
July 3, 2007:82–108

used to judge success, some recent studies also include MACCE.

Short-term clinical success. Short-term clinical success requires, in addition to procedural success, the relief of signs and symptoms of myocardial ischemia.

Longer-term clinical success. Longer-term clinical success requires that the initial clinical success remains durable and that the patient has persistent relief of signs and symptoms of myocardial ischemia for 6 to 9 months after the procedure. Restenosis remains the principal cause of a lack of clinical success over the first year following a successful procedure. This directly leads to target lesion revascularization (TLR), target vessel revascularization, and target vessel failure. Thereafter, clinical events are usually caused by progression of disease at other sites. Clinically important restenosis may be judged by the frequency with which subsequent TLR procedures are performed after the index procedure. Incomplete revascularization, new lesion formation, and stent thrombosis may also limit long-term clinical success, especially in subsequent years (50).

Patient and Lesion Characteristics Related to Procedural Success and Complication Rates

Angioplasty procedural success and complication rates are influenced by a variety of patient and target lesion characteristics. These characteristics must be taken into consideration through risk adjustment when assessing adverse event rates. In addition, they must also be weighed in determining procedure appropriateness.

Patient clinical characteristics. The clinical factors associated with an increased risk of an adverse outcome after intervention include advanced age, female gender, acute coronary syndrome (especially STEMI), chronic renal insufficiency, heart failure, and multivessel coronary disease (7,12,14,15). Patients with impaired renal function, particularly patients with diabetes, are at increased risk for contrast-induced nephropathy (51).

Target lesion anatomic factors. Particular lesion morphologic characteristics are predictive of immediate outcome with coronary intervention (7,12,14,52). Lesion length, presence of thrombus, and degenerated saphenous vein grafts are independently associated with abrupt vessel closure and major ischemic complications. Chronic total occlusions (greater than or equal to 3 months) are associated with a lower procedural success rate. On the basis of these observations, a previous ACC/AHA Clinical Task Force on Clinical Privileges in Cardiology (13) proposed a classification scheme based on lesion morphology to estimate the likelihood of procedural success and complications. This scheme was subsequently modified by others (52) and has served as a useful guide for assessing the risk of an adverse outcome associated with a particular lesion. More recent experience indicates that improved devices and techniques have higher success rates in more complex lesions (53–56). As a result, lesion morphology may be less predictive of complications currently than it has been in the past (57).

Strategies for Risk Stratification and Operator Evaluation

Several large retrospective studies of patients undergoing PCI have identified clinical and angiographic characteristics that correlate with procedural success, in-hospital morbidity, and mortality (21,22,44) (Table 2). These observations have been used to develop multivariate logistic regression models that can stratify patients before the procedure. Model reliability is best assessed by relative predictive accuracy (C-statistic: moderate is greater than 0.80, excellent is greater than 0.90) and scaling accuracy (the Hosmer-Lemeshow statistic). Several models predict periprocedural mortality with C-statistic greater than 0.80 (Table 2). Prediction of other events is typically less accurate (58–60). Model utility also must consider the frequency and clinical importance of the event measured. Very infrequently occurring events, even if severe, may not allow adequate evaluation of operators with low volume. Results of several years of experience should be considered in order to have sufficient numbers of events to be adequately assessed from a statistical standpoint. Operators and catheterization laboratories should be encouraged to submit information to large databases that allow for evaluation of risk-adjusted outcomes.

Impact of the Facility on Procedural Success

Physical facility requirements. The physical facility in which interventional procedures are performed has an important impact on procedural success. The facility must provide radiologic equipment, monitoring, and patient support equipment to enable operators to perform at the best of their ability. The video and "cine" image quality of radiologic imaging equipment must be optimal to facilitate accurate catheter and device placement and enable proper assessment of procedure results. Physiologic monitoring equipment must provide continuous, accurate information about the patient's condition. Requisite support equipment must be available and in good operating order to respond to emergency situations.

Overall institutional system requirements. The interventional laboratory must have an extensive support system of specifically trained laboratory personnel. Cardiothoracic surgical, respiratory, and anesthesia services should be available to respond to emergency situations in order to minimize detrimental outcomes. The institution should have systems for credentialing, governance, data gathering, and quality assessment. Prospective, unbiased collection of key data elements on consecutive patients and consistent feedback of results to providers brings important quality control to the entire interventional program. The ACC/AHA/SCAI 2005 Guideline Update for PCI (15) recommends that each interventional program performing elective PCI

Table 2. Odds Ratios* for Significant Independent Risk Factors† for Short-Term Mortality Related to PCI

Source	New York State	Northern New England	Michigan BMC2	ACC-NCDR	ACC-NCDR Update		COAP
No. of patients	50,046	15,331	10,796	100,253	No acute MI (142,817)	Acute MI (30,926)	19,358
Incidence (%)	0.58	1.1	1.6	1.4	N/A	N/A	1.6
Years	2003	1994–1996	1997–1999	1998–2000	1998–2001	1998–2001	1999–2000
Clinical							
Acute MI less than 12–24 h	8.6	5.5	2.8	1.3			+
Age	+	+	+	+	+	+	+
Cardiac arrest			3.7				
CHF	3.2	8.6					1.6
COPD				1.3	1.7	1.5	1.8
Diabetes				1.4	1.25		
Female	1.5		1.8				1.4
IABP pre		26.2		1.7		1.9	
Peripheral vascular disease	2.6	3.3	1.6				1.6
Prior CABG	1.4						
Priority (salvage, emergent urgent, elective)		+		+	+	+	+
Renal insufficiency	3.1	6.4	5.5	3.0	3.5	2.0	3.5
Shock	22.1	32.2	11.5	8.5	9.8	8.8	9.8
Anatomic							
ACC lesion score, C		2.9					
Ejection fraction	+	+		+	+	+	+
LMT lesion				2.0	1.5	2.1	
Number of diseased vessels	+		+				
Prox LAD lesion				2.0	1.3	1.3	+
SCAI lesion score				+	+	+	
Thrombus			+				
Procedural							
Lytic use				1.4		1.25	
Nonstent use				1.6	1.6	1.4	
C-statistic	0.905	0.88	0.90	0.89	0.85	0.87	0.87

*Values are odds ratios for binary variables unless otherwise noted; †specific definitions of risk factors may vary from series to series; + relationship exists for continuous or ordinal variables (61–66). ACC-NCDR = American College of Cardiology National Cardiovascular Data Registry; BMC2 = Blue Cross Blue Shield of Michigan Cardiovascular Consortium; CABG = coronary artery bypass graft; CHF = congestive heart failure; COAP = clinical outcome assessment program; COPD = chronic obstructive pulmonary disease; IABP = intra-aortic balloon pump; LAD = left anterior descending; LMT = left main trunk; MI = myocardial infarction; PCI = percutaneous coronary intervention; SCAI = Society for Cardiovascular Angiography and Interventions.

should have in-house surgical support. Institutions that do not have in-house surgical support and are performing primary PCI only for STEMI, should have an established, well-organized system for emergency transfer to surgery at another institution.

Components of Operator Competence

Cognitive Knowledge Base

The knowledge needed to perform PCI, including that expected to be acquired in ACGME-approved interventional training programs, has been addressed by expert panels (7,8,20,67,68). The core knowledge is now tested by the ABIM Interventional Cardiology certifying examination which has been administered since 1999. Through 2003, physicians trained by a nontraditional pathway were eligible to take the examination based on either practice-based procedure activity and experience or by completion of an interventional training program. Since 2003, only individuals who have completed an ABIM-qualified training program are eligible to take the certifying examination. Individuals who train in interventional cardiology should become ABIM certified in interventional cardiology.

Training programs and the qualifying examination (20,69) require that interventional cardiologists be knowledgeable in anatomy, physiology, and pathophysiology of the cardiovascular system. In particular, one should understand the biology of coronary artery disease, be knowledgeable about the pathophysiology of myocardial ischemia and MI, and understand the dynamics of cardiac dysfunction. Interventionalists should possess a fundamental knowledge of stents and be familiar with the polymers and drugs that are incorporated into stents, coagulation cascade, thrombosis, and the pharmacology, therapeutic application, and risks of antiplatelet, antithrombin, and fibrinolytic drugs that are used in association with PCI. Competent operators must have knowledge of the indications for PCI and adjunctive and alternative use of medical therapy and surgery for patients with coronary artery disease based on an in-depth understanding of published clinical trials. Coronary interventionalists must understand the role of primary angioplasty compared with fibrinolytic therapy for STEMI and the alternative therapeutic approaches for treating STEMI that depend upon the time of presentation, anticipated door-to-balloon time, and the presence or absence of ongoing symptoms and/or electrocardiographic abnormalities.

Cognitive knowledge must be bolstered by clinical skills and experience that support the rational selection of optimal treatment strategies for each patient. Such decisions are based on symptoms, anatomy, and associated risk factors. Thus, equally important to knowing the indications for PCI is an understanding of its limitations and contraindications, particularly as these relate to comorbid systemic diseases and special anatomical subsets. Physicians performing these procedures should be conversant with the applicable guidelines (e.g., PCI, CABG, STEMI, unstable angina/NSTEMI [15,70–72]).

Coronary interventionalists must also have a thorough knowledge of specialized equipment, techniques, and devices used to perform PCI competently, including:

1. The theoretical and practical aspects of X-ray imaging, radiation physics and safety, and other equipment to generate digital images; quality control of images; image archiving; consequences of exposure of patients and personnel to ionizing radiation; and methods of reducing patient and staff radiation exposure (73).
2. Specialized catheterization recording and safety equipment (physiological data recorders, pressure transducers, blood gas analyzers, defibrillators) (74).
3. Catheters, guide wires, balloon catheters, stents, atherectomy devices, ultrasound catheters, intra-aortic balloon pumps, puncture site sealing devices, contrast agents, distal protection devices, and thrombus extraction devices.

Operators must be knowledgeable about the prevention, prompt recognition, and treatment of procedural complications. It is extremely important to have the knowledge and skills to diagnose and manage vessel perforation, no reflow, coronary dissection, expanding hematoma, pseudoaneurysm, arterial venous fistulas, and retroperitoneal hemorrhage. Interventionalists must also be cognizant of systemic complications, including cerebrovascular events and contrast-related nephropathy.

Technical Skills

Many of the skills required to perform coronary interventional procedures are closely related to those needed to perform diagnostic cardiac catheterization and coronary angiography. These include manual dexterity and the ability to obtain percutaneous arterial and venous access and maintain sterile surgical technique.

Most of the other required technical skills are unique to coronary interventional procedures and can only be acquired during training and by performing actual procedures under the direction of an experienced interventionalist. These include the manipulation and operation of guide catheters, coronary angioplasty guide wires, coronary angioplasty balloon catheters, specialized atherectomy devices, stents, and intracoronary ultrasound catheters. Such training appropriately occurs in standardized training programs that are ACGME-approved and lead to eligibility for board certification.

Nonballoon Devices

A special area of competence involves use of lesion assessment tools. Intracoronary devices commonly used by interventional cardiologists for assessment of intraluminal coronary anatomy and/or physiology include intravascular ultrasound (IVUS) or intracoronary ultrasound (ICUS), Doppler flow wires, and pressure wires. Competency in the use of angioscopy, optical coherence tomography, spectroscopy, intravascular thermography, and intravascular magnetic resonance imaging is beyond the scope of this document. Expertise in device manipulation and image interpretation is required to use these intravascular assessment devices safely and effectively. The risks of these devices is the same as those with PCI and include vessel spasm; myocardial ischemia; coronary artery dissection; plaque disruption; thrombosis; air, plaque, or thrombotic embolization; acute occlusion; coronary artery perforation; and contrast nephropathy, stroke, and access site complications. Therefore, only an interventional cardiologist skilled in transluminal coronary techniques such as balloon angioplasty and stenting who is able to diagnose and treat complications of interventional procedures should employ these devices. Recommendations regarding the use of IVUS, Doppler flow wires, and pressure wires are published in Appendix C of the ACC/AHA Guidelines for Coronary Angiography (75).

It is also important to ensure quality image acquisition, measurement, and reporting for each of the intravascular assessment devices. For ICUS, the reader is referred to the ACC Clinical Expert Consensus Document on Standards for Acquisition, Measurement and Reporting of Intravascular Ultrasound Studies (76). No such documents are available for Doppler analysis of coronary flow reserve and pressure wire analysis of fractional flow reserve, but many of the general principles in the IVUS document may be of some benefit in guiding appropriate use of these other modalities.

Relationships of Operator and Institutional Experience and Activity to Outcomes in Coronary Interventional Procedures

Evidence Reviewed

Computerized literature searches of English language publications, review of recent abstract publications, and solicitation of manuscripts under review for publication from

Table 3. Published Data Relating Hospital Coronary Angioplasty Volume to Complication Rates

Study	Data Source	No. of Patients/ Hospitals Studied	Conclusions	Comments
Hartz et al. (78)	1989–1991 Wisconsin Medicare	2,091/16	No relation between volume and outcome	Very low number of cases and hospitals examined
Ritchie et al. (86)	1989 California State (Adm)	24,883/110	Increased CABG (not death) less than 20 cases per yr; finding is valid for both acute MI and nonacute MI patients	
Jollis et al. (85)	1987–1990 MEDPAR (Adm)	217,836/1,194	Death and CABG increased with low volume (risk increases with Medicare patient volume* (less than 100–200 total per yr for death, 200–300 per yr for CABG)	
Kimmel et al. (84)	1992–1993 SCAI	19,594/48	Fewer major complications for labs with greater than 400 cases per yr	Able to risk adjust more completely than most other analyses
GUSTO (IIb) Angioplasty Substudy Group (36)	GUSTO IIb trial	565/59	No difference, 200–625 vs. greater than 625 cases per yr for acute MI patients	All operators greater than or equal to 50 cases per yr
Kato et al. (79)	1991 HCFA (RAND Corp.)	113,576/862	Except for Medicare volume* less than 50, higher volume hospitals had higher mortality rates	
Stone et al. (80)	PAMI II trial	1,100/34	No difference, less than 500, 501–1,000, greater than 1,000 cases per yr for acute MI patients	
Jollis et al. (77)	1992 Medicare (Adm)	97,498/984	Incremental decrease in death and bypass surgery as hospital Medicare volume* less than 100, 100–200, greater than 200 per yr	
Tiefenbrunn et al. (83)	Second National Registry of MI (U.S.)	4,939/?	Increased acute MI mortality for hospital less than 25 acute MI cases per yr	
Hannan et al. (82)	1991–1994 NY State	62,670/31	Death alone and same-stay CABG increased with annual caseloads less than 600	Risk-adjusted
Zahn et al. (81)	1992–1995 German Hospital Consortium	4,625/?	For patients with acute MI; increased mortality in hospitals with less than or equal to 40 acute MI PTCA per yr	No risk-adjusted
Moscucci et al. (22)	1998–1999 NY State and MI	11,374/8	In-hospital death increased for hospital volume less than 400	Risk-adjusted
Hannan et al. (21)	1998–2000 NY State	107,713/34	Death, same-day CABG, same-stay CABG increased for hospital volume less than 400	Risk-adjusted

*Medicare patients usually constitute 35% to 50% of total interventional caseload.
Adm = administrative data set; CABG = coronary artery bypass graft; GUSTO = Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes; HCFA = Health Care Financing Administration; MEDPAR = Medicare provider analysis and review; MI = myocardial infarction; PAMI = Primary Angioplasty in Myocardial Infarction; PTCA = percutaneous transluminal coronary angioplasty; SCAI = Society for Cardiovascular Angiography and Interventions.

many physicians and epidemiologists expert in the field were used to compile the relevant available scientific evidence relating institutional and operator activity level to outcomes (Table 3). In general, greater weight was given to recent, fully peer-reviewed publications of high quality. No single work was considered definitive. It was recognized that many analyses were limited to some extent by lack of capacity to fully adjust expected outcomes for differences in patient characteristics, changes and advances in the field of interventional cardiology, and inability to generalize the results to a broader population.

Relationship of Institutional Volume to Procedural Outcome

The preponderance of data suggest that, on average, hospitals in which fewer coronary interventions are performed have a greater incidence of procedure-related complications, notably death and need for bypass surgery for failed intervention, than hospitals performing more procedures. Multiple data sources support the existence of a curvilinear, perhaps logarithmic, statistical relation between caseload and outcome (Fig. 1). However, for CABG, the continued importance of the relationship between volume and outcomes has been recently confirmed using contemporary clinical data (87). For PCI, the majority of the studies available either predate the widespread introduction in interventional practice of coronary stenting and adjunctive use of glycoprotein receptor blockers, or were obtained through analysis of Medicare claims data or other administrative data. Recognized limitations of Medicare data include the need to extrapolate the total number of proce-

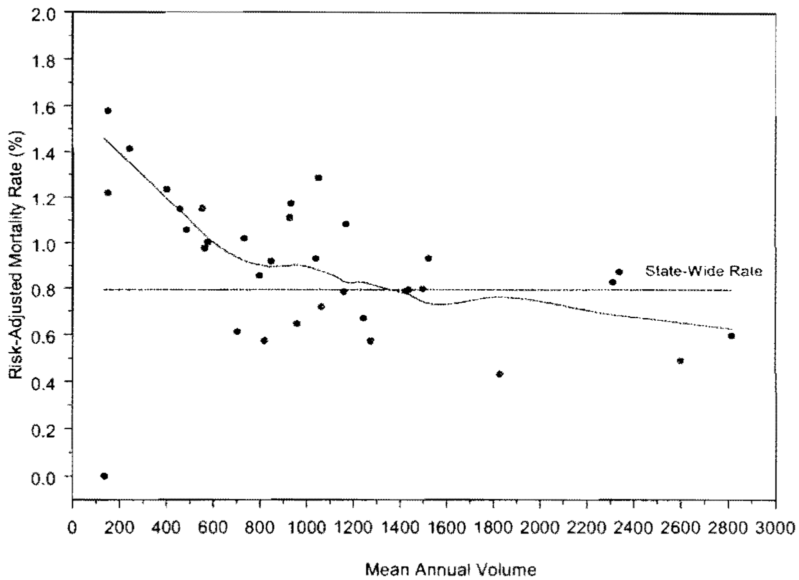

Figure 1. Mean Annual Hospital PCI Volume and Risk-Adjusted In-Hospital Mortality Rate in New York State, 1998–2000

Reprinted with permission from Hannan EL, Wu C, Walford G, et al. Volume-outcome relationships for percutaneous coronary interventions in the stent era. Circulation 2005: 112:1171–9 (21). PCI = percutaneous coronary intervention.

dures from the number of Medicare procedures, the incomplete reporting in Medicare claims of comorbidities that might be important predictors of adverse outcomes (16,17), and the possibility of miscoding complications as comorbidities (18).

The direct relationship between institutional volume and outcomes has been recently confirmed by 2 more contemporary analyses of large clinical registries. The first study compared data collected between 1998 and 1999 in a multicenter PCI registry in Michigan with data from the New York State data registry (22). An institutional annual volume less than 400 cases per year was found to be independently associated with an increased risk of in-hospital death compared with hospitals with annual volumes of at least 400 (adjusted odds ratio [OR] 1.77, 95% confidence interval [CI] 1.16 to 2.70). The second study (21), based on the New York State data registry, evaluated 107,713 procedures performed in 34 hospitals in New York State during 1998 to 2000. The same hospital volume threshold of less than 400 procedures per year was found to be associated with an increased risk of in-hospital mortality (adjusted OR 1.98, 95% CI 1.17 to 3.35), "same day" CABG surgery (adjusted OR 2.07, 95% CI 1.36 to 3.15) or "same stay" CABG surgery (adjusted OR 1.51, 95% CI 1.03 to 2.21). Figure 1 from the New York study presents the continuous relationship between hospital volume and risk-adjusted in-hospital mortality.

It is important to underscore that advancements in technology have resulted in a progressive improvement in outcomes of PCI, and that this improvement has at least in part offset the adverse institution volume–outcome relationship. In a recent study evaluating temporal trends in the volume–outcome relationship in the state of California, it was found that over time, the disparity in outcomes between low- and high-volume hospitals had narrowed, and that outcomes had improved significantly for all hospitals (88). The author of this study concluded that given these improvements, lower minimum volume standards might be justifiable in less populated areas, where the alternative is no access to angioplasty at all. Importantly, procedural volume is only one of many factors contributing to the variability of measured outcomes (58,82,89). Furthermore, there is no clear "cut-off" above or below which hospitals, or groups of hospitals in aggregate, perform well or poorly. There are institutions with low volumes that appear to achieve very acceptable results. For an individual institution, however, such an impression must be tempered by the statistical imprecision of the estimate of risk.

Volume and Outcomes Relationship for Primary PCI in Acute MI

The relationship between operator and institutional volume and outcome of primary PCI for acute MI has been examined nearly exclusively at hospitals with onsite cardiac surgery. In an analysis including 62,299 patients with acute MI and enrolled in the National Registry of Myocardial Infarction, Magid et al. (90) analyzed data from 446 acute-care hospitals providing primary angioplasty services. Hospitals were classified as low volume (less than 16 procedures per year), intermediate volume (17 to 48 procedures per year), and high volume (more than 49 procedures per year). In high-volume hospitals, mortality for acute MI patients was significantly lower with primary angioplasty when compared with fibrinolysis, while in low-volume hospitals, there were no differences in mortality rates between primary angioplasty and fibrinolysis. Two other analyses from the same registry and 2 studies using the New York State data registry have shown a direct relationship between hospital volume of primary angioplasty and mortality. In the analysis by Canto et al. (91), hospital volume was divided in quartiles. In-hospital mortality was 28% lower in patients treated in the highest volume quartile (greater than 33 primary PCIs per year) when compared with patients treated in the lowest volume quartile (less than 12 primary PCIs per year). Similar results were obtained by Cannon et al. (92). In this analysis, a procedure volume greater than 3 PCIs per month was found to be associated with a lower in-hospital mortality rate when compared with a procedure volume of less than 1 PCI per month, or with a procedure volume between 1 and 3 PCIs per month.

Recently, Hannan et al. (21) reported data from the New York State Coronary Angioplasty Reporting System Registry collected in the years 1998 to 2000, a period when stenting was used in a large majority of the STEMI patients. A trend toward an increased odds ratio of in-hospital mortality was observed for low-volume operators when compared with high-volume operators both for a volume cut of 8 procedures per year (OR 1.40, 95% CI 0.89 to 2.20) and with a volume cut of 10 procedures per year (OR 1.27, 95% CI 0.87 to 1.87). Importantly, a significant increase in the odds of in-hospital mortality was observed with lower institutional volume of primary PCI, regardless of whether the institutional volume cut point was set at 36 procedures per year (OR 2.01, 95% CI 1.27 to 3.17), 40 procedures per year (OR 1.73, 95% CI 1.1 to 2.71), or 60 procedures per year (OR 1.45, 95% CI 1.01 to 2.09).

Volume and outcomes relationship for PCI in hospitals without onsite cardiac surgery. There is only 1 report indicating a relationship between institutional PCI volume and outcome in hospitals without onsite cardiac surgery. Wennberg et al. (93) reported that among Medicare recipients, there was no difference in mortality after primary/rescue PCI (emergency procedure on the same day for STEMI) performed at hospitals with or without cardiac surgery onsite. However, they did report a higher mortality for PCI patients, excluding primary/rescue PCI, at hospitals without cardiac surgery onsite (adjusted OR 1.38, 95% CI 1.14 to 1.67; $p = 0.001$). The relationship between institutional volume and PCI affecting this outcome was confined mainly to hospitals without cardiac surgery onsite performing 50 or fewer nonprimary/rescue PCIs in Medicare recipients per year. Among hospitals performing more than 100 PCIs in Medicare recipients, mortality was not higher in hospitals without surgery onsite (adjusted OR 0.76, 95% CI 0.52 to 1.11; $p = 0.16$). These hospitals likely perform more than 200 PCIs per year based on the assumption that 100 Medicare PCIs represent approximately 200 total PCIs per year.

Taken together, these data suggest that the *relationship* between institutional volume of PCI patients (excluding primary/rescue PCI) and mortality in hospitals without surgery onsite may be similar to the relationship in hospitals with surgery onsite. For facilities without onsite surgery, it is mandatory that there be an established, well-organized plan for transfer for surgery if needed.

Relationship of Individual Operator Volume to Procedural Outcome

Several large studies have assessed the potential relation between individual operator caseload and procedural complications (93). Recently, McGrath et al. (94) analyzed relatively contemporary data (calendar year 1997) from the Medicare database. Based on a slightly different assumption than Wennberg et al. (93) that Medicare patients represent 35% to 45% of total PCI procedure volume, they estimated that 30 PCIs per operator per year on Medicare patients could be extrapolated to a total procedure volume of 70 PCIs per operator per year (94). A significant relationship between operator volume and outcomes was also reported in their study, with better outcomes observed in patients treated by high-volume operators when compared with patients treated by low-volume operators. Similar results were obtained in the study by Hannan et al. (21) in the analysis of data collected from the 107,713 procedures performed in the 34 hospitals performing PCI in New York State during 1998 to 2000. Operator volume thresholds were set at 75 procedures per year based on ACC/AHA recommendations, and at slightly higher levels of 100 and 125 procedures per year. There were no differences in risk-adjusted mortality between patients undergoing PCI performed by lower volume operators and patients undergoing PCI performed by higher volume operators for any of the 3 volume thresholds that were examined. However, for all 3 volume thresholds, significant differences for "same day" CABG surgery and for "same stay" CABG surgery were observed. For example, patients undergoing PCI with operators performing less than 75 procedures per year had a 65% increased odds of undergoing same-day CABG surgery, and a 55% increased odds of undergoing "same-stay" CABG surgery.

Further confirmation of the adverse operator volume–outcome relationship with contemporary PCI comes from an analysis by Moscucci et al. (95) of another regional, audited, clinical PCI registry. In that analysis including 18,504 procedures performed in 14 Michigan hospitals in calendar year 2002, operator volume was subdivided in quintiles (1 to 33 PCIs per year, 34 to 89 PCIs per year, 90 to 139 PCIs per year, 140 to 206 PCIs per year, and 207 to 582 PCIs per year). The primary end point was a composite of MACE, including death, CABG, stroke, transient ischemic attack, MI, and repeat PCI at the same lesion site. Stent utilization was greater than 80%, and greater than 70% of patients received a glycoprotein ($GP_{IIb/IIIa}$) receptor inhibitor. After adjustment for comorbidities, patients treated by operators in the 2 lower volume quintiles (Quintiles 1 and 2) had a 63% increase in the odds of MACE

JACC Vol. 50, No. 1, 2007
July 3, 2007:82–108

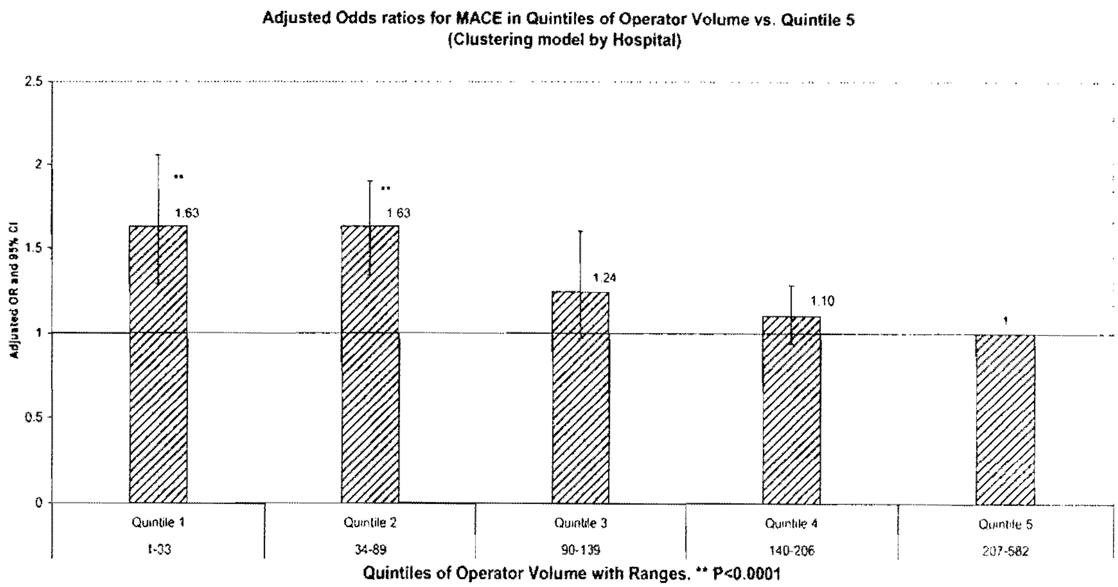

Figure 2. Adjusted Odds Ratios for MACE by Quintile of Operator Volume

Reprinted with permission from Moscucci M, Share D, Smith D, et al. Relationship between operator volume and adverse outcome in contemporary percutaneous coronary intervention practice: an analysis of a quality-controlled multicenter percutaneous coronary intervention clinical database. J Am Coll Cardiol 2005; 46:625–32 (95). MACE = major adverse cardiac events.

(Fig. 2). No significant relationship was observed between operator volume and risk of in-hospital death. The adverse relationship between operator volume and outcomes appeared to be relatively independent of patient risk. A detailed analysis of individual operator risk-adjusted outcomes revealed the presence of several low-volume operators with better than expected outcomes, and of a few high-volume operators with worse than expected outcomes, thus suggesting that there are exceptions to the rule, and that low-volume operators should be tracked over a longer period of time to ascertain their true performance (Fig. 3).

Combination of Individual Operator Volume and Institutional Volume on Procedural Outcome

The combined impact of hospital volume and operator volume on adverse outcomes was assessed by Hannan et al. (21). Patients undergoing PCI performed by operators with volumes below 75 per year in hospitals with volumes below 400 per year were found to have significantly higher odds of dying in the hospital than patients undergoing PCI performed by operators with volumes of 75 or more in hospitals with volumes of 400 or more (OR 5.92, 95% CI 3.25 to

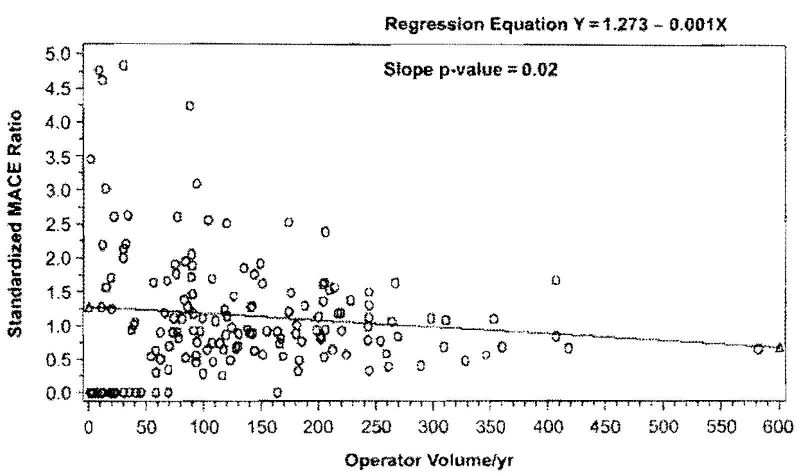

Figure 3. Linear Plot of Standardized MACE Ratios (Observed/Predicted Rates) Versus Annual Operator Volume

Reprinted with permission from Moscucci M, Share D, Smith D, et al. Relationship between operator volume and adverse outcome in contemporary percutaneous coronary intervention practice: an analysis of a quality-controlled multicenter percutaneous coronary intervention clinical database. J Am Coll Cardiol 2005; 46:625–32 (95). MACE = major adverse cardiac events.

10.97). Also, patients undergoing PCI performed by operators with annual volumes of below 75 in hospitals with annual volumes below 400 experienced significantly higher same-day CABG rates than patients with high-volume operators (greater than 75 annually) in high-volume hospitals (greater than 400 annually), with an OR of 4.02. For same-stay CABG surgery the respective OR was 3.19. It should be noted that the magnitude of these ORs demonstrates that the increase in adverse outcomes compound when patients undergo PCIs performed by low-volume operators (less than 75 annually) in low-volume hospitals (less than 400 annually).

In summary, analysis of more contemporary data supports the hypothesis that technological advancements have not completely offset the influence of "practice" in determining proficiency of contemporary PCIs. However, procedure volume is only a poor substitute for quality and outcomes; therefore, it should not be used as a replacement for appropriately risk-adjusted outcomes. Nevertheless, it is easy to measure, and its potential implications are easily understood by patients undergoing PCI. As such, it seems appropriate to continue to include procedure volume among the several indirect quality indicators of contemporary PCI practice.

However, it is also important to underscore that there are significant limitations to the simplistic interpretation of procedure volume statistics as a measure of competence and quality. First, it is uncertain whether this relationship is a result of the "practice makes perfect" principle, or the fact that patients are more frequently referred to high-quality operators. Second, it remains unclear where the "cut-off" number should be set. Third, studies have shown significant variability in the volume–outcome relationship within the same registry, with some low-volume operators having better than expected outcomes, and a few high-volume operators having worse-than-expected outcomes. Furthermore, at present, few or no data exist linking operator volume to case selection, appropriateness of procedures, periprocedural MI, long-term clinical outcome, or cost-effectiveness, each of which measures a component of quality of care, or linking clinical outcomes to operator experience as measured by the number of years in practice, total procedure volume over a lifetime career, or board certification.

The development of national, regional, and state registries for outcome assessment is also promoting a shift of the paradigm surrounding quality of PCI from a mere collection of procedure volume to objective assessment of clinical outcomes. In addition, the past decade has been characterized by substantial advancement in methodology, scientific rigor, and acceptance of risk adjustment. Factors related to in-hospital mortality following PCI are now well defined, and progress is being made toward the development of statistical models for other outcomes. Clearly, the calculation of risk-adjusted outcomes using data from clinical registries is a more accurate way to assess outcomes than using volume as a surrogate, and as more registry data become available, procedure volume will likely no longer be used as a replacement or a surrogate for quality assessment.

Yet, limitations related to the effect of random variation and to the evaluation of rare events continue to exist. These limitations make it difficult to assess the true performance of very-low-volume operators. In such situations, close scrutiny of case selection and close monitoring of outcomes on a case-by-case basis might serve as a substitute/complement to risk adjustment.

In summary, while there are inherent limitations in using procedure volume as a surrogate of quality and outcomes, recent data suggest that there is still a relationship between experience and outcomes. In the analysis of the New York State data, the relationship appeared to be at a level of 75 procedures per year, with further improvement in outcomes observed at a volume threshold of greater than 100 procedures per year. In the analysis of the Michigan data, the relationship was at a level of 100 procedures per year. On the basis of these data, it is recommended that the operator volume threshold continue to be 75 procedures per year. Independent of procedure volume, all operators should participate in a regional or national program for outcome assessment and quality improvement. In addition, it is recognized that there are limitations in the application of the risk-adjustment methodology in the evaluation of rare events and of low-volume operators, and that there might be substantial variations in the volume–outcome relationship. For operators that do not meet a threshold of 75 cases per year measured in 2-year intervals, it is recommended that a case-by-case review, case selection, and prior experience including the total number of cases in a lifetime career be included in their evaluation. They could also partner with higher volume operators to perform cases together to gain further experience.

Ongoing Quality Improvement and Maintenance of Competence

Maintenance of competence in interventional procedures should be accomplished for both the individual physician operator and for the institutions in which cardiac interventional procedures are performed. The goals in setting criteria for maintaining competence include:

1. Ensuring quality of patient care and outcomes;
2. Enabling quality interventionalists and institutions to continue to perform PCI;
3. Providing standards that all institutions and operators should strive to achieve.

Institutional Maintenance of Quality

It is recommended that all institutions have a regular (at least monthly) catheterization laboratory conference. The opportunity for ongoing dialogue and collaboration among angiographers, interventional operators, and cardiothoracic surgical colleagues is highly desirable. New developments in the angioplasty literature should be reviewed, and procedural complications should be discussed.

Maintenance of competence also requires that patient outcomes be determined longitudinally for each procedure by the institution's quality assessment program. Participation in a state, regional, or national database is highly encouraged. This allows institutions to measure risk-adjusted outcomes and compare them to regional and national benchmarks for improving quality of care.

It is recommended that lower volume institutions (less than 400 interventions per year) consider holding conferences with a partnering, more highly experienced institution. It is also recommended that any institution that falls outside the risk-adjusted national benchmarks in mortality or emergency same-stay CABG during 2 of 3 contiguous 6-month periods have an external audit looking for opportunities to improve quality of care.

Individual Maintenance of Quality

To maintain a cognitive knowledge base, it is recommended that individual operators attend at least 30 h of interventional cardiology continuing medical education (CME) every 2 years. This could include catheterization conferences and PCI meetings in addition to expanding the use of simulation cases for procedure use and competence.

To ensure appropriate patient selection and quality of technical skills, it is recommended that all operators have 5 randomly selected cases and all major complications reviewed each year by the catheterization laboratory director or a Quality Assessment Committee at the institution. Any operator performing less than 75 cases per year should have 10 cases reviewed per year. These performance evaluations should include feedback to the operator. If it is determined that the quality of PCI care being provided does not meet national benchmarks, the catheterization laboratory director should have the discretion of making recommendations for improving quality and reassessing over the next 6 months. If disagreements concerning corrective action occur, external review is often helpful.

Quality Assurance

Definition of Quality in PCI

Satisfactory quality in PCI may be defined as selecting patients appropriately for the procedure and achieving risk-adjusted outcomes that are comparable to national benchmark standards in terms of procedure success and adverse event rates. To achieve optimal quality and outcomes in PCI it is necessary that both the physician operator and the supporting institution be appropriately skilled and experienced.

Institutional Quality Assurance Requirement

In the United States, responsibility for quality assurance is vested in the health care institution that is responsible to the public to ensure that patient care conducted under its jurisdiction is of acceptable quality. Quality assessment review should be conducted both at the level of the entire program and at the level of the individual practitioner.

Each institution that performs PCI must establish an ongoing mechanism for valid peer review of its quality and outcomes. The program should provide an opportunity for interventionalists as well as physicians who do not perform angioplasty, but are knowledgeable about it, to review its overall results on a regular basis. The review process should tabulate the results achieved both by individual physician operators and by the overall program and compare them to national benchmark standards with appropriate risk adjustment. Valid quality assessment requires that the institution maintain meticulous and confidential records that include the patient demographic and clinical characteristics necessary to assess appropriateness and to conduct risk adjustment.

Role of Risk Adjustment in Assessing Quality

A raw adverse event rate that is not appropriately risk adjusted has little meaning. Data compiled from large registries of procedures performed in recent years have generated multivariate risk adjustment models for adverse event rates for PCI in the current era. Six multivariate models of the risk of mortality following PCI have been published (62,64,96–99).

Although these models differ somewhat, they are consistent in identifying acute MI, shock, and age as important risk stratification variables for mortality. The ACC-NCDR® reported an univariate in-hospital mortality of 0.5% for patients undergoing elective PCI, mortality of 5.1% for patients undergoing primary PCI within 6 h of the onset of STEMI and mortality of 28% for patients undergoing PCI for cardiogenic shock (64). Thus, it is clear that, in order to assess PCI mortality rates, patients should be stratified by whether they are undergoing elective PCI, primary PCI for acute STEMI without shock, or primary PCI for STEMI with shock.

Challenges in Determining Quality

Given the complexity of case selection and procedure conduct, quality is difficult to measure in PCI and is not determined solely by adverse event rates even when properly risk adjusted. Accurate assessment of quality becomes more problematic for low-volume operators and institutions because absolute event rates are expected to be small. Thus, particularly in low-volume circumstances, quality may be better assessed by an intensive case-review process conducted by recognized experts who can properly judge all of the facets of the conduct of a case. Case review also has merit in high-volume situations as it can identify subtleties of case selection and procedure conduct that may not be reflected in pooled statistical data.

Table 4. Key Components of a Quality Assurance Program

Clinical proficiency
- General indications/contraindications
- Institutional and individual operator complication rates, mortality, and emergency coronary artery bypass grafting
- Institutional and operator procedure volumes
- Training and qualifications of support staff

Equipment maintenance and management
- Quality of laboratory facility (see ACC/SCAI Expert Consensus Document on Catheterization Laboratory Standards [100])

Quality improvement process
- Establishment of an active concurrent database to track clinical and procedural information and patient outcomes for individual operators and the institution. Participation in multicenter database is highly encouraged.

Radiation safety
- Educational program in the diagnostic use of X-ray
- Patient and operator exposure

Requirement for Institutional Resources and Support

A high-quality PCI program requires appropriately trained, experienced, and skilled physician operators. However, the operator does not work in a vacuum. An operator needs a well-maintained high-quality cardiac catheterization facility to practice effectively. In addition, the operator depends on a multidisciplinary institutional infrastructure for support and response to emergencies. Thus, to provide quality PCI services, the institution must ensure that its catheterization facility is properly equipped and managed, and that all of its necessary support services, including data collection, are of high quality and are readily available.

The Quality Assessment Process

Quality assessment is a complex process that includes more than a mere tabulation of success and complication rates. Components of quality in coronary interventional procedures include appropriateness of case selection; quality of procedure execution; proper response to intraprocedural problems; accurate assessment of procedure outcome both short- and long-term; and appropriateness of postprocedure management. It is important to consider each of these parameters when conducting a quality assessment review. A quality program performs appropriately selected procedures while achieving risk-adjusted outcomes, in terms of procedure success and complication rates, that are comparable to national benchmark standards. It is accepted that quality assurance monitoring is best conducted through the peer-review process despite the political challenges associated with colleagues evaluating each other. There has been considerable controversy surrounding efforts to define standards, criteria, and methodologies for conducting quality assessment. There are many challenges to conducting this process in a fair and valid manner.

The cornerstone of quality assurance monitoring is the assessment of procedure outcomes in terms of success and adverse event rates. Other components of quality assurance monitoring include establishing criteria for assessing procedure appropriateness and applying proper risk adjustment to interpret adverse event rates. As adverse events should be rare, a valid estimate of a properly risk-adjusted adverse event rate generally requires tabulating the results of a large number of procedures. This adds an additional challenge to the valid assessment of low-volume operators and institutions. The responsible supervising authority should monitor the issues outlined in Table 4.

In addition, mere tabulation of adverse event rates, even with appropriate risk adjustment, is inadequate to judge operator or program quality. Such tabulations do not address numerous other quality issues—in particular, appropriateness. Thus, the quality assessment process should also conduct detailed reviews of both cases that have adverse outcomes, to determine the cause(s) of the adverse event, and of uncomplicated cases, in order to judge case selection appropriateness and procedure execution quality. These reviews should be conducted by recognized experienced interventionalists, drawn either from within the institution or externally, if a requisite number of appropriately qualified unconflicted individuals are not available.

Conclusions and Recommendations for PCIs

In formulating conclusions and recommendations it is important to emphasize that the ultimate goal of setting standards is to facilitate the attainment of optimal patient outcomes. Optimal outcome is most likely when operators select clinically appropriate patients for interventional procedures and perform these procedures at a requisite level of proficiency. Institutional and programmatic quality is ultimately determined by its success in achieving that goal.

Success and Complication Rates

Coronary interventional procedures may be complex and technically demanding to perform. Complications of these procedures may be life-threatening and can occur unpredictably. Nonetheless, recent clinical studies have demonstrated that despite increased clinical and angiographic complexity, procedural and clinical success has remained high and complications have remained low. Angiographic success (at least 1 lesion successfully dilated by greater than 20%, with a residual stenosis of less than 50%), excluding

JACC Vol. 50, No. 1, 2007
July 3, 2007:82–108

STEMI patients, occurs in over 95% with an average mortality rate of less than 1%, a Q-wave MI rate of less than 1%, and an emergency CABG rate of less than 1%.

Risk Adjustment

Several large retrospective studies have identified both clinical and angiographic characteristics of PCI that correlate with procedural success, hospital morbidity, and mortality. These studies have been used to develop multivariate logistic regression models that can stratify patients into risk groups before the procedure which have moderate predictive value for mortality (C-statistic 0.85 to 0.90), and slightly less predictive value for morbidity (C-statistic 0.67 to 0.78).

Volume–Activity Relationships

Analysis of more contemporary data supports the hypothesis that technological advancements have not offset the influence of "practice" in determining proficiency of contemporary PCIs. There are statistical associations between activity levels and short-term complication rates (emergency CABG and mortality) (17,58,85,89,97,101) for both institutions and for individual operators. In particular, low-volume operators operating at low-volume hospitals had an increased mortality rate. However, procedural volume is only one of many factors contributing to the variability of measured outcomes. Furthermore, there is no clear "cut-off" above or below which hospitals or individual operators perform well or poorly. Procedural volume continues to be correlated with outcomes, but should not serve as a substitute for a well-controlled analysis of results and does not ensure quality. The development of national, regional and state registries for outcome assessment is promoting objective assessment of clinical outcomes.

The expected low complication rate for coronary interventional procedures presents a major statistical power problem when attempting to estimate the true complication rate of the low-volume operator with meaningful precision. In such situations, close scrutiny of case selection and close monitoring of outcomes on a case-by-case basis would serve as a complement to risk adjustment.

Highly complex procedures require much more skill and experience, and should be undertaken by operators possessing these attributes. Complex cases appropriate for interventions should be referred, not denied.

Recommendations for Institutional Maintenance of Quality

It is recommended that all institutions have a regular (at least monthly) catheterization laboratory conference. Patient outcomes should be determined longitudinally for each procedure by the institution's quality assessment program. Participation in a state, regional, or national registry is highly encouraged to allow institutions to measure risk-adjusted outcomes and compare them to national benchmarks for improving quality of care.

For both institutional and individual volume assessments, ongoing 2-year volumes should be measured, then averaged to arrive at annual statistics. It is recommended that lower volume institutions (less than 400 per year) consider holding conferences with a more experienced partnering institution, with all staff expected to attend on a regular basis.

It is also recommended that any institution that falls more than 2 standard deviations outside the risk-adjusted national benchmarks in mortality or emergency same-stay CABG during 2 of 3 contiguous 6-month periods have an external audit looking for opportunities to improve quality of care.

An institution offering coronary interventional procedures should have a physician-director who is responsible for the program's overall quality. The director should be certified in interventional cardiology by the ABIM, with a career experience of more than 500 procedures. The director should perform procedures at the facility that he or she directs.

Recommendations for Individual Maintenance of Quality

To maintain an appropriate cognitive knowledge base for PCIs, it is recommended that individual operators attend at least 30 h of PCI CME every 2 years. The overall performance of physicians whose complication rates exceed national benchmark standards for 2 of 3 contiguous 6-month periods should be reviewed by the program director, with careful attention to statistical power and risk-adjustment issues. It is recommended that the operator volume threshold continue to be 75 procedures per year. Monitoring of physicians with an annual procedural volume of less than 75 should be particularly detailed because of the difficulty of estimating their true complication rate. These performance evaluations should include feedback to the operator.

If it is determined that the quality of PCI care being provided does not meet national benchmarks, the catheterization laboratory director should have the discretion of making recommendations for improving quality and reassessing over the next 6 months. These recommendations could include establishing a defined mentoring relationship with an experienced operator. If the operator in question disputes this assessment, then external review may be helpful in determining the most appropriate methods of assuring quality performance.

Percutaneous Noncoronary Interventions

Introduction

Noncoronary interventions are a growing and important contribution to the field of interventional cardiology. The majority of procedures have had their origin in the pediatric population, and several have expanded to the adult patient. The purpose of this section is to discuss the training and experience necessary for the safe and successful performance of valvuloplasty, alcohol septal ablation, and percutaneous repair of ASD/PFO.

The knowledge, skills, and training necessary for competency in noncoronary interventional procedures are different from that required for coronary interventions. Therefore, special study of the anatomy, physiology, and pathology of these conditions is a prerequisite for safe and effective treatment. Furthermore, an in-depth understanding of the clinical indications for treatment and the unique complications of these treatments are essential.

Although the scope of this document is focused on competency, this section will expand the discussion somewhat to describe some anatomical and procedural details. Such details are well known for PCI, and their performance is widespread, whereas these noncoronary procedures, in the estimation of this Writing Committee, warrant some discussion of background information and procedural alternatives.

Disorders of the Atrial Septum

Criteria for Competency

The knowledge base required for performing PCI is different than that required for percutaneous closure of ASD and PFO. Extensive knowledge of structural cardiac anatomy, especially that of the atrial septum and the adjacent structures, is required, as is the understanding of the impact of abnormal anatomy and function, and the relative value of therapeutic options (85,101–105). Therefore, specific training and experience is necessary to safely and successfully treat this subgroup of patients. The Food and Drug Administration guidelines on the use of device closure of PFOs in these patients state that only patients who have failed anticoagulation or have a compelling medical reason to not be anticoagulated are appropriate for device closure. These guidelines should be fully discussed with patients during the informed consent process. In addition, complications such as cardiac perforation, device embolization, thrombus formation on the device, infective endocarditis, arrhythmias, and early as well as late erosion of the device through the atrial wall or aorta should be disclosed. Currently, 2 studies are underway comparing percutaneous closure of PFO to standard oral anticoagulation, which should clarify the indications for interventional treatment.

Since these procedures are relatively new to interventionalists trained in adult cardiology, no pre-existing guidelines are available on which to base current opinion. In the absence of such guidelines, we arrived at these recommendations from discussions with colleagues actively performing these percutaneous closures.

Cardiologists in Training Programs

Acquisition of the knowledge and skills necessary to perform percutaneous procedures to treat ASD and PFO should be incorporated into the formal training of interventional cardiologists. There are no data regarding the minimum number of cases required for maintenance of competency and proficiency. A survey of Pediatric Cardiology Interventional Catheterization training programs concluded that a minimum of 10 percutaneous ASD closures is necessary for a trainee to gain clinical competence with the procedure (102).

With this in mind, it is recommended that interventional cardiologists who intend to perform these procedures independently, should be involved in these procedures during training with at least 10 of these cases being secundum ASD closures. Furthermore, as part of the procedure, the fellow should be fully conversant in the use of transesophageal echocardiography and/or intracardiac echocardiography. He or she should understand how to obtain the appropriate views to image necessary structures in order to perform the procedure safely and to exclude other anatomical problems such as a primum or sinus venosus ASD, anomalous pulmonary venous drainage, fenestrated or multiple ASD, or lipomatous hypertrophy of the septum. Obviously, not all fellows in training will be able to gain this experience and, therefore, concentrating the experience in training should be limited to a few trainees.

Cardiologists in Practice

Interventional cardiologists in practice who were not specifically trained in ASD/PFO closure but would like to perform these procedures should be fully credentialed in interventional techniques in their institution. The first several cases should be done with a proctor. To ensure safety and success, it seems prudent that the first 10 cases be proctored by someone fully credentialed in these techniques such as a pediatric cardiologist or adult cardiologist trained in congenital heart disease. Proctors should also be present for the first 3 to 5 cases if a different device is to be used after the initial credentialing proctorship.

Maintenance of Competency for Percutaneous ASD/PFO Closure

To maintain physician proficiency and competency in percutaneous ASD/PFO closure, a minimum of 10 cases per year is recommended. Similarly, to maintain catheterization laboratory proficiency, a minimum of 10 cases per year should be performed in each institution each year. To achieve this experience, it may be necessary to concentrate the procedures in the hands of only a few operators. A multidisciplinary program, including neurology consultation for PFO closure, prospective evaluation of case selection, and evaluation of clinical outcomes is critical to ensure appropriateness and maintain safety and efficacy. Laboratories and individual operators that are not active enough to maintain quality outcomes should reconsider treating these patients.

Quality Assurance

The quality improvement process used for oversight of ASD/PFO closure should include concurrent case review, and will also benefit from regular case conferences to discuss indications, procedural techniques, and case outcomes. It is particu-

JACC Vol. 50, No. 1, 2007
July 3, 2007:82–108

larly useful in any developing procedural area to share results with other institutions through informal and formal conferences. Because there are, as of yet, no large databases of outcomes for these procedures, participation in local, regional, and national registries is encouraged. Focusing the performance of these procedures in the hands of a few experienced operators is also recommended.

Hypertrophic Cardiomyopathy and Alcohol Septal Ablation

Hypertrophic cardiomyopathy is the most common genetic cardiovascular disease, with a prevalence in the general population estimated to be 0.2% (103). Physicians performing these procedures should have extensive knowledge of the outcomes, limitations and complications of medical therapy (104), dual chamber pacing and surgical myectomy (105–107), and alcohol septal ablation (105–114). No comparative trial against surgical myectomy has been performed.

Criteria for Competency

Acquisition of competence. It is strongly recommended that alcohol septal ablation be offered within a multidisciplinary program that includes the contribution of experienced cardiac surgeons, echocardiographers, general cardiologists, and electrophysiologists. Although there are currently no data regarding the minimum number of procedures required for training and for credentialing, a minimum number of 10 procedures seems to be appropriate.

Maintenance of competence. It is recommended that individual operators perform a minimum of 6 cases per year to maintain competence in performance of septal ablation for hypertrophic cardiomyopathy. Each institution should employ a multidisciplinary program with prospective evaluation of case selection and clinical outcomes. Such an approach is critical for any institution offering alcohol septal ablation as a treatment option for symptomatic patients with hypertrophic obstructive cardiomyopathy.

Quality assurance. Quality assurance in such low-volume procedures requires an approach similar to that outlined for ASD and PFO closures, as previously described.

Valvular Heart Disease

Cognitive Knowledge Base

Physicians performing invasive procedures on stenotic cardiac valves must have extensive knowledge of the pathoanatomy, the hemodynamic alterations, the clinical course, and the outcomes of various therapeutic options. Complications of aortic (115,116) and mitral (117–119) valvuloplasty should be well understood.

Criteria for Competency

Acquisition of competence. Mitral valvuloplasty is one of the most challenging cardiac procedures. The presence of a "learning curve" has been well described (120,121). Thus, training in the performance of mitral valvuloplasty requires the acquisition of clinical skills for the evaluation of indications for the procedure and the assessment of suitable valve morphology. It requires the development of proficiency in the performance of transseptal cardiac catheterization, device manipulation, and online evaluation of hemodynamic parameters. The interventionalist must be able to recognize and manage complications specific to mitral valvuloplasty, including acute mitral regurgitation, cardiac perforation, pericardial tamponade, and stroke. Although a learning curve has been well described, there are currently no specific data regarding the minimum numbers needed for competency. Nonetheless, 5 to 10 cases should be done with an experienced colleague before attempting to perform balloon valvuloplasty independently. Any program offering mitral valvuloplasty as an alternative to mitral valve replacement or surgical commissurotomy for the treatment of mitral stenosis should include a thorough quality assurance program and close monitoring of case selection and clinical outcomes. As with other infrequently performed procedures, concentration of experience among a small subset of interventional cardiologists within an institution is appropriate.

Maintenance of competence. With the low prevalence of mitral stenosis in the United States, maintaining experience is difficult. Given this limitation, concentration of this experience among institutional and perhaps regional centers may be appropriate.

Quality assurance. Quality assurance in such low-volume procedures requires an approach similar to that outlined for ASD and PFO closures, as previously described.

Percutaneous Ventricular Assist Devices

Percutaneous ventricular assist devices are becoming available. They require training and proctored supervision to attain competence, as well as periodic use or refresher drills to maintain competence. As with other seldom-used techniques, experience should be concentrated among a limited number of operators and laboratory staff who have received appropriate training.

Laboratory and Staff Competence

In order for laboratories to become competent in the performance of noncoronary cardiac procedures, the supervising or performing operator should be fully credentialed in the procedure. Initially, this may require off-site training, simulation training, a visiting proctor, or a combination of these approaches. The operator responsible for the performance of the procedure in the catheterization laboratory should supervise the staff in acquiring the necessary skills and equipment for the procedure. As is the case for the operators of lower volume procedures, there should be a small number of dedicated staff members trained to perform specific noncoronary interventions, concentrating the experience. If and when a specific procedure becomes more common, then the training may be expanded to the remainder of the staff and operators.

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APPENDIX 1. AUTHOR RELATIONSHIPS WITH INDUSTRY—ACCF/AHA/SCAI WRITING COMMITTEE TO UPDATE THE CLINICAL COMPETENCE STATEMENT ON CARDIAC INTERVENTIONAL PROCEDURES

Name	Consultant	Research Grant	Scientific Advisory Board	Speakers' Bureau	Steering Committee	Stock Holder	Other
Dr. Thomas Aversano	None	None	None	None	None	None	None
Dr. William L. Ballard	None	None	None	None	None	None	None
Dr. Robert H. Beekman, III	• AGA Medical	None	None	None	None	None	None
Dr. Michael J. Cowley	None	None	None	None	None	None	None
Dr. Stephen G. Ellis	• Boston Scientific • Celera • Cordis • Guidant • Viacon	• Celera • Centacor/Lilly • Cordis	• Boston Scientific • Cordis • Viacon	None	None	None	None
Dr. David P. Faxon	• Bristol-Myers Squibb/Sanofi	None	• Boston Scientific	None	None	• Medical Technology Informational	None
Dr. Edward L. Hannon	None	None	None	None	None	None	None
Dr. John W. Hirshfeld, Jr.	None	None	• Bracco Inc. • Bristol-Myers Squibb/Sanofi	None	None	None	None
Dr. Alice K. Jacobs	None	None	None	None	None	None	• Wyeth–Spouse's Employer
Dr. Mirle A. Kellett, Jr.	None	None	None	None	None	None	None
Dr. Stephen E. Kimmel	None	None	None	None	None	None	None
Dr. Spencer B. King, III	• Bristol-Myers Squibb • CV Therapeutics • Sanofi/Aventis	None	• Medtronic	• Bristol-Myers Squibb • Sanofi	None	None	• Novoste–Royalties
Dr. Joel S. Landzberg	None	None	None	None	None	None	None
Dr. Louis S. McKeever	None	None	None	None	None	None	None
Dr. Mauro Moscucci	None	• BlueCross/ BlueShield	None	• Aventis • Pfizer	None	None	• Cordis–Fellowship Training Grant
Dr. Richard M. Pomerantz	• Medacorp. • Sanofi/Aventis	None	None	• Sanofi/Aventis	None	• Pfizer	None
Dr. Karen M. Smith	None	None	None	None	None	None	None
Dr. George W. Vetrovec	Merck	• Cordis/Johnson & Johnson • NHLBI	None	• Lilly • Pfizer	None	• Johnson & Johnson	None

This table represents the relationships of committee members with industry that were reported orally at the initial writing committee meeting and updated in conjunction with all meetings and conference calls of the writing committee during the document development process. It does not necessarily reflect relationships with industry at the time of publication.

APPENDIX 2. PEER REVIEWER RELATIONSHIPS WITH INDUSTRY—ACCF/AHA/SCAI 2007 UPDATE OF THE CLINICAL COMPETENCE STATEMENT ON CARDIAC INTERVENTIONAL PROCEDURES

Name	Representation	Consultant	Research Grant	Scientific Advisory Board	Speakers' Bureau	Steering Committee	Stock Holder	Other
Dr. John C. Giacomini	• Official–AHA	None	None	None	None	None	None	None
Dr. Lawrence Laslett	• Official–ACC Board of Governors	None	None	None	None	None	• General Electric	None
Dr. Carl J. Pepine	• Official–ACC Board of Trustees	• Abbott • CV Therapeutics	• Abbott • AstraZeneca • Berlex Laboratories • Pfizer	None	None	None	None	• Educational grant–AstraZeneca, CV Therapeutics, GlaxoSmithKline, King Pharmaceuticals, Monarch Pharmaceuticals, Pfizer, Sanofi-Aventis, Schering-Plough, Wyeth-Ayerst Laboratories
Dr. Albert P. Rocchini	• Official–AHA	None	None	None	None	None	None	None
Dr. Samuel J. Shubrooks	• Official–ACC Board of Governors	None	None	None	None	None	None	None
Dr. Alan Yeung	• Official–AHA	• Medtronic	• Abbott • Boston Scientific	• Abbott • Boston Scientific • Cordis	None	None	• Boston Scientific	None
Dr. Gregory Dehmer	• Organizational–Society for Cardiovascular Angiography and Interventions	None	None	None	None	None	None	None
Dr. John Hodgson	• Organizational–Society for Cardiovascular Angiography and Interventions	• Volcano Corp	• Boston Scientific • GE Medical • Lilly • RADI Medical • Volcano Corp	• Volcano Corp	• GE Medical • Pfizer	None	• Technology Solutions Group • BioInfo Accelerator Fund • Volcano Corp	• Management–Mytogen Technology Solutions Group • BioInfo Accelerator Fund
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Dr. Douglass A. Morrison	• Organizational–Society for Cardiovascular Angiography and Interventions	None	None	None	None	None	None	None
Dr. Mark Reisman	• Organizational–Society for Cardiovascular Angiography and Interventions	None	None	• Abbott • Boston Scientific • Cordis • Medtronic	• Boston Scientific • Cordis	None	None	None
Dr. Barry Uretsky	• Organizational–Society for Cardiovascular Angiography and Interventions	None	None	None	None	None	None	None
Dr. Mazen Abu-Fadel	• Content–ACCF Cardiac Catheterization and Intervention Committee	None	None	None	None	None	None	None
Dr. Peter Berger	• Content–Individual Reviewer	• Boston Scientific • Cordis/Johnson & Johnson • Genentech • Guilford	• Cardiokinetix • Conor • Cordis/Johnson & Johnson • Datascope • Guilford • Lilly • The Medicine Company • Medtronic • Sankyo • Sanofi-Aventis	• Arginox • Bristol-Myers Squibb • Sanofi-Aventis • Schering-Plough	None	None	• Lumen, Inc	None

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APPENDIX 2. Continued

Name	Representation	Consultant	Research Grant	Scientific Advisory Board	Speakers' Bureau	Steering Committee	Stock Holder	Other
Dr. Robert O. Bonow	• Content-PCI Guideline Writing Committee	None	None	None	None	None	None	None
Dr. Jose G. Diez	• Content-ACCF Cardiac Catheterization and Intervention Committee	None	None	None	None	None	None	None
Dr. Ted E. Feldman	• Content-ACCF Cardiac Catheterization and Intervention Committee	• Boston Scientific • Cardiac Dimensions • Cordis • Myocor	• Abbott • Atritech • Boston Scientific • Cardiac Dimensions • Cordis • Evalve	None	None	None	None	None
Dr. James Ferguson	• Content-Individual Reviewer	None	None	None	None	None	None	None
Dr. Tommaso Gori	• Content-AHA Diagnostic & Interventional Cardiac Catherization Committee	None	None	None	None	None	None	None
Dr. Hani Jneid	• Content-AHA Diagnostic & Interventional Cardiac Catheterization Committee	None	Pfizer	None	None	None	None	None
Dr. Fred M. Krainin	• Content-ACCF Cardiac Catheterization and Intervention Committee	None	None	None	None	None	• Boston Scientific • Johnson & Johnson • Medtronic	None
Dr. Glenn Levine	• Content-AHA Diagnostic & Interventional Cardiac Catheterization Committee	None	None	None	None	None	None	None
Dr. Charanjit S. Rihal	• Content-ACCF Cardiac Catheterization and Intervention Committee	None	None	None	None	None	None	None
Dr. Dan M. Roden	• Content-Individual Reviewer	• Abbott • Alza • Arpida • AstraZeneca • Bristol-Myers Squibb • CV Therapeutics • EBR Systems • First Genetic Trust • GlaxoSmithKline • Genzyme • Johnson & Johnson • Lexicon • Lundbeck • Medtronic • Merck • NPS Pharmaceuticals • Novartis • Pfizer • Sanofi-Synthelabo Groupe • Solvay • Thornton Medical • Wyeth • Yamanouchi	None	None	None	None	None	None
Dr. Carlos Ruiz	• Content-ACCF Cardiac Catheterization and Intervention Committee	None	None	None	None	None	None	None
Dr. Michael J. Silka	• Content-Individual Reviewer	None	None	None	None	None	None	• General Electric

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JACC Vol. 50, No. 1, 2007
July 3, 2007:82–108

APPENDIX 2. Continued

Name	Representation	Consultant	Research Grant	Scientific Advisory Board	Speakers' Bureau	Steering Committee	Stock Holder	Other
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Dr. Cynthia M. Tracy	• Content–Individual Reviewer	None	• Guidant Corp • Medtronic	None	None	None	None	None
Dr. E. Murat Tuzcu	• Content–AHA Diagnostic & Interventional Cardiac Catheterization Committee	None	None	None	None	None	None	None
Dr. Matthew Wolff	• Content–ACCF Cardiac Catheterization and Intervention Committee	None	None	None	None	None	None	None
Dr. Yerem Yeghazarans	• Content–Individual Reviewer	None	None	None	• Pfizer • Sanofi-Aventis	None	None	None

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Attachment E

ACCF/AHA/SCAI 2007 Update of the Clinical Competence Statement on Cardiac Interventional Procedures: A Report of the American College of Cardiology Foundation/American Heart Association/American College of Physicians Task Force on Clinical Competence and Training (Writing Committee to Update the 1998 Clinical Competence Statement on Recommendations for the Assessment and Maintenance of Proficiency in Coronary Interventional Procedures)

Spencer B. King, III, Thomas Aversano, William L. Ballard, Robert H. Beekman, III, Michael J. Cowley, Stephen G. Ellis, David P. Faxon, Edward L. Hannan, John W. Hirshfeld, Jr, Alice K. Jacobs, Mirle A. Kellett, Jr, Stephen E. Kimmel, Joel S. Landzberg, Louis S. McKeever, Mauro Moscucci, Richard M. Pomerantz, Karen M. Smith, George W. Vetrovec, Mark A. Creager, John W. Hirshfeld, Jr, David R. Holmes, Jr, L. Kristin Newby, Howard H. Weitz, Geno Merli, Ileana Piña, George P. Rodgers, and Cynthia M. Tracy

J. Am. Coll. Cardiol. 2007;50;82-108; originally published online Jun 25, 2007;
doi:10.1016/j.jacc.2007.05.006

Attachment F

Published in final edited form as:
Circ Cardiovasc Qual Outcomes. 2010 September 1; 3(5): 506–513. doi:10.1161/CIRCOUTCOMES.109.908541.

Comparative Effectiveness of STEMI Regionalization Strategies

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Abstract

BACKGROUND—Primary percutaneous coronary intervention (PCI) is more effective on average than fibrinolytic therapy (FT) in the treatment of ST-segment elevation myocardial infarction (STEMI). Yet most U.S. hospitals are not equipped for PCI and FT is still widely used. This study evaluated the comparative effectiveness of STEMI regionalization strategies to increase the use of PCI against standard emergency transport and care.

METHODS AND RESULTS—We estimated incremental treatment costs and quality-adjusted life expectancies of 2,000 patients with STEMI who received PCI or FT in simulations of emergency care in a regional hospital system. To increase access to PCI across the system, we compared a base case strategy to 12 hospital-based strategies of building new PCI labs or extending the hours of existing labs, and one emergency medical services (EMS)-based strategy of transporting all patients with STEMI to existing PCI-capable hospitals. The base case resulted in 609 (569, 647) patients getting PCI. Hospital-based strategies increased the number of patients receiving PCI, the costs of care, and quality-adjusted life years (QALYs) saved, and were cost effective under a variety of conditions. An EMS-based strategy of transporting every patient to an existing PCI facility was less costly and more effective than all hospital expansion options.

CONCLUSION—Our results suggest that new construction and staffing of PCI labs may not be warranted if an EMS strategy is both available and feasible.

Keywords

cost-benefit analysis; fibrinolysis; Percutaneous coronary intervention; ST-segment elevation myocardial infarction; thrombolysis

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Disclosures: The funding organizations had no role in the design and conduct of the study; collection management, analysis, and interpretation of the data; and preparation, review or approval of the manuscript.

Conflict of Interest Disclosures: None

Background

For patients with ST-segment myocardial infarction (STEMI), primary percutaneous coronary intervention (PCI) is better than fibrinolytic therapy (FT) at reducing mortality if administered in a timely manner.[1–3] However, PCI is available only at hospitals with cardiac catheterization labs and FT remains the standard of care in the majority of US hospitals.[4] One recent study indicates that 80% of the US population lives within a one-hour drive of a PCI facility, but empirical estimates suggest far fewer than 80% of eligible patients with STEMI actually receive PCI.[5, 6]

To increase access to PCI, there is considerable interest in regional planning for the procedure,[7,8] but few opportunities are available to evaluate regionalization strategies in head-to-head comparisons. In this study, we used our recently developed triage and allocation model[9] to compare the incremental benefits and costs of two approaches for increasing patient access to PCI: 1) *hospital-based strategies*, in which new PCI capacity is added to a region through hospital lab construction and staffing and 2*) an emergency medical service* (*EMS)-based strategy*, in which patients with STEMI are transported by EMS to existing PCI-capable hospitals.

Methods

To estimate the costs and effectiveness of alternative strategies for increasing access to PCI, we compared a strategy of standard emergency resources and transport procedures (the base case) with 13 scenarios in which hospital PCI capability was expanded (the hospital-based strategies) and one scenario in which EMS was used to transport all patients with suspected STEMI to an existing PCI-capable hospital (the EMS strategy). The strategies and scenarios are presented in Table 1. The base case (A) assumed that EMS providers transport patients to the closest hospital, regardless of which reperfusion method is available at the time of arrival. This scenario assumed no new PCI lab construction and no new staffing of existing PCI labs. In the base case, two hospitals were capable of performing PCI full time, 12 were capable part-time (Monday through Friday, 7 am – 5 pm), and two were capable of providing FT only. In scenario B, a high-volume hospital that was capable of providing FT only was selected for PCI expansion. This hospital built and staffed a part-time PCI lab and operated it Monday through Friday, 7 am to 5 pm. In this scenario, we assumed that back-up coronary artery bypass graft (CABG) surgery could be provided off site, saving the cost of building and staffing a new suite dedicated to the procedure. In scenario C, we added a CABG suite to the costs in scenario B. All new construction scenarios were tested both with and without a new on-site CABG suite (D and E, G and H, I and J, K and L, M and N). One scenario (F) involved only an increase in staffing hours at two existing PCI-capable hospitals and therefore construction of a new PCI lab and CABG suite were not necessary. The EMS strategy (O) involved EMS transport of patients with suspected STEMI to existing PCI-capable hospitals. In this scenario, we used the regional configuration of hospital PCI capability that existed in scenario A.

We simulated EMS transport, reperfusion strategy, clinical outcomes and costs for 2,000 patients, representing approximately one year of STEMIs in a municipal area the size of Dallas County. We bootstrapped the simulation 500 times and estimated the bootstrap mean and confidence intervals at the 2.5 and 97.5 percentiles.

Patients

Patient data were sampled from the Atlantic Cardiovascular Patient Outcomes Research Team (C-PORT) Trial.[10] C-PORT was a randomized controlled trial of 451 patients with STEMI conducted from July 1996 through June 1999 that compared PCI and FT at 11 community-based hospitals in Maryland and Massachusetts. Clinical data needed for the mortality predictive model were available for 408 of the 451 subjects recruited into C-PORT. All hospital-, EMS- and patient-level variables were used in or computed from a model of Dallas County that was built using ArcGIS version 9.1 (Environmental Systems Research Institute, Redlands, CA). The model is described further in previous work.9

Outcomes

We used the Percutaneous Coronary Intervention-Thrombolytic Predictive Instrument (PCI-TPI) to predict 30-day mortality for each patient.11, 12 For individual patients, the PCI-TPI trades off the incremental mortality benefit of PCI over FT with delays to treatment. Rates of post MI stroke, congestive heart failure (CHF) and re-infarction at 30 days and six months were taken from the outcomes literature (Table 2). Survival for each additional year was stochastically estimated from rates published in 2007 National Center for Health Statistics (NCHS) age- and sex-adjusted actuarial tables. We assumed a small additional mortality risk due to MI up to five years after the initial event, an approach that has been shown in previous work[22] to calibrate well with five-year survival rates after STEMI.23 In our main analysis we added 0.005 risk of mortality for patients treated with PCI and 0.015 for patients treated with FT. In a sensitivity analysis, we added 0.01 risk to both groups, to explore how results would change if longer-term mortality were equal in the two treatment groups.

For every year survived, we adjusted for reduced quality of life from complications related to the index event or to the mode of reperfusion. Utility estimates for stroke, CHF and re-infarction were drawn from the Cost Effectiveness Analysis Registry[24] (Table 2). We used high and low estimates from a search of the Registry to estimate the upper and lower bounds for each utility measure. We assumed the higher bound in our main analysis, and the lower bound in a sensitivity analysis. Future years were discounted at 3% per year in our main analysis and at 5% in sensitivity analyses.

Our main analysis thus assumed unequal risk of death in the two treatment groups at year one after the index event, a high quality of life after complications, and a 3% discount for future years. In sensitivity analyses, we changed these assumptions individually and simultaneously to account for uncertainty surrounding survival, quality of life, and discounting.

Costs

We updated a previously developed framework for hospital operations and costs[25] to 2008 U.S. dollars, using the National Income and Product Accounts (NIPA) GDP deflator.[26] We assumed that newly purchased lab equipment and facilities would be in use for 10 years.

In randomized controlled trials comparing PCI and FT, the initial costs of PCI have been higher typically, but additional complication and procedure rates in the FT arm have been found to yield similar cumulative costs.[27-29] Two studies from the mid-1990s drew different conclusions: one using registry data found lower costs in the FT group[30] and another using administrative data found lower costs in the PCI group.[31] Our base case assumed equal costs for PCI and FT over the lifetime of patients. In each successive scenario, we added costs when new construction, staffing, in-hospital CABG back-up or diverted transport was needed.

SAS version 9.1 (SAS Institute, Cary, NC) was used for all statistical analyses.

Results

Table 3 shows the number of new PCI patients, total costs, QALYs saved and cost per QALY for each of the 14 scenarios. In the base case (A), 609 (95% confidence interval: 569, 647) primary PCI procedures – representing 30.4% of all patients with STEMI – were performed annually in 14 hospitals. Roughly 250 of these were performed during weekdays at a time when elective procedures would otherwise be scheduled. With 14 PCI labs operating on 260 weekdays per year, we assumed that demand for elective PCI was already being met and that no additional elective procedures would be performed as a result of new capacity. In this context, new construction and staffing costs could not be defrayed with elective procedures.

The costs and effectiveness of each successive scenario (B-O) were compared with the base case (A). An additional 82 patients had access to PCI after construction of a new part-time lab in a hospital seeing more than 200 patients with STEMI annually (B). This scenario resulted in nearly $4.8M additional costs over 10 years and the additional 82 PCI procedures performed over this period saved 157.4 QALYs. The cost per QALY saved was $30,399, well under the costs of other accepted life-saving therapies. When that same hospital built a new lab and staffed it full time (D), an additional 272 PCI treatments could be performed in a year and the cost per QALY saved dropped to $14,765. If a new program of on-site CABG back-up was needed for this new lab, costs increased to $85,032 per QALY saved in the part-time scenario (C) and to $31,021 in the full time scenario (E). Building a new lab was most cost-effective if it could be opened full time and if a new on-site CABG back-up program was unnecessary (D). Costs per QALY saved are graphed for each scenario in Figure 1.

Expansion of PCI capability in the two highest volume hospitals that already had a part-time PCI lab in place (F) resulted in 304 additional procedures and 605.2 QALYs saved at a cost of $10,000 per QALY saved. This expansion, involving only the additional costs of night and weekend on-call staff, was the most cost effective of hospital-based scenarios. We explored a series of combinations involving new lab construction and expansion of part-time PCI labs to full-time hours (G-N). When compared with the base case, each scenario cost less than $100,000 per QALY saved.

Finally, we estimated the incremental costs and effectiveness of one EMS strategy for increasing access to PCI (O). In this scenario, EMS personnel identified patients with STEMI prior to hospital arrival and transported directly to PCI-capable hospitals. Because our previous work on EMS triage strategies for PCI[9] showed this approach to achieve the largest reduction in short-term mortality, we selected direct transport as the EMS strategy of interest for the present study. A strategy of inter-hospital transfer performed almost as well in our previous work and is of interest for our future work. For the present study, we assumed the EMS transport strategy would cost an additional $1,000 per diverted patient.

In 2,000 patients, this strategy resulted in 1,391 diversions at a cost of nearly $1.4M and a cost per QALY saved of $506. Because it was less costly and more effective than any of the hospital-based strategies, we considered the EMS strategy to be dominant. It would no longer be the most cost-effective strategy if the average cost per diverted patient rose to more than $19,769 (a 20-fold increase). Alternatively, it would no longer be the most cost effective strategy if the most favorable hospital-based scenario (F) cost less than $306,231 (a 20-fold decrease).

We assumed 100% adherence to each tested strategy, including that all patients call 9-1-1 for assistance. This assumption could lead to an overestimate of benefit for the EMS strategy in an actual regional emergency system, where nearly half of all patients with STEMI arrive at the hospital via transportation other than EMS.32 Evidence suggests patients who arrive via EMS are older, higher risk, and more likely to benefit from PCI than those who arrive by other means.[32] To test the sensitivity of our results to 100% adherence, we iteratively reduced the EMS strategy's total benefit by the average benefit per diverted patient until the strategy was no longer more effective than the next most effective hospital strategy. This method would indicate how many walk-ins would be needed until the EMS strategy was no longer dominant. In the EMS strategy (O), 1391 patients were diverted, producing a total benefit of 2749.8 QALYs, or an average benefit of 1.98 QALYs per diverted patient. The next most beneficial strategy (M) produced 1247.0 QALYs. To fall below this level of benefit, 762 of 1391 diversions (55%) would have to be replaced by walk-ins. The EMS strategy would therefore continue to be more effective and less costly than the next best hospital strategy if at least 45% of all patients with STEMI were to call 9-1-1 for assistance. Below that number, the EMS strategy would continue to be more cost effective but would not dominate hospital strategies. This calculation is conservative if patients who are more likely to benefit from PCI are more likely to call 9-1-1, as the evidence suggests they are.

Conclusion

To increase access to PCI in our model of a large urban, suburban and rural region, an EMS strategy of transporting all patients to existing PCI-capable hospitals was more effective and less costly than 13 hospital-based strategies of new construction and staffing. While hospital strategies were cost-effective under a variety of conditions, the EMS strategy dominated in all of the scenarios we tested and in multivariate sensitivity analyses. Our results strongly suggest that construction and staffing of new PCI hospitals may not be warranted if an EMS strategy is both available and feasible. Demonstration programs have shown that EMS detection and diversion of patients with STEMI for delayed PCI are both safe and effective.[33,34] Our results suggest that, in EMS systems where STEMI detection and diversion are feasible, such a strategy is more effective and less costly than hospital-based regionalization alternatives. This finding persisted even when the estimated new cost of an EMS strategy was multiplied by a factor of nearly 20, or when its expected benefits were decreased by 55% or more.

Expansion of access to timely PCI is widely considered to be critical for improving outcomes after STEMI. To accomplish this goal, a range of regionalization approaches have been reviewed or evaluated in the research literature.[35-39] In order to understand the potential of STEMI regionalization strategies in their full context, however, it is critical that the benefits, risks and costs of all hospital- and EMS strategies be compared in head-to-head match-ups. While the preferred method to compare such strategies might be a randomized effectiveness trial,[40] such an approach would not likely be feasible given the large numbers needed to measure rare outcomes after heart attack, as well as the ethical problem of randomizing patients to receive FT when timely PCI is known to be superior.

In this context, the use of mathematical modeling to compare predicted outcomes from PCI expansion strategies is a promising approach. The model we employed combined empirical data from clinical, health systems and geographic sources with clinical predictive instruments to perform head-to-head comparisons of regionalization strategies. Our model for estimating outcomes was sensitive to the number of new PCI treatments resulting from an expansion strategy, and therefore to the regional population's baseline rate of access to PCI. In our model of Dallas County, we estimated a baseline access rate of 30.4%. Two aspects of our model explain why our baseline rate was 50 percentage points lower than a recent national estimate indicating that 80% of the population lives within a one-hour drive of a PCI-capable hospital.[4] First, patients in our base case were transported to the closest hospital even if PCI was available within a one-hour drive. Second, the 80% estimate assumes that hospitals with a PCI lab operate the lab 24 hours per day, 7 days per week. Of the 16 hospitals in our model of a large county, 14 had a PCI lab but only two operated the lab full-time. In the base case, we operated the part-time PCI labs from Monday through Friday, 7 am to 5 pm. Two classic papers on the circadian and weekly patterns of heart attack onset estimate that approximately 39% begin during these weekday hours.[41,42] We used these estimates to stochastically estimate STEMI onset day and time. In our model, therefore, approximately 61% of patients with STEMI onset in locations served by a part-time lab received immediate FT in the local hospital or delayed PCI after transport to a more distant full-time lab. We believe that our method of accounting for the part-time operation of PCI labs is reflective of actual operations in a region that has not yet introduced regionalization measures. Assuming full-time operation at all hospitals would have led to a significant overestimate of the true baseline access rate.

Nevertheless, in regions with a higher baseline rate of access to primary PCI, we would expect that an EMS strategy would fare better and the hospital strategies would fare worse than in our model. In a hospital strategy, the high fixed costs of construction can be defrayed only by increasing the number of patients with newly created access to PCI. In an EMS strategy, new costs are substantially lower and vary with the number of new transports that are needed. This relatively low variable cost is the primary advantage of an EMS strategy. A second advantage was explored in our previous work: the opportunity to select for transport to existing PCI hospitals only those patients who are predicted to benefit most from PCI. We did not exploit this opportunity in the present study; we transported every patient with suspected STEMI directly to a PCI-capable hospital regardless of predicted benefit. The EMS strategy dominated hospital strategies on the basis of its low variable costs and its potential to reach every patient with STEMI, but we believe an even stronger case could be made for a strategy that involves selective transport of only those patients who are individually predicted to benefit from delayed PCI.

Public policy remains unsettled on the optimal strategy to increase access to PCI. In some states, Certificate of Need laws are used to control the widespread diffusion of high cost and volume-sensitive procedures such as PCI. In 2008, these laws existed in 36 States, but only 23 had provisions for cardiac catheterization services review.[43] From 2001 through 2006, American Hospital Association (AHA) data show a steady increase of 50-125 new hospitals with PCI capability in the US each year, in both urban and rural areas.[44,45] There is substantial contradictory activity in the public arena that is aimed both at curtailing and at sustaining the diffusion of PCI labs. We believe our approach to comparing alternative strategies can help clarify the impact of such decisions.

For several reasons, Dallas County represents an ideal place to test our model. First, Dallas has a diversity of urban, suburban and rural areas. The majority of Census tracts in Dallas County are designated as urban (comprising 69.7% of the county's dry land area), but a substantial portion of the county is suburban and rural. Second, there is significant variation in PCI capability at hospitals inside the county. Our model showed that just 30.4% of the county's population lived closest to a PCI-capable hospital, leaving substantial room for growth in the availability of PCI. Third, Dallas is bordered to the north, east and south by sparsely populated areas and to the west by Dallas-Fort Worth Airport, creating natural and man-made barriers to EMS transport outside the County's borders. These factors allowed us to test the EMS strategy inside a diverse yet nearly closed emergency system.

While Dallas offered an excellent choice for the first test of our model, large and less densely populated regions are of great interest for further testing. In rural areas where access to PCI is lowest, the need for further study is especially urgent. Empirical evidence suggests that new hospital PCI capability results in modest new access to PCI.[37] To answer the question about what works best in urban, suburban and rural counties, head-to-head comparisons of all available strategies are needed. Our triage and allocation model can help planners and policy-makers decide on the approach that best fits the specific features of a county or region.

Our main finding, that an EMS strategy is more effective and less costly than any hospital strategy, was based on the estimated societal impact of alternative regional planning strategies in the care of patients with STEMI. The implications for individual hospitals are less clear. However, if it were recast to take in the hospital perspective, our model could help to inform the business case for regional planning. This would lend a great deal of clarity to discussion about the implications of our main finding.

In some circumstances, we recognize that a hospital strategy may be warranted even when it is dominated by an EMS strategy. First, resource constraints may preclude EMS strategies from being considered. Ambulance staff must be able to identify patients with STEMI accurately, the vehicles must be equipped with electrocardiograms, and EMS-hospital handoff should be organized to pre-notify receiving hospitals. Second, hospital expansion may be of particular importance in some suburban and rural settings, where the risks of exceptionally lengthy drive times to PCI hospitals can be prohibitive. Third, hospital strategies may be acceptable or desirable if the geographic distribution of PCI hospitals is inequitable and hospital expansion could lead to outcome improvements for a presently underserved population.

Our study has limitations. First, there are limitations inherent to simulations, insofar that they incorporate empirical data from multiple sources and resort to assumptions where empirical data are not available. Our simulation was no different in this regard. However, we conducted a wide range of multivariate sensitivity analyses and the results were robust to all potential changes. Perhaps the strongest assumptions we made concerned the costs of EMS transport and hospital lab construction, which were estimated from a study of new construction and staffing at U.S. hospitals from the mid-1990s. We chose this model because it allowed us to compare a range of hospital costs in discrete categories and thus to compare 13 alternative hospital strategies with each other and with the EMS strategy. We updated the cost model using the most reliable index for inflation of medical care and construction costs, the National Income Products Account (NIPA) GDP deflator. In a sensitivity analysis, our main finding was robust to changes in baseline costs by a factor of nearly 20 across the board. A second important assumption included adherence to the tested strategies. We assumed that 100% of patients use 9-1-1, an assumption that would lead to overestimates of benefit in the EMS strategy in locales where hospital walk-ins occur at a high rate. In a post hoc sensitivity analysis, our findings were robust until 55% or more of patients arrive to the hospital by means other than EMS. A third important set of assumptions included the utility weights for quality adjustment. In sensitivity analyses, we used high and low estimates from a search of the Cost Effectiveness Analysis Registry to estimate the upper and lower bounds for each utility measure in our model. Quality adjustment had minor effects on the ordering of preferred hospital strategies, but did not change the main result showing that the EMS strategy was both more effective and less costly than all hospital strategies.

A second limitation was that we conducted the study in a single county. We selected Dallas County for its size, diversity, and composition of urban, suburban and rural districts, but the primary advantage of this setting was its self-contained emergency system. Further research is planned in a broadly representative sample of U.S. counties.

In summary, while expansion of hospital PCI capability can be cost-effective for improving quality-adjusted survival after STEMI, a strategy of EMS transport to existing PCI-capable hospitals was dominant in a regional hospital system with 30% baseline access to PCI. Further inquiry is needed into the relationship of regional health system characteristics and optimal strategies for increasing access to PCI, and we have begun a five-year research project funded by the Agency for Healthcare Research and Quality (AHRQ) to explore these relationships. Our results suggest that regional planners should consider EMS strategies for increasing access to PCI before adopting strategies involving new construction or increased staffing of PCI hospitals.

Acknowledgments

Dr. Concannon was assisted by Daniel J. Baldor, B.A., in the preparation of the manuscript.

Funding Sources: Dr. Concannon was supported by the Agency for Healthcare Research and Quality (R01 HS010282, T32 HS00060-12; and K01 HS017726) and by the Tufts Medical Center-Pfizer Career Development Award. Dr. Kent was also supported through AHRQ (R01 HS010282). Dr. Selker, Dr. Griffith and Ms. Beshansky were supported by the Immediate Myocardial Metabolic Enhancement During Initial Assessment and Treatment in Emergency (IMMEDIATE) care trial, National Heart, Lung, and Blood Institute (U01 HL 0778241). Scientific assistance was also provided through the Tufts Clinical and Translational Science Award (UL1 RR025752).

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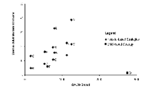

Figure 1. STEMI Regionalization Strategies - Cost per Quality Adjusted Life Year
Quality-adjusted life years saved are presented on the x-axis and cost in 2008 dollars on the y-axis. The base strategy is positioned at (0,0). Hospital strategies (B-N) are depicted with a diamond. The EMS strategy (O) is depicted with a square.

Table 1

STEMI Regionalization Strategies

Scenario	Strategy	Hospital Capabilities		
		Full-time PCI Hospitals	Part-time PCI Hospitals	FT-only Hospitals
Base Case				
A	No new construction or staffing	2	12	2
Hospital Strategies				
B	One new part-time lab*	2	13	1
C	One new part-time lab and CABG suite	2	13	1
D	One new full-time lab†	3	12	1
E	One new full-time lab and CABG suite	3	12	1
F	Night and weekend staffing for two part-time labs	4	10	2
G	Night and weekend staffing for two part-time labs and one new part-time lab	4	11	1
H	Night and weekend staffing for two part-time labs and one new part-time lab and CABG suite	4	11	1
I	Night and weekend staffing for two part-time labs and one new full-time lab	5	10	1
J	Night and weekend staffing for two part-time labs and one new full-time lab and CABG suite	5	10	1
K	Night and weekend staffing for two part-time labs and two new part-time labs	4	12	0
L	Night and weekend staffing for two part-time labs and two new part-time labs and CABG suites	4	12	0
M	Night and weekend staffing for two part-time labs and two new full-time labs	6	10	0
N	Night and weekend staffing for two part-time labs and two new full-time labs an CABG suites	6	10	0
EMS Strategy				
O	No new construction or staffing - EMS transports only to PCI-capable hospitals	2	12	2

*Staffed Monday-Friday 7 am to 5 pm

†Staffed 24 hours/day 7 days/week

Table 2

Follow up Events, Quality of Life Estimates and Event Rates

Event	Quality of Life (Lower)	Quality of Life (Upper)	Event Rates (PCI)	Event Rates (FT)
Mortality				
- in-hospital			0.04[13]	0.063[13]
- 4-6 weeks			0.05[1]	0.07[1]
- 6-18 months			~ 0.095[1]	~ 0.135[1]
Non-fatal Reinfarction	0.73[14]	0.91[14]		
- in-hospital			0.025[13]	0.064[13]
- 4-6 weeks			0.03[1]	0.07[1]
- 6-18 months			~ 0.05[1]	~ 0.1[1]
Total Stroke	0.60[15]	0.85[16]		
- in-hospital			0.0022[13]	0.0145[13]
- 4-6 weeks			0.01[1]	0.02[1]
- 6-18 months			0.022[10]	0.04[10]
Rescue PCI				
- in-hospital			0.133[17]	0.63[17]
- 4-6 weeks			0.19[10]	0.49[10]
- 6 months			0.236[10]	0.496[10]
CABG				
- in-hospital			0.082[17]	0.12[17]
- 4-6 weeks			0.124[10]	0.186[10]
- 6 months			(flat)	(flat)
CHF	0.63[18]	0.85[19]		
- in-hospital			(flat)	0.18[20]
- 4-6 weeks			0.152[21]	(flat)
- 6 months			(flat)	(flat)

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Table 3

Cost Effectiveness of Strategies to Increase Access to PCI

Incremental cost-effectiveness ratios are presented in the last column, measured as the cost in 2008 dollars per quality-adjusted life year saved. Strategies are presented in order from least to most cost-effective. Results assume: risk of death is unequal for the two treatment groups through 5 years after treatment; an upper bound for health-related quality of life if survival with STEMI is followed by stroke, CHF, or re-infarction; and future years discounted at 3%.

Scenario	Strategy	PCI Patients N=2,000 % (s.d.)	New PCI Patients (n)	Costs in 2008 Dollars (1000s)	QALYs Saved (95% CI)	Cost per QALY (95% CI)
Base Case						
A	No new construction or staffing	30.4 (1.0)				
EMS Strategy						
O	No new construction or staffing - EMS transports only to PCI-capable hospitals	100 (0.0)	1391	1,391	2749.8 (2678.4-2936.6)	506 (474-519)
Hospital Strategies						
F	Night and weekend staffing for two part-time labs	45.6 (1.1)	304	6,052	605.2 (550.8-788.8)	10,000 (7,673-10,988)
I	Night and weekend staffing for two part-time labs and one new full-time lab	59.2 (1.1)	576	13,863	1125.6 (1109.4-1210.6)	12,316 (11,451-12,496)
G	Night and weekend staffing for two part-time labs and one new part-time lab	49.7 (1.1)	385	10,837	754.0 (719.2-877.0)	14,373 (12,357-15,068)
D	One new full-time lab	44.0 (1.1)	272	7,811	529.0 (544.8-650.2)	14,765 (12,013-14,337)
M	Night and weekend staffing for two part-time labs and two new full-time labs	61.3 (1.1)	617	21,674	1247.0 (1147.2-1356.0)	17,381 (15,984-18,893)
K	Night and weekend staffing for two part-time labs and two new part-time labs	50.3 (1.1)	398	15,622	788.6 (803.0-1039.0)	19,810 (15,035-19,454)
J	Night and weekend staffing for two part-time labs and one new full-time lab and CABG suite	59.2 (1.1)	576	22,462	1125.6 (1109.4-1210.6	19,956 (18,555-20,247)
H	Night and weekend staffing for two part-time labs and one new part-time lab and CABG suite	49.7 (1.1)	385	19,436	754.0 (719.2-877.0)	25,778 (22,162-27,025)
B	One new part-time lab	34.5 (1.0)	82	4,785	157.4 (37.2-302.8)	30,399 (15,802-128,623)

Scenario	Strategy	PCI Patients N=2,000 % (s.d.)	New PCI Patients (n)	Costs in 2008 Dollars (1000s)	QALYs Saved (95% CI)	Cost per QALY (95% CI)
E	One new full-time lab and CABG suite	44.0 (1.1)	272	16,410	529.0 (544.8-650.2)	31,021 (25,239-30,122)
N	Night and weekend staffing for two part-time labs and two new full-time labs and CABG suites	61.3 (1.1)	617	38,873	1247.0 (1147.2-1356.0	31,173 (28,667-33,885)
L	Night and weekend staffing for two part-time labs and two new part-time labs and CABG suites	50.3 (1.1)	398	32,820	788.6 (803.0-1039.0)	41,619 (31,588-40,872)
C	One new part-time lab and CABG suite	34.5 (1.0)	82	13,384	157.4 (37.2-302.8)	85,032 (44,201-359,787)

MICHIGAN CON REQUIREMENTS FOR INITIATION OF PPCI PROGRAM

Liz Pielsticker, MD, FACC

Section 5. Requirements for approval -- applicants proposing to initiate an adult diagnostic cardiac catheterization service with provision to perform primary PCI for patients experiencing AMI (ST elevation or new left bundle branch block) without on-site open heart surgery services

Sec. 5. (1) An applicant proposing to initiate primary PCI service without on-site open heart surgery services shall submit documentation demonstrating all of the following:

(a) The applicant's adult diagnostic cardiac catheterization service performed a minimum of 400 diagnostic procedures (excluding diagnostic electrophysiology studies and right heart catheterizations) during the most recent 12 months preceding the date the application was submitted to the Department. Mobile cardiac catheterization laboratories are not eligible to apply under Section 5.

(b) The interventional cardiologists (at least two) to perform the primary PCI are experienced interventionalists who have each performed at least 75 interventions annually as the primary operator at an open heart surgery facility during the most recent 24 months preceding the date the application was submitted to the Department, and annually thereafter.

(c) The nursing and technical catheterization laboratory staff: are experienced in handling acutely ill patients and comfortable with interventional equipment; have acquired experience in dedicated interventional laboratories at an open heart surgery facility; and participate in an un-interrupted 24-hour, 365-day call schedule. Competency should be documented annually.

(d) The catheterization laboratory is well-equipped, with optimal imaging systems, resuscitative equipment, intra-aortic balloon pump (IABP) support, and must be well-stocked with a broad array of interventional equipment.

(e) The cardiac care unit nurses are adept in hemodynamic monitoring and IABP management. Competency should be documented annually.

(f) A written agreement with an open heart surgery facility that includes:

(i) Involvement in credentialing criteria and recommendations for physicians approved to perform primary PCI;
(ii) Provision for ongoing cross-training for professional and technical staff involved in the provision of primary PCI to ensure familiarity with interventional equipment; and competency should be documented annually;
(iii) Provision for ongoing cross training for Emergency Department, Catheterization Laboratory and Critical Care Unit staff to ensure experience in handling the high acuity status of primary PCI patient candidates and competency should be documented annually;
(iv) Regularly held joint cardiology/cardiac surgery conferences to include review of all primary PCI cases;
(v) Development and ongoing review of patient selection criteria for primary PCI patients and implementation of those criteria;
(vi) A mechanism to provide for appropriate patient transfers between facilities and an agreed plan for prompt care;

(vii) Written protocols, signed by the applicant and the open heart surgery facility, must be in place, with provisions for the implementation for immediate and efficient transfer (within 1 hour from cardiac catheterization laboratory to evaluation on site in the open heart surgical facility) of patients requiring surgical evaluation and/or intervention 365 days a year, the protocols shall be reviewed/tested on a regular (quarterly) basis; and
(viii) Consultation on facilities, equipment, staffing, ancillary services, and policies and procedures for the provision of interventional procedures.
(g) A written protocol must be established and maintained for case selection for the performance of primary PCI that is consistent with current practice guidelines set forth by the American College of Cardiology and the American Heart Association.
(h) A system to ensure prompt and efficient identification of potential primary PCI patients and rapid transfer from the Emergency Department to the Catheterization Laboratory must be developed and maintained so that door-to-balloon targets are met. CON Review Standards for CC Services CON-210 Approved December 11, 2007 Effective February 25, 2008 Page 5 of 12

(i) Because primary PCI must be available to emergency patients 24 hours per day, 365 days a year, at least two physicians credentialed to perform primary PCI must commit to functioning as a coordinated group willing and able to provide this service at the hospital on a 24-hour per day, 365 day per year call schedule, with ability to be on-site and available to operate within 30 minutes of identifying the need for primary PCI. These physicians must be credentialed at the facility and actively collaborate with administrative and clinical staff in establishing and implementing protocols, call schedules, and quality assurance procedures pertaining to primary PCI designed to meet the requirements for this certification and in keeping with the current guidelines for the provision of primary PCI promulgated by the American College of Cardiology and American Heart Association.

(2) An applicant shall project a minimum of 48 primary PCI procedures will be performed in the second 12 months of operation after initiation of service, and annually thereafter. Primary PCI volume shall be projected by documenting, as outlined in Section 13, and certifying that the applicant treated or transferred enough ST segment elevation AMI cases during the most recent 12 months preceding the date the application was submitted to the Department to maintain 48 primary PCI cases annually. Factors that may be considered in projecting primary PCI volume are the number of thrombolytic eligible patients per year seen in the Emergency Department (as documented through hospital pharmacy records showing the number of doses of thrombolytic therapy ordered for AMI in the Emergency Department) and/or documentation of emergency transfers to an open heart surgery facility for primary PCI.

Facility No	Type	Facility Name	Facility City	Beds Total Acute Care H25_L4E	AODP
500080	H	HENRY FORD MACOMB HOSPITAL - MT. CLEMENS	MT. CLEMENS	1	
100020	H	PAUL OLIVER MEMORIAL HOSPITAL	FRANKFORT	8	
400020	H	KALKASKA MEMORIAL HEALTH CENTER	KALKASKA	8	
020010	H	MUNISING MEMORIAL HOSPITAL	MUNISING	11	
760010	H	DECKERVILLE COMMUNITY HOSPITAL	DECKERVILLE	15	
490030	H	MACKINAC STRAITS HEALTH SYSTEM, INC.	ST. IGANCE	15	
320040	H	HARBOR BEACH COMMUNITY HOSPITAL	HARBOR BEACH	17	
090020	H	BAY REGIONAL MEDICAL CENTER (WEST CAMPUS	BAY CITY	20	
230021	H	EATON RAPIDS MEDICAL CENTER	EATON RAPIDS	20	
500100	H	SOUTHEAST MICHIGAN SURGICAL HOSPITAL	WARREN	20	
070020	H	BARAGA COUNTY MEMORIAL HOSPITAL	L'ANSE	24	
640021	H	MERCY HEALTH PARTNERS, LAKESHORE CAMPUS	SHELBY	24	
030032	H	ALLEGAN GENERAL HOSPITAL	ALLEGAN	25	
790032	H	CARO COMMUNITY HOSPITAL	CARO	25	
790031	H	HILLS & DALES GENERAL HOSPITAL	CASS CITY	25	
150021	H	CHARLEVOIX AREA HOSPITAL	CHARLEVOIX	25	
230022	H	HAYES GREEN BEACH MEMORIAL HOSPITAL	CHARLOTTE	25	
140010	H	BORGESS-LEE MEMORIAL HOSPITAL	DOWAGIAC	25	
260011	H	MIDMICHIGAN MEDICAL CENTER - GLADWIN	GLADWIN	25	
340021	H	SPARROW IONIA HOSPITAL	IONIA	25	
360021	H	NORTHSTAR HEALTH SYSTEM	IRON RIVER	25	
270022	H	GRAND VIEW HEALTH SYSTEM	IRONWOOD	25	
520051	H	BELL MEMORIAL HOSPITAL	ISHPEMING	25	
590201	H	SPECTRUM HEALTH UNITED MEMORIAL - KELSEY	LAKEVIEW	25	
310021	H	ASPIRUS KEWEENAW HOSPITAL	LAURIUM	25	
510020	H	WEST SHORE MEDICAL CENTER	MANISTEE	25	
770010	H	SCHOOLCRAFT MEMORIAL HOSPITAL	MANISTIQUE	25	
760041	H	MARLETTE REGIONAL HOSPITAL	MARLETTE	25	
480020	H	HELEN NEWBERRY JOY HOSPITAL	NEWBERRY	25	
660020	H	ASPIRUS ONTONAGON HOSPITAL	ONTONAGON	25	
800041	H	BRONSON LAKEVIEW HOSPITAL	PAW PAW	25	
320030	H	SCHEURER HOSPITAL	PIGEON	25	
670021	H	SPECTRUM HEALTH REED CITY HOSPITAL	REED CITY	25	
760030	H	MCKENZIE MEMORIAL HOSPITAL	SANDUSKY	25	
590030	H	SHERIDAN COMMUNITY HOSPITAL	SHERIDAN	25	

190011	H	CLINTON MEMORIAL HOSPITAL	ST JOHNS	25
060020	H	ST. MARY'S OF MICHIGAN STANDISH HOSPITAL	STANDISH	25
460052	H	HERRICK MEDICAL CENTER	TECUMSEH	25
130100	H	SOUTHWEST REGIONAL REHABILITATION CENTER	BATTLE CREEK	26
330050	H	SPARROW HEALTH SYSTEM - ST. LAWRENCE CAM	LANSING	30
630150	H	STRAITH HOSPITAL FOR SPECIAL SURGERY	SOUTHFIELD	34
310020	H	PORTAGE HOSPITAL	HANCOCK	36
630060	H	DMC SURGERY HOSPITAL	MADISON HEIGHTS	36
710030	H	ROGERS CITY REHABILITATION HOSPITAL	ROGERS CITY	36
390030	H	BRONSON VICKSBURG HOSPITAL	VICKSBURG	39
470010	H	BRIGHTON HOSPITAL	BRIGHTON HOSPITAL	41
730060	H	HEALTHSOURCE SAGINAW, INC.	SAGINAW	45
630013	H	OAKLAND REGIONAL HOSPITAL	SOUTHFIELD	45
160020	H	CHEBOYGAN MEMORIAL HOSPITAL	CHEBOYGAN	46
690020	H	OTSEGO MEMORIAL HOSPITAL	GAYLORD	46
350010	H	ST. JOSEPH HEALTH SYSTEM - TAWAS	TAWAS CITY	49
330010	H	INGHAM REGIONAL MEDICAL CENTER - PENN	LANSING	53
610030	H	MERCY HEALTH PARTNERS - GENERAL CAMPUS	MUSKEGON	57
700030	H	ZEELAND COMMUNITY HOSPITAL	ZEELAND	57
110040	H	COMMUNITY HOSPITAL WATERVLIET	WATERVLIET	58
750020	H	THREE RIVERS HEALTH	THREE RIVERS	60
590010	H	CARSON CITY HOSPITAL	CARSON CITY	61
830240	H	HUTZEL WOMEN'S HOSPITAL	DETROIT	61
620010	H	GERBER MEMORIAL HOSPITAL	FREMONT	61
500030	H	ST. JOHN NORTH SHORES HOSPITAL	HARRISON TWP.	63
320020	H	HURON MEMORIAL HOSPITAL	BAD AXE	64
180010	H	MIDMICHIGAN MEDICAL CENTER CLARE	CLARE	64
590060	H	SPECTRUM HEALTH UNITED MEMORIAL - UNITED	GREENVILLE	65
300010	H	HILLSDALE COMMUNITY HEALTH CENTER	HILLSDALE	65
740030	H	ST. JOHN RIVER DISTRICT HOSPITAL	EAST CHINA	68
810010	H	FOREST HEALTH MEDICAL CENTER, LLC	YPSILANTI	68
730030	H	COVENANT MEDICAL CENTER - N MICHIGAN	SAGINAW	71
530010	H	MEMORIAL MEDICAL CENTER OF WEST MICHIGAN	LUDINGTON	73
540030	H	MECOSTA COUNTY MEDICAL CENTER	BIG RAPIDS	74
810040	H	ST. JOSEPH MERCY SALINE HOSPITAL	SALINE	74
130080	H	OAKLAWN HOSPITAL	MARSHALL	77
410070	H	MARY FREE BED REHABILITATION HOSPITAL	GRAND RAPIDS	80

700010	H	NORTH OTTAWA COMMUNITY HOSPITAL	GRAND HAVEN	81	
170020	H	CHIPPEWA COUNTY WAR MEMORIAL HOSPITAL	SAULT STE MARIE	82	
800020	H	SOUTH HAVEN COMMUNITY HOSPITAL	SOUTH HAVEN	82	
810080	H	CHELSEA COMMUNITY HOSPITAL	CHELSEA	83	
750010	H	STURGIS HOSPITAL	STURGIS	84	
460020	H	EMMA L. BIXBY MEDICAL CENTER	ADRIAN	88	X
080010	H	PENNOCK HOSPITAL	HASTINGS	88	
650010	H	WEST BRANCH REGIONAL MEDICAL CENTER	WEST BRANCH	88	X
820040	H	HENRY FORD COTTAGE HOSPITAL	GROSSE POINTE FARMS	89	
110070	H	LAKELAND HOSPITAL, NILES	NILES	89	
200020	H	MERCY HOSPITAL - GRAYLING	GRAYLING	90	
830410	H	REHABILITATION INSTITUTE	DETROIT	94	
220020	H	DICKINSON COUNTY HEALTHCARE SYSTEM	IRON MOUNTAIN	96	
840010	H	MERCY HOSPITAL	CADILLAC	97	X
210010	H	ST. FRANCIS HOSPITAL	ESCANABA	98	
120010	H	COMMUNITY HEALTH CENTER OF BRANCH COUNTY	COLDWATER	102	
780010	H	MEMORIAL HEALTHCARE	OWOSSO	111	
370010	H	CENTRAL MICHIGAN COMMUNITY HOSPITAL	MT. PLEASANT	118	
740010	H	ST. JOSEPH MERCY PORT HURON HOSPITAL	PORT HURON	119	X
830520	H	KARMANOS CANCER CENTER	DETROIT	123	
040010	H	ALPENA REGIONAL MEDICAL CENTER	ALPENA	124	
820250	H	OAKWOOD HERITAGE HOSPITAL	TAYLOR	125	
290010	H	GRATIOT MEDICAL CENTER	ALMA	130	X
630080	H	ST. JOHN MACOMB-OAKLAND HOSP (OAKLAND)	MADISON HEIGHTS	133	X
470020	H	ST. JOSEPH MERCY LIVINGSTON HOSPITAL	HOWELL	136	
630014	H	HURON VALLEY-SINAI HOSPITAL	COMMERCE	153	
610010	H	MERCY HEALTH PARTNERS - HACKLEY CAMPUS	MUSKEGON	154	X
740020	H	PORT HURON HOSPITAL	PORT HURON	163	X
440010	H	LAPEER REGIONAL MEDICAL CENTER	LAPEER	183	X
630176	H	HENRY FORD WEST BLOOMFIELD HOSPITAL	WEST BLOOMFIELD	191	X
700020	H	HOLLAND HOSPITAL	HOLLAND	193	
820170	H	OAKWOOD SOUTHSHORE MEDICAL CENTER	TRENTON	193	
610020	H	MERCY HEALTH PARTNERS - MERCY CAMPUS	MUSKEGON	196	
630177	H	PROVIDENCE MEDICAL CENTER-PROVIDENCE PAR	NOVI	200	
500020	H	HENRY FORD MACOMB HOSPITAL - WARREN CAMP	WARREN	203	X
130031	H	BATTLE CREEK HEALTH SYSTEM	BATTLE CREEK	204	X
410060	H	METROPOLITAN HOSPITAL	GRAND RAPIDS	208	

240030	H	NORTHERN MICHIGAN REGIONAL HOSPITAL	PETOSKEY	214	
580030	H	MERCY MEMORIAL HOSPITAL	MONROE	217	X??
110050	H	LAKELAND HOSPITAL, ST. JOSEPH	ST. JOSEPH	224	
830080	H	CHILDREN'S HOSPITAL OF MICHIGAN	DETROIT	228	
410080	H	SAINT MARY'S HEALTH CARE	GRAND RAPIDS	230	
560020	H	MIDMICHIGAN MEDICAL CENTER-MIDLAND	MIDLAND	230	
820010	H	OAKWOOD ANNAPOLIS HOSPITAL	WAYNE	247	
520050	H	MARQUETTE GENERAL HEALTH SYSTEM	MARQUETTE	264	
730050	H	ST. MARY'S OF MICHIGAN	SAGINAW	268	
630070	H	CRITTENTON HOSPITAL MEDICAL CENTER	ROCHESTER	270	
830500	H	DETROIT RECEIVING HOSPITAL	DETROIT	273	
820190	H	ST. MARY MERCY LIVONIA HOSPITAL	LIVONIA	273	
730020	H	COVENANT MEDICAL CENTER - COOPER	SAGINAW	275	
730061	H	COVENANT MEDICAL CENTER - HARRISON	SAGINAW	277	
500060	H	MOUNT CLEMENS REGIONAL MEDICAL CENTER	MOUNT CLEMENS	288	
820030	H	WILLIAM BEAUMONT HOSPITAL, GROSSE POINTE	GROSSE POINTE	289	X
630050	H	BOTSFORD HOSPITAL	FARMINGTON HILLS	305	
410010	H	SPECTRUM HEALTH BLODGETT HOSPITAL	GRAND RAPIDS	306	X
630120	H	POH MEDICAL CENTER	PONTIAC	308	X
330020	H	INGHAM REGIONAL MEDICAL CENTER	LANSING	310	
630110	H	DOCTORS' HOSPITAL OF MICHIGAN	PONTIAC	321	X
820070	H	GARDEN CITY HOSPITAL	GARDEN CITY	323	
820230	H	HENRY FORD WYANDOTTE HOSPITAL	WYANDOTTE	323	
380010	H	ALLEGIANCE HEALTH	JACKSON	325	
630130	H	PROVIDENCE HOSPITAL AND MEDICAL CENTER	SOUTHFIELD	340	
250050	H	MCLAREN REGIONAL MEDICAL CENTER	FLINT	342	
500070	H	ST. JOHN MACOMB-OAKLAND HOSP (MACOMB)	WARREN	348	X
500110	H	HENRY FORD MACOMB HOSPITAL	CLINTON TOWNSHIP	349	
090050	H	BAY REGIONAL MEDICAL CENTER	BAY CITY	356	
630160	H	WILLIAM BEAUMONT HOSPITAL, TROY	TROY	361	
390010	H	BORGESS MEDICAL CENTER	KALAMAZOO	372	
280010	H	MUNSON MEDICAL CENTER	TRAVERSE CITY	377	
390020	H	BRONSON METHODIST HOSPITAL	KALAMAZOO	380	
830450	H	SINAI-GRACE HOSPITAL	DETROIT	383	
250040	H	HURLEY MEDICAL CENTER	FLINT	383	
630140	H	ST. JOSEPH MERCY OAKLAND HOSPITAL	PONTIAC	395	
250072	H	GENESYS REGIONAL MEDICAL CENTER	GRAND BLANC	410	

830220	H	HARPER UNIVERSITY HOSPITAL	DETROIT	506
810030	H	ST. JOSEPH MERCY ANN ARBOR HOSPITAL	ANN ARBOR	513
330060	H	EDWARD W SPARROW HOSPITAL	LANSING	587
820120	H	OAKWOOD HOSPITAL AND MEDICAL CENTER	DEARBORN	632
410040	H	SPECTRUM HEALTH BUTTERWORTH HOSPITAL	GRAND RAPIDS	755
830190	H	HENRY FORD HOSPITAL	DETROIT	762
830420	H	ST. JOHN HOSPITAL & MEDICAL CENTER	DETROIT	769
810060	H	UNIVERSITY OF MICHIGAN HOSPITALS	ANN ARBOR	848
630030	H	WILLIAM BEAUMONT HOSPITAL, ROYAL OAK	ROYAL OAK	1,031
			Total	**25,111**

AOD/TP	AOD/P-PCI	A/PD/T/P	
			1
			8
			8
			11
			15
			15
			17
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			25

154 Acute Care Hospitals
86 <100 beds 3 have diagnostic labs
3 have pediatric labs
18 diagnostic labs
30 theraputic labs
11 Primary PCI labs

of the hospitals with greater than 100 beds nir
of hospitals with greater than 150 beds only d
convenant medical center are without labs

25
25
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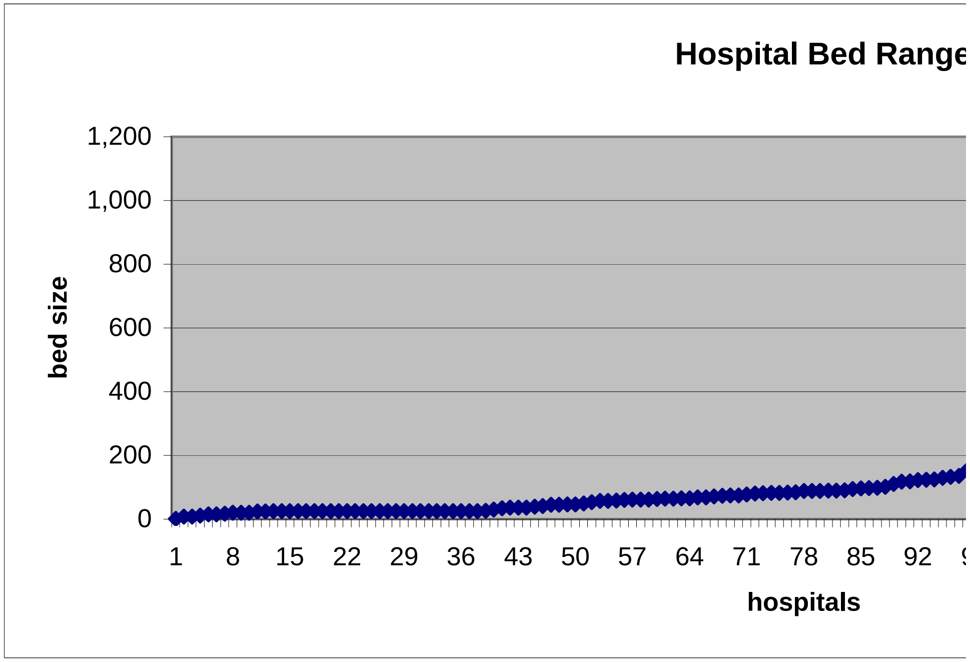

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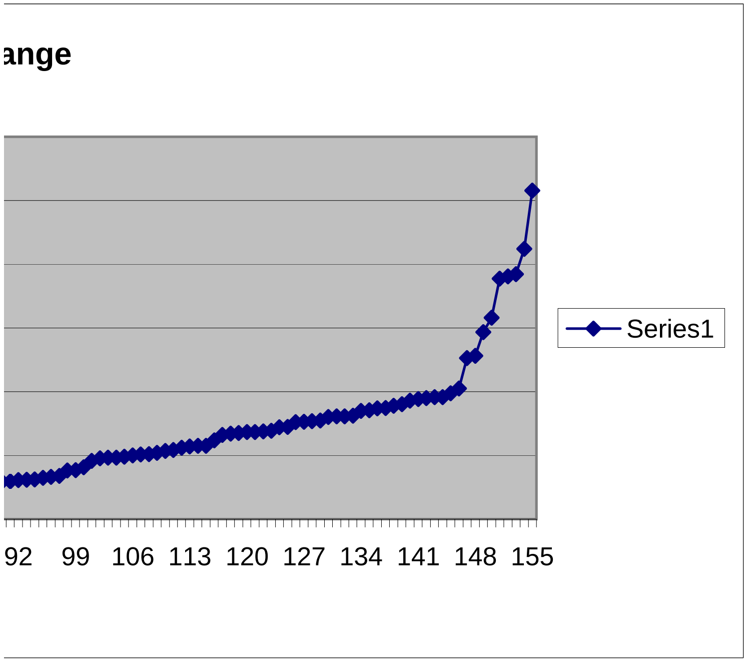
		133
		136
	X	153
		154
		163
		183
		191
	X	193
	X	193
X		196
X		200
		203
		204
	X	208

X			214
			217
X			224
		X	228
	X		230
X			230
	X		247
X			264
X			268
X			270
			273
	X		273
X			275
			277
X			288
			289
	X		305
			306
			308
X			310
			321
	X		323
	X		323
X			325
X			340
X			342
			348
X			349
X			356
X			361
X			372
X			377
X			380
X			383
	X		383
X			395
X			410

X		506
X		513
X		587
X		632
	X	755
X		762
X		769
	X	848
X		1,031

ne have no labs
letroit receiving and
(55 out of 57)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92
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113
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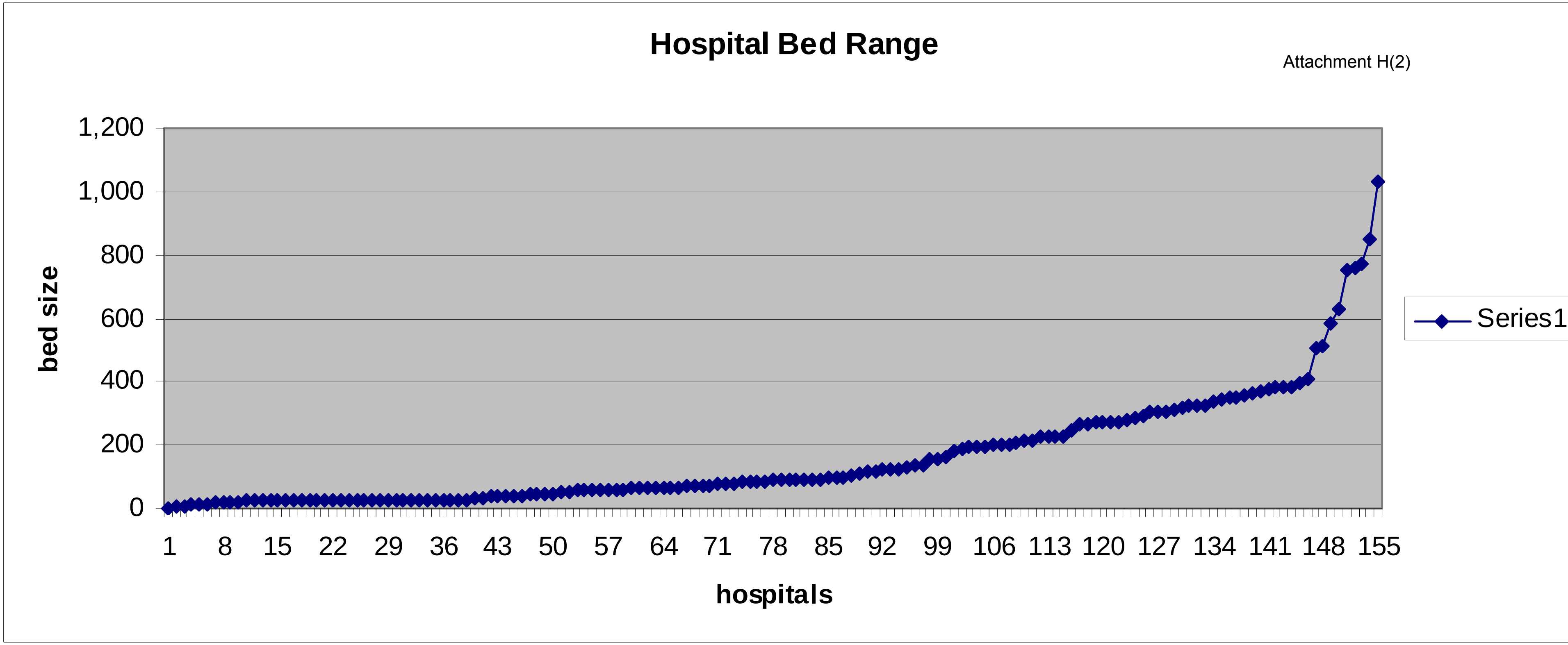
127
134
141
148
155



154 Acute Care Hospitals

86 <100 beds

3 have diagnostic labs

3 have pediatric labs

18 diagnostic labs

30 theraputic labs

11 Primary PCI labs

Of the hospitals with greater than 100 beds, nine have no labs (59 out of 68 do)

Of hospitals with greater than 150 beds only Detroit Receiving and

Convenant Medical Center are without labs (55 out of 57)