

UPMC REHAB GRAND ROUNDS

FALL 2020



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Disclosures

Drs. Orada and Watson report no relationships with proprietary entities producing health care goods and services.

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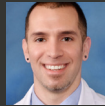
*UPMC Presbyterian Shadyside and UPMC Mercy are rated as high performing for rehabilitation by *U.S. News & World Report*.

Cancer Pre-habilitation



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Clinical Vignette

AB is a right-hand-dominant, 47-year-old female with a past medical history significant for remote cervical cancer status/post hysterectomy and a new diagnosis of right breast invasive lobular carcinoma (ER+/PR+, Her2/Neu-). She currently is pending cancer treatment. AB has been evaluated by a breast oncologic surgeon and plastic surgeon with plans to undergo a double mastectomy with right sentinel lymph node biopsy and reconstruction. She also has an upcoming consultation with a medical oncologist to discuss systemic treatment options (chemotherapy, endocrine therapy, or both) after her surgery.

AB was a college volleyball athlete and had “chronic rotator cuff issues” in the past. She was doing well until about three months ago when she experienced more pain in her right shoulder. There were no inciting events precipitating the increased pain. Prior to her breast cancer diagnosis, AB was seen by an orthopaedic surgeon and had a magnetic resonance image (MRI) taken of her right shoulder, which showed a superior labrum anterior and posterior (SLAP) tear.

AB endorses acute on chronic “deep” and “sharp” shoulder pain located inside her shoulder. The pain is particularly exacerbated when reaching upward, reaching back to unhook her bra, and lifting heavy objects. AB has no shoulder pain at rest, and she denies neck pain, left-sided pain, other joint pains, or arm and hand weakness. Because of her new cancer diagnosis, she has not had any formal treatment for her shoulder pain, including physical therapy. She takes ibuprofen as needed for the pain. AB admits to a sedentary lifestyle.

On general exam, the patient has a BMI of 32. She is neurovascularly intact and has no signs or symptoms of cervical radiculopathy or brachial plexopathy. Her active range of motion (AROM) abduction/forward flexion is only to 160 degrees and is limited by pain. Passive ROM is full. Her pain ratings can escalate to 10/10. She has a positive Obrien’s test and mildly positive Hawkin’s test. Other provocative maneuvers were negative. AB was referred to the UPMC Hillman Cancer Center Rehabilitation Clinic for “pre-habilitation” to address decreased range of motion in her right arm.

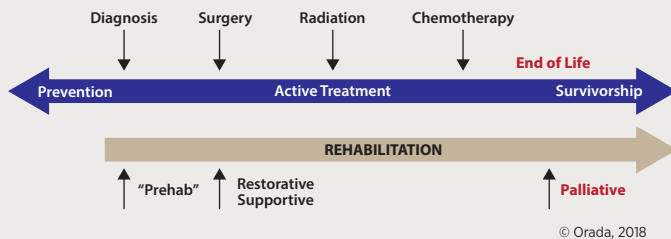
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Cancer Rehabilitation

Cancer rehabilitation is a subspecialty of physical medicine and rehabilitation which focuses on reducing or eliminating the side effects, complications, and associated treatments of cancer to improve survivor's functional independence and quality of life.¹

Additionally, cancer rehabilitation should be integrated throughout the oncology continuum and delivered by trained rehabilitation professionals with the expertise to diagnose and treat a patient's physical, psychological, and cognitive impairments. This is done in an effort to maintain or restore function (i.e., range of motion, strength, ability to perform activities of daily living [ADLs] independently), reduce symptom burden, maximize independence, and improve quality of life in this medically complex population.^{2,3}



During cancer treatment, physical activity declines for reasons including fatigue, schedule disruption, decreased motivation from the psychological impact of illness, and the effects of cancer itself. Prior levels of activity may not resume for years following treatment; however, a life-altering event, such as a cancer diagnosis may, instead, serve as an initial motivator to make positive behavioral changes.

Goals of cancer rehabilitation, therefore, should generally target improving health-related quality of life (HRQoL) and the maintenance of functional capacity. Therapies should facilitate functional recovery after acute declines in function, prevent chronic impairments and pain from developing, and ultimately allow patients to maintain their independence.^{4,5}

This topic is highly relevant since breast cancer is the most common cancer in women and has the highest incidence of all cancer types. There are approximately 250,000 new cases of invasive breast cancer yearly (in the US),⁶ driven by increases in hormone receptor-positive breast cancer in all racial/ethnic

groups and over 300,000 total cases (including noninvasive), overall. Yet, from 1989 to 2015, rates of mortality from breast cancer decreased by 39%.⁷ As a result, this increased survivorship means that approximately 3.8 million people are currently being treated for – or are living following treatment for breast cancer in the United States.⁶ Furthermore, approximately 150,000 women in the U.S. currently are living with metastatic breast cancer.⁸

Specific Anticipated Impairments in Breast Cancer

Cancer is now being considered a chronic disease as more patients survive thanks to the robust research and tireless efforts by our oncology colleagues. Many cancer survivors experience side- and late-effects as a result of cancer-directed treatments. These impairments include, but are not limited to, shoulder dysfunction, contractures, axillary cording, upper quadrant pain, lymphedema, neuropathy, fatigue, cognitive dysfunction, sexual side effects, and cardiovascular complications.⁹

The purpose of cancer pre-habilitation is to prevent or reduce the complications commonly seen during cancer-directed treatments. After breast cancer surgery, approximately 50% of breast cancer survivors experience loss of shoulder ROM, with approximately 15% experiencing severe functional restrictions.⁹⁻¹²

A common impairment seen shortly after surgery for cancer is axillary cording, which is composed of sclerosed and thrombosed lymphatics that can cause pain.¹³ Also known as axillary web syndrome (AWS), cording can affect up to 20% and 70% of patients after sentinel and completion axillary lymph node dissection, respectively.¹⁴⁻¹⁶

If acute pain symptoms are not addressed after breast cancer surgery, breast cancer survivors may experience “postmastectomy pain syndrome” or upper quadrant pain – a chronic pain condition that can occur following surgery to the breast.¹⁷ In one population-based study, about 47% of breast cancer survivors endorsed persistent pain two to three years after treatment.¹⁸ Undeniably, nearly all patients experience some degree of fatigue during cancer treatment, and up to one third endure persistent fatigue for years after treatment completion.¹⁹

Table 1: Activities to Perform for the First Week Immediately Following Breast/Axillary Surgery	
Spine	Cervical spinal rotation
	Lateral Bending
Wrist	Flexion
	Extension
	Circumduction
Elbow	Flexion
	Extension
Shoulder	Pendulum exercises, wall-walking, pectoralis stretch

Cancer Pre-habilitation

Cancer pre-habilitation has many common elements with rehabilitation; however, the aim is to prepare the patient’s body for anticipated stressors (i.e., surgery, chemotherapy) to decrease morbidity and mortality and facilitate faster functional recovery. Breast cancer pre-habilitation shares many features with pre-habilitation for other malignancies since many physical and psychological interventions are not unique to one cancer type. Due to the unique risk factors associated with breast cancer and the distinct morbidity associated with hormonal therapy/chemotherapy, lumpectomy/mastectomy, and lymph node dissection, there are important features specific only to breast cancer pre-habilitation.

Breast cancer patients should perform basic ROM exercises for the affected arm (Table 1) during the first week after surgery. These exercises can result in significantly better ROM, with function returning to near baseline²⁰ and should include shoulder flexion/extension, wall-walking, and gentle seated pectoralis muscle stretches one week after drain removal. (Figure 2)

In predicting the potential magnitude of the benefit of pre-habilitation, data suggest that baseline ROM and pain scores prior to mastectomy correlate with the postoperative likelihood of pain and return to function.²² Further, this does not exclusively apply to patients without pathology in the limb prior to mastectomy; rehabilitating a shoulder with

baseline impairment prior to surgery (essentially a combined rehabilitation/pre-habilitation) allows for similar postoperative accelerated recovery benefits.²²⁻²⁴ Benefits are not only seen when preparing a healthy shoulder for breast cancer-related surgery, but also if a shoulder had baseline impairment due to other, unrelated pathology. Beyond targeting the upper extremity, pre-habilitation can improve general exercise tolerance and cardiovascular health, which is particularly relevant given potential cardiotoxicity of common chemotherapeutic agents such as doxorubicin and paclitaxel.²⁵

Specific Role of HIIT

High-Intensity Interval Training (HIIT) has been one of the more frequently studied exercise regimens in cancer pre-habilitation. Instead of a steady aerobic pace, it involves running, cycling, or other exercise being performed at maximum effort for a brief period of time (from ~30 seconds to a few minutes) followed by a short, low-intensity recovery period.



Figure 2: Additional sample exercises for patient instruction following surgical treatment of breast cancer;²¹ here shown with a live model. These are to be performed after drain removal, as well. **A.** Shoulder blade stretch; **B & C.** Wand exercise; **D.** Chest wall stretch; **E & F.** Shoulder blade squeeze; **G & H.** Shoulder stretch.

Then, the high-intensity activity is repeated. Researchers that combined HIIT with either resistance training (RT) or aerobic training (AT) found improvements in “cancer related fatigue” in both intervention groups, but reported the greatest improvement in HIIT + resistance training.²⁶ Patients had the greatest benefit for assessments of cognitive functioning in the HIIT-RT group, while those in the HIIT-AT arm demonstrated the greatest benefit for emotional functioning. Neither group experienced major adverse events, even despite patients having PICC lines present during exercise sessions. However, patients in the HIIT-AT group had significantly higher rates of diarrhea than those in the RT-HIIT and control groups by unknown mechanism(s).

Because patients with lung cancer have an average three-week period from diagnosis to surgery, researchers²⁷ designed a pre-habilitation program using HIIT for deconditioned patients following a lung cancer diagnosis. During this period (with a median number of eight sessions), patients achieved significant decreases in resting heart rate while making significant improvements in VO₂ max, peak watts generated, and the six-minute walk test (6MWT).²⁴

In a similarly-abbreviated four-week HIIT intervention with additional resistance training as part of a “4-pillared pre-habilitation program”,²⁸ patients received nutritional supplements (protein supplements twice daily) and psychological interventions (meeting for 90 minutes with a trained psychologist). The study demonstrated excellent feasibility metrics with a high attendance rate (90%), high level of patient satisfaction and no adverse events. After surgery, the intervention group had significantly better 6MWT and significantly faster returns to baseline functional capacity.

Pre-habilitation programs condensed to a two-week timeframe for patients newly-diagnosed with lung cancer prior to lobectomy were able to demonstrate significant benefits.²⁹ The multimodal program consisted of aerobic and resistance exercises, respiratory training, nutrition counseling with whey protein supplementation, and psychological guidance. The participants dramatically improved their 6-minute walk distance by one day prior to surgery, and they retained a significant residual difference at 30 days after surgery. Although the intervention group’s distance declined after surgery, the decline was smaller compared with the control group’s, and their walking distance was still 21.5 meters above their baseline before the pre-habilitation therapy. Forced vital capacity (FVC) was also significantly better. Despite these improvements, there were no differences in procedural complication rates or hospital length of stay (LOS).

Given the opportunity for behavioral change following a life-altering diagnosis, it is worthwhile to consider the literature on exercise benefits on rates of recurrence *after* a patient is already diagnosed with breast cancer. Data from the *Nurses’ Health Study* found a lower rate of recurrence for women who exercised at least 9 MET/yr/week.³⁰ Moreover, women who were active at the time of diagnosis had lower mortality than inactive patients, but this benefit was only sustained if they maintained their baseline activity level after diagnosis.³¹

Nutritional Components of a Comprehensive Pre-habilitation Program

Nutrition may have a role in breast cancer incidence, recurrence, and mortality, and treatment for breast cancer can significantly impact nutritional status.

The diets of patients undergoing chemotherapy are often low in fruit, legumes, dark green vegetables, and orange vegetables, implying potential insufficient intake of most minerals, B-vitamins, and Vitamin C. Decreased protein intake, which may be seen in the setting of chemotherapy, predisposes patients to sarcopenic obesity, a condition of low lean mass and higher than normal fat mass. These patients should ideally consume 1.2g to 1.5g protein per kilogram of body weight³² for maintenance of lean mass.

Patients with low BMI (< 20) at baseline or those who have lost > 10% of their weight in < 6 months are at increased risk of complications from malnutrition. One risk is decreased bone mineral density, which may be compounded in patients receiving certain anti-estrogen therapies. Alternatively, *gaining* weight after diagnosis is associated with worse outcomes, so patients should be counseled and monitored to control weight loss to 5% to 10% of body weight. Practitioners should restrict calories, recommend nutrient-dense foods, and reduce simple sugars and added fats. This strategy has been shown to reduce tumor growth and inflammatory response, delay the aging process, and increase rodent/human life expectancy.³² Ultimately, it is important to not disregard nutritional therapies even if a patient is at a healthy BMI at baseline as this may not adequately reflect nutritional status or how a patient will respond to breast cancer treatments.

More directly, malnutrition and malnourishment may negatively impact overall “resilience,” with sarcopenia and fatigue directly impeding patients’ abilities to participate in the exercise components of pre-habilitation/rehabilitation.

Approximately 40% of patients receiving oncologic treatment of any type may be malnourished, with higher rates in hospitalized patients versus those treated as outpatients. Rates of malnutrition are lower in breast cancer relative to other cancer types, but increase with the extent of cancer spread (i.e., local versus regional versus metastatic). Poor oral intake is most commonly a result of anorexia (reported by 62.5% of patients), loss of taste (42.2%), nausea (29.9%), and difficulty swallowing (25.6%).^{33,34}

By utilizing a diet rich in fruits, vegetables, whole grains, and omega-3 fatty acids researchers achieved significant decreases in fatigue with significant improvements in sleep quality.⁴¹ Soy intake is thought to have estrogen-promoting qualities and may directly promote growth of, and interact with, tamoxifen in ER+ tumors.³² This effect has not been conclusively demonstrated and remains an area of investigation.

Psychological Therapies and Benefits of Pre-habilitation

Many multimodal pre-habilitation strategies include psychologic therapies to benefit mental health in the setting of cancer diagnosis and treatment. The individual contribution of stress management training without additional exercise or dietary interventions has varying reported levels of benefits. Psychologists demonstrated benefits of lower depression scores through relaxation and guided imagery techniques although quality of life (QoL) did not significantly improve.³⁵ In a systematic review,³⁶ four of seven studies pertained to patients being treated for breast cancer with stress management strategies. The interventions did not affect surgical outcomes such as length of stay (LOS), rate of complications, mortality, or analgesic requirements, but demonstrated improved immunologic function, psychological and somatic symptoms, and QoL. Additionally, many of the studies showed improvement in depression scores with residual benefit extending up to three months postoperatively.

Models of Cancer Pre-habilitation Used in Other Cancer Diagnoses

In one meta-analysis of various exercise pre-habilitation programs for patients with pulmonary malignancies,³⁷ researchers pooled 10 randomized controlled trials (RCTs) with a total of 676 participants of varying regimen: aerobic training + inspiratory muscle training; aerobic + strength + inspiratory muscle training; aerobic + strength training; multicomponent

training; aerobic training alone. In this pooled dataset, they found significant improvement in 6MWD, VO₂ peak, dyspnea, postoperative hospitalization, and pulmonary complications. Of note, these studies were heterogenous in their protocols, methodologic quality, and interventions.

In one pilot study of patients treated for colorectal malignancies,³⁸ researchers followed 12 patients through six educational exercise sessions during neoadjuvant therapy for rectal cancer. Primary outcome in the study was feasibility, as adherence cannot be assumed given the high morbidity during this period. Overall adherence was good, with 64 completed exercise education sessions out of 72 potential sessions. Moreover, despite a small sample size, the study demonstrated significant improvements in VO₂ peak, depression measures, and a QoL “emotional function” domain.

Patient Buy-In for Pre-habilitation

Ultimately, the best pre-habilitation program is any one in which patients are willing and able to participate. Implementing behavioral change amid a new cancer diagnosis and ensuing treatment is a delicate undertaking. Qualitative interviews with patients during chemotherapy sessions³⁹ proposed several insights that should underlie a strategy for proposing and facilitating behavioral therapies. First, participants reported awareness of the benefits of a healthy lifestyle, but “breast cancer treatment may put motivation for lifestyle change on hold.”^{33,34,40}

Many respondents were also overwhelmed by the sheer volume of information they received related to their diagnosis and treatments. One application of this insight is to always offer guided exercise interventions, as this would make participation less daunting and leave little room for uncertainty and anxiety. Although the data have shown video demonstration to be generally noninferior to in-person demonstration,⁴¹ individual cases may warrant a closer “hand-holding” approach.

Overall, “individualization is the key” when designing pre-habilitation regimens for patients. Many participants feel that counseling often provides lifestyle information they already know.³⁹ Also, participants comment that there often is not enough time in counseling sessions to ask questions, because counselors often use most of the available time for routine questions. Worse, a lot of these questions about lifestyle make participants feel guilty, which may result in them dreading the sessions. Therefore, any lifestyle program should have as few barriers to participation as possible.

Future Direction

Research should attempt to further identify the simplest interventions with the lowest potential barriers to participation, especially in the setting of fatigue and psychological effects of cancer diagnoses and treatment. Moreover, studies also should generate cost-effectiveness data or other measures to encourage reimbursement for these therapies, as they would likely benefit patients, providers, and payers. Research should address the benefit of multimodal interventions in patients with breast cancer that have shown benefit in other populations.

Clinically, cancer rehabilitation continues to gain recognition in the oncology world as an integral part of care in the cancer care continuum. Indeed, accreditation bodies are now starting to recognize the importance of supportive care services, including the availability of rehabilitation care services, as an essential part of comprehensive cancer care. Ultimately, the inclusion of these modalities will become standard of care with informed medical and surgical oncologists as part of an integrated care model. Also, as additional data are generated to support outcomes benefits for patients, payers may incentivize health systems to incorporate pre-habilitation/rehabilitation programs for their own benefit as well.

Clinical Vignette Outcome

AB was neurovascularly intact. She had no signs and symptoms of cervical radiculopathy and/or brachial plexopathy. Her main symptoms were mostly mechanical, confirming rotator cuff dysfunction/SLAP tear. She had not received any conservative treatments since her breast cancer diagnosis.

AB was initiated on a pre-habilitation program. Symptomatic treatment included nonsteroidal anti-inflammatory drugs (NSAID), cryotherapy, and activity modifications that included avoiding activities that exacerbate her symptoms including excessive overhead activities, lifting and pushing heavy objects, or reaching behind the back. She was given a referral to physical therapy for ROM exercises, posterior capsular stretching exercises, and strengthening of the dynamic stabilizers of the shoulder. A conditioning program also was introduced in anticipation of her planned bilateral mastectomy with right sentinel lymph node biopsy and immediate reconstruction.

Since starting physical therapy and a home exercises program, the patient reported 70% improvement with pain and shoulder ROM. She was happy with her progress but admitted anxiety about her upcoming surgery.

AB underwent surgery without complications. She was initially lost to follow-up, but when she returned to the clinic approximately six months after her surgery, she completed her postoperative outpatient physical therapy and continued with her home exercises program. Her home exercise program for the shoulder continues to employ assisted ROM exercises with a wand. She also continues with shoulder stretches to avoid tightening of the pectoralis muscle. Her strengthening routine includes using a Theraband® to work her scapular muscles, trapezius, and serratus anterior muscle groups to help maintain her scapular mechanics. She was very appreciative of the improvement she made prior to her surgery and continued her progress despite having had the major surgery. She stated, “I’m glad I learned all the exercises before the surgery. If not, I’d probably still be having difficulty with my shoulder.”

Summary and Key Takeaways

1. Personalization is key. With wide disparity in oncologic presentations, baseline impairments, comfort with technology, dietary limitations, and others, no two pre-habilitation/rehabilitation regimen should be identical.
2. Multi-pillared pre-habilitation programs addressing specific impairments (i.e., upper extremity effects of mastectomy), general cardiovascular health, psychological interventions, and nutrition will provide the greatest short-term benefits and opportunities for long-term lifestyle improvements.
3. Know when to leave little space for ambiguity, such as when demonstrating exercise maneuvers or providing transportation (if resources allow), versus when to ask fewer questions and allow the patient to steer the course in psychiatric therapy settings.
4. If a patient is overweight at the onset of therapy, target a 5% to 10% weight reduction through the incorporation of 1.2g to 1.5g protein/kg bodyweight from poultry, fish, and low-fat dairy; advise on the consumption of foods rich in unsaturated fats (particularly omega-3 fatty acids) and of whole fruits and vegetables; minimize intake of refined carbohydrates, all to minimize fatigue, lower risk of sarcopenia, and possibly reduce rates of recurrence.

If a patient is at a healthy weight at baseline, encourage them to maintain their current body weight with at least a moderate activity level, and educate them on the likelihood that their tastes and appetite will be affected by chemotherapy.

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*UPMC Presbyterian Shadyside and UPMC Mercy are rated as high performing for rehabilitation by *U.S. News & World Report*.

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