The Role of Rehabilitation for Women with Cancer

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KEYWORDS

• Cancer pain • Cancer survivors • Function recovery • Lymphedema • Quality of life • Rehabilitation • Survivorship

KEY POINTS

- Survivorship and rehabilitation are vital components of the oncological plan of care.
- Rehabilitation interventions improve the quality of life and function of women with cancer.
- Symptoms associated with cancer and its treatment are amenable to medical management.
- Rehabilitation services, including physiatry, physical therapy, occupational therapy, speech and language pathology, and neuropsychology, help improve cognitive and physical function.
- Treatments for psychological stress improve function and performance status.

INTRODUCTION

"Cancer rehabilitation is medical care that should be integrated throughout the oncology care continuum and delivered by trained rehabilitation professionals who have it within their scope of practice to diagnose and treat patients' physical, psychological, and cognitive impairments in an effort to maintain or restore function, reduce symptom burden, maximize independence and improve quality of life (QOL) in this medically complex population."[1] Within the United States, it is estimated that over 2 million new cases of cancer will be diagnosed in 2024, with women representing 48.6% of the total. Although breast represents the majority, women can develop a

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variety of malignancies specific to organ system and gender (Fig. 1).[2] The number of cancer survivors living in the United States is also increasing, due to improvements in early detection, treatment advances, and the growth and aging of the population (Table 1).[3] The scope of survivorship, especially when considering the wide range of experiences from time of initial diagnosis to end of life for different malignancies, is broad. Physical, emotional, social, and spiritual well-being, in the context of QOL, play important roles when optimizing survivorship care plans.[4] Understanding gender-specific cancer diagnoses and treatment effects is important to support the survivorship and rehabilitation needs for women.

ONCOLOGICAL PATHOLOGIES COMMON TO WOMEN

Breast Cancer

With an estimated incidence over 300,000 in 2024, breast cancer accounts for over 30% of all new cancer diagnoses in women.[2] It is the most common malignancy impacting women in the United States, with about 1 in 8 persons affected within their lifetime. According to the American Cancer Society (ACS), women between the ages of 40 and 44 years with average risk can consider yearly screening with a mammogram, and women aged 45 to 54 years should get a mandatory screening mammogram yearly.[5] After the age of 54 years, survivors can choose between annual or biennial testing. For those with a high risk of disease secondary to family history or genetic mutations, MRI should be used in addition to mammography.[5] Examples of genetic signatures include hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) activity, and they can be categorized as positive (+) or negative (−). The main subtypes ordered by prevalence are HR+/HER2-, HR-/HER2-, HR+/HER2+, and HR-/HER2+. With better screening, enhanced surveillance methods, and diminished toxicity profiles of treatment, the 5 year survival rate has improved to 90.8% as of 2019.[6]

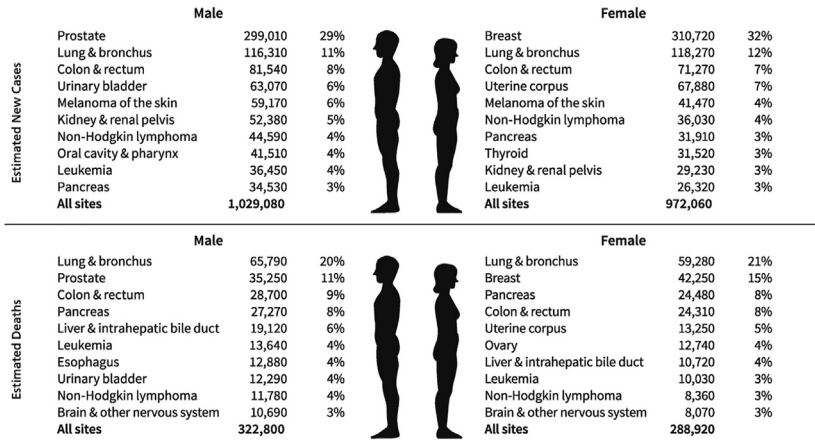

Fig. 1. Estimated incidence and number of death of new cancer cases in the United States stratified by gender.[2] Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data. ©2024, American Cancer Society, Inc., Surveillance and Health Equity Science.

Table 1
Estimated number of female cancer survivors in 2022[3]

Years Since Diagnosis	Number	Percent	Cumulative Percent
0 to <5	2,802,390	29	29
5 to <10	2,063,560	21	50
10 to <15	1,598,790	16	66
15 to <20	1,173,480	12	78
20 to <25	806,370	8	87
25 to <30	527,280	5	92
30+	767,040	8	100

Gynecologic Cancer

Human papillomavirus (HPV) is the primary cause of cervical cancer and is most often transmitted through skin-to-skin contact. Current ACS recommendations suggest all children between the ages of 9 and 12 years receive the HPV vaccine, with access available up until the age of 26 years. Screening every 3 to 5 years with the use of a primary HPV or Papanicolaou test (better known as Pap test or smear) should start at the age of 25 years and continue until the age of 65 years. No further evaluations are necessary for individuals with hysterectomy or aged 65 years with a 10 year history of negative testing. However, cervical pre-cancer assessments should continue for at least 25 years after initial diagnosis, regardless of age.[5] For 2023, cervical cancer accounted for 13,960 of new cases (0.7% of all new cancer cases) in the United States and had a 5 year survival rate of 67.2%.[7]

Endometrial cancer originates from the inner lining of the uterus. There are no specific screening tests for endometrial cancer, but addressable risk factors include excess body weight and lack of physical activity. Consideration should be made for individuals with early onset menstruation, late menopause, hormone replacement therapy, history of hereditary nonpolyposis colorectal cancer (Lynch syndrome), increasing age, and polycystic ovary syndrome as these are associated with higher risk of diagnosis. Women who have Lynch syndrome should be offered yearly testing, including endometrial biopsy from the age of 35 years.[5] There were an estimated 66,200 cases of uterine cancer in the United States (3.4% of all cancer cases in 2023) and a 5 year survival rate of 81.0%.[8] The risk of developing ovarian cancer also increases with age and Lynch syndrome, but additional factors include breast cancer 1 and 2 gene mutations, cigarette smoking, excess body weight, hormone replacement therapy, and history of breast or ovarian cancer.[8] Again, there are no available routine screening tests, but some women opt for preventative hysterectomy based on their medical profiles. Ovarian cancer incidence in 2023 was 19,710 (1.0% of all cases), but 5 year survival was lower at 50.8% due to diagnosis at time of increased severity of disease.[9]

Behavior Modification

Addressing specific behaviors may help decrease the chance of developing cancer in women, such as cessation of tobacco use and incorporation of a consistent physical activity program. The American College of Sports Medicine recommends 150 to 300 minutes per week of moderate intensity or 75 to 150 minutes per week of vigorous aerobic exercise with twice weekly strength training, which in addition to helping with performance status can potentially decrease the risk of breast, endometrial, and

ovarian cancers.[10] Diets integrating more fruits, vegetables, and whole grains while limiting processed foods, red meat, refined grains, and sugary drinks can also play a role. Moderation of alcohol consumption to one drink per day for women, along with following appropriate screening guidelines, is also recommended.[5]

CONDITIONS ASSOCIATED WITH CANCER

Cancer Pain

Pain is one of the most common complaints of cancer survivors regardless of whether the tumor is localized or has spread beyond initial presentation.[11] Patients should be screened during each encounter to understand potential sources, including disease recurrence, new malignancy, or treatment effects from cancer itself. It is prudent to differentiate cancer-related pain and non-cancer pain as approaches can vary drastically for optimal management. For example, shoulder pain in breast cancer survivors can be due to underlying shoulder arthropathy or possible bony metastasis. If conservative measures and therapeutic interventions are not successful, opioids can be considered for cancer-related pain while utilizing adjuvant and non-opioid analgesics.[12] The World Health Organization Four-Step Ladder is a useful tool to determine the appropriate types of analgesic based on pain complaints (**Fig. 2**).[13] Several different agents can be considered when treating mild, moderate, and severe cancer pain (**Table 2**).[14]

If oral pharmaceutical agents are not sufficient or tolerated for adequate analgesic relief, interventional procedures with ultrasound or fluoroscopic guidance can also be utilized to manage pain. Intraarticular corticosteroid injections for adhesive capsulitis have been documented to be safe in populations with breast cancer who have active cancer or are undergoing active treatment.[15] Chemodenervation with botulinum toxin or phenol has been shown to relieve pain related to cervical dystonia or spasticity after radiation treatment.[16] Selective nerve blocks, such as pectoral or dorsal spinal, can successfully manage postmastectomy pain syndrome and increase QOL.[17] Additionally, selective stellate ganglion blocks show promise as an option for reducing pain in postmastectomy pain syndrome. Superior hypogastric plexus and ganglion impar

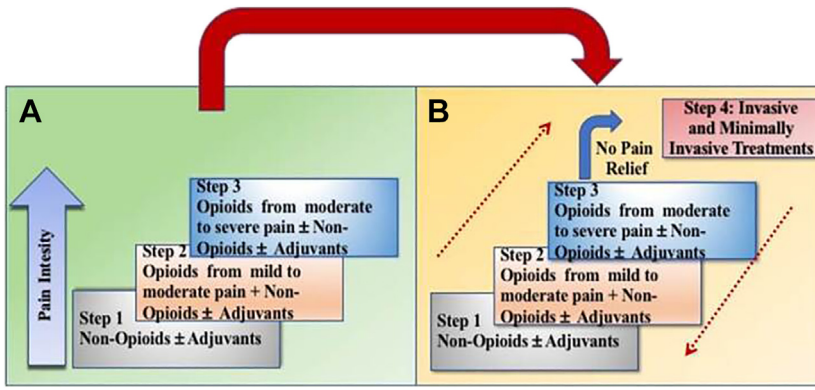

Fig. 2. WHO analgesic ladder.13 Transition from the original WHO 3 step analgesic ladder (*A*) to the revised WHO fourth-step form (*B*). The additional step 4 is an "interventional" step and includes invasive and minimally invasive techniques. This updated WHO ladder provides a bidirectional approach. (*With permission from* Dr. Marco Cascella, MD. Anekar AA, Hendrix JM, Cascella M. WHO Analgesic Ladder. Published April 2, 2023. Accessed April 22, 2024. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554435/.)

Table 2
Common analgesics used to treat cancer pain[13]

Types of Pain		
Mild Non-opioids • Paracetamol • Nonsteroidal anti-inflammatories	Mild to moderate Weak opioids (in combination with non-opioids) • Codeine • Dihydrocodeine • Tramadol Low-dose strong opioids	Moderate to severe Strong opioids • Buprenorphine • Diamorphine • Fentanyl • Hydromorphone • Morphine
Breakthrough Immediate-release opioids • Hydrocodone • Oxycodone	Bone Bisphosphonates Denosumab Dexamethasone Radiation therapy	Cancer-related neuropathic Adjuvants • Duloxetine • Gabapentin • Pregabalin • Tricyclic antidepressants Opioids (in combination with adjuvants)

blocks can also provide analgesia for visceral pain associated with uterine, ovarian, and cervical cancers.[18]

Malnutrition

Malnutrition in cancer is a result of increased inflammatory cytokines, metabolic alterations, and inadequate availability of nutrients due to anorexia from disease and its treatment effects.[19] Optimizing nutrition is a vital cornerstone in cancer survivorship to maintain QOL, support adequate treatment effects, and limit adverse clinical outcomes. Although enteral tube feeding and parental nutrition can be applied to patients with cancer, improvement of oral intake is the preferred method to address patient needs.[20] As part of a multidisciplinary therapeutic strategy, appetite stimulants can play a vital role in mitigating cancer-associated anorexia. Mirtazapine, a specific noradrenergic and serotonergic antidepressant, can increase appetite in patients with cancer-associated anorexia without depression.[20] Other agents such as the antipsychotic olanzapine, the cannabinoid dronabinol, and the progestin megestrol acetate have also shown benefit in increasing appetite.[21] However, the side effect profiles of these agents are more consequential than mirtazapine, especially megestrol acetate that can increase the risk of venous thromboembolisms.[22]

SEQUELAE OF CANCER TREATMENT

Cancer-Related Cognitive Impairment

Cancer-related cognitive impairment (CRCI) refers to changes in cognitive function in noncentral nervous system cancers that occur during or after cancer treatment. Up to 75% of survivors experience cognitive changes during and 60% after treatment, respectively.[23] Deficits are usually mild to moderate and can include challenges with attention, executive functions, processing speed, and short-term and working memory.[24] The duration of impairments varies, and although many resolve within 6 to 12 months of treatment, difficulties can persist for years or decades.[25] CRCI affects women with various malignancies, including breast, lung, colorectal, ovarian, leukemia and lymphoma.[26] Cognitive impairment can be affected by age, cancer diagnoses themselves, oncological treatments (such as chemotherapy, hormone therapies, and targeted therapies), and psychological factors. CRCI can negatively impact QOL, as

cognitive function is related to independence in decision-making as well as instrumental activities of daily living (ADL), return to work, self-confidence, and social relationships.[22]

Rehabilitation professionals play a key role in assessing for and treating CRCI in women with cancer. Neuropsychological evaluation provides objective assessments of various cognitive domains and psychological factors (including anxiety, depression, and fatigue) that may affect cognitive function.[24] Integration of these into the care plan helps guide management and treatment interventions, including cognitive rehabilitation and behavioral therapies. Cognitive rehabilitation is typically completed by speech and language pathology (SLP), with focus on building metacognitive awareness, compensatory strategy training, environmental modifications, retraining of cognitive skills, and structured and functional tasks.[27] Behavioral therapies include counseling, mindfulness and meditation, and self-efficacy. Exercise therapy and pharmacologic interventions are also recommended; however, more research is needed to assess their effectiveness.[28] Evidence is lacking specifically regarding medication options for cognitive dysfunction.[29] However, considerations should be made given that cognitive dysfunction can lead to impairments in attention, concentration, memory, and multi-tasking.[30] In combination with rehabilitation interventions, pharmaceutical options can play a role in supporting patients' participation and progress. Stimulants, such as methylphenidate and modafinil, may aid in cancer-related cognitive changes.[31,32]

Cancer-Related Fatigue

Cancer-related fatigue (CRF) is defined as a distressing, persistent, and subjective sense of physical, emotional, or cognitive tiredness or exhaustion. It can result from cancer and its treatment. Symptoms often are not proportional or correlated to recent activity.[33] Factors associated with CRF include chemotherapy, depression, female gender, insomnia, neuroticism, pain, poor performance status, and radiation therapy.[34] CRF is frequently associated with breast cancer after chemotherapy or radiation, but when both interventions are combined, symptoms are far more significant.[35] In women, it can also impact cognitive, physical, and social functioning as well as QOL and self-confidence. Diagnosis is important given that prevalence is 1.4 times greater than that in men.[36]

Multidimensional assessment tools are necessary when evaluating CRF as it is known to have a combination of affective, cognitive, and physical domain impairments.[34] The Brief Fatigue Inventory and the European Organization for Research and Treatment of Cancer-QOL Questionnaire C30 are helpful to determine the impact of symptoms.[33] Evaluation should be initiated at the time of cancer diagnosis and continued during regular intervals within the treatment and posttreatment period. Cognitive behavioral therapy and physical activity are beneficial for CRF.[34] Specifically, for patients with breast cancer, yoga, as well as aerobic and resistance exercises, can improve symptoms.[37] Continued programs with vigorous and rhythmic exercise, such as aerobic resistance training, aerobic yoga, and traditional yoga, remain valuable after completion of oncological treatments for breast cancer.[36] Although there are no standard protocols to help with CRF, medications such as antidepressants, psychostimulants such as methylphenidate and modafinil, and steroids may be of helpful.[30,31,38]

Chemotherapy-Induced Peripheral Neuropathy

Chemotherapy-induced peripheral neuropathy (CIPN) is a toxic side effect from systemic treatment of malignancy. It is induced by specific types of treatments, including chemotherapy, targeted agents, and immunotherapy medications that are commonly used in breast and gynecologic cancers (**Table 3**). For women, CIPN was reported in up to 47% of individuals even after 6 years from completion of treatment.[39] It presents

in a stocking and glove distribution with involvement of longer axons and is typically characterized as a sensory axonal peripheral neuropathy.[40] Symptoms include burning, cold sensitivity, impaired motor function of the hands or feet, numbness, pain, and tingling. Onset can occur anytime during or after chemotherapy treatment.[38]

Functional impairments are common in CIPN. Patients report difficulty with cooking, dressing, typing, and writing, which in turn may affect home and work roles. Occupational therapy (OT) is a valuable resource to address these needs, specifically with upper extremity symptoms. For the lower extremities, physical therapy (PT) can be valuable as survivors may have fall risk due to changes in balance and gait. Slower gait and increased disability can lead to 1.8 times increase in falls.[38] Both PT and OT can apply manual therapy techniques, such as soft tissue massage, to decrease pain and increase blood flow in affected areas. Supervised exercise programs may also be valuable to address motor weakness and range of motion deficits. For women receiving taxane-based treatments, exercise before and during treatment decreased symptoms of CIPN and improved health-related QOL.[41] Both compression and kinesiotape are useful to help with sensory symptoms. Burning, pain, and tingling may improve with proper application of modalities, including ultrasound and transcutaneous electrical nerve stimulation. Considerations for durable medical equipment, such as canes and walkers, and orthotics, including ankle foot orthoses, may be helpful for individuals experiencing motor symptoms and gait instability. Early intervention with therapy can help address and prevent functional decline. However, medical management may also help to alleviate symptoms.

Clinicians can treat neuropathic pain with adjuvant medications and adjust doses based on symptom severity and potential side effects.[42] Although topical agents such as capsaicin and menthol have shown some benefit, challenges may arise if large areas of the body require application. Gabapentinoids, such as gabapentin or pregabalin, are commonly utilized as first-line treatments. However, the selective serotonin and norepinephrine reuptake inhibitor duloxetine is one of the only pharmaceutical agents with evidence supporting clinical benefit.[43] It can also be used to help with musculoskeletal pain associated with aromatase inhibitors, commonly associated with the treatment of breast cancer.[44]

Lymphedema

Lymphedema is described as swelling secondary to dysfunction of the lymphatic system. Damage to the lymph nodes and collectors may be due to surgery and radiation for cancer treatment. For patients with breast cancer, the prevalence of lymphedema is 21.4% with increased risk secondary to higher body mass index and axillary lymph node dissection.[45,46] Lymphedema is also common within gynecologic and colorectal

Table 3
Common causes of chemotherapy-induced peripheral neuropathy[38]

Chemotherapy	Targeted therapy
Platinum-based Compounds	Bortezomib
• Carboplatin	Immunotherapy
• Cisplatin	Thalidomide
Taxanes	
• Taxol	
• Taxotere	
Vinca Alkaloids	
• Vinblastine	
Vincristine	

malignancies. Female survivors of ovarian, endometrial, and colorectal cancers, who met criteria for lymphedema, demonstrated point prevalences of 37%, 33%, and 31%, respectively.[47] Symptoms include achiness, heaviness, numbness and tingling, and swelling in the affected area causing difficulty with ADLs and mobility. Breast cancer-related lymphedema (BCRL) has become a significant financial burden on the health care system, and with 5 year survival rates of 90%, it can significantly impact QOL long term.[48]

The cornerstones for management of early-stage lymphedema include comprehensive multidisciplinary assessment at the time of initial diagnosis, early referral to therapy after surgery, and patient education regarding weight loss, skin changes, and nail care.[47] Treatment options can be broken down into nonsurgical and surgical options (**Table 4**).[49] Evaluation by a certified lymphedema therapist (CLT) can be helpful in creating the lymphedema plan of care. CLTs are either PT, OT, or SLP that assess skin condition, measure volume of swollen areas, and predict impact on function. Complete decongestive therapy remains the standard of care in BCRL and consists of manual lymphatic drainage (MLD), compression prescription, exercise, and skin care education to reduce the risk of cellulitis and progression of swelling. The application of MLD results in a sequenced and manual method to move fluid from an impaired area to a competent area in the body for improved lymphatic fluid distribution. Then compression with bandaging to reduce swelling in phase I followed by compression garments to maintain reduction in phase II result in sustainable volume reduction. Exercise is encouraged to facilitate muscle pumping action for further fluid decompression. The risk of cellulitis with skin breakdown can be addressed with further skin care education (**Fig. 3**). Additional treatment options may include intermittent pneumatic compression, nonpneumatic active compression devices, and low-level laser therapy.[50] For appropriate patients, lymphedema surgery may be considered, including vascularized lymph node transfer or lymphaticovenous anastomoses.[51]

Pelvic Floor Dysfunction

Pelvic floor dysfunction (PFD) refers to a wide range of disorders that affect the function of the pelvic floor musculature, leading to challenges with defecation, pelvic pain, pelvic organ prolapse, sexual dysfunction, and voiding.[52] It can occur in women with bladder, colorectal, and gynecologic malignancies, including cervical, endometrial, ovarian, uterine, vaginal, and vulval, and is typically due to radiation or surgery. Prevalence can vary widely between diagnoses and their treatments, but approximately 50% of colorectal cancer survivors experience anorectal, bowel, sexual, and urinary dysfunction after intervention.[53] With resection of rectal cancer, 37% to 90% experience low anterior resection syndrome and significant bowel dysfunction.[54] Other common symptoms in gynecologic cancers include dyspareunia, urinary incontinence, and fecal incontinence at rates of 7% to 58%, 4% to 76%, and 2% to 37%, respectively.[55]

Table 4
Nonsurgical and surgical options for treatment of lymphedema[48]

Nonsurgical Treatments	Surgical Treatments
Complete decongestive therapy	Reductive techniques
• Manual lymph drainage	• Direct excision
• Compression therapy	• Liposuction
• Exercise	Physiologic techniques
• Skin care	• Lymphatico-lymphatic bypass
• Compression garments	• Lymphatico-venous bypass
Advanced pneumatic compression therapy	• Lymph node transfer

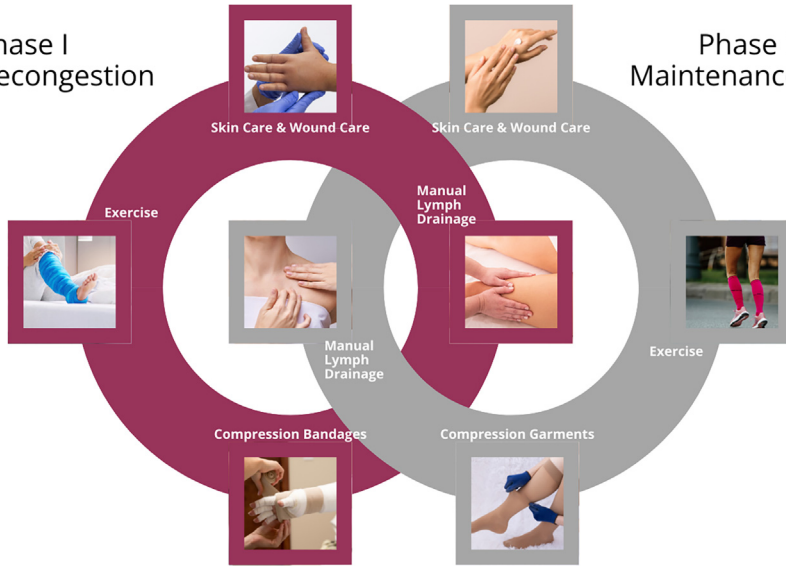

Fig. 3. Complex decongestive therapy.[68]

For women, PFD can negatively impact emotional, physical, psychological, and social well-being as well as QOL.[56] Pelvic floor rehabilitation is performed by PT and OT with specialized training. Interventions include biofeedback, dilator education and progression, joint mobilization, myofascial release, neuromuscular electrical stimulation, and trigger point massage.[57] Pelvic floor muscle training, which includes repetitive voluntary contraction of pelvic floor muscles, has been shown to have positive effects for many PFDs.[58] Bowel medications, including fiber supplements, stimulants, and osmotic laxatives, may be effective to treat constipation associated with PFD.[59]

Psychological Stress and Sexual Dysfunction

Women are at risk for psychological effects from cancer and its treatment. Conditions such as anxiety, depression, and impaired body image are common in breast cancer survivors and can present several years after initial diagnosis.[60,61] Prolonged and significant cancer-related impairments are associated with anxiety and depression in breast cancer as well. After treatment, concerns about breast symmetry or changes in skin texture and sensitivity could lead to impaired self-image. Early identification can lead to appropriate referrals to improve QOL and survival.[62] Cognitive-behavioral and psycho-educational therapies help to improve anxiety and depression, leading to better adjustment in terms of the survivor's diagnosis, mood, and QOL.[63] Addressing physical function through exercise is important as well, as psychological symptoms are predictive of impaired performance status.[64] Body perception exercises and relaxation techniques found in mindfulness-based cognitive therapy reduce stress levels.[62] Yoga has a role to improve anxiety, depression, and fatigue regardless of stage of diagnosis.[65] Selective-serotonin reuptake inhibitors and anxiolytics are also important in management.[66]

Sexual dysfunction is another common impairment and can occur in 30% to 80% of women with cancer.[60] Symptoms associated with sexual dysfunction include dyspareunia as well as decreased ability to orgasm, arousal, desire, and lubrication. Malignancies most often associated with these challenges are breast, cervical and

endometrial. In addition, treatments such as chemotherapy, hormonal therapies, radiation, and surgery may exacerbate the condition. Treatment requires a multidisciplinary approach, especially with emphasis on PFD therapy to address health education and persistent symptom management. Social support groups also help to validate experiences and decrease associated stress.[60] Consideration can be made for over-the-counter moisturizers and lubricants, or prescription of estrogen versus selected estrogen receptor modulators based on the clinical diagnosis.[67]

SUMMARY

The impact of cancer on women is significant. With almost half of all new cases per year in the United States attributed to women, and continually increasing survival rates due to earlier diagnosis, improved treatments, and behavior modification, QOL and functional status are becoming priorities in the oncological care continuum. Rehabilitation intervention and medical management allow for application of rehabilitation principles to a variety of malignancies common in women. By addressing cognitive, physical, and psychological challenges associated with cancer and its treatment, women have the opportunity for better functional and performance status, which translates into better QOL.

CLINICS CARE POINTS

- Cancer rehabilitation treats physical, psychological, and cognitive impairments to maximize independence and QOL.
- Women with cancer have a wide range of experiences, based on the pathology and prognosis of malignancy and its subsequent impact on physical, emotional, social, and spiritual well-being.
- Conditions such as cancer pain and malnutrition benefit from medical management.
- Sequelae of cancer treatment (such as CRCI, CRF, CIPN, lymphedema, PFD, psychological stress, and sexual dysfunction) respond to rehabilitation interventions, including PT, OT, SLP, and psychology.
- Integration of rehabilitation and survivorship into the oncological plan of care is necessary for optimization of outcomes, including QOL and function.

DISCLOSURES

The authors have nothing to disclose.

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