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Contemporary Issues in Cancer Rehabilitation

The Case for Prehabilitation Prior to Breast Cancer Treatment

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Abstract

Cancer rehabilitation in breast cancer survivors is well established, and there are many studies that focus on interventions to treat impairments as well as therapeutic exercise. However, very little is known about the role of prehabilitation for people with breast cancer. In this narrative review, we describe contemporary clinical management of breast cancer and associated treatment-related morbidity and mortality considerations. Knowing the common short- and long-term sequelae, as well as less frequent but serious sequelae, informs our rationale for multimodal breast cancer prehabilitation. We suggest 5 core components that may help to mitigate short- and long-term sequelae that align with consensus opinion of prehabilitation experts: total body exercise; locoregional exercise pertinent to treatment-related deficits; nutritional optimization; stress reduction/psychosocial support; and smoking cessation. In each of these categories, we review the literature and discuss how they may affect outcomes for women with breast cancer.

Breast Cancer Treatments and Related Adverse Effects

Breast cancer is the most common and second most deadly malignancy among North American women [1,2]. Earlier detection and improved treatment options have resulted in high survival rates for early-stage cancer, increasing the number of women living with a history of treatment. Oncology-directed treatment for breast cancer is individualized to diagnostic, prognostic, and individual factors, and most often is multidimensional, including surgery, radiotherapy, chemotherapy, targeted therapy, and hormone therapy. Unfortunately, adverse effects resulting from surgery and neo- and/or adjuvant treatments produce chronic and latent impairments that deteriorate health-related quality of life (HRQOL) [3].

Surgery (eg, lumpectomy or mastectomy and breast reconstruction) is a cornerstone of disease management for stage I-III breast cancer [4]. Tumor resection and cosmetic surgeries are associated with numerous adverse effects including lymphedema, loss of strength, and compromised range of motion of the shoulder, arm, and cervical spine, collectively recognized as upper-quadrant dysfunction [5-8]. Other localized persistent and late effects include axillary web syndrome and ipsilateral brachial plexopathy [9-11]. Particularly when surgery is combined with other therapies, patients may also experience more systemic impairments such as pain, fatigue, and decreased ability to participate in activities of daily living [6,12-14]. Ultimately, these postoperative impairments can significantly reduce physical capacity, which further exacerbates deconditioning and undermines return to work and other meaningful activities that have eventual social and economic consequences [15,16].

Adjuvant radiation is indicated in 60%-70% of patients with stage I-III breast cancer [4]. Radiotherapy further complicates postoperative outcomes and can contribute independent adverse effects, such as persistent or latent fatigue, pain, lymphedema, muscle weakness or radiation fibrosis, nerve dysfunction, and skin damage [8,17,18]. Particularly concerning is the increased risk of secondary cancers and cardiac toxicity resulting from chest irradiation [8,17]. In fact, although radiation attenuates breast cancer—related deaths, benefits of treatment are offset by increased cardiovascular-related mortality, especially a decade after completion of treatment [19].

Systemic therapy for breast cancer includes immunotherapy, hormonal therapy, targeted drugs, and cytotoxic chemotherapy. Cytotoxic chemotherapy is indicated in up to 90% of the patient population, often within 6

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weeks after surgery [20]. Common chemotherapy drugs include cyclophosphamides, 5-fluorouracil, cisplatin, and taxanes, often administered in combination [21]. Chemotherapy is commonly accompanied by unfavorable treatment-related effects such as nausea, debilitating and persistent fatigue, hair loss, peripheral neuropathy, cognitive impairment, early menopause, and impaired cardiac function [21-23]. In hormone-sensitive breast cancer, adjuvant endocrine therapy (eg, aromatase inhibitors, tamoxifen, and gonadotropin-releasing hormone agonists) is often used and is associated with improved disease-free survival [24]. Despite clinical utility, the risk of adverse cardiac outcomes has been shown to reduce overall survival benefit for some hormone treatment regimens [25]. The musculoskeletal system is also adversely affected through hormone therapy via arthralgias, myalgias, and reduced bone mineral density [26].

Secondary, or latent, morbidities associated with breast cancer treatments are similarly problematic and undermine return to well-being. Cardiotoxicity is a well-established, and potentially fatal, side effect of the treatment paradigm for breast cancer, resulting from chemotherapy, radiation, hormonal therapies, and targeted therapies [27]. One in 5 patients with breast cancer will develop some type of treatment-related cardiac morbidity and have nearly twice the risk of cardiovascular-related mortality compared to healthy women [28,29]. The cardiotoxic effect of breast cancer treatment has recently been recognized as the leading cause of death in older cancer survivors and is commonly characterized by a decrease in left ventricular ejection fraction, asymptomatic or symptomatic congestive heart failure, abnormal cardiac function, and biological markers of heart failure and function [30,31]. In particular, anthracycline-based chemotherapy and the targeted drug trastuzumab, used in combination or independently, can increase the risk of cardiotoxicity to 27% [32].

Collectively, local and systemic therapy for breast cancer challenge the patient's physiological and psychosocial reserves and undermine HRQOL. Prospective data looking at HRQOL from the prediagnosis to 18-months posttreatment period report significant deterioration in global HRQOL that maintains a downward trend [33]. Unfortunately, these deficits in HRQOL are present up to 10 years posttreatment, especially in younger breast cancer survivors and those receiving adjuvant therapy, highlighting the need for enhanced supportive care services across the treatment experience to attenuate the severity of dysfunction in the acute posttreatment and survivorship period [34-36].

The Case for Prehabilitation in Breast Cancer

Breast Cancer Rehabilitation

Breast cancer rehabilitation is most commonly introduced after locoregional therapy (surgery or radiation) and/or after systemic therapy, with an acute postoperative focus on restoring function of the upper quadrant through mobility and flexibility exercises to mitigate shoulder-related impairments [37,38]. Earlier implementation of postoperative rehabilitation significantly expedites return to baseline range of motion compared with traditional rehabilitation, which is initiated after removal of surgical drains [39]. In light of evidence that suggests an important role of earlier intervention, and to further optimize care, a prospective model of care for breast cancer rehabilitation has been suggested [40]. This model of care highlights the need to identify preoperative measures of physical and psychosocial well-being, with an emphasis on follow-up throughout the treatment trajectory to rapidly identify and treat adverse effects that are amenable to rehabilitation. Unfortunately, adherence to breast cancer rehabilitation can be low, especially among patients who do not have a history of participating in regular exercise before treatment or among those who lack financial resources to attend the prescribed frequency and duration of rehabilitative care [41]. Strategies that can emphasize the importance of rehabilitation in addition to expediting recovery may reduce the need for intensive and/or prolonged rehabilitation.

In addition to rehabilitative exercise, the broad and impactful value of general cardiovascular and musculoskeletal training for women during/after breast cancer treatment underscores recommendations for integration into breast cancer survivorship paradigms [42,43]. A recent meta-analysis of 33 randomized controlled trials (RCTs), including 2659 breast cancer survivors during and after treatment, showed significantly improved social and emotional well-being, anxiety, depression, physical fitness, body composition (eg, muscle mass and body mass index), and overall HRQOL for exercising participants [44]. Epidemiological research also shows survival benefits for women who are active after a breast cancer diagnosis [45,46], with one showing a dose-response association between physical activity and risk of overall and breast cancer–specific mortality in which an increase of 10 metabolic equivalent hours per week (the equivalent of brisk walking for 3 hours per week) in postdiagnosis physical activity was shown to decrease the risk of total mortality by 24% [46].

Early investments into understanding the effects of physical movement for women with breast cancer may improve patient engagement in rehabilitative and exercise regimens. To date, very little attention has been paid to the potential value of the postdiagnosis/pretreatment setting when patients may be able to invest in optimized posttreatment outcomes. Given that treatment tolerance and recovery may be compromised due to poor preoperative physical condition, strategies to improve pretreatment physiological