

PALLIATIVE CARE SECTION

Special Communication

Chronic Pain in the Cancer Survivor: A New Frontier

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ABSTRACT

Objective. This monograph is intended to clarify the clinical problem of chronic pain in cancer patients.

Design. A pertinent literature review on chronic pain syndromes in cancer patients was undertaken using Medline. Further, the treatment strategies for cancer versus chronic pain are contrasted and clarified.

Results. With increasing cancer survivorship come new challenges in patient care. In the United States, the cancer-related death rate has dropped by 1.1% per year from 1993–2002. Seventy-five percent of children and two out of three adults will survive cancer, whereas 50 years ago just one out of four survived. The net effect of these trends and opportunities is a large and rapidly growing population of persons living longer with cancer and/or as cancer survivors. While agreement exists on the best strategies for assessment and treatment of most acute cancer pain syndromes, little consensus exists on the treatment of chronic pain in the patient with slowly progressive cancer or the cancer survivor.

Conclusions. The landscape of “cancer pain” is shifting quickly into a chronic pain situation in many instances, thereby blurring previous lines of distinction in treatment strategies most suited for “chronic” versus “malignant” pain. Adopting chronic pain treatment strategies including pharmacologic and other pain control techniques, rehabilitation care, and psychological coping strategies may lead to optimal outcomes. Lastly, as cancer evolves into a chronic illness, with co-morbid conditions, recurrent cancer, and treatment toxicities from repeated antineoplastic therapies, pain management challenges in the oncologic patient continue to increase in complexity.

Key Words. Treatment Outcome; Cancer Pain; Chronic Pain; Palliative Treatment; Persistent Pain; Standards of Care; Survivorship

Introduction

The overall state of cancer pain care has improved over the past two decades through

the widespread use of traditional therapies. Improved cancer therapy has led to increasing life expectancy and cure rates in most types of cancers; in some tumor types long-term survival has increased dramatically. The American Cancer Society has stated a goal in the coming decade of making cancer into a chronic disease state in which long-term control is possible, even in the absence of a conventional “cure.” A recent report from the

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Institute of Medicine is titled “From Cancer Patient to Cancer Survivor: Lost in Transition” [1]. This report points out that the number of cancer survivors in the United States has more than tripled to around 10 million people over the past 30 years. The authors also note that although survival rates are increasing, no one knows at what cost to the health and well-being of the survivors. More than six million cancer survivors are over age 65, creating a huge challenge to the Medicare system, while in the under age 65 set more than 10% of survivors are uninsured. While most survivors return to work, 20% will have work limitations up to 5 years later. It is clear that there are numerous challenges presented by this growing patient population, with chronic pain among them.

Opioid-based strategies like the World Health Organization ladder have been validated in the treatment of active cancer pain syndromes, whereas the use of chronic opioid treatment in the treatment of chronic pain remains controversial. Chronic pain in cancer survivors is a poorly studied and understood entity. Incidence, prevalence, and basic epidemiological data are, with a few exceptions, lacking. Only within the last decade has attention been directed toward the identification and treatment of chronic pain syndromes in cancer survivors.

The goals of this monograph will be to provide an overview of the prevalence and types of chronic pain occurring in cancer patients as a direct consequence of their cancer or cancer treatment and to help providers recognize these syndromes and their presentations. Further, therapeutic insights will be presented that may help providers decrease the occurrence of chronic pain in cancer survivors. The most commonly known surgery, chemotherapy, and radiation therapy associated chronic pain syndromes will be described.

Epidemiology of Chronic Pain in Cancer Survivors

A total of 1.4 million Americans were newly diagnosed with cancer in 2004, approximately 4,000

Table 1 Incidence of developing chronic postoperative pain by type of surgery

Type of Surgery	Reported Incidence of Chronic Pain
Limb amputation	30–80%
Thoracotomy	22–70%
Cholecystectomy	3–56%
Inguinal hernia	0–37%

Modified from Perkins and Kehlet [9].

Table 2 Factors which predict chronic pain postoperatively

a. Preoperative factors: chronic preoperative pain >1-month duration; repeated surgery; psychological traits including passive coping skills; worker's compensation claims
b. Intraoperative factors: type of surgery, risk of nerve trauma
c. Postoperative factors: severe pain poorly controlled; radiation therapy to the area; chemotherapy; anxiety

Modified from Perkins and Kehlet [9].

per day [2]. In the same year 564,000 US deaths were attributed to cancer, about 22% of all deaths. It is estimated that over 10 million in the United States are living with cancer at the present time, around 3% of the population. The prevalence of pain at the time of cancer diagnosis and early in the course of disease is estimated to be 50%, increasing to 75% in advanced stages. The prevalence of chronic pain in cured cancer patients is less well studied, but some data exist.

Posttreatment pain syndromes may stem from chemotherapy, radiation therapy, or surgery. Post-chemotherapy painful peripheral neuropathy is well described with the use of vincristine, platinum, taxanes, thalidomide, bortezomib, and some other agents. Radiation-induced neural damage and pain may surface decades after radiotherapy completion, confounding the diagnosis in some cases. Finally, postsurgical pain syndromes come in many varieties, including post-mastectomy, post-amputation, post-thoracotomy, and other chronic pain states (Table 1). The prevalence of chronic pain in breast cancer survivors is estimated to be at least 50% [3]. The prevalence of phantom limb pain (PLP) after amputation is estimated to be between 7% and 72%, depending on the “cut off” points applied to evaluate the pain severity [4]. Long-term severe pain after thoracotomy may have a prevalence as high as 50% [5]. The incidence of pain following treatment for head and neck cancer may be as high as 50%, with more than 50% disabled 1 year after diagnosis highly correlated to pain scores [6–8]. Perkins and Kehlet identified several risk factors that predispose surgical patients to chronic pain (Table 2) [9]. Many of these “predisposing factors” for chronic pain are oncologic in nature, including preexisting pain, repeat surgery, psychological vulnerability, radiation, chemotherapy, and finally depression and anxiety.

Existential consequences of unrelieved cancer pain have been well reported [10]. Fear that post-survival pain may be a dire prognostic indicator and other factors may lead to underreporting of pain by cancer survivors. The types of pain that

occur are often complex, difficult to diagnose, may be myalgic or neuropathic, and might be less responsive than somatic pain to usual treatments. Radiation-induced plexopathy may occur up to 20 years after cancer treatment that occurred so long ago may be unrecognized as an etiology by many providers [8]. Detailed knowledge of painful conditions that can occur in survivors is necessary to optimize treatment and this understanding may be absent even among oncologists and pain specialists.

Chronic Pain Secondary to Treatment for Cancer

Most chronic pain in cancer survivors is a consequence of cancer treatment. Survival is the principle goal in cancer treatment and the prevalence of chronic pain, disfigurement, or other adverse treatment-related effects in survivors may be either underappreciated or considered a recognized and subordinate risk in a quest for survival by both providers and patients [11]. Survival accompanied by suffering and a poor quality of life, however, is not the intended goal. Many chronic pain treatment strategies can be employed to optimize the quality of life and functionality of the cancer survivor. In the following sections, specific treatment-related pain syndromes will be identified with epidemiologic data, prevention strategies, and specific treatment options where they exist. The three mainstays of cancer treatments, surgery, radiation, and chemotherapy can all lead to chronic pain syndromes when used alone. A therapeutic trend to improve cancer treatment success is the combination use of these three modalities, with the probability of additive or even synergistic toxicity in some cases.

Surgery

Chronic pain is a potential consequence of any surgery [9]. The magnitude of chronic postoperative pain has only recently been clarified. In a survey of all chronic pain patients in the United Kingdom, surgery was the second most common etiology of chronic pain (with degenerative diseases being the most common cause) [12]. Predictors of the development of chronic postoperative pain include preoperative pain, repeat surgery, psychological vulnerability (including personality disorders and neuroticism), nerve damage, and previous chemotherapy or radiation therapy (Table 2). Depression and anxiety are well known to amplify painful symptoms and complaints.

Chronic pain after common surgical cancer treatments will be reviewed.

Breast Surgery

Chronic pain after breast surgery is seen in as many as 50% of mastectomy patients. Postmastectomy pain syndrome has been well described and Jung et al. characterized four distinct types of chronic post-mastectomy pain, including: phantom breast pain, intercostobrachial neuralgia, neuroma pain (including scar pain), and other nerve injury pains (including long thoracic, thoracodorsal, etc.) [13]. Pain can be present in the arm, neck, shoulder, axilla, chest wall or breast. Paresthesia, dysesthesia, allodynia, hyperalgesia, and loss of shoulder function have all been reported. Pain in the breast region in women who have had modified radical mastectomy as well as breast-conserving surgical treatment with axillary node dissection has been reported to be present in 39% of survivors by one investigator with 8% of patients reporting pain that interfered considerably with their daily life [14]. In the same study, 36% of women reported pain in the ipsilateral arm 30 months after surgery and 8% had pain that interfered considerably in their daily life. Perkins and Kehlet have reviewed the subject of chronic pain as an outcome of surgery and have concluded that 50% of women suffer pain 1 year after surgery for breast cancer and that moderate to severe pain is reported by 10% [9].

Choice of surgical procedure and technique influence the occurrence of chronic pain. While intuitively, providers may believe that breast-conserving treatment results in a decreased incidence of chronic pain when compared with modified radical mastectomy, this has not been shown to be true and in fact there is some evidence that breast-conserving surgery with axillary node dissection may result in a higher incidence of chronic pain [15]. This is likely related to increased use of chemotherapy and radiotherapy in patients undergoing more conservative resection. In addition, women who have a breast prosthesis implanted may also have a higher incidence of chronic pain.

Sensory abnormalities in the intercostobrachial nerve distribution have been reported by 61% of women in whom the nerve was preserved and 80% of women for whom the nerve-sparing procedure was not utilized. A total of 25–50% of these women with sensory changes developed intercostobrachial neuralgia. Extent of axillary dissection correlates directly with increased incidence of pain and axillary dissection increases the likelihood of

arm problems in general as well as psychological distress [16].

Tasmuth et al. have shown that an increased incidence of chronic posttreatment pain in breast cancer patients is related to the intensity of acute postoperative pain, the type of operation, involvement of regional lymph nodes, and radiotherapy [17]. The severity of acute postoperative pain is in fact the best predictor of chronic pain in breast cancer survivors. While increased postoperative pain may be related to the prevalence of underrecognized neuropathic pain and less skilled postoperative pain management, it is also related to prevalence of depression and anxiety in patients undergoing surgery, surgical technique (traction and nerve-sparing procedures), and postoperative complications such as bleeding or infection. Whether or not the presence of preoperative pain is a predictor of chronic pain in patients undergoing breast surgery for cancer is an unresolved question. An additional question is whether the use of regional anesthetic nerve block techniques perioperatively could favorably impact the incidence of long-term pain.

Postoperative radiation therapy is a risk factor for pain in both the breast and arm. Keramopoulos and colleagues showed a correlation between axillary radiation and the incidence of chronic arm pain [18].

The general prognosis for prediction of persistence of pain in the breast area within the first postoperative year is one of gradually decreasing pain. Postoperative pain in the breast area is likely to gradually diminish for up to 1 year following surgery. However, postoperative neuropathic pain in the form of phantom breast pain and/or arm pain is usually much more chronic and problematic [3]. Recently, the preemptive use of anti-neuropathic pain medications (gabapentin and mexilitine) has been investigated in the setting of mastectomy with promising, but preliminary results [19,20].

In summary, the incidence of chronic pain after breast surgery may be as high as 50% with up to 10% of women complaining of moderate to severe chronic pain. Predictors of chronic pain after surgery include poorly controlled postoperative pain, extent of axillary dissection, radiation therapy, and overall psychological state.

Thoracotomy

The etiology of postthoracotomy pain is likely due to intercostal nerve injury and the difficulty controlling acute pain immediately postoperatively

[12]. The presence of preoperative pain or emotional distress in patients undergoing thoracotomy has not been shown to be predictive of postoperative chronic pain.

Intaoperative factors may be important in predicting the incidence of chronic pain after thoracotomy. While studies are somewhat contradictory and of mostly moderate quality, there does seem to be a decreased incidence of chronic pain in patients undergoing video-assisted thoracoscopic surgery when compared with open thoracotomy and perhaps a decreased incidence of chronic pain in patients undergoing anterolateral vs posterolateral open thoracotomy [5]. Preoperatively initiated epidural analgesia is more effective at decreasing the incidence (and severity) of chronic pain than postoperative epidural analgesia or intravenous patient-controlled analgesia [21,22].

The natural history of postthoracotomy pain is of severe immediate discomfort with a gradual improvement over months following surgery. The prevalence of pain at 3 months after surgery is 80% and decreases to 60% at 1 year reporting pain significant enough for analgesic use [17]. Chronic pain after thoracotomy may have an incidence as high as 50% with up to half of these patients reporting moderate to severe pain [23]. Optimal therapies for this chronic chest wall pain remain speculative and include medical management, intercostal nerve blockade, and other blocks, but recent work has included development of a rat model of postthoracotomy pain allowing critical evaluation of numerous treatment strategies [24].

Limb Amputation

The incidence of PLP after amputation varies from 7% to 72%, depending on the cut points applied for pain [4]. Phantom sensations, phantom pain, and stump pain are common phenomena seen in the post-amputation period. Phantom sensation is present in nearly all amputees with a subset reporting pain.

Risk factors predisposing for chronic PLP include preamputation pain, female gender, severe postoperative pain, a poorly fitting prosthesis, and a more proximal amputation. Approximately two-thirds of patients with PLP also suffer from stump pain. There may be a higher incidence of PLP after amputation for cancer than for noncancer causes. The use of chemotherapy increases the incidence of PLP [25]. The presence of PLP decreases during the first year after surgery but pain present after this time is likely to persist unchanged indefinitely. The com-

plex interplay of pain and disability with regards to PLP has been carefully evaluated by Borsje and colleagues [4]. The strongest correlation for ongoing impaired function was the level of the amputation, closely followed by severe stump pain and significant phantom sensation. An interesting finding was a negative correlation between *frequency* of phantom pain and impairment, indicating that if phantom pain was experienced more frequently, it does not result in more impairment due to it. The authors hypothesize that subjects who experience phantom pain frequently learn coping strategies, whereas the “infrequent” phantom pain patient experiences more impairment even with less overall pain, due to the lack of “being used to it.”

Head and Neck Cancer

Treatment for head and neck cancer usually involves surgery, radiation, and chemotherapy treatments. These therapies typically cause severe side effects such as facial deformity, speech and swallowing difficulties, and chronic pain in the oral cavity, neck, face, or shoulder. The incidence of chronic pain approaches 40% at 1 year and 15% at 5 years, with 50% of patients diagnosed with head and neck cancer taking medical disability 1 year post diagnosis highly correlated with ongoing pain scores [6–8,26].

The accessory nerve and the nerves of the superficial cervical plexus are commonly injured and can cause typical and identifiable neuropathic pain syndromes. Detailed follow-up examination of 153 patients 1 year following neck dissection surgery with or without radiotherapy revealed the following morbidity: the incidence of neck pain was 33%, shoulder pain 37%, myofascial pain 46%, with associated loss of sensation in 65% [7]. The optimal treatment of these chronic post-head and neck cancer surgery symptoms remains speculative, but some pilot research is focused on the use of early postoperative physical therapy techniques to prevent chronic shoulder pain syndromes [27].

Radiotherapy

As noted above, radiotherapy used as an adjunctive therapy in breast cancer or head and neck cancer increases the incidence of chronic pain. Radiation toxicity is generally divided up into early and late effects. Early or acute effects including nausea, skin reactions, diarrhea, and neutropenia usually are self-limited. Late effects including

connective tissue fibrosis, neural damage, and secondary malignancies can occur long after completion of radiotherapy [28]. A recent large retrospective cohort study revealed an association between previous pelvic radiation and hip fractures, with an increase in lifetime fracture rate from 17% (control) to 27% (radiation group) [29]. Radiation therapy is a risk factor for pain in both the breast and arm in women treated for breast cancer presumably due to connective tissue fibrosis and neural damage [30,31]. Radiation-induced brachial plexopathy is a well-defined clinical entity known to occur after radiotherapy for the treatment of breast carcinoma [32]. There is a considerable range in estimates of incidence likely due to inconsistencies of dosage, technique, and concurrent chemotherapies, but the incidence of disabling painful brachial plexopathy is likely between 1% and 5% and mild plexopathy may occur in up to 9% of women undergoing radiotherapy for breast cancer [33]. There is no specific clinical presentation of radiation-induced plexopathy that can distinguish this syndrome from tumor recurrence as a cause of plexopathy with great accuracy, but tumor recurrence tends to involve the lower trunks of the plexus and radiation tends to involve C5, C6, or C7 roots. Imaging such as magnetic resonance imaging or position emission tomography/computed tomography study may help distinguish tumor recurrence from neural damage syndromes. Nerve conduction studies are normal in roughly 10% of patients with radiation-induced brachial plexopathy [34].

The onset of symptoms ranges from 6 months to 20 years with most patients developing symptoms within 3 years with a median time to onset of 1.5 years. Initial presentation can be dysesthesia, pain or weakness progressing to pain and global limb weakness often progressing to a flaccid arm [35]. In one study of 33 patients with radiation-induced brachial plexopathy, the authors reported that 17 patients required opioids for treatment of their pain and suggested early institution of opioid treatment. These authors also reported that three of 33 patients had a good response to chemical sympathectomy. Once onset of plexopathy occurred, progression was often inexorable and led to loss of useful hand function in a time range of 6 weeks to 5 years. Two patients who underwent amputation as a treatment for brachial plexus pain suffered from PLP afterward. A single patient (out of 33) had spontaneous remission of pain after 2 years [36].

Generally, toxicities are felt to be more prevalent with “short-course” radiotherapy techniques, which utilize higher doses per fraction, although recent work is calling this dogma into question noting significant toxicities with standard, more fractionated techniques administered over 6 weeks [37]. Frequency and size of each treatment (fraction) has been shown not to affect the occurrence of brachial plexopathy but “high dose” techniques are strongly associated with an increased incidence of brachial plexopathy. Numerous confounders exist when attempting to attribute late toxicities to radiotherapy, as more techniques now combine chemotherapy, surgery, and radiation. Thus, some have advocated the terminology “treatment-related toxicity” vs assigning the etiology to a specific modality [38,39].

Pelvic pain after radiotherapy may be due to pelvic insufficiency fracture, enteritis, visceral dysfunction, or neural damage [40]. Chronic pelvic pain has been reported as a consequence of prostate brachytherapy. Wallner and colleagues have reported three patients who developed painful urination within 1 month after brachytherapy whose pain persisted longer than 3 years [41]. Brachytherapy-related dysuria is thought to typically resolve within 6–24 months after implantation [42]. Twenty percent of patients receiving brachytherapy have been reported to complain of dysuria 1 year after treatment [39]. These patients describe pain either localized to the prostate or diffusely throughout the urinary tract or pelvis that is either only present during urination or exacerbated during urination. Many authors have speculated that they believe post-radiation pelvic pain syndromes are underreported.

Radiation myelopathy is defined as injury to the spinal cord by ionizing radiation. Generally paresthesia, especially abnormalities in thermesthesia and algesthesia, and muscle weakness, which begins in the legs, are the earliest symptoms and signs. Symptoms such as gait disturbance, hemiplegia, and transverse signs may ensue. Radiation myelopathy may present with pain or dysesthesia at or below the level of injury [43].

Late post-radiation chronic pain syndromes have an onset greatly delayed from the radiotherapy, often by many years. Thus, clinicians should be aware of this syndrome so that appropriate treatment can commence. As noted above, an electromyography study will reveal characteristic changes confirming the diagnosis. Recent research has focused on limiting radiation-induced toxicities through either alteration of the treatment pro-

ocols or coadministration of various protective agents [37].

Chemotherapy

Painful peripheral neuropathy is frequently a dose limiting side effects of certain chemotherapeutic regimens. Mild chemotherapy-induced peripheral neuropathy is commonly seen during chemotherapeutic cycles with these agents leading to reduced dose or elimination of the offending agent in subsequent courses [37]. Typically, this neuropathic pain will then resolve with or without symptomatic treatment. However, in a small number of patients, the neuropathy does not resolve and may continue to be intensely painful chronically. Prevalence during treatment varies from agent to agent, the intensity of treatment (dose intensity and cumulative dose), other concurrent therapies such as surgery and radiotherapy, and the use of combination chemotherapy. Estimates of prevalence range from 4% to 76% during chemotherapy treatment [33,36]. Preexisting nerve damage such as neuropathy caused by diabetes, alcoholism, inherited neuropathy or paraneoplastic syndrome may increase the incidence and severity of chemotherapy-induced peripheral neuropathy.

Commonly used current neurotoxic agents include paclitaxel, docetaxel, vincristine, cisplatin, oxaliplatin, thalidomide, and bortezomib. There is an increased incidence of neurotoxicity if two or more neurotoxic agents are combined. These neuropathies are generally sensory and nonpainful. Painful chronic neuropathic pain as a direct consequence of chemotherapy appears to be less common. Treatments currently include all antineuropathic pain medications, physical medicine techniques including desensitization therapy, and in refractory cases interventional pain therapies such as spinal cord stimulation [35]. Ongoing research efforts are focused on mechanisms of neural injury to ultimately lead to protective or preventative strategies [44,45].

Lastly, chemotherapeutic toxicity may be attributable to corticosteroids, which are coadministered in many chemotherapeutic protocols, and in some cases such as myeloma, the corticosteroid is an intergral chemotherapeutic agent.

Osteonecrosis is a well-described complication of steroid use. Morbidity is related to progressive joint damage often leading to decreased range of motion, pain with movement, and arthritis. Weight-bearing joints are most commonly involved and the disease often requires joint replacement to restore function and relieve pain.

The shoulder, elbow, wrist, hand, and vertebral bodies can also be involved. Osteonecrosis typically develops within 3 years of steroid treatment.

Osteonecrosis or avascular necrosis may occur as a complication of either intermittent or continuous corticosteroid treatment. It most commonly involves the femoral head and presents with pain in the hip, thigh or knee that is worse with movement, with or without localized tenderness. Humeral head disease presents similarly with pain in the shoulder, upper arm or elbow. It may occur in any bone in the body. Focal osteonecrosis may mimic boney tumor and may result from steroid therapy as well as radiation and chemotherapy. There is little correlation between the degree of bone involvement and the intensity of associated pain. Physician awareness of the incidence and severity of this complication is low and a uniform diagnostic approach is not used. Fifty-five percent of adult patients treated for lymphoblastic disease developed avascular necrosis that was disabling a mean of 3.5 years after treatment [43]. Nonspecific bone pain first occurred in five of nine adult males during reintensification block of chemotherapy containing high doses of dexamethasone. Mattano and colleagues found a 14% risk of developing osteonecrosis following multiple, prolonged courses of corticosteroids in children aged 10–20 years old, who were treated for acute lymphoblastic leukemia [46]. Children less than 10 years of age had a risk of only 0.9% in the same study. These authors hypothesize that the maturing bones of adolescents may be more susceptible to the development of osteonecrosis.

General Principles of Treating Chronic Pain

Chronic pain in survivors may occur as a consequence of severe, poorly controlled acute cancer pain. Patients who endure severe, inadequately controlled pain during the acute treatment phase of their disease are more likely to develop chronic pain later on. This is not unique to cancer pain patients but is known to occur in pain patients in general [47]. Every effort should be made to control pain well at the time of diagnosis, after surgery, during chemotherapy, and radiation treatment. Good acute pain control *may* reduce the incidence of chronic pain in cancer survivors [48].

Psychological factors influence chronic pain in patients cured of cancer [49]. The expression and ability to cope with pain heavily impact on the magnitude of debility caused by the chronic pain-

ful condition. Patients who use active coping strategies report less chronic pain than those who use passive strategies. Active strategies are an attempt by the patient to control pain and to continue to function in spite of pain while passive strategies involve relinquishing the control of pain entirely to others. Catastrophizing is a tendency to ruminate on and exaggerate the threat of pain and to adopt a helpless orientation to pain. Patients who have this personality trait (“catastrophizing”) have been shown to report a greater intensity of pain and have a predilection for developing *chronic* pain even before they experience pain [50]. Early institution of behavioral medicine strategies in the treatment of both acute and chronic cancer pain may result in an improved quality of life for survivors. Extrapolation from the chronic pain literature reveals effectiveness of the use of so-called “cognitive-behavioral” psychological therapies to help chronic pain patients retain control of their pain and functionality [51]. Promotion of wellness behaviors and the use of physical therapy and physical medicine techniques early in cancer recovery may help to diminish the intensity and incidence of chronic pain in long-term survivors. For example, perhaps *all* mastectomy or radical neck dissection patients should be put through a course of physical therapy as a part of routine care.

The distinction between acute cancer-related pain and chronic pain is rarely entirely clear. Many patients will suffer repeated bouts of acute pain, during chemotherapy cycles for example, or perioperatively. Some of these acute episodes may linger on to become subacute lasting for some months, or ultimately lasting longer in the case of the chronic pain syndromes. Cousins and Siddall have argued for the definition “persistent pain” for pain lasting longer than 3 months, to allow adequate time for the expected healing phase. Cousins and Siddall have further argued that this “persistent pain” represents a disease state to itself with unique nervous system pathophysiology and treatment strategies [47]. Recognition of specific chronic pain syndromes in various cancer survivor groups, with aggressive, appropriate treatment may help to improve quality of life in this growing patient population.

In this complex patient, it is imperative to develop a mechanism-based diagnosis and treatment approach. Distinguishing between neuropathic and nociceptive pain, visceral and somatic pain, bone pain, spontaneous and evoked pain, incident pain, voiding pain, allodynic pain, and understanding temporal and activity-related pat-

terns can help optimize selection and timing of appropriate remedies. Whereas the typical patient response to acute pain, including reducing activity and splinting the affected area, is adaptive and helpful, this same response to chronic pain does not allow the optimal outcome. Chronic pain patients typically gradually avoid activity becoming progressively deconditioned and enter a cycle of inactivity, reduced socialization, altered sleep-wake cycles, and medication misuse, all termed "maladaptive behaviors" [52].

Lastly, the same interdisciplinary treatment paradigms apply to cancer survivors as apply to all chronic pain patients [53]. Attention not just to pain and other symptoms but including social, emotional, and spiritual issues will result in improved quality of life and outcome measures. The therapeutic focus in chronic pain shifts to a management and adaptive coping strategy rather than a continual search for the cure of the pain. The proper balance of interventional measures, pharmacological treatments, behavioral interventions, and physical medicine approaches will produce the best outcome. Cancer survivors may be deconditioned following their treatment. Reconditioning measures, physical and occupational medicine referrals, and/or personal training regimens should always be considered as part of the treatment plan. These patients may suffer from addictive disorders as do many chronic pain patients and this should not be overlooked in cancer survivors [54]. There may be social impediments to treatment such as lack of prescription coverage or health insurance. These factors are not unique to cancer survivors nor should they be unnoticed in treating cancer survivors for chronic pain. Providers should recognize their own strengths and weaknesses and involve other specialists such as chaplains, social workers, psychologists, occupational and physical therapists, vocational rehabilitation counselors, spiritual advisors and family members whenever needed and possible. Flor and colleagues and Buse et al. have shown the effectiveness of organized centers for multidisciplinary care of chronic pain vs single-discipline treatment [55,56]. These centers combine medical management of pain and symptoms with physical, occupational, and vocational therapies. Additionally, group educational sessions are integrated to promote wellness behaviors and family dynamics are addressed as well (see Table 3). This multidisciplinary approach to chronic pain management uses medications and the aforementioned techniques to permit func-

Table 3 Characteristics of "chronic pain patients and behaviors" vs "wellness behaviors/chronic pain recovery"

Chronic pain patients and behaviors
• Demanding, angry, passive-dependent personality traits
• Limited insight into self-defeating behavior patterns
• Facial grimacing, moaning, crying, blaming
• Focus on pain, catastrophizing
Wellness behaviors/chronic pain recovery
• Takes responsibility for own actions
• Sets realistic goals, exercises regularly, positive attitude
• Practices pain-reducing techniques and coping strategies
• Seeks out support including family, religious, or community groups

Adapted from Obata, et al. [21].

tional restoration. This treatment strategy will serve the patient with chronic cancer pain well, keeping in mind unique aspects of post-cancer syndromes. For example, when a patient with chronic cancer pain has a significant pain exacerbation, one must consider the possibility of recurrent cancer [57].

Conclusion

Optimal treatment of the cancer survivor with chronic pain is an evolving clinical story borrowing current best practices from the chronic non-cancer arena. Areas on ongoing research include defining the magnitude of these chronic pain syndromes, uncovering mechanisms of chronic pain, and preventative strategies. Newer, minimally invasive surgical approaches, different radiation, and chemotherapeutic protocols will hopefully decrease the development of chronic painful conditions. Lastly, there is evidence that optimal treatment of acutely painful conditions may lower the incidence of chronic pain. Also, careful attention to the patients emotional and psychological state is imperative as part of pain treatment to assist in optimal coping with the pain.

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