

Mariam Abuladze

Physical therapy and Rehabilitation for Improvement of Quality of Life of
Breast Cancer Patients Undergoing Chemotherapy

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Relevance and Aims of the study

One of the most critical factors that cancer survivors need to consider when it comes to their rehabilitation is the availability of effective and personalized rehabilitation programs. The most common issues that cancer survivors experience are pain and fatigue, as well as psychosocial issues. They are also more prone to experiencing cardiovascular disease (Institute of Medicine, 2006, Stewart BW. World Cancer Report 2014, Burg MA et al, Adorno G, Lopez EDS, Loerzel V, Stein K, Wallace C, et al. 2015)(1,2). The goal of oncology rehabilitation is to help patients maintain or improve their physical and psychological health. Rehabilitation programs can help them manage their cancer as a chronic condition. Aside from being a vital part of cancer rehabilitation, exercise can also improve the quality of life for cancer survivor and help them maintain a healthy and balanced lifestyle (Lisy K, Langdon et al 2019; Reilly CM, et al 2013)(3,4). In addition exercise can help prevent the disease returning. These are the reasons why guidelines supporting the use of exercise in cancer rehabilitation have been published (Cormie P, et al. 2017, Jones LW et al, 2016)(5, 6). Cancer rehabilitation programs are designed to help people with cancer improve their quality of life. They are based on exercise and various forms of education (Gilchrist SC, Barac A, Ades PA, Alfano CM, Franklin BA, Jones LW, et al. Cardio oncology et al 2019)(7). Exercise-based oncology rehabilitation programs can help people with cancer reduce mortality and improve their quality of life. These programs also help people manage their risk factors and improve their functional capacity. Oncology rehabilitation can be delivered in groups and is commonly used to provide peer support. It can help people with cancer return to a more normal lifestyle (Dittus KL et al, 2015) (8). Compared to cardiac rehabilitation, the effects of cancer treatment and the disease itself may vary depending on the patient's physiological system. This suggests that the multidisciplinary approach to cancer rehabilitation may be more important. Studies have shown that exercise-based oncology programs can improve the quality of life for people with cancer (Shiraz I et al 2014) (9). Two studies concluded that rehabilitation of breast cancer survivors can improve their quality of life and reduce fatigue. However, no study has examined the effects of exercise-based group therapy on the quality of life of individuals with cancer (Myrhaug HT, et al 2020, Scott DA et al, 2013)(10,11).

There are no standardized guidelines for the implementation of exercise-based cancer rehabilitation programs (Canestraro A et al, 2013) (12). Also, the lack of access to these programs is a major issue that needs to be resolved in order to implement them into clinical practice. The healthcare service outcomes of patients with cancer can vary depending on their conditions and the type of rehabilitation program they choose. For instance, the length of stay in a hospital may be different from that of other patients. Although there are promising results from retrospective studies and pre-to- post investigations on the feasibility of exercise- based cancer rehabilitation, there is limited evidence on its effects on various outcomes, such as patient mortality and readmissions. Most people with cancer will experience cognitive and physical issues as a result of their treatment. These effects can lead to reduced quality of life and decrease their survival rate. These functional issues can also affect their participation in various vocational and social roles. The negative effects of cancer treatment on various body systems are known to be present in different types of cancers. These effects can affect the functioning of individuals' multiple body systems and increase their lifespan. Although there is growing evidence that rehabilitation can improve the quality of life for people with cancer, it is not widely used. This is because it is not yet integrated into the oncology care system (Mewes JC, et al, 2012, Gordon LG, et al, 2005, Khan KA, et al, 2019) (13,14,15).

The lack of adequate care for cancer survivors is a growing concern globally. Due to the increasing number of people diagnosed with cancer, the need for comprehensive cancer care is expected to increase. This issue should be addressed in order to reduce the morbidity burden (Smith SR, et al, 2020, Padgett LS, et al, 2020, Salerno EA, et al, 2019, Sommer MS, et al, 2018) (16,17,18,19).The WHO launched the Rehabilitation 2030 initiative in 2017 to provide high-quality rehabilitation services to individuals with non-communicable diseases. It aims to create a package of interventions that will help strengthen health systems and improve the accessibility of rehabilitation services. The WHO identified oncology as a priority area due to the various effects of cancer, such as its persistent and

late effects. (Gimigliano F, et al, 2017, World Health Organization, 2019, Krug E, 2019) (20,21,22).

High-quality cancer care is a tenant of guideline-concordant care, which is the process of providing standardized interventions for a specific disease or condition based on the best evidence. These guidelines can improve the quality of care and safety. The National Academy of Science has developed a set of best practices for the development of medical and scientific guidelines. These guidelines include a robust review of the evidence, an expert consensus, and the endorsement of a professional organization or society. The goal of these guidelines is to improve the quality of the development process and ensure that the recommendations are based on the best evidence. Although there is a wide variety of clinical pathways and guidelines for cancer treatment, they may not be followed properly in certain areas. Although rehabilitation is often included in cancer guidelines, the exact role of this modality in the treatment of the disease has not been established. This uncertainty can contribute to the uncertainty regarding the availability of rehabilitation services for patients. A comprehensive review of the guidelines on oncology rehabilitation is needed to improve the quality of these services for those with cancer (Committee on Improving the Quality of Cancer Care: 2013, 1 Institute of Medicine (US) Committee on Standards for Developing Trustworthy Clinical Practice Guidelines 2011, Zebrack B, et al 2017) (23,24,25).

Breast cancer is the most common type of cancer that affects women over 35 years old. It is treated through various forms of therapy, such as surgery, radiation therapy, and systemic treatments. The most common adverse effects after cancer treatment are pain, fatigue, and upper limb impairment. These are often caused by the post-chemotherapy and radiotherapy treatment. As the number of breast cancer survivors continues to increase, rehabilitation goals are to improve the quality of life and prevent or minimize the effects of these treatments.

Breast cancer patients undergo various medical procedures such as chemotherapy, surgery, and hormone therapy. They are also faced with side effects, such as fatigue. In addition, patients are prone to

experiencing decreased physical activity during and after treatment (Schmitz KH, et al, 2010) (26). For patients undergoing chemotherapy, physical activity can also be used as an effective adjuvant for breast cancer treatment. It can help decrease the symptoms of the disease and improve the quality of life for those who are suffering from it. (Friedenreich CM: The role of exercise in cancer progression and mortality: observational and molecular epidemiologic evidence, 2017, Cancer Res 2016, Buffart LM, et al, 2014) (27,28,29). After breast cancer treatment, regular physical activity can help improve the quality of life for patients. It can also help prevent various health conditions such as diabetes and heart disease. Long-term effects of physical activity are also known to be associated with the treatment of breast cancer. (Adraskela K, et al,2017, Volaklis KA, at al, 2013, Runowicz CD, et al, 2016) (30,31,32).

One of the most important factors that a rehabilitation program must consider is the individual's fitness level. It is important that cancer survivors are fit and ready to live their lives. Aside from being physically active, a healthy lifestyle is also important to prevent the disease from recurring (Lucas AR, et al, 2017) (33). The design of an intervention should be focused on the improvement or restoration of quality of life, which is affected by various factors such as cancer and treatment. There are also many studies that do not provide clear information regarding the exercise programs that are available for women with breast cancer (Neil-Sztramko SE, et al, 2017) (34). There is a lack of consensus on the rehabilitation of women with breast cancer following surgery. There are also no specific guidelines for the rehabilitation of patients undergoing various treatments, like chemotherapy. Literature about importance of physical rehabilitation techniques during chemotherapy is scarce (Cheville AL, et al, 2009, Pergolotti M, et al, 2015, Pace A, et al, 2016, Worku T, et al, 2017) (35,36,37,38). Aim of our study was to see the effect of physical therapy and rehabilitation of breast cancer patients during chemotherapy. Primary endpoint was to compare quality of life between control and intervention group.

Literature review

Cancer is a major cause of mortality worldwide, WHO estimates suggest nearly one in six deaths were caused by cancer accounting for approximately 10 million deaths in 2020 (World Health Organization, 2018) (39) accounting for 21% of all fatalities in both men and women. It was, however, the prominent cause of death among women aged 40 to 79 and men aged 60 to 79, As of 2019, the overall decline in cancer mortality rate was 32%. (Siegel, et al, 2019) (40).

However, as the overall treatment of cancer improves, a new challenge arises which comes in the shape of cancer rehabilitation which runs alongside or after the treatment of cancer (Chasen, et al, 2008) (41). Thus, cancer rehabilitation must be considered a multidisciplinary field, with doctors, therapists, and social workers, along with several others being involved depending on the needs of the patient. Cancer can inflict physical or psychological impairments that may impede a person's capacity to operate as a contributing member of society. Functional impairments typically involve cognitive function loss, speech and motor control deficits, and, across several cases, sensory loss. Tumors in various organs can impact a patient's functionality in diverse ways, spinal cord tumors, for instance, might cause complications like sensory or motor loss, incontinence, or other neurological dysfunctions. The lymphatic drainage or range of motion of the axilla may become compromised by other cancers, such as breast cancer. Rehabilitation problems are defined as distinct problems that may impact either one or multiple organ system. These specific problems that may be limited to an organ system or affect several are referred to as Rehabilitation problems. These Rehabilitation problems usually relate to ambulation, mobility, or any aspect that may affect a person's physical ability to function independently. Cancer patients, on the other hand, must cope with both the physical and psychological components of their illness, which can have an impact on their functional capacity. 80% of patients who had cancer for more than a year had difficulty ambulating (Ganz PA, et al 1990) (42). Almost all

cancers generated activity restrictions and vocational challenges (Moinpour C. 1994) (43).Cancers that affect the activity of daily life (ADL) however usually cause their effect through the physical symptoms of cancer such as breast cancer, cancer of the respiratory system, and nervous system tumors causing shortness of breath or paralysis and paresis. Cancers of the head and neck may lead to communication and speech problems. Cancers that impact activity of daily living (ADL) frequently do so through physical symptoms, such as breast cancer, cancer of the respiratory system, and nerve system tumors that induce shortness of breath, paralysis, and paresis respectively. Head and neck cancers can impair communication and speech. Recreational activities are usually restricted, and vocational problems arise due to the activity limitation.

As previously stated, cancer patients may experience psychological issues throughout their treatment or thereafter, with psychological issues being reported in practically all cancer sites. Psychological issues in cancer patients have long been recognized, with as many as 78% of nervous system cancer patients reporting psychological issues or anxiety as early as 1978 (“WHOQOL: Measuring Quality of Life.” 2014) (44). Thus, adequate psychological support must be provided to cancer patients throughout their treatment and after to reduce any distress that may be caused.Due to its elusive roots in many aspects of human life such as medical, cultural, and vocational ones, the cancer rehabilitation effort may be met with wildly varying results throughout the rehabilitation process. Thus, the cancer rehabilitation effort must account for advances in the cancer, pain management, fatigue and other physical issues as well as physiological issues such as the compromised immunity of many cancer patients. The varying requirements of cancer rehabilitation thus brought about the division of rehabilitation goals into restorative, supportive, palliative, and preventive. Restorative aims to return the patient into his pre-morbid state or at least as close to that as possible by reducing the functional impairment to a minimum. Supportive aims to help the patient cope with what has been permanently lost of his physical

and functional ability and to adapt to maximize the patient's leftover functionality. Palliative, as the name suggests, deals with terminally ill patients which direct it towards patient comfort and minimizing end-of-life complications. Preventive aims to minimize the probability of adverse events in cancer patients through education strategies. Restorative care strives to return the patient to their pre-morbid state, or as close to it as possible, by minimizing functional impairment. The goal of supportive care is to aid the patient to cope with what has been permanently lost of their physical and functional capacity, as well as to adapt in order to optimize the patient's residual functioning. Through education strategies, preventive care aims to reduce the likelihood of adverse outcomes in cancer patients. Thus, cancer rehabilitation has become a vastly multidisciplinary effort due to the variety of efforts and variety of possibilities in terms of disease progression. This has led to the effort in cancer rehabilitation being distributed among various settings and facilities ranging from outpatient care facilities to patients' accommodations in their own homes.

Cancer QOL in different regions:

Due to the widespread prevalence of cancer, the focus on HR-QOL for cancer has become the focus of many researches and interventions in many countries. The cultural and social differences between different regions may lead to different approaches to the improvement of HR-QOL. For example, researchers found that in the western regions of Saudi Arabia women were less likely to be affected by their appearance throughout rehabilitation for breast cancer (Imran, M. et al, 2019) (45). Cancer QOL can also vary in its different results across different regions with the prevalence of different symptoms and side effects varying between nations (Hashemi, S.-M., et al 2019) (46). For example, a recent meta-analysis found that in breast cancer patients in Germany, insomnia was one of the least faced symptoms during breast cancer rehabilitation, while in Japan and Spain it was nausea and vomiting (Sun Y, et al, 2013) (47). Cancer QOL may also vary due to the financial aspect of treatment

and rehabilitation as was demonstrated by researchers in the Malwa region of Punjab. The researchers found that while a judicious diagnosis and appropriately timed chemotherapy greatly improved QOL, the financial burden of the situation the patients are in is often debilitating and distressing (Singh, H., et al, 2014) (48). As a result, Cancer QOL can vary wildly due to social, regional and even unknown factors. However, the ongoing debate of customizing QOL interventions has not been settled yet in different countries and it is yet to be determined if the customization would be advantageous.

Quality of life and cancer rehabilitation:

The WHO defines quality of life as “A state of complete physical, mental, and social well-being not merely the absence of disease.” The concept of quality of life no longer encompasses only the physical health of patients, it includes mental and psychosocial problems as well. Thus, aspects such as the emotional and social conditions of the patient have become pivotal and central to the modern method of rehabilitation. While health related QOL (HR-QOL) is usually interchanged with the general term of QOL, HR-QOL is more appropriate for use in the rehabilitation setting as it encompasses the positive and negative aspects of physical, emotional, social and cognitive function within the relative process of rehabilitation (Osoba D. et al, 1994) (49). Cancer related QOL may be of special interest due to the huge strides taken forward in cancer treatment with survival rates increasing indubitably as mentioned earlier. Thus, it has become one of the main objectives of cancer research and treatment to strive forward toward the improvement of QOL. Since cancer is also a broad term, different cancers may affect the HR-QOL in varying ways. Thus, the need for monitoring QOL in cancer patients throughout rehabilitation has risen. As a result, improving quality of life has become one of the primary goals of cancer research and therapy. Considering cancer is such a broad term, different cancers may have varying impacts on HR-QOL. Consequently, there is a greater demand for monitoring QOL in cancer patients during their rehabilitation. Rehabilitation can hence be

monitored and improved upon with the use of QOL questionnaires through the identification of the specific deficits or issues that a single patient might face throughout their rehabilitation. Rehabilitation may thus be evaluated and improved using QOL surveys by identifying specific deficits or challenges that a single patient might have had throughout their rehabilitation.

Research as early as the 60s began the use of questionnaires to monitor patient progress throughout their rehabilitation (Osoba D. et al, 1994) (50). These early questionnaires however focused on the disease progression through its clinical appearance and evaluation of the tumor size and progression, which omitted other aspects of the rehabilitation process mainly through the lack of patient input and feedback throughout the process. In order to track patients' progress during their rehabilitation, researchers first used questionnaires in the 1960s (Izsak FC, et al, 1971;) (51). These early questionnaires, however, were primarily concerned with evaluating the disease's progression through its clinical manifestations including the tumor's size and growth, leaving out other parts of the rehabilitation process, predominately due to the absence of patient participation and feedback throughout the process. However, QOL questionnaires have since improved and now have a more holistic focus on the various aspects of QOL. As a result, QOL assessment has become essential for research and rehabilitation and has become crucial towards the shaping of rehabilitation strategies and policy decisions (Grant M, et al, 1990) (52).

QOL does not have a fixed standard for patients who share the same group, cancer, or background; QOL can vary depending from patient to patient, regardless of how similar their cancer or underlying condition is. For example, a patient's physical activity patterns may impact their QOL in a variety of ways. Physical exercise has been demonstrated to improve physical function, immunological function, fatigue reduction, and overall body shape improvement in cancer patients throughout their rehabilitation (Galvão, et al, 2005, Kirshbaum, et al, 2007, Knols, Ruud, et al. 2005) (53,54,55). Dependence on others for ADL may also be

psychologically debilitating, thus the positive effect of exercise on functional independence may also serve to eliminate some of the negative psychological effects of cancer during rehabilitation (MacVicar MG, et al, 1986) (56). Exercise may also improve body image which may be psychologically debilitating during rehabilitation. Cancer patients may also opt to group psychotherapy to reduce the psychosocial stress that may occur during rehabilitation. This relies on the concept of normalizing the situation that many patients may be in as well as encourage patients to support one another throughout the treatment hence improving the overall QOL (Courneya KS, et al, 1997)(57).

The goal is to minimize the side effects of cancer treatment, especially those that do not go away after the therapy has concluded. Breast cancer patients are prone to experiencing fatigue and depression, and these conditions can affect their quality of life immediately following treatment. In an overview of the literature on exercise for cancer survivors, Mustian and colleagues noted that there is a growing body of evidence suggesting that exercise can improve the quality of life for those who have survived the disease (Karen M. Mustian, et al, 2009) (58). They found that a survey of over 500 breast cancer survivors revealed that physical activity and performance were associated with a positive correlation with the quality of life (Penttinen HM, et al, 2011) (59). The researchers conducted a review of the 21 randomized trials that examined the effects of exercise on the quality of life of cancer survivors (Duncan M, et al, 2017) (60). They found that regular exercise programs, such as yoga and resistance training, can improve the quality of life for these individuals. In a study with 55 breast cancer survivors, the researchers found that organized exercise programs could improve the quality of their lives (Mirandola D, et al, 2014) (61).

Challenges in Cancer Rehabilitation

Fatigue - Inactivity/Disuse Syndrome:

Cancer patients are susceptible to a general decline in activity as a result of repeated medical interventions or, in some cases, hospitalization. Inactivity/Disuse syndrome refers to the de-conditioning and diminished

functional capability of bodily systems that may occur independently of the underlying condition (Fialka-Moser, V et al, 2003) (62). The most basic manifestation of this condition is in the musculoskeletal system, where muscles that are not utilized often atrophy and joints that are retained in the same position might result in contractures of the patient's ligaments and tendons, lowering the QOL of the cancer patient. Asthenia fatigue syndrome, more commonly known as asthenia, is one of the most commonly reported symptoms in advanced cancer patients (Bruera A. et al, Oncology 1992) (63). Asthenia can be defined as reduced vitality, energy or vigor which is noticeable when performing activities of ADL or low effort activities. Asthenia may be caused by many chronic conditions such as cancer or its treatment, chronic infection and many other metabolic abnormalities. Furthermore, treatment of asthenia is similar to treatment of chronic nausea in that the underlying condition must be addressed (Hinshaw, D. B, et al, 2002) (64). Non-pharmacologic methods such as physiotherapy and occupational therapy may also prove useful in the treatment of asthenia regardless of the finding of the cause.

One of the most pressing issues encountered during cancer rehabilitation is fatigue. As a matter of fact, it is so widespread that cancer-related fatigue is labeled as cancer related fatigue (CRF). CRF can be defined as a "persistent, subjective sense of tiredness related to cancer and cancer treatment that interferes with usual functioning" (Mock V, et al, 2000) (65). In fact, CRF is so common that it was shown that 95% of cancer patients scheduled to receive chemotherapy or radiotherapy will experience some level of fatigue (Hofman, Maarten, et al. 2007) (66). CRF can vary in severity and may affect QOL in various ways. CRF may for example result in mild discomfort or may present as severe enough to limit ADL of patients. The inherent problem with CRF is that the desire to rest and relax in patients is higher, however this may prove more detrimental and may result in inactivity/disuse syndrome. Therefore, resting in an attempt to counteract CRF may actually serve to prolong and perpetuate the fatigue due to the catabolism of muscles. As a result, patients who present with CRF are advised to physically exercise regularly and maintain a healthy lifestyle to reduce their symptoms. Many studies have shown that the most effective way to counteract CRF is

regular exercise despite the fact the fatigue is perpetuated by ADL. The reasoning is that the exercise helps produce adaptive changes resulting in better physiological performance of the body. These changes may be gains in muscle mass and plasma volume, improved lung ventilation and perfusion, increased cardiac reserve, and a higher concentration of oxidative muscle enzymes. The rationale is that exercise promotes adaptive changes that result in improved physiological performance of the body. Gains in muscle mass and plasma volume, enhanced lung ventilation and perfusion, increased cardiac reserve, and a higher concentration of oxidative muscle enzymes may be among these improvements (Dimeo, et al, 2001) (67). Thus, exercise may prevent CRF by normalizing regular day to day activity and increasing the body's ability to adapt to the CRF. The effect of regular exercise on CRF was first seen as early as 1983 by Winningham (Winningham ML, et al, 1983) (68). Winningham coaxed cancer patients onto a 10-week bicycle ergometer training program of 30 minutes, 3 times per week. This resulted in a substantial increase in physical activity and decrease in fatigue in patients on chemotherapy. Winningham also went on to prove in later researches that an exercise program would reduce mood disturbance, somatic complaints (MacVicar MG, et al, 1989) (69), total body weight, and body fat percentage (Winningham ML, et a, 1989) (70), and increased the maximal physical performance of women with breast cancer undergoing chemotherapy.

In a study, Mustian and colleagues noted that exercise can help reduce the fatigue that occurs during and following cancer treatment. They found that psycho-oncology and exercise therapy are more effective than usual pharmaceutical interventions (Mustian KM, et al, 2017) (71). Review of 14 randomized controlled trials revealed that breast cancer patients can improve their physical activity levels through supervised and personalized exercise programs. The researchers also noted that the intensity and training approaches used in these programs can vary depending on their level of fatigue (Zimmer P, Baumann FT, Oberste M, et al: 2017, Meneses-Echavez JF, et al, 2014) (72,73). The recommendations for exercise include a combination of resistance and aerobic exercise. A review of 25 randomized clinical trials revealed that

breast cancer patients who participated in regular exercise had lower fatigue levels (McNeely ML, et al, 2010, Juvet LK, et al, 2017) (74,75).

Cancer and sexuality:

An important factor of cancer rehabilitation that is commonly overlooked is the sexual aspect of it. This might be due to the stigma associated with openly discussing one's sexual life or the practitioner's inability to discuss with the patient a potentially distressing aspect of the patient's life. However, the sexual aspect of rehabilitation is vital within the framework of QOL as the inability to sexually perform whether it's for physical or psychological reasons can be distressing for cancer patients. It has been discovered that a significant portion of women struggles with sexual interaction due to breast cancer. In fact, it has been reported that about 50% of female breast cancer patients may struggle with global and profound sexual dysfunction (Ganz PA, et al, 1998, Schover LR, et al, 1997) (76,77). It has been shown that breast cancer patients often avoid sexual intercourse due to negative emotional effects. However, it has also been shown that early resuming of sexual activity has a positive effect on the sexual function of patients (Schover LR. 1994) (78).

Female cancer patients specifically can have their sexual lives affected more directly, nonetheless. The more direct effect is seen in patients with ovarian and cervical cancer. Patients with advanced ovarian cancer often undergo pelvic exenteration surgery after which many do not attempt to reestablish a sexual life. Cervical cancer patients may also present with fibrosis, pain on penetration due to vaginal stenosis and decreased lubrication. In fact, female cancer patients may avoid sexual activity completely following pelvic surgery or radiotherapy (Lotze W 1990, DePompolo RW, 1994) (79,80). This may be due to the anatomical deformity of the site of cancer or due to the psychologically debilitating effect of cancer itself. However, vaginal dilators can prevent stenosis, artificial lubrication, and the discussion about changes from customary sexual positions might help with the readjustment of the sexual life

during rehabilitation (Urbanek V, et al, 1996, Smith DB,et al, 1992) (81,82).

Testicular cancer patients on the other hand are at risk of infertility and hormonal changes if treated with radiotherapy or following an orchiectomy. This leads to the need for a pretreatment discussion of the reproductive concerns and may develop the need for sexual counseling before the treatment and throughout the rehabilitation. Sperm banking may become a necessary precaution for the treatment of pelvic cancers in men. In addition, radiation in the pelvic region may also lead to fatigue, diarrhea,urine and fecal incontinence and dermatologicalsymptoms. All of the changes associated with treatment of testicular cancers may also lead to loss of libido and sexual dysfunction.

Sexual problems arise with prostate cancer patients as well. Prostate cancer is the most common cancer in men with the condition accounting for about 25% of all cancers in men (Jemal A, et al, 2009) (83). The treatment for prostate cancer often leads to some sort of debilitating effect with common treatments being radical prostatectomy, radiation and androgen therapy. The most commonly reported aftereffect of treatment of prostate cancer is urinary incontinence due to the perineal nerve followed shortly after by erectile dysfunction and difficulty with ejaculation. This led to the development of tools such as topical intraurethraltherapies, oral medication, vacuum-assisted devices, intracavernosal injection therapy, and penile prosthesis (Duncan GG, et al, 2000, Kihara K, et al, 1998, Krongrad A, et al, 1998, Litwin MS, et al,1999, Litwin MS, et al, 1998, Moore KN, et al, 1999) (84,85,86,87,88,89)

The treatment and diagnosis of breast cancer in young women are very different from that of older women due to their unique psychosocial and medical context. In younger women, the disease is more advanced than in older women. Early detection is also more challenging because the younger population is not routinely screened.Compared to older women,

younger women are more likely to have breast cancer that is estrogen-receptor-negative. They also have a poor 5-year prognosis. Breast conserving surgery is often associated with a higher likelihood of local recurrence in young women. On the other hand, compared to older women, those who have undergone a mastectomy have a similar rate of recurrence. Young women are also more likely to have high productivity and are in a development phase when they start families, careers, and settle down (Axelrod D, et al, 2008, Shannon C, et al, 2003, Baucom DH, 2005) (90,91,92). During this time, sexual intimacy is an important aspect in life. Being diagnosed with breast cancer can be very challenging for young women. They also have to deal with other demanding roles such as being a mother, an employer, and a partner. It is important to note that women under 50 are often married, have children at home, and are in committed relationships. Compared to older women, those without children are more likely to be single. This unique situation highlights the vulnerability of younger women. Young breast cancer survivors, known as YBCSs, typically have lower emotional well-being and quality of life. They also experience more disruptions in their body image, higher depressive symptoms, communication issues, premature menopause, and fertility concerns (Fobair P, et al, 2006, Basson R. et al, 2005) (93,94). Studies have shown that breast cancer treatment and the diagnosis of the disease can have detrimental effects on a woman's sexual functioning. In a study conducted by Fobair (Fobair P, et al, 2009) (95), about half of the women experienced moderate or severe sexual issues in the first few months after their diagnosis. These findings suggest that the impact of the disease on a woman's sexual health is significant. The sexual sphere is very important to the development of young women.

The effects of breast reconstruction or a mastectomy can trigger negative feelings about one's body image. It can be especially hard for younger women due to their high expectations of body image. Although the types of surgery that are performed on the breast are not directly related to sexual functioning, they can still affect one's body image (Bakewell RT, et al, 2005, Alder J, et al, 2008) (96,97). Although breast reconstruction has

been associated with fewer sexual problems, there were no differences in the quality of life for both men and women. The reduction in breast sensitivity could lead to changes in foreplay, and the more that one has breast caressing, the more disruptions in sexual life can occur (Ganz PA, et al, 1999, Avis NE, 2004) (98,99). One of the most crucial factors that can affect a woman's menopausal status is the use of chemotherapy. According to a study conducted by Ochsenkuhn, the effects of chemotherapy on sexual desire were not as significant as those of other treatments (Gilbert E, et al, 2010;) (100). The use of chemotherapy can induce an abrupt menopause, which can be very stressful for young women. Aside from experiencing hot flashes and night sweats, they can also experience other symptoms such as sleep disturbance and joint pain¹⁰¹. Many YBCSs experience menopausal symptoms. This condition is unexpected and can occur at any stage in a woman's life. Chemotherapy during a reproductive age can also cause damage to the hair follicles, which can lead to irregular menses, temporary amenorrhea, or irreversible amenorrhea. The effects of this treatment on fertility are dependent on the age of the women. The chances of a woman entering menopause significantly increase with age. For younger women, the use of chemotherapy can cause them to tolerate higher doses of the medication than older ones. For instance, those under 40 can develop amenorrhea in around 4 to 8 months compared to those over 40 who can experience it in 2 to 4 months. In addition, in vitro fertilization can only fulfill one's biological needs by satisfying psychological and interpersonal desires (Knobf MT, 2006) (102). Table 1 summarizes the complexity of factors related to sexual functioning in Breast Cancer Patients.

Table 1 - Complexity of factors related to sexual functioning in Breast Cancer Patients.

Complexity of factors related to sexual functioning in Breast Cancer Patients
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Physical therapy and Rehabilitation for Improvement of Quality of Life of Breast Cancer Patients Undergoing Chemotherapy

Medical and Biological	Psychological/Intrapersonal	Interpersonal/relationship	Sociocultural
Breast cancer treatment modality (surgery radiation therapy, hormonal therapy, chemotherapy) and its side effects	Prior sexual experiences	The quality of relationship with the partner	Social norms
menopausal status	Emotional well-being (depression, anxiety)	Social support from partner	cultural values
antidepressants	Negative expectations regarding sexual interactions	Attractiveness of women breast cancer treatment for her partner and vice versa	stereotypes
Drugs	body image	Communication	Discriminations
Age	self-esteem	Prior sexual life with the partner	Religious beliefs
Fatigue	Sense of femininity	The importance of sex for quality of relationship	

	Level of stability of identity; role of breast as an element of female identity	The importance of breast as a part of a foreplay	
		Partners` sexual problems	

Radiotherapy's effects on the breast are usually limited to pain and inflammation. In some cases, it can cause chronic fibrosis, which can affect the position of the body during intercourse. The study conducted by Dow and Lafferty (Dow KH, et al, 2000) (103) revealed that the sexual adjustment experienced during the first week of RTH was related to the development of a pattern of side effects. These side effects included fatigue, skin reactions, and severe headaches. Six months after the start of the treatment, the researchers found that the most common side effects were still present. The sexual adjustment period decreases with the end of treatment. This is because the effects of RTH peak at the end of its treatment. It then improves to near normal levels six months later. There are mixed results when it comes to the effects of endocrine therapy on sexual function. Some studies suggest that it does not affect sexuality, while others claim that it can lead to problems with sex. Hormonal therapy is frequently a cause of abrupt menopause. Tamoxifen (Bakewell RT, et al, 2005, Alder J, et al, 2008, Ganz PA, et al, 1999) (104,105,106) is a weak estrogenic agent, but it can have a stronger effect on the uterine and vaginal epithelium. In premenopausal women, this can lead to abnormal uterine bleeding and vaginal dryness.

Breast cancer patients' sexual activity drops significantly one year after the surgery. A study conducted by Burwell and colleagues revealed that more women experienced problems with their sexual function immediately after their treatment ended¹⁰⁷. Although these problems would diminish over time, they still occur in some women a year after their surgery. The short-term effects of chemotherapy on sexual

functioning are minor, but they can be long-term when the patient experiences a menopausal transition (Burwell SR, et al, 2006) (108). According to a study conducted by Ochsenkuhn (Ochsenkuhn R, et al, 2011) (109), premature menopause results in a significant decline in sexual function among young women. The findings suggest that women who stopped menstruating after undergoing chemotherapy were more prone to experiencing these issues (Wimberly SR, et al, 2005) (110). The effects of sexual dysfunction on a person's sexual satisfaction and activity can last for a long time. Five years after having surgery, the sexual problems and activities of the women in the group were not significantly different. About three-fourths of them were pre-menopausal, and most of them experienced night sweats, hot flashes, and vaginal dryness. It is believed that these problems started as a result of menopause. After CHT, premenopausal women have impaired sexual desire. They experienced decreased breast sensitivity, vaginal dryness, and reduced sexual activity for several years following diagnosis (Ganz PA, et al, 2002) (111). A study conducted on the effects of breast cancer surgery on sexual functioning revealed that the number of sexual activities decreased significantly over the 10-year period and that the prevalence of problems related to cancer was lower than that of the 5-year period. However, the researchers did not find evidence of a significant impairment in the quality of life after the operation. About 68% of the women who had undergone the procedure reported experiencing sexual dysfunctions a few years after the operation, which is higher than the percentage of healthy women (Joly F, et al, 2000) (112). The only way to predict a person's sexual desire is by assessing their relationship quality. Chemotherapy was associated with a higher likelihood of experiencing various sexual dysfunctions, such as pain, orgasm, and lubrication. These results support the model suggested by Basson (Basson R. 2000) (113). Table 2 sums up factors important to women's sexual adjustment.

Table 2 - Factors important to women's sexual adjustment

Factors important to women's sexual adjustment
• The quality of the first sexual experience after surgery (Wimberly SR, et al 2005) (114)
• How frequent partner initiates sexual activity ²⁰ ; if the partner initiates sex women are able to become aroused and enjoy sexual act although some of them do not feel sexual desire and do not initiate sexual contact
• Perceptions of partner positive emotional involvement in the relationship
• The females' perceptions of their male partners' reaction to breast cancer diagnosis
• Communication about sex within relationship
• Prior sexual life
• The quality of couple relationship
• The importance of breasts in the foreplay
• Partner initial reaction on naked BCSs

Pain

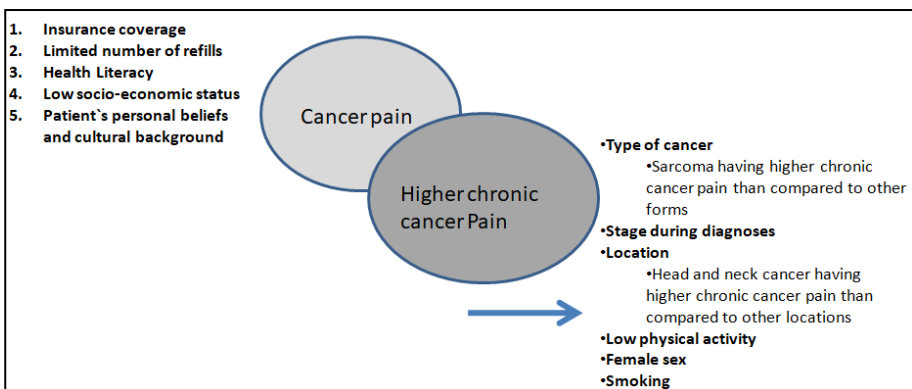
During the course of their treatment, patients with cancer often experience pain, which can make it hard to care for themselves and maintain their daily activities. When the disease is found at later stages, it can cause severe and constant pain, which can affect their quality of life (Prommer, et al, 2015, Pain management for patients with cancer. 2018, R. Sutradhar, et al, 2017) (115,116,117). Even after the treatment of cancer has completed, it is still possible for pain to remain persistent. It is

believed that around 50% of cancer survivors will experience chronic pain for a long time. The pain that patients experience is caused by the cancer itself, as well as the damage that it has caused to the nerve fibers (S.Y. Yoon, et al,2018) (118).Using a scale to determine the severity of pain can help healthcare providers identify the most effective treatment options and create a tolerable level of pain. The WHO has also published guidelines that help healthcare providers manage pain (B.M. Scarborough, et al, 2018, A.A. Anekar, 2022) (119,120).Although cancer survivors and patients with moderate to severe pain may experience some degree of discomfort, they are often managed poorly. Opioids are known to provide adequate analgesic effects for higher pain levels, but they can also cause issues with addiction and adverse effects.Non-opioid therapy is also an alternative for patients who are not able to take the initial treatment of opioids (P. Reis-Pina, et al, 2015) (121). Because of the development of new cancer treatments, patients have a better chance of surviving. Having the proper control over pain can help patients improve their quality of life after their cancer treatment.Although around 50% of cancer patients experience significant distress due to their pain, various barriers such as those affecting the healthcare provider can prevent them from effectively managing their disease (R. Sutradhar, et al, 2017, R. McKee, et al, 2018) (122, 123) Some factors that can limit a patient's ability to take pain medication include their insurance coverage, the number of refills, and their health literacy level. According to health professionals, limitations on pre-authorization and the need for prior authorization can prevent patients from managing their pain (M.F. Ilowite, et al, 2018, C. Rodriguez, et al,2019) (124,125). Compared to families with higher socioeconomic status, those with low socioeconomic backgrounds are more prone to experiencing distress and pain. Their lack of knowledge and access to resources can lead to disability and long-term suffering. Many of these individuals also experience constant or frequent pain, which can affect their daily lives. The severity of the pain that a patient experiences can affect their social isolation, fatigue, and poor sleep (O. Erol, et al, 2018)(126).Different factors can affect a patient's perception of

pain. For instance, a lack of familiarity with a patient's cultural background and spiritual beliefs can put them at risk of being undertreated. Beliefs about being dependent on medication or experiencing suffering can also result in underreporting (E. Gallagher, et al, 2017, G. Can, et al, (2019) (127,128). Miscommunications can affect the treatment of patients. To minimize these issues, health providers should regularly address all of the patient's concerns and questions. Knowing the type of cancer helps in managing the pain associated with the illness. Those who have advanced cancer are more prone to experiencing chronic pain (M.M. Russo, 2019, N.N. Sanford, et al. 2010-2017) (129,130). One of the most common reasons why people with cancer are prone to experiencing chronic pain is due to the damage caused by the tumor. Other factors such as being female and having low physical activity are also known to increase the risk of experiencing this type of pain (J.B. Epstein, et al, 2019) (131).

If a patient is not satisfied with the medication they are currently taking, it is important that they consider switching to another drug (Figure 1). This can help them improve their treatment plan and reduce their side effects (O. Corli, et al,2019) (132).

Figure 1 – Factors effecting cancer pain



The role of non-pharmacological interventions in cancer pain management is increasing. Nurses can play a vital role in managing

chronic pain by implementing non-pharmacologic interventions such as massage, foot reflexology, muscle relaxation, and meditation. A review of the literature has revealed that these can help breast cancer survivors improve their pain levels (Hikmat, R. et al, 2022) (133). Nurses can easily master non-pharmacologic interventions for managing cancer pain. They can also play a vital role in the management of this condition. Given the lack of evidence supporting the use of drugs for this condition, it is important to explore the various non-pharmacologic options available (Brown, R. Pet al, 2013) (134). Additionally, regular breathing exercise can help manage their chronic pain. It can also improve their health and well-being. According to various studies, this type of exercise has a long history of being used in Asian countries. According to a recent research, BE has the potential to relieve pain in different conditions, such as chronic non-cancer pain and labor pain. Other pain conditions that can be treated with this drug include those that are caused by procedures. Despite the positive effects of BE on various conditions, its underlying physiologic mechanism is still not well understood. A review of the studies that examined the effects of BE on cancer survivors revealed that most of them concentrated on the treatment of acute pain. They also found that the drug did not affect the long-term effects of chronic pain. Despite the high prevalence of chronic pain, the majority of the studies that examined the drug's effects on cancer survivors focused on the management of acute pain (Wang, H et al. 2022, Hamood, R. 2018) (135,136). According to the systematic reviews, the quality of the studies that examined the effects of BE varied significantly due to the varying aspects of its treatment protocol. Some of the studies did not provide sufficient information about the development of the intervention and the scientific evidence supporting its design. This could explain the contradictory findings regarding the effects of the drug on cancer survivors. Pain is one of the most commonly faced symptoms in terminal cancer patients. It is estimated that approximately 40-90% of all cancer patients experience pain that may or may not be related to their tumor (Caraceni A, et al, 1999) (137). The pain me be directly associated with

the tumor but it may also be associated with metastatic growth or pain due to the treatment itself (Portenoy RK, et al, 1999) (138). 80-90% of pain in terminally ill cancer patients is well managed following the WHO analgesics ladder for pain relief (Grond S, et al, 1991, Zech DF, et al, 1995, Walker VA, et al, 1988) (139,140,141). Non-pharmacological treatments such as physiotherapy, acupuncture, transcutaneous nerve stimulation (TENS), and psychological techniques may also assist in the pain management of terminally ill cancer patients (Fallon M, et al, 2006) (142). Due to the rising survival rates and prevalence of cancer, many people are now faced with the effects of this disease on their lives. One of the most common problems that cancer survivors and patients experience is pain. A recent meta-study revealed that about 55% of cancer patients experience pain during their treatment, and 40% after their cancer has been cured. In addition to interfering with one's daily activities, pain can also affect a person's quality of life. Unfortunately, cancer pain is often under-treated and underestimated (Torre, L.A, et al, 2012, Ferlay, J. et al, 2018, Van den Beuken-van Everdingen et al, 2016, Pachman, et al, 2012) (143,144,145,146).

Cachexia-Anorexia syndrome

The word cachexia derives from Greek with “kakos” meaning bad and “hexis” meaning condition (Tisdale MJ. 1997) (147). Cachexia can be defined by anorexia, involuntary weight loss, poor performance, and ultimately death (Bruera E. 1997) (148). Approximately half of all cancer patients suffer from cachexia throughout their rehabilitation. Typically, cancers of hematologic origin rarely cause cachexia while solid tumors are the main culprits (Larkin M. 1998, Inui A. 1999) (149,150). Cachexia may be due to reduced food intake due to physical obstruction of the gastrointestinal tract, pain, depression, constipation, malabsorption, debility or the side effects of treatment such as opiates, radiotherapy, or chemotherapy (Inui, A, 2002) (151). Cachexia may also be due to dysregulated leptin production, hypermetabolism of the tumor, disrupted carbohydrate and lipid metabolism, altered protein metabolism or

gastrointestinal dysfunction (Flier JS. 1998, Schwartz MW, et al, 1995, Schwartz MW, et al, 1997, Inui A. 1999, Tisdale MJ. Et al, 2000; Nelson KA, et al,1994) (152,153,154,155,156,157). Treatment of Cachexia in terminally ill patients is generally limited to increasing the caloric intake and pharmacological manipulation of the body's metabolism to prevent further wasting .Since causes of cachexia can vary even among cancer patients, it is advised that the physician pinpoint the cause of the cachexia in order to be more efficient in treating it. Although anorexia can be treated with nutritional supplements, it is not reversible with this type of therapy. Currently, there are no approved treatments for this condition. The characteristics of cancer cachexia are still considered promising for the development of future treatment options. One of the most promising non-pharmacological ways to improve the survival rate of patients with this condition is by regular exercise. The ability to examine the skeletal muscle's response to exercise is a necessary and justified part of the cancer cachexia treatment process. Consequences of cachexia can include reduced anticancer therapy tolerance, increased susceptibility to treatment toxicity, and decreased patient quantity and quality of life (Evans WJ, et al, 2008) (158).

Although there are already various diagnostic criteria for cachexia, cancer-specific criteria are based on the percentage of weight loss that patients have experienced over the past six months (>5% weight loss over the past 6 months). A cachectic patient is characterized by reduced food intake and muscle function. They may also have psychosocial impairment (Fearon K, et al, 2011) (159). The loss of skeletal muscle can affect a cancer patient's physical and metabolic health. It can also impair their quality of life. Due to the importance of maintaining muscle mass, therapies that can improve the survival rate of cancer patients are being studied. Despite the growing evidence that regular exercise can improve the survival of cancer patients, little is known about the potential of exercise to treat or prevent cancer cachexia (Wolfe RR. 2006) (160). Although physical inactivity has been known to play a role in the development of various chronic diseases, it has not been shown to play a

significant role in the progression of cancer. Both the preclinical and cachectic cancer models have shown that regular physical inactivity can lead to various health conditions. In patients with advanced cancer, the basal metabolic rate increases, which results in a reduction of total energy expenditure (Gibney E, et al, 1997) (161). Patients with pancreatic cancer have similar physical activity levels to those with cerebral palsy or spinal cord injury. However, in recent studies, they showed that the level of physical activity decreased during the latest stage of the disease. This suggests that the development of chronic fatigue and muscle wasting may be influenced by the lack of physical activity. More studies are needed to identify the role of physical inactivity in these conditions (Moses AW, et al, 2004) (162).

Chronic nausea

Patients suffering from cancer often experience nausea and vomiting. Although nausea and vomiting can be caused by various factors, the evidence supports that the use of radiotherapy and chemotherapy is the most common reason. About 40% to 70% of individuals with other chronic diseases, such as inflammatory bowel disease or hepatitis C, experience nausea and vomiting. As their condition worsens, these symptoms become more common (Grond S, et al, 1994; Fainsinger R, 2001, Greenstein AJ, et al, 1975) (163,164,165). The complex physical and neurological phenomenon of nausea and vomiting involves different parts of the gastrointestinal tract and central nervous system. In supportive and palliative care, nausea may be caused by radiotherapy, platinum-based chemotherapy, and other drugs such as antibiotics and opiates. It can also be caused by disease-related factors, such as metabolic syndrome, elevated intracranial pressure, gastrointestinal issues, and bowel obstruction. Most nausea and vomiting episodes will respond to treatment for the underlying cause (Grunberg SM, et al, 2004, Campora E, et al, 1991, Feyer CP, et al, 1996, Bajorunas DR. et al, 1990, Fallowfield LJ. Et al, 1992) (166,167,168,169,170). It is estimated that 70% of advanced cancer patients complain of nausea and vomiting throughout their illness (Mannix KA. 2002, Stephenson, J. at al 2006, Davis, M. at al, , 2000, Naeim, A. at al, 2008) (171,172,173,174). Nausea may be caused by the drug or by the tumor's direct influence on one of the body organs that

might cause vomiting, such as the gastrointestinal organs or the brain (Twycross, R. G. 2002, Glare, P. A., et al, 2008) (175,176) Treatment of the underlying condition in the case of chronic nausea is the best course of action. In patients with advanced cancer, there are two critical questions that need to be answered in order to assess the effects of nausea and vomiting. First, what is the likely mechanism of this symptom? Second, what receptors are involved? It is important to consider multiple mechanisms that can cause nausea and vomiting, and the management of these should take into account. One of the most important features of this procedure is identifying the possible causes of these symptoms. For patients with advanced cancer, the assessment will also focus on the use of new drugs, such as those being used for chemotherapy. This includes the timing of vomiting, gastric discomfort, recent bowel movements, headaches and confusion, and obstruction. An initial evaluation of the mouth, pharynx, and other internal organs should be carried out. It should also include palpation for various intra-abdominal masses, monitoring for bowel sounds, and a rectal examination. Some of the investigations that may be useful include a full blood count, a serum calcium concentration test, a liver function test, and a urine analysis. In addition, abdominal films may be used to check for fluid levels in the intestine. A contrast-enhanced CT scan is sometimes indicated when there is a suspicion of elevated intracranial pressure or a possible vestibular or cerebral involvement. A similar procedure can also be used to check for signs of lymphadenopathy or progressive disease.

In patients with cancer, there are various potential causes of emesis. One of these is the use of drugs, such as anticholinergics and opiates. In addition, some other potential causes of emesis include anxiety and stress, as well as gastric irritation and fear/anxiety. Proton pump inhibitors, anxiolytics, and cognitive behavioral therapy can also help stop irritation. If the cancer is directly related to the constipation, then radiotherapy should be considered. The key to successful drug administration is identifying the likely mechanisms by which a particular drug can be blocked. Table 3 shows a summary of the various receptors involved.

Table 3 - Antiemetic drugs by class and their dosages, effects and indications

Antiemetic drugs by class and their dosages, effects and indications				
Antiemetic	Class	Dosage (per 24 hrs)	Main mechanism of action/receptor	Indication
Metoclopramide	Prokinetic	30-80mg	Increases peristalsis in the upper gut	Gut stasis
Cyclizine	Antihistamine	150mg	Dopamine D2 receptor antagonist Vestibular and vomiting centers Histamine H1 antagonist	Intestinal obstruction Vestibular causes
Haliperidol	Butyrophenone	1,5-10mg	Dopamine D2 receptor antagonist	chemical/drug causes, hiccup
Levomepromazine	Ophenothiazine	6,25-50mg	Blocks dopamine and serotonin receptors in the CTZ	Most causes, used as a second-line antiem

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				etic
Ondasetron	Antiserotoninergic	8-16mg	Blocks 5HT3-receptors in the CTZ and gut	Nausea and vomiting related to chemotherapy, radiotherapy and surgery
Granisetron	Antiserotoninergic	1-2mg	Blocks 5HT3-receptors in the CTZ and gut	Nausea and vomiting related to chemotherapy, radiotherapy and surgery
Dexamethasone	Corticosteroid	8-16mg	Reduces inflammatory edema, has an ill-defined, non-specific central antiemetic effect	Adjunct in raised intracranial pressure

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				e and chemotherapy related nausea and vomiting
Hyoscine butylbromide	Anticholinergic	60-300mg	Reduces gastrointestinal secretions and motility	Intestinal obstruction
Octreotide	Somatostatin analogue	250-750mg	Acetylcholine reduces gut secretions Somatostatin receptor agonist	Intestinal obstruction
Aprepitant	Neurokinin receptor antagonist	125mg 1 hour before chemotherapy 80mg once daily for 2 days	Neurokinin receptor antagonist	Adjunct in raised intracranial pressure and chemotherapy-related nausea and vomiting

Metoclopramide is most commonly used for treating nausea and other gastrointestinal disorders. Its side effects include depression and anxiety. For treating nausea and other gastrointestinal disorders, the drug haloperidol is used. However, it should be caution for patients with Parkinson's disease. Its side effects can include sedation, additional pyramidal effects, and tardive dyskinesia. Granisetron, Ondansetron, and Troisetron are 5HT₃ receptor antagonists that are used to treat nausea and other gastrointestinal conditions. Their main indications are for treating cancer and other procedures. This drug is a powerful D₂-receptor antagonist that has the ability to work across various receptors. It can induce sedation, which is usually associated with nausea and vomiting. In certain clinical situations, non-pharmacologic measures may be utilized. For instance, in the treatment of obstructive upper gut tumors, laser therapy and stenting may be required. In addition, in the end of life, a ventilating gastrostomy may be performed to treat intractable vomiting. Ovarian and pelvic cancer, including those that are related to the lower gut, can respond to radiotherapy or chemotherapy. Nasogastric tubes can be utilized for these patients. For those with a reasonable prognosis, colostomy can be performed to treat the obstruction. Other environmental measures such as relaxation, diversion, and avoidance of unpleasant smells are also commonly utilized. Some people report that they benefit from acupuncture, though there is not enough evidence supporting its widespread use. One of the most common forms of treatment for breast cancer is chemotherapy. This treatment involves the use of powerful antiemetic drugs. However, even with these drugs, nausea and vomiting can still occur in up to 70% of patients. In addition to destroying the cancer cells, chemotherapy drugs can also damage healthy tissues in the body. This is why prolonged treatment for cancer can negatively affect the functioning of individuals. Their functional status is related to various aspects of their physical, social, psychological, and cognitive health (B. Kurt, S. Kapucu 2018, Ü. Özdemir 2017, E. Ballatori et al, 2007) (177,178,179). A study revealed

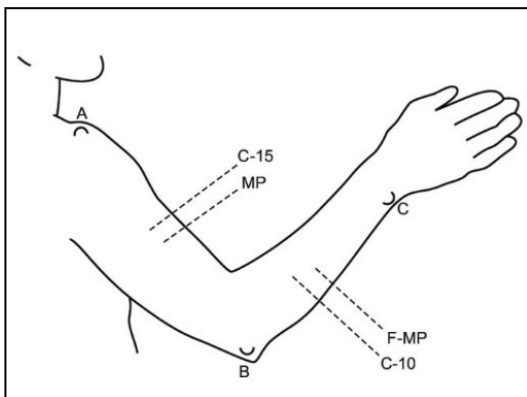
that prolonged exposure to chemotherapy drugs can negatively affect the functioning and nutritional status of patients. Many cancer patients resort to alternative and complementary medicine to reduce nausea and vomiting (C. Farre et al, 2013) (180). A study conducted in Turkey revealed that about 22.1% and 84.1% of cancer patients use complementary and alternative medicine (CAM) methods. This figure is significantly higher than the average in other countries (N. Uysal et al 2016, Y. Tokem, et al, 2011) (181,182). Various forms of complementary and alternative medicine (CAM) are used by patients to reduce and prevent nausea and vomiting associated with chemotherapy. These include yoga, meditation, and herbal treatments. According to the literature, breathing is one of the most relaxing exercises that can be performed during a regular day (H. Aksu et al, 2007) (183). Handbooks for patients who are undergoing chemotherapy contain information about the importance of deep breathing exercises to prevent nausea and vomiting. It is also believed that breathing can help reduce stress levels and anxiety. Having this type of information can help patients avoid experiencing severe distress and improve their functional status (Hastalar et al, 2018, Hasta ve et al, 2018) (184,185).

Lymphedema

Breast cancer related lymphedema may be a persistent and upsetting condition that's assessed to influence between 12.5% and 49% of female patients who experience surgical lymphatic vessel/node extirpation or radiation treatment, with a lower rate in sentinel node-negative patients (Brouwers MC, et al, 2010) (186). It can develop directly after surgery, radiation treatment, or months and even a long time later (Petrek JA et al, 2001) (187). American Cancer Society (ACS) guidelines 2012 provide signs around how to measure arm circumferences in lymphedema. They recognize four points to a degree: a) the metacarpal-phalange joints; b) the wrists; c) 10 cm distal to

the horizontal epicondyles; and d) 12 cm proximal to the horizontal epicondyles (Harris SR et al, 2012) (188). Circumferential estimations should be taken preoperatively, postoperatively, and amid observing treatment. To warrant treatment, it is vital to have a distinction between the two arms of more than 2.0 cm at any of the four estimation focuses, given that tumor inclusion within the axillaries or brachial plexus, contamination, and axillaries vein thrombosis have been ruled out (Harris SR et al, 2012, Rogan S et al, 2016) (189,190). Lymphedema is a disease process that is characterized by insufficient drainage of interstitial fluid mostly involving the extremities. Secondary lymphedema is commonly found in the developed world often as a complication of malignancies or surgical treatment of cancer. While Lymphedema is a physical condition a major impact of it may be the psychological distress even following the completion of treatment for cancer itself. Patients often complain of pain, heaviness, swelling, inability to find proper fitting clothing, and in some cases frequent infections (Chang, David W., et al, 2016) (191). Figure 2 shows Points for objective circumference measurements to diagnose lymphedema, as suggested by Starritt et al (Starritt EC, et al, 2004) (192).

Figure 2 -
Points for objective circumference measurements to diagnose lymphedema



Studies have shown that regular physical activity can be safely used in patients suffering from breast cancer-associated lymphoedema. They also noted that the subjective effects of exercise can be influenced by the training. It has been shown that home-based and water-based exercises can improve the quality of life and functional limitations in patients with this condition (Letellier ME, et al, 2014) (193).

During the "early phase" of recovery, it is important that patients are informed about the importance of taking part in daily life activities. After a patient has developed a problem, such as a complication following a breast cancer surgery, physiatrist are called to manage it properly. Unfortunately, there is not enough evidence supporting the use of acupuncture or manual lymphatic drainage in treating lymphedema. There are also conflicting guidelines regarding the use of laser therapy and compression bandages. The guidelines for treating secondary upper limb lymphatic disease do not provide specific criteria for choosing the right treatment method or for assessing the effectiveness of lymphatic drainage procedures. They do not specify the duration, intensity, or parameter of the procedure (Inui A, et al, 1999)(194).

The American Cancer Society's guidelines on pain management recommend the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and acupuncture, though they do not provide an absolute view of the treatment of pain. Currently, there is not enough evidence supporting the use of electrocortical modifications in the treatment of antalgic gait in patients with breast cancer. A randomized clinical trial has revealed that these modifications may explain the effectiveness of TENS in treating intercostobial nerve pain. Guidelines for treating fatigue emphasize the importance of identifying the factors that can affect a person's fatigue, as well as taking the necessary steps to improve their physical activity and cognitive skills. One of the guidelines emphasizes the importance of physiotherapy and therapeutic exercise, though it does not provide specific recommendations on the type of exercise that is ideal. In addition, there are many reviews of rehabilitation exercises, though they

do not provide enough evidence to support their recommendations. Most of the guidelines on body image cover concerns. However, they do not provide recommendations on the treatment of metastatic patients. This means that there are no recommendations for the management of vertebral collapse or bone pain. Other rehabilitative issues that are not covered in the literature search include the management of axillary web syndrome and lymphangitis. Although the guidelines do not provide specific recommendations on the treatment of these conditions, they do recommend the use of Kinesio-taping (Fearon KC, et al, 1999, Billingsley KG et al, 1996) (195,196).

Although there are many benefits of having a definitive prosthesis or breast expander, there are no guidelines that provide advice on rehabilitation for patients with this type of device. For instance, while it is important to maintain a healthy body, it is not always recommended to follow a microsurgical approach after the initial phase. Existing guidelines do not address gender differences in the approach to rehabilitation after radical surgery. The survival rate of women with breast cancer has significantly improved worldwide, which is why it is important for patients to maintain a high level of social, vocational, psychological, and physical function following their cancer treatment. It is also important that rehabilitation programs include psychosocial support services, which are not included in the guidelines. This is because they can help patients maintain a high level of social and psychological function.

Arthralgia

Although the exact mechanisms by which exercise can improve the quality of life for people with arthralgia are still not known, it has been suggested that regular physical activity can help decrease the intensity and duration of pain. There are still many unanswered questions regarding the effects of this drug. These include its nature and the appropriate intensity and methods for its use (Irwin ML, et al, 2015, Yang GS et al, 2017) (197,198).

Cardiotoxicity

A study conducted on breast cancer patients revealed that exercise reduces the risk of cardiovascular events. Runowicz and colleagues recommend that women with this type of cancer be taught about the importance of exercise in their health (Runowicz CD et al, 2016) (199). This could have a positive effect on the severity of cardiovascular events or cardiotoxicity.

Cancer-Related Cognitive Impairment

Cancer-Related Cognitive Impairment - CRCI refers to a type of cognitive impairment that occurs in patients with cancer. It can affect various aspects of their cognitive function, such as attention, language, and reasoning. Although the exact prevalence and incidence of this condition is still unknown, it is widely believed that it can affect a number of individuals (Wefel et al., 2004) (200). Patients with cancer may experience changes in their cognitive abilities due to their treatment or the presence of the disease. Different factors such as age, social and psychological factors, and genetic predisposition can also affect the development of cognitive impairment. Various forms of cancer treatment, such as radiotherapy, chemotherapy, targeted therapy, and surgery, can result in cognitive impairment. These effects can negatively affect a person's quality of life and function in different areas of their life (Mehnert et al., 2007) (201). Different types of cancer can have cognitive dysfunction, which can occur during the diagnosis, treatment, and even years after the cure. Most studies on this issue focus on women with breast cancer, though investigations have also been conducted on other malignancies, like colorectal, prostate, lung and hematological malignancies (Cruzado et al., 2014; Scherwath et al., 2013) (202,203). A comprehensive review of 19 studies revealed that physical activity can improve the cognitive function of breast cancer patients. It also showed that exercise can reduce chronic inflammation. The findings support the idea that exercise can help improve the processing speed and prevent cancer-related cognitive

impairment (CRCI) (Zimmer P, et al, 2016, Hartman SJ et al,2018) (204,205).

Neuropathy

As the field of oncology continues to evolve, peripheral neuropathy is becoming an increasingly important issue. It can greatly affect the quality of life of patients. The knowledge about the mechanisms of peripheral neuropathy has significantly improved over the past decade. This has led to the development of effective treatment plans. In patients with cancer, the reduction of deep tendon reflexes is frequently detected on a neurologic examination. New therapeutic approaches can be developed to treat peripheral neuropathy and prevent it from interfering with cancer care. Various mechanisms can cause peripheral neuropathy in cancer patients. In one study, 48% of the patients had clinically evident neuropathy. In another study, 30% of the patients with no known cause of neuropathy and tumors of varying types showed signs of neuromuscular disease, with the highest incidences in those with bronchogenic or ovarian cancers. This condition is regarded as the most common type of paraneoplastic disorder, affecting up to 5% of patients with cancer. A specific antibody can only be identified in around half of cases (Teräväinen H et al, 1977, Paul T et al, 1978, Anderson NE et al, 1987, Mallecourt C et al, 2000) (206,207,208,209).

People suffering from peripheral neuropathy, which affects adults, are more prone to experiencing chronic alcoholism and metabolic disturbances than cancer. These conditions are also more common causes of this disorder. Vulnerable oncologic patients are especially prone to experiencing neuropathic pain due to how nutritional status can affect the development of the condition (Chaudhry V et al, 2003, Barnouin J, et al, 2012) (210,211).

New generation of chemotherapy drugs that are commonly used for treating cancer are peripheral neurotoxic agents such as thalidomide, vinorelbine, and taxanes. Early exposure to these agents can lead to

underestimation of the severity of their effects due to how long it can take for nerve injury to manifest. The use of these drugs in patients who have been treated with neurotoxic substances can also increase the impact of these drugs (Laguëny A et al, 1986, Cella D et al, 2003) (212,213). Vinca alkaloid vinorelbine is one of the least toxic of the various types of vinca alkaloids. It differs from other semisynthetic compounds such as vincristine and vinblastine in that it does not suppress microtubule growth. Vinca compounds have similar properties to those of taxanes when it comes to the treatment of microbubbles. In a phase I study, vinorelbine was not able to provide a therapeutic effect after being followed by paclitaxel. There was also a sufficient degree of neurotoxicity to stop the treatment (Ngan VK et al, 2001, Fazeney B et al, 2016) (214,215). Thalidomide has been used successfully for the treatment of various cutaneous and systemic inflammatory disorders. This drug thalidomide can cause axonal neuropathy, which affects the sensory and proximal portions of the body. It is typical for this type of toxic neuropathies. Although duration and dosage of treatment are not known factors that can increase the risk of neuropathy, a study suggests that smokers may be protected from this condition. Thalidomide neuropathy has been known to have long-lasting effects (Calabrese L, et al, 2000, Chaudhry V et al, 2002, Clemmensen OJ et al, 1984 Fullerton PM et al, 1968) (216,217,218,219).

Oxaliplatin is a useful chemotherapeutic agent for gastrointestinal malignancies and has neurotoxic effects. It has also been reported that it can increase sensory nerve activity by acting on certain sodium channels. There have been several clinical trials suggesting that oxaliplatin toxicity can be safely treated with either carbamazepine or Gabapentin. However, none of these trials have resulted in a benefit. Most patients with neuroneuropathies that were treated with chemotherapy show signs of recovery, though they may experience more symptoms during the course of treatment. Because of the platinum-based therapy's concentration in certain nerve cells, patients with platinum-neuropathies

may not recover completely (Holmes J et al 1998, Gamelin E et al 2002, Wilson RH et al, 2002, Gregg RW et al, 1992) (220,221,222,223).

Taxanes, such as docetaxel and paclitaxel, have gained widespread acceptance for treating cancer. They are plant derived the mitotic spindle poisons. Like the vinca alkaloids, they cause microtubular gating. In patients with advanced ovarian cancer, paclitaxel administration as a 24-hour infusion has been shown to cause orthostatic hypotension. About 95% of these patients experienced sensory-motor neuropathy after taking the drug combination with cisplatin (Jerian SM et al, 1993) (224). The combination of docetaxel and platinum compounds can have synergistic effects. Most patients with nerve damage are at risk of experiencing sensory neuropathy. These symptoms usually appear during the course of treatment. Although taxane neurotoxicity can cause significant functional loss, it usually plateaus. This condition is similar to other chemotherapy-induced neuropathy in that it usually improves with sufficient time (Chaudhry V, et al, 1994, Hilkens PH et al, 1997, Br J et al 1997) (225,226,227). Neuropathy as a critical illness is a relatively new condition that can affect patients in intensive care units. It is characterized by a metabolic syndrome and occurs when patients are undergoing extreme stress. This condition was first described in 1984 by Bolton and colleagues. It affects patients who are in intensive care units and are experiencing multiple organ failure. Although critical illness neuropathy can usually present after a prolonged period of respiratory therapy, it can also occur in patients who are in an intensive care unit for less than a week. Clinicians usually recognize it when patients show signs of muscular wasting. A polyneuropathy involving the axons can be confirmed through electromyography. It can also show evidence of chronic and diffuse denervation. Although critical illness neuropathy can have varying degrees of involvement, it usually affects the sensory and motor peripheral nerves (Bolton CF et al, 1984, Lacomis D, et al, 1998, Bednarik J et al, 2003) (228,229,230).

The mischaracterization of neuromuscular blocking agents as a means to improve positive pressure ventilation is often made. In fact, neurophysiologic testing can help clarify this distinction. Besides demonstrating denervative electrical conduction, neurophysiologic testing can also show preserved nerve conduction velocity. If the loss of F waves or nerve conduction slows down significantly, then the clinician should consider developing a condition known as acute inflammatory bowel disease, or an acute inflammatory demyelinating polyradiculoneuropathy AIDP, which is characterized by severe respiratory failure and weakness. Table 4 shows Size and function relationships in peripheral nerve. AIDP can be triggered by trauma, infection, or surgery. It is important to identify a case of AIDP syndrome as treatment with plasmaphereses or gamma immunoglobulins can help decrease the severity of the condition. Other conditions such as diabetes mellitus and alcoholism can also result in peripheral neuropathy. The injury to the nerve can be cumulative, and malignancy can sometimes reveal a subclinical form of this disorder (Gutmann L et al, 1999) (231).

Table 4 - Size and function relationships in peripheral nerve

Size and function relationships in peripheral nerve			
Conduction fiber size, mm	Type of fiber	Velocity, m/sec	Function
10,18	A	70	a-motor neuron 1 degree spindle afferents
6,12	A	50	Touch and pressure afferents
4,8	A	30	g-Efferents; - degree spindle afferents

2,6	B	10	Autonomic: preganglionic
0,2,3	C	2	Temperature, Nociception, Autonomic: postganglionic

Many cancer patients with peripheral neuropathy have to deal with their symptoms, which can often overshadow their progress in their recovery. These symptoms can include pain, functional loss, and dysautonomia, which can affect a person's quality of life and safety. Regenerating nerve can cause paresthesias and cramping, and these can become the focus of patient complaints. Anticipation can help prevent these issues from developing into serious problems. While patients often complain about neuropathic pain, there is a difference between dysautonomia and other disorders. For instance patients should be aware of the risks of orthostatic hypotension especially during nocturnal micturition. For people with peripheral neuropathy, regular check-ups for orthostatic hypotension are important. They can also benefit from occupational and physical therapy assessments. Some of these tools include canes, walkers, toilet and kitchen aids, and brace systems. In addition to regular therapy, patients with neuropathy should also be taught about the safety devices and techniques they should use. Although these efforts do not cure their condition, they can help improve their function (OConnell PG et al, 1991, Kouidi EJ et al, 2001, Streckmann F et a, 2014) (232,233).

A systematic review conducted by Streckmann and colleagues revealed that exercise is more effective than strength training for treating peripheral neuropathies in reducing symptoms of CIPN in patients²³⁴. In a randomized controlled trial, a six-week home-based resistance exercise program and standardized walking program were shown to improve the symptoms of CIPN in patients who received chemotherapy for cancer (Streckmann F et al, 2018) (235).

Management of neuropathic pain

One of the most common symptoms of polyneuropathy is pain. Although it is not always the case that neuropathy patients experience pain, the degree of it does not correlate with the severity of the injury. Most patients with nociceptive neuropathy do not show signs of polyneuropathy, which can include reduced vibration sense or deep tendon reflexes. During the recovery phase, pain may appear more frequently due to the immaturity of the nerve's reinnervation. Table 5 shows the various neuropathies that can be associated with pain.

Table 5 - Neuropathies that can be associated with pain

Neuropathies associated with pain
Mononeuritis/mononeuropathy
entrapment syndromes (eg carpal tunnel syndrome)
post-traumatic/amputation neuromas
infection/inflammation(eg herpes zoster, shingles, postheraptic neuropathy)
Diabetic syndromes
Cranial mononeurpathies (eg trigeminal and glosopharyngeal neuralgia)
Brachial and lumbosacral neuritis
Ischemic/angiopathic
Polyneuropathies

Toxins

Airesic

Thallium

Drugs

Isoniazid

Platinum compounds

Vinca alkaloids

Taxanes

Thalidomide

Nitrofurantoin

Disulfiram

Metabolic/nutritional

Diabetes mellitus

Hypothyroidism

Chronic alcoholism

Pellagra

Beriberi

Malignancy

Amyloid

Hereditary

Hereditary sensory neuropathy

Amyloid

Fabry Disease

Inflammatory

Sjogren syndrome

Gullain-Barre syndrome

Different types of pain can be distinguished from one another by their characteristic qualities. For instance, neuropathic pain can have an electric or a non-linear quality. Patients with this condition often experience persistent numbness or burning sensations. In patients with neuropathic pain, allodynia is a condition wherein mild stimuli, such as the weight of bed sheets, become overpowering. The most common and persistent symptom of this disorder is a tingling or numbness in the stocking glove distribution. Some patients may stop taking cancer medications due to the unbearable pain they are experiencing.

For many years, strong anticholinergic tricyclic drugs, such as doxazopin or amitriptyline, were the primary treatment for neuropathic pain. These have since been replaced by more effective and natural alternatives, such as the combination of doxazopin and Gabapentin. Unfortunately, the newer generation of serotonin reuptake inhibitors and less anticholinergic medications are not as helpful for treating neuropathic pain (Collins SL et al, 2000) (236).

The added burden of drug intoxication can overwhelm the already compromised autonomic system in patients with cancer. For these individuals, pharmacologic intoxication can lead to various adverse effects, including cardiac rhythm disturbance, constipation, agitation, and orthostatic hypotension. Different dosage of Gabapentin can be used by patients for various conditions. Some people can benefit from doses as low as 200 mg per day, while others require higher doses. They should be counseled about the appropriate amount of medication to take, as some

people take the bulk before sleeping. One of the most common anticonvulsants is carbamazepine, which can be used for treating paroxysmal pain. However, it can also cause side effects such as leukopenia that are usually not desirable for cancer patients. Although some people use carbamazepine for treating non-paroxysmal neuropathy, the experience with this drug is more limited. Oxcarbazepine, a similar medication, has also been advocated for treating painful neuropathy. However, the published experience of this drug is more limited (Backonja MM et al, 2002, Tremont-Lukats IW et al, 2000) (237,238). Another new drug known as lamotrigine is reportedly promising for treating neuropathic pain. Although it doesn't induce hepatic enzymes, it can cause dermatologic reactions. Other agents such as capacicin can also help relieve neuropathic pain. In addition, patients should be aware of the potential side effects of this drug, such as an increase in the burning dysesthesia.

Most painful cramps occur at night and are usually caused by the reinnervation of an injured nerve. They can also accompany other metabolic conditions such as thyroid disorders and electrolyte imbalance. Quinine can be used at a lower dosage than the usual 325 mg. Since most of the toxic effects of quinine occur due to its dose, the minimal effective amount is usually taken once every two weeks. For some patients, however, a small amount of this drug can be obtained over the counter. Quinine can antagonize multidrug resistance, which is a secondary benefit of this medication. Phenytoin and abapentin can also help (Kanaan N et al, 2001, Lum BL et al, 1993) (239,240).

Neuroprotective Agents

The use of neuroprotective agents to protect the peripheral nerve from the effects of chemotherapy can help minimize the risk of morbidity and increase the therapeutic dose. Two strategies have been developed to prevent the toxic effects of the drugs while also promoting nerve regeneration. The specialized properties of the peripheral nerve make it

vulnerable to injury, and its metabolic requirements are high. Apart from its surface area, the distance between the nerve's axon terminal and the cell body also contributes to its susceptibility to toxic effects (Griffin JW, et al, 1988) (241).

Promoters of peripheral nerve regeneration can help strengthen and hasten the nerve's recovery from neurotoxic injury. Various clinical trials have been conducted on these strategies. Among the compounds that have been tested are thiol drugs that contain sulfur. Although Glutathione, cysteine, and methionine are amino acids that can help fight against oxidative stress, they can also hinder the delivery of these compounds to the tumor. Their use as neuroprotectants has been limited due to these issues. A number of studies conducted on the use of parenteral reduced glutathione showed that it did not reduce the effectiveness of chemotherapy (Cascinu S, et al,2002) (242).The military developed a drug known as amifostine (S-2-ethyl phosphorothioic acid, WR 2721, ethiofos) as a radiation protectionant. It has been used to prevent platinum neuropathy. Because it's a prodrug that requires to be dephosphorylated in order to be active, it can provide selective protection. Injected into the bloodstream as an intravenous infusion, amifostine must be given before the use of chemotherapy. However, it is not yet clear if this procedure should be done subcutaneously. To avoid anaphylaxis, it is important to use a lipoic acid-based alternative. Amifostine is widely available as a nutritional supplement. It has demonstrated the ability to protect against various neurotoxins, such as cisplatin, aminoglycoside, and lead. In addition, it can help with the metabolism of pyruvate, which is vital to nerve recovery and growth (Bergstrom P, et al, 1999, Conlon BJ et al, 1999, Gurer H et al, 1999,Rybak LP et al, 1999, Konrad T et al, 1999) (243,244,245,246,247).

Various neurotrophic factors are being studied for their therapeutic potential in the treatment of various neuro disorders, such as peripheral neuropathy. One of the most widely-known is the neurotrophic factor known as nerve growth factor. Other factors that have been identified are

the brain-derived neurotrophin, CNTF, GDNF, and ILGF. Unfortunately, the results of neurotrophic clinical trials have been disappointing. They suggest that these agents work best in combination rather than individually. One of the main concerns about these agents is that they can promote growth of malignancy. Despite their promising laboratory results, these agents have not been shown to be effective in treating neuropathy. Due to its ability to stimulate the growth of cancer cells, Insulin like growth factors have been identified as potential therapeutic agents for treating various types of cancer. These include breast cancer, prostate cancer, and colon cancer (Hayakawa K, et al, 1999) (248). When these therapies are available, it will be important to monitor the effects of these agents on the peripheral nervous system (Beech DJ et L, 1996, Apfel SC: 2001, Lee CT ET AL, 1996) (249,250,251). One of the most promising neurotrophic agents that has been studied for treating neuropathy is the pyrimidine isoxaonine. This drug can stimulate the regeneration of the peripheral nerve after various axonal injuries. Isaxonine's hepatic toxicity is enough to limit its clinical use (Kleinman D, et al, 1996) (252). Another promising neurotrophic agent that has been studied for its therapeutic potential is the methionine-containing sextapeptide known as Org2766. Unfortunately, the results of these clinical trials have been disappointing due to the drug's delivery problems (Duhamel G, et al,1982) (253). In one clinical trial, melatonin was shown to prevent chemotherapy-induced peripheral neuropathy but it is not always possible to use this drug in combination with other therapies (Lissoni P, et al,1997) (254).

Dyspnea

The American thoracic society defines dyspnea as “a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity... [it] derives from interactions among multiple physiological, psychological, social, and environmental factors, and may induce secondary physiological and behavioral responses” (Parshall MB , et al, 2012) (255). It has been estimated that approximately 55% of cancer patients display some level of dyspnea (Bruera, Eduardo, et

al 2000) (256). Dyspnea associated with cancer may be caused by the stimulation of chemoreceptors in the blood or mechanoreceptors in the lung. Similar to other issues that are targeted in palliative care, identification of the cause of the dyspnea may play a huge role in targeting it and rehabilitation. However, there are also other management strategies designed to combat dyspnea in palliative care. Management of dyspnea in palliative is usually done through a combination of pharmacologic and non-pharmacologic methods. Pharmacological methods may include opioids and adjuvants (Gallagher, Romaine et al, 2003) (257). The use of opioids was often frowned upon in cases of dyspnea due to concerns of respiratory depression following some studies (Jennett S et al, 1968) (258), however, it has been proven that even in patients with severe COPD there was no evidence of respiratory depression due to the use of opioids (Munck L, et al, 1990, Young I et al, 1989) (259,260). Other non-pharmacologic methods that may be used include avoiding exacerbating activities, keeping the room cool and moist, and avoiding irritants.

Rehabilitation strategies in Cancer patients

The two Category A guidelines for breast cancer rehabilitation address the needs of patients with various impairments. These include pain, fatigue, cognitive deficits, neuropathy, and other side effects. The guidelines from the American Cancer Society and ASCO recommend that patients undergo rehabilitative activities that minimize their ability to function. For patients with other conditions such as sexual dysfunction and musculoskeletal impairment, rehabilitation should be carried out when these symptoms are present. Various interventions such as massage therapy, music therapy, and yoga are also supported by ASCO. These can help patients manage their pain and improve their quality of life (Runowicz CD, et al, 2016, Greenlee H, et al, 2017) (261,262). Based on the treatment timing and the onset of the symptoms, rehabilitation should be considered for patients with various conditions such as post-operative upper extremity exercises and management of lymphatic

drainage (Thill M et al, 2018) (263). Two Category A guidelines from the American Cancer Society (ACS) and the National Institute of Health and Care Excellence (NICE) recommend various interventions for men with prostate cancer. One of these includes rehabilitation programs for those who are taking anti-androgen therapy. The other recommendation is for people who are experiencing urinary incontinence (Skolarus TA , et al, 2014, Parker C, et al, 2015) (264,265). The ACS has released a list of rehabilitation recommendations for people with head and neck cancer. These include treatment for various conditions such as dysphagia, temporomandibular joint disorder, and mobility issues caused by the disease. The Cancer Council Australia has also released a Category A guideline that focuses on nutritional intervention for individuals with this condition. The five Category B guidelines recommend referring patients for rehabilitation after cancer treatment based on various factors such as the type of surgery, the treatment timetable, and the presentation of symptoms (Talwar B et al, 2016, Binczak M et al, 2014) (266,267). The American College of Chest Physicians has issued a single Category A guideline that provides recommendations for patients with lung cancer who are at high risk of experiencing persistent cough. Four Category B guidelines follow suit and recommend rehabilitation for those who have symptoms that are severe or present at a level of concern. The European Respiratory Society and the European Society of Thoracic Surgery have also issued guidelines that recommend the use of supervised exercise as a part of an enhanced recovery after surgery (Brunelli A, et al, 2009, Batchelor TJP et al, 2019, Brunelli A et al, 2013) (268,269,270).

The American Thyroid Association has released a Category A guideline that provides rehabilitation strategies for individuals with symptoms related to fatigue and shortness of breath. Another guideline from the AAO recommends voice management therapy, which includes the assessment of the vocal cord mobility and the restoration of voice (Smallridge RC, et al, 2012) (271). The NCCN's Cancer Survivorship guideline provides a comprehensive view of cancer types and their treatment. It offers rehabilitation recommendations based on the specific

symptoms and severity of their condition. It also helps patients and their healthcare providers identify the appropriate interventions. Some of the common symptoms of cancer include pain, fatigue, and hormone-related symptoms (National Comprehensive Cancer Network , 2019) (272). The ACSM created exercise guidelines for cancer survivors in 2009 after reviewing the research on exercise and cancer. Although the guidelines are similar to those of the US Physical Activities Guidelines, they provide specific recommendations for different types of cancer and treatment. The main message to cancer survivors is to stay active and avoid inactivity. According to the American Cancer Society's guidelines, individuals who have survived the disease should engage in at least 150 minutes of vigorous aerobic exercise per week and two days of resistance exercise at a high intensity. They also recommend flexibility exercises for all major muscle groups as part of their exercise program. For older adults, regular exercise can help improve their balance. The guidelines also suggest incorporating exercise into a survivor's routine for certain conditions, such as breast reconstruction and peripheral neuropathy. Although the exact effects of exercise on cancer are not known, the findings of the current research suggest that it is safe to exercise (Schmitz KH , et al, 2010, Nadler M , et al, 2017, Schwartz AL, et al, 2007, Schwartz AL, et al, 2002, Jones LW, et al, 2012, Wolin KY, et al, 2012) (273,274,275,276,277,278,279).

Rehabilitation of cancer pain

The WHO released guidelines in 1986 regarding the management of cancer pain. These guidelines were developed to provide evidence-based treatments for cancer pain, and they help in making informed decisions regarding the use of opioids. The organization has also updated these guidelines on the use of adjuvants and analgesics (World Health Organization , 2018) (280). The WHO guidelines are aimed at addressing the needs of adolescents and adults over the age of 60. They provide a variety of treatment options that can be utilized without the need for immediate opiate medication. Before starting the first step of the ladder,

health providers should assess the patient's pain level. A poor assessment of pain can lead to unnecessary treatment and inadequate pain control. Having a comprehensive history and a focused assessment of pain can help identify changes that can affect a patient's quality of life (E. Gallagher, et al, 2017, M. Shkodra, et al, 1992) (281,282). For patients with mild pain, the first step is to start taking nonopioid drugs. Depending on the patient's presentation, these may be used for better control of their condition, such as neuropathic pain. In addition to these, other agents such as antidepressants and anticonvulsants can also be added to the treatment. After treating moderate pain, healthcare providers may add nonsteroidal anti-inflammatory drugs or other non-opioids when appropriate. For patients with severe pain, they may need stronger doses of pain medication. Some may benefit from counseling if their symptoms worsen due to anxieties or depression (World Health Organization, 2018) (283).

After they had undergone treatment using the WHO guidelines, patients reported a significantly lower pain rate and a good or excellent pain control. There have been many studies that suggest that these guidelines can help provide effective pain relief even in severe cases. It is important that healthcare providers talk to their patients about the possibility of managing their pain at a tolerable level. In addition to discussing the possible side effects of drugs, healthcare providers should also talk about the risks associated with abuse and misuse. This should include the factors that can affect a patient's care, such as the availability of medication, barriers to treatment, and history of opioid abuse (C.L. Carlson, et al, 2016) (284). Although the use of drugs for treating cancer has become standard, there are still many potential rehabilitation strategies that can help patients manage their pain. Unfortunately, many healthcare providers and patients are not aware of these potential benefits. The goal of cancer rehabilitation is to improve the functioning of cancer survivors and their pain relief. This process involves a multidisciplinary team, which is composed of physical therapists, nurses, and other healthcare providers. The role of the physical therapist is to

provide a comprehensive assessment and treatment plan for the patient's pain (Glare, P.A, et al, 2014, Bennett, M.I, et al, 2019) (285,286). For patients who are suffering from pain, traditional rehabilitation techniques include manual techniques and general exercises. However, there has been a substantial increase in the awareness of the benefits of educational interventions. These can no longer be disregarded (Egan, M.Y, et al, 2013) (287). Despite the abundance of literature about the various benefits of rehabilitation, there is still a lack of evidence supporting the use of pain relief as a rehabilitation strategy for cancer survivors (Nijs, J , et al, 2016, Nijs, J , et al, 2018) (288,289).

Patient education refers to a process utilized by healthcare providers to provide patients with information that can help them improve their health. Over the years, the field of rehabilitation has been heavily impacted by the increasing importance of education. In the treatment of cancer, studies have shown that educational programs can help patients with pain intensity (Koongstvedt, P, et al, 2001, Louw, A, et al, 2016, Lee, Y.J, et al, 2014) (290,291,292). In a study, researchers discovered that educational programs were more effective than usual care in reducing the intensity of pain. They also found that these programs were beneficial in reducing the pain interference that patients experience. In 2016, Prevost and colleagues reported that over 80% of the studies that were conducted had shown that the participants gained better knowledge about pain. They also noted that 45% of the studies improved their adherence with the use of prescribed analgesics. A review of the studies conducted by Oldenmenger et al. revealed that many of the subjects had a hard time understanding the side effects of certain drugs and how they can affect their health. Another study conducted by the researchers revealed that educational programs were associated with a significant increase in medication adherence (Bennett, M.I. et al, 2009, Koller, A, et al, 2012, Prevost, V, et al, 2016, Oldenmenger, W.H, et al, 2018) (293,294,295,296). Those studies could not find a link between the level of pain knowledge and the intensity of the pain, nor did they find a correlation between adherence to medication and these outcomes. Also,

the effect sizes of these studies were small, and they lacked clinical relevance. Only 20% of the patients experienced a reduction in their pain, and only one study reported a response rate of more than 50% (Oldenmenger, W.H , et al, 2018) (297). The limited effectiveness of these interventions could be explained by the narrow scope of their studies. They were focused on a biomedical approach to treating pain, which means that they could not provide a comprehensive solution to the issue. The level of education that cancer nurses and doctors provide regarding the treatment of their patients with pain is evidenced by the fact that they mainly cover the various aspects of the disease. However, it is also important to note that they should add a more comprehensive explanation of pain pathophysiology to the curriculum. Research has shown that this type of knowledge can help improve the quality of care for those with chronic musculoskeletal pain. The goal of educational approach is to remove the barriers that prevent people from managing their pain. It focuses on the patient's knowledge and experience of pain, as well as his or her behavior related to it. This method aims to transform the way people think about and manage their pain. Different types of education are available for cancer patients, such as face-to-face meetings, video, and leaflet. In addition, the studies that were included did not examine the mechanisms by which pain was related to cancer treatment (Bennett, M.I , et al, 2009, Koller, A, et al, 2012, Prevost, V, et al, 2016) (298,299,300).

Physical therapy

Various studies have shown that regular exercise can improve the quality of life and other health outcomes for people who are suffering from cancer. It can also help prevent them from experiencing negative effects from the disease (Kennedy MA,et al 2020)(301).For example, A meta-analysis conducted on the effects of exercise on the quality of life and fatigue in prostate cancer patients revealed that it had significant benefits for both, but it did not find a significant effect on the overall quality of life. Further, the study revealed that the global health status of men with

prostate cancer was similar to that of men with other conditions, despite having a higher risk of experiencing sexual and urinary dysfunction (Clark JA, et al, 2003) (302). There are relatively few studies on the various aspects of physical activity and rehabilitation programs. They show varying options for patients and provide varying levels of evidence. A comprehensive review of 14 randomized controlled trials RCTs revealed good evidence for the short-term effects of various interventions, but also highlighted the significant differences between them. Another review of 10 studies revealed the initial evidence for the feasibility of exercise in improving psychological and physiological function during rehabilitation (Bluethmann SM, et al. 2015, Spence RR, et al. 2010) (303,304). Other studies conducted with small sample sizes looked into the various ways in which cancer patients can participate in programs related to their health. For instance, Cox et Al. compared the effectiveness of a weight loss intervention involving 37 cancer survivors with a telephone-delivered and internet-based program (Cox M, et al. 2017) (305). The results of the telephone group showed that the cancer survivors' health outcomes were better than those in the group that was delivered through a traditional program. In another study, Ritvo and colleagues will analyze the effects of a 12-week physical activity program on the physical health of 106 breast cancer survivors. The participants will be provided with a home-based program and a variety of devices, including smartphones and wearable technology. A systematic review of 14 randomized studies revealed that group activities, such as those involving behavioral modification, had the biggest effect on the physical health of breast cancer survivors. It also noted that community-based programs could help improve the functional status of older cancer survivors (Swartz MC, et al. 2017, Ritvo P, et al. 2017) (306,307).

Studies on the effects of exercise on the quality of life and the physical activity levels of cancer patients are currently being conducted. For instance, a randomized trial revealed that a supervised exercise program during chemotherapy significantly improved the quality of life and the physical activity levels of patients two years after the treatment (Kirkham

AA, et al. 2018) (308).The duration and intensity of an exercise program are two of the most critical factors that affect the quality of life for cancer survivors. In a study, researchers found that high-intensity training and low-intensity exercises can have similar effects on the physical and emotional well-being of women (Schmitt J, et al. 2016) (309).Table 6 summarizes exercise recommendations/guidelines for breast cancer survivors from different reviews.

Table 6 - Exercise recommendations/guidelines for breast cancer survivors from different reviews

Recommendations/guidelines for breast cancer survivors from different reviews
Strength training exercises 2 times/week
150min of moderate or 75 min of vigorous physical activity/week
normal daily activities as soon as possible
Prevent inactive lifestyle
Advise patients about healthy weight
Emphasize strength training for women treated with adjuvant chemotherapy or hormone therapy
Need for nutrition counseling
Need for physical activity
Need for weight management

It is feasible to use high-intensity interval workouts as part of a low-intensity training program for cancer survivors. A study also showed that strength training and endurance training can improve the quality of life for breast cancer patients (Schulz SVW, et al. 2018) (310). Although

numerous studies have shown that exercise programs with low numbers of participants can improve the quality of life for cancer survivors, they lack sufficient evidence to confirm their effectiveness. Other investigations have shown that cardiac rehabilitation facilities can be used effectively by cancer patients (Mazor M, et al. 2018, Melchiorri G, et al. 2017) (311,312). A study conducted on a group of breast cancer patients revealed that an exercise program could be integrated into a cardiac rehabilitation facility's program. However, it did not meet its primary objective of improving the participants' adherence and increasing their aerobic exercise capacity. In another study, researchers noted that the various topics covered in cancer rehabilitation programs are similar to those utilized in cardiac rehabilitation facilities (De Jesus S, et al. 2017, Dittus KL, et al. 2015) (313, 314). Although many studies have examined the link between physical activity and reduced mortality and recurrence, they are still not able to provide definitive answers. There are various methodologies and approaches that have yielded varying results (Friedenreich CM: 2016) (315). The findings of a population-level study conducted by Emaus and colleagues showed that there was a relationship between physical activity, body mass index and blood pressure, and lipids. They also found that the timing of the diagnosis and the duration of active lifestyle affected the risk of breast cancer recurring. The results of the study revealed that a low-level physical activity lifestyle is associated with a higher likelihood of death. In a rehabilitation program for cancer patients, Adamo and colleagues noted that aerobic fitness can improve survival. There are also studies that look into the mechanical effects of exercise on the molecular and cellular levels. In particular, they noted that the activation of the immune system could be a potential factor that could prevent cancer recurring. After six months of regular exercise, the patients' lymphocyte activation levels increased (Jakobisiak M, et al. 2003, Hutnick NA, et al. 2005) (316,317).

Specific exercise therapy

An exercise is defined as any physical activity that causes an increase in the body's energy expenditure. It can be done in a systematic manner and is designed to improve or maintain health-related outcomes. Resistance and aerobic training are usually considered when talking about exercise therapy for cancer patients. A review of 53 studies revealed that regular exercise can help improve the quality of life for those who are suffering from the disease. The results of the studies also indicated that exercise is safe for people who are suffering from cancer. Although the guidelines and studies supporting the benefits of exercise for cancer patients have been presented, no recommendations have been made yet for the use of exercise in the treatment of pain (Mishra, S.I.; et al. 2012, Mishra, S.I.; et al, 2012, Stout, N.L.; et al, 2017, Zeng, Y.; Huang, et al,2014. Bourke, L; et al, 2015) (318,319,320,321,322,323).

For cancer patients, specific exercise therapy can help them improve their function by restoring their natural functions. Unfortunately, there is not enough evidence supporting the effectiveness of this type of exercise in treating pain. There has been a lot of research conducted on the effects of upper limb exercises on the functioning of the affected limbs after breast cancer, head, neck, and other diseases. After radiotherapy and surgery, various factors can affect upper limb function and range of motion. These include the formation of scar tissue and fibrosis, nerve damage, pain, and axillary cording. In order to restore and optimize the muscle and joint function, specific exercises are prescribed (McNeely, M.Let al, 2010, Sierla, R.; et al, 2013, De Groef, A, et al, 2015) (324,325,326).Although it's usually presumed that pain will reduce after a certain period of time, it can also be a primary indication for performing specific exercises. For instance, for neuropathic and nociceptive pain, performing certain exercises can improve blood flow and reduce inflammation. Only four randomized controlled trials have been published so far that analyzed the effectiveness of various exercise techniques in treating cancer (Tatham, B.; et al, 2013) (327). Breast cancer patients can benefit from various exercise programs, according to some reviews.According to one study, including two groups of shoulder pain patients, the effects of exercise on

pain intensity were not different. But in a randomized controlled trial, the researchers found that engaging in active exercises for three months was associated with a reduction in pain intensity (McNeely, M.L.; et al,2010, De Groef, A.; et al, 2015) (328,329). Almost all studies that examined the effects of exercise on the shoulder range of motion and function found that it was beneficial. In addition, several studies showed that the initial or delayed start of certain exercises after surgery did not affect the pain intensity or incidence up to two years following the operation. A meta-analysis and review of the effects of a training program for patients with head and neck cancer revealed that it can reduce pain. However, the results didn't prove to be clinically relevant (Carvalho, A.P.; et al, 2012) (330). There is currently no proof supporting the use of exercise therapy for the relief of pain in cancer survivors or patients. Several possible reasons can be considered for this. First, the programs were designed with the goal of improving physical impairments, such as strength and range of motion. The lack of a comprehensive analysis of the available trials suggests that they were not designed to test the effectiveness of certain pain relief exercises. Instead, they were focused on finding out if these could help patients manage their pain. This means that the trials were not able to identify the most effective ways to treat their conditions. Most studies only looked at the intensity of pain. Other dimensions of pain, such as disability, are also relevant to the treatment of pain. It is important to note that the underlying mechanisms of the patient's pain complaint were not considered when it came to the exercise therapy. There are various factors that can affect the development and maintenance of pain after cancer treatment. It is not yet clear which type of exercise therapy is most effective for treating this condition and which type of exercises are appropriate for patients. Although the limited research on the subject has shown that certain exercises are safe, it is still not clear which ones are best for treating pain.

A meta-analysis conducted by Nakano, Frist, and colleagues revealed that regular exercise can improve the quality of life for cancer patients. They also found that those who exercise regularly have lower pain levels and

better physical symptoms (Nakano, J.;et al, 2018, Mishra, S.I.;et al, 2012) (331,332).

The researchers found that regular exercise can reduce the pain levels of cancer patients. They noted that those who participated in regular exercise had lower pain levels than those who did not exercise. However, the effects of the exercise were small and the difference between the three types of exercises was not significant. Two studies conducted by the Cochrane Collaboration revealed that regular exercise is also beneficial for cancer patients. These studies analyzed the effects of exercise on various aspects of health, such as pain. The researchers found that the effects of exercise on the quality of life were small. A review of the four studies revealed that regular exercise reduces the pain levels of people who have cancer. It also found that the effects were small. The other findings of the study suggest that general physical activity can have various positive effects. Although exercise is a type of physical activity, it has different positive effects on different aspects of health. For instance, it can reduce the risk of heart disease and improve the quality of life for people with cancer. However, the results of the studies on pain were not very encouraging (Lahart, I.M.; et al, 2018) (333). The reviews of the various studies on the effectiveness of exercise therapy in treating pain revealed that it can be very beneficial (Mishra, S.I.; et al, 2012) (334). However, it was not clear which modality or type of exercise was most effective. In the case of pain management, exercise is often considered to be very important due to its potential to improve the central nervous system's inhibition and anti-inflammatory effect. In people with chronic musculoskeletal pain, the response to exercise can vary, and it can also lead to hyperalgesia. There is not enough evidence supporting the effects of exercise on the processing of pain in cancer patients (Lima, L.V.; et al,2017, Naugle, K.M.; et al, 2012, Rice, D.; et al, 2019) (335,336,337). In particular, exercise is very beneficial for people who are suffering from arthralgia, a condition that is commonly caused by hormone therapy. In a large randomized controlled trial, it was revealed that regular exercise can improve the pain levels in patients (Nahm, N.; et al. 2018, Yang, G.S.;

et al. 2017) (338,339). Although exercise is generally safe and well-tolerated for cancer patients, there is not enough proof supporting the effects of it on the relief of pain after treatment. The exact exercise techniques that can be used to achieve this are not known. However, it is often recommended to use a combination of strength and aerobic training to reduce pain (Irwin, M.L.; et al. 2015) (340).

Mind-Body Exercise Therapy

The goal of mind-body exercises is to enhance the mind's ability to positively affect the symptoms and functions of one's body, such as pain (Husebø, A.M.L.; et al. 2017) (341). They can also be used to rehabilitate cancer patients. In addition to being used for rehabilitation, pilates has also been shown to reduce pain in women with breast cancer. A review of the studies revealed that it was more effective than the control group's interventions (Pinto-Carral, A.; et al, 2018) (342). Only breast cancer patients were included in the study. In addition, yoga is becoming more popular as a cancer rehabilitation technique. According to a review of 29 RCTs, regular yoga sessions can improve a person's perceived stress levels, fatigue, and general quality of life. Although there have been several studies showing that mind-body exercises can reduce pain, they were not able to provide conclusive proof. For breast cancer survivors, the results of three randomized controlled trials could not provide proof of beneficial effects. Practicing yoga and meditation can help breast cancer patients feel better about themselves, and it can also reduce their stress levels. In addition, massage therapy can help improve the quality of life for those suffering from pain (Pan, Y.; et al. 2015) (343). Although mind-body exercises are commonly regarded as complementary therapies, evidence supporting their use in cancer rehabilitation is still lacking. For instance, while pilates can relieve pain, it is not yet clear if yoga can also help patients with cancer. Simple meditation exercises have been shown to provide significant benefits related to mental health and quality of life for breast cancer survivors, and 6- to 8-week Mindfulness Based Stress Reduction Intensive Course (MBSR) programs have resulted in significant

improvements in psychological status and quality of life for patients who recently had a diagnosis of breast cancer. To our knowledge, no studies have explored the benefit of simple meditation exercises during the initial postoperative days for breast cancer-related surgery. Therefore, we explored whether a simple meditation intervention (a 15- min DVD-based instruction of paced breathing and a simple gratitude meditation) in addition to massage therapy would provide more benefit than massage therapy alone to breast cancer patients undergoing autologous tissue reconstruction.

Manual Therapy and Massage Therapy

Manual therapy is different from massage therapy in that it focuses on improving the physical and mental well-being of the patient. For most massage therapists, it's about promoting relaxation. On the other hand, physical therapists' main goal is to improve their physical function and reduce pain. Therapeutic massage is a type of relaxation that involves manipulation of the soft tissues of the body. It is commonly used for the treatment of cancer patients. According to a survey, about 11% of breast cancer patients have used massage. Unfortunately, there are no quantitative measures of its effectiveness.

Studies on the use of massage therapy and manual therapy in cancer therapy are being conducted. They examine the effects of these procedures on the joint range of motion and the soft tissues. In addition, these procedures are designed to restore the range of motion and prevent injury to the articular cartilage. In addition, certain procedures such as the activation of the mechanoreceptors can help reduce pain. A review of the literature revealed that the use of passive mobilization can help decrease the duration of pain and improve the quality of life following breast cancer surgery (Egmond, D.L.; et al, 2014, Le Vu, B.; et al, 1997) (344,345). Despite the overwhelming evidence supporting the use of massage therapy in cancer patients, the research on its effects on the various tissues of the body is still not enough to provide a definitive answer. The review found that massage can reduce the duration of pain in 79% of the studies. However, its effects on the intensity of the pain

were small and did not provide clinical relevance. The meta-analyses revealed that the massage effect on pain intensity was small. The standardized mean difference between the two groups was 0.20, which is less than the difference between the active and passive comparators. The conclusion of the review revealed that the effects of massage therapy are not clinically relevant. Instead, they suggest that other effects can be achieved through the procedure. These include a reduction in stress and anxiety, as well as an enhancement of one's sense of well-being. The two studies that were reviewed were very low-quality and included various types of cancer. They also did not find sufficient evidence supporting the use of massage therapy in patients with advanced or metastatic disease (Fellowes, D.; et al. 2004, Shin, E.S.; et al. 2016, Boyd, C.; Crawford, et al, 2016) (346,347,348). Massage therapy is commonly considered to be a safe and effective alternative medicine technique for managing various health problems (J. Finnegan-John, et al, 2013) (349). Different types of massage therapy techniques are commonly used in clinical practice. Some of these include Japanese massage, Chinese massage, Tai massage and Swedish massage. These techniques can trigger relaxation and improve the appearance and function of the human body's soft tissues (A. H. Ng, G. et al 2018.) (350). Practicing massage therapy can help improve various aspects of one's well-being, such as increasing one's heart rate variability, reducing fatigue, and improving mood disturbance. Breast cancer survivors have a high acceptance rate for massage therapy. It can also be used in the management of fatigue (M. Listing, et al, 2009) (351). Several small-scale studies have been conducted in the past few years to examine the effects of massage on the fatigue of breast cancer patients. There have also been reports of a reduction in the severity of the condition known as chronic fatigue syndrome (CRF). Three systematic reviews and review protocols related to the use of massage therapy for the management of cancer symptoms have been published (Kinkead, P. J. et al, 2018) (352). A review conducted by Finnegan-John and colleagues focused on the use of complementary and alternative medicine (CAM) interventions for managing the fatigue of patients with different types of cancer. The other two studies, which were conducted by Wang and Pan, focused on the effects of massage on the relief of the condition (K. Wang, et al, 2018) (353).

Manual therapy includes a number of tissue mobilization treatments, including as superficial and deep muscle massage, myofascial release,

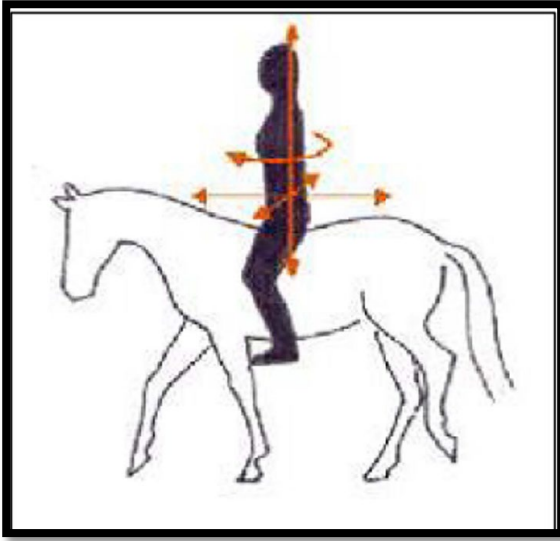
trigger point acupuncture, manual traction, and muscular articulation and mobility, all of which may play a significant part throughout therapy. Increasing the pressure pain threshold, analgesia of localized, referred, and general physical pain, and a decrease in CMP complaints are the key objectives of these exercises, along with the general rest and relaxation and release of fibrotic tissue found in muscle and fascia (Villar RR, et al, 2017) (354). Massage therapy has been documented to be helpful in outpatient and inpatient settings, including the postoperative period. In regard to surgical breast cancer patients, Drackley et al. reported significant reduction in pain, stress, and muscle tension, as well as an increase in relaxation, for patients who received massage on postoperative day 1 after mastectomy. According to studies, massage therapy (MT) can be an effective treatment for the relief of pain related to musculoskeletal conditions. However, it is not always clear how to use it and what the ideal treatment technique should be (Babatunde OO, et al. 2017) (355). It has been shown that manual therapy can reduce pain in patients. Various mechanisms explain how this type of therapy works. These include the effects of repetitive movement, the psychological impact of physical contact, and the biomechanical effects of this type of therapy (Hurley MV, et al. 2008) (356). Various techniques can be used during manual therapy in order to release tension and promote muscle relaxation. These include deep and superficial muscle massage, trigger point therapy, myofascial release, and manual traction. These procedures can help reduce the discomfort and promote the healing of tissues. The goal of these techniques is to improve the overall condition of the body (Vernon H. 2007) (357).

Equine assisted therapy

Through human and horse interactions, the equine-facilitated support program assists in minimizing the negative impacts of cancer diagnosis and treatment, regaining positive through experiential therapy, clients can work through their unfinished business and relieve psychological distress. In addition, Equine assisted therapy (EAET) uses horses as

metaphors and catalysts for addressing clinical issues. The core concept of is based on the psychodrama technique and the theory of experiential therapy. This modality is not only beneficial for individuals, but it can also help improve their psychological health. In previous studies, it has been shown that participants who undergo treatment have significantly reduced their psychological symptoms and improve their well-being. In EAET, the therapist and the horse handler work together to ensure that the client is safe and that the horse is treated properly. Activities such as horse grooming, riding, and walking are combined with traditional therapy tools such as role-playing and role-reversal (Lynne Murphy et al, 2019) (358). The use of horses in therapeutic settings has been shown to have positive effects on the psychological and social well-being of children and adults with disabilities. This type of intervention involves using the unique characteristics of horses to improve individuals' gross motor, self-help, and social skills (Benda, W., et al. 2003, Borioni, N., 2012, Boswell, S., et al, 2009) (359,360,361). Most studies conducted on hippotherapy involved participants being placed on a live horse, which was led by a horse leader. Their goal was to improve their motor function, not develop any skills related to riding. The goal of hippotherapy is to help the participants maintain a balanced position while the horse moves. During the session, two people walked on the other side of the animal to balance the riders. The horse's movements challenged the participants' core, pelvis, hips, legs, and spine. A licensed therapist then guided the participants through a variety of activities to improve their posture and reach their goals (Ratliffe, K. T., & Sanekane, C. 2009) (362). Figure 3 shows patient`s balanced position while the horse moves.

Figure 3 - patient`s balanced position while the horse moves.



About 35% of the studies indicated that therapeutic horseback riding was more effective than hippotherapy when it came to introducing participants to the concept of improving their riding skills. This type of intervention was carried out by a certified therapeutic horsemanship instructor, not a licensed therapist. Unlike hippotherapy, therapeutic riding involves the use of various equipment such as saddling, grooming, and horseback care. Only 19% of the studies used horse exercise without a certified instructor or therapist (Hammer, A, et al, 2005) (363). The studies all focused on horse gaits, and one of the most common factors that were discussed was trotting. This is a type of movement that increases the horse's velocity and difficulty. In most of the studies, only 16% mentioned trotting, while the other 87% were kept at a walk. Although trotting was a common factor discussed, it was not studied as a variable. Eight studies also looked into various aspects of horse gaits, such as weaving through obstacles and stretching (Aranda-Garcia, S., et al, 2015, Borioni, N., et al, 2012, Beinotti, F., et al, 2013) (364,365,366).

Breast cancer and Rehabilitation

Around 2.1 million women worldwide are diagnosed with breast cancer annually. This disease is the most deadly type of cancer in women (.

Iacoviello, et al, 2000) (367). According to the World Health Organization, around 627, 000 women died from breast cancer in 2018. This figure is about 15% of all deaths related to other malignancies (World Health Organization, Breast cancer. 2020) (368). Breast cancer is a type of cancer that can be age-specific. Its various characteristics, such as its clinical symptoms and molecular profile, are different from those of other types of cancer (M.A.E. Watanabe, et al., (2010) (369). Various factors, such as the age, grade of the tumor, the receptor type, and the expression of the ER by the tumor cells, should be considered in the treatment of breast cancer (N.A. Taylor, et al., 2017) (370). Breast cancer could be categorized into five molecular subtypes, including luminal A (ER+ and/or PR+, HER-2 negative) (26.55%), luminal B with HER-2 negative (ER+ and/or PR+, HER-2 negative) (31.38%), luminal B with HER-2 positive (ER+ and/or PR+, HER-2+) (24.14%), HER-2 enriched (ER-, PR-, HER-2+) (8.62%), and basal-like or triple-negative (ER-, PR-, HER-2 negative, CK5/6+ and/or EGFR+) (9.31%) (B. Kondov, et al., 2018) (371). Some women with breast cancer have a specific genetic mutation that can lead to the development of the disease. Most of the time, these mutations are in the genes BRCA1 or 2. Other genes that are known to be associated with breast cancer include CDH1, PTEN, and TP53 (Gulley, J.L. et al, 2023) (372). The American Joint Committee for Cancer's (AJCC) staging system is a combination of a clinical and a pathologic approach. It is based on the concept of the TNM system, which indicates that the tumor is referred to as "T," the nodes are called "N," and the disease is referred to as "M." (De_Vita, et al, 2015) (373). Breast carcinoma TNM anatomic stage group AJCC UICC 8th edition is shown in Table 7.

The definitions for tumor classification are the same whether assessed clinically or pathologically. A designation of cT or pT is used to indicate whether the staging is based on clinical or pathologic criteria. Pathologic classification is preferred when available.

- Tx – Primary tumor is unable to be assessed.

- T0 – No evidence of primary tumor.
- Tis – Carcinoma in situ.
- Tis (DCIS) – Ductal carcinoma in situ.
- Tis (Paget) – Paget disease of the nipple not associated with invasive carcinoma and/or DCIS in the underlying breast parenchyma. Carcinoma in the breast parenchyma associated with Paget disease is categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget disease should still be noted.
- T1 – Tumor ≤ 20 mm in greatest dimension.
- T1mi – Tumor ≤ 1 mm in greatest dimension.
- T1a – Tumor >1 mm but ≤ 5 mm in greatest dimension (round any measurement 1.0 to 1.9 mm to 2 mm).
- T1b – Tumor >5 mm but ≤ 10 mm in greatest dimension.
- T1c – Tumor >10 mm but ≤ 20 mm in greatest dimension.
- T2 – Tumor >20 mm but ≤ 50 mm in greatest dimension.
- T3 – Tumor >50 mm in greatest dimension.
- T4 – Tumor of any size with direct extension to the chest wall and/or the skin (ulceration or macroscopic skin nodules)*.
- T4a – Extension to chest wall, not including only pectoralis muscle adherence/invasion.
- T4b – Ulceration and/or ipsilateral satellite nodules and/or edema (including peau d'orange) of the skin, which do not meet the criteria for inflammatory carcinoma.
- T4c – Both (T4a and T4b).

•T4d – Inflammatory carcinoma**.

Regional lymph nodes (N) — Lymph node classification criteria differ depending on whether the nodes are clinically or pathologically assessed. A designation of cN or pN is used to make the distinction. Pathologic classification is preferred when available. Regional lymph nodes include axillary nodes, ipsilateral intramammary nodes, internal mammary nodes, and supraclavicular nodes. Intramammary nodes reside within the breast tissue and are coded as axillary lymph nodes for staging purposes. Supraclavicular lymph nodes are classified as regional lymph nodes for staging purposes. Metastases to any other lymph node, including cervical, or contralateral axillary lymph nodes are classified as distant (M1).

●cNX* – Regional lymph nodes cannot be assessed (eg, previously removed).

●cN0 – No regional lymph node metastases (neither by imaging nor clinical exam).

●cN1 – Metastasis to movable ipsilateral level I, II axillary lymph nodes(s).

•cN1mi** – Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm).

●cN2 – Metastasis to ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in ipsilateral internal mammary nodes in the absence of clinically evident axillary node metastases.

•cN2a – Metastasis to ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures.

•cN2b – Metastasis only in ipsilateral internal mammary nodes, and in the absence of clinically evident axillary node metastases.

●cN3 – Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in

ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastases; or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement.

•**cN3a** – Metastasis to ipsilateral infraclavicular lymph node(s).

•**cN3b** – Metastasis to ipsilateral internal mammary lymph node(s) and axillary lymph nodes.

•**cN3c** – Metastasis in ipsilateral supraclavicular lymph node(s).

Distant metastasis (M)

●**M0** – No clinical or radiographic evidence of distant metastases (no pathologic M0; imaging studies are not required to assign the cM0 category).

•**cM0(i+)** – No clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumor cells that are no larger than 0.2 mm are present in circulating blood, bone marrow, or other nonregional nodal tissue in a patient without symptoms or signs of metastases.

●**M1** – Distant detectable metastases as determined by classic clinical and radiographic means and/or histologically proven metastases larger than 0.2 mm (AJCC cancer staging manual , 2023) (374).

Table 7- Breast carcinoma TNM staging AJCC UICC 2010

Physical therapy and Rehabilitation for Improvement of Quality of Life of Breast Cancer
Patients Undergoing Chemotherapy

When T is...	And N is...	And M is...	Then the stage group is...
Tis	N0	M0	0
T1	N0	M0	IA
T0	N1mi	M0	IB
T1	N1mi	M0	IB
T0	N1	M0	IIA
T1	N1	M0	IIA
T2	N0	M0	IIA
T2	N1	M0	IIB
T3	N0	M0	IIB
T0	N2	M0	IIIA
T1	N2	M0	IIIA
T2	N2	M0	IIIA
T3	N1	M0	IIIA
T3	N2	M0	IIIA
T4	N0	M0	IIIB
T4	N1	M0	IIIB
T4	N2	M0	IIIB
Any T	N3	M0	IIIC
Any T	Any N	M1	IV

The management of breast cancer should be done in a multidisciplinary manner with the input of various medical specialists, such as the surgeon, pathologist, radiologists, and radiation oncologists. After the diagnosis, it is important that the patient's medical oncologist and other specialists thoroughly confirm the histology and the receptor and prognostic markers.

Surgery

Early breast cancer is a type of cancer that can be removed through surgery -T1-3, N0-1 tumours. The disease can be managed through various procedures, such as surgical removal and the use of adjuvant therapy. Multidisciplinary planning and discussion is necessary in order to improve the outcomes of treatment. Although routine imaging procedures such as CT scans and liver ultrasound are not recommended, they should be considered when assessing individuals at high risk of developing metastatic disease. Breast cancer patients usually require a radical removal of primary tumor. This usually involves either a wide local resection or a mastectomy. According to EORTC 10801 and NSABP B-06, there is no difference in the survival rate of patients who receive breast conservation therapy compared to those who receive lumpectomy and radical mastectomy. A simple axillary node dissection and a simple

mastectomy are less invasive procedures that preserve the axillary nerve and the pectoralis major muscle. They can also lead to sequelae, such as numbness of the skin. During the 1970s, a new type of breast-conserving surgery called a quadrantectomy was introduced. This operation involves removing the cancer with a margin of about 2.0cm of breast tissue, because of poor cosmesis this procedure is majorly abandoned now. Wide local excision is the is most commonly performed surgery nowadays for patients with early breast cancer. Multiple randomized trials have shown that following breast-conserving and breast radiotherapy has similar survival rates and local control rates as with a total mastectomy . Wide local excision, and breast irradiation, is preferred way of treatment of most T1–2 breast cancers. If a breast-conserving procedure is not feasible due to the size of the tumor, then neoadjuvant chemotherapy may be. It has been shown that this strategy can reduce the size of the tumor and improve the survival rate. Axillary lymphadenopathy can be inaccurately diagnosed. More than 30% of the positive nodes are pathologically impalpable. The clearance of the axilla is the important step in the treatment of cancer. It allows for the control of the disease in the region, except for the presence of extra capsular or fixed tumors beyond the lymph node. But overtreatment can also be problematic for patients with low-grade cancers. The goal of a sentinel lymph node biopsy is to identify and remove the first lymph node that is draining for pathological examination. Patients with node-negative disease should avoid getting axillary clearance. Patients with positive nodes can be treated with either axillary radiotherapy or dye and radio labeled colloid injection. There have been several studies that show that the procedure is more effective than axillary node removal and sampling. After breast-conserving surgical procedures, the risk of local relapse is reduced by about 30% to 10%. In addition, breast irradiation can prevent one death from cancer every four years. This benefit is recommended for all women with invasive breast cancer. The whole breast is treated with tangential fields to a dose of 40Gy in 15 fractions (or an equivalent dose fractionation regimen).

Adjuvant treatment

Despite effective local therapy with surgery and radiotherapy many women with early breast cancer carry occult micro metastases. These can lead to overt metastatic disease and eventually death. There is now a body of evidence supporting the use of systemic therapy as a treatment option for breast cancer. The goal of these therapies is to reduce or eliminate the microscopic systemic disease of breast cancer in women who have previously had their entire local tumor removed. Combination chemotherapy reduces recurrence rates and mortality by approximately one-third in all groups of women. This results in an absolute gain in DFS and OS which is greatest in women at high risk. The standard of adjuvant therapy is the combination of AC +T (4 cycles of doxorubicin hydrochloride (Adriamycin) and cyclophosphamide followed by 12 cycles of weekly Paclitaxel). About 60% of breast cancer cells are ER-positive. With adjuvant hormone therapy, patients have better survival rates. They also experience fewer symptoms than with chemotherapy.

Rehabilitation

Aside from the psychological distress that may be caused by breast cancer throughout its treatment and thereafter, the physical implications of breast cancer are may be very harmful to the patient's ADL and consequently, the QOL. Restricted arm movement, lymphedema and pain are some of the most common physical consequences of breast cancer or its treatment. As with all cases, early rehabilitation may be crucial in maintaining physical wellbeing. Physical therapy following breast cancer has been shown to improve shoulder motion in post-operative breast cancer patients as early as 1976 (Pollard K, et al 1976) (375). Arm mobilization generally begins on the first or second postoperative day, with joint rotation to tolerance but restricted abduction and flexion to 40 degrees. By day 4, flexion is gradually advanced to 45 degrees and increased by 10 to 15degrees per day if tolerated. Abduction is held at 45 degrees until the drains are removed and adapted to the patient's tolerance (Hoskins CN, et al, 2000) (376). These plans however are adapted to the patient's needs and according to their post-operative complications. The guidelines of the American Cancer Society (2012)

recommend complete decongestive therapy for lymphedema management. They also suggest using compression garments at night and keeping them on throughout the day if evidence shows that they can only prevent swelling and minimize the amount of limb volume (Harris SR, . et al. 2012) (377). For secondary lymphedema management, there are various interventions that can be performed. These include a complete decongestive therapy, manual lymphatic drainage, self-massage, compression bandaging, and intermittent pneumatic compression. In addition to these, other procedures such as low-level laser therapy and oral medications can also be utilized (Rogan S, et al. 2016) (378). Although the guidelines of the CPG recommend the use of manual lymphatic drainage in patients with no metastasis, they do not support the use of compression bandaging and other similar procedures. In studies, compression bandaging can reduce edema volume in the intensive phase of the treatment (Moseley AL, et al. 2007, Haghigat S. et al. 2010) (379,380). Although there are still many randomized trials to be conducted, a recent meta-analysis revealed that pneumatic compression can reduce the volume of edema in patients during the intensive phase of the treatment. The guidelines of the American Cancer Society (2012) also do not support the use of various drugs such as diosmin, coumarin, and selenium compounds in patients. Due to the conflicting results of studies, they do not believe that these drugs can be effective in treating edema (Szuba A. et al. 2002) (381). Conservative treatment of lymphedema is split into two phases with the first being concerned with skin care, compressive bandaging and manual lymphedema treatment (MLT) (Consensus Document of the International Society of Lymphology Executive Committee. 1995, Ko DS, et al, 1998) (382,383). Even simple elevation of the edematous limb may be effective. Patients should be instructed to use their arm sparingly and avoiding hot and cold exposure. Simple muscle exercises may also be used as part of phase one to encourage lymph movement. Phase two aims to maintain and build on what has been successfully established in the first phases. This includes low stretch elastic stockings that maintain constant pressure to reduce the edema. MLT may be used as seen necessary to maintain the results achieved in the first phase.

Aims and Hypotheses

The purpose of this study is to adapt an evidence-based exercise program and rehabilitation techniques for breast cancer patients undergoing adjuvant chemotherapy and test the efficacy of this approach combining physical therapy, massage therapy, equine therapy (intervention group) compared to chemotherapy only (control group) for improving quality of life.

Hypothesis :Participants in the Intervention group will have better quality of life than controls.

Outcome measures: The primary outcome of this study was the mean difference in Quality of life scores between groups after the four CT cycles and intervention. Data were collected using European Organization for the Research and Treatment Cancer Quality of Life Questionnaire (EORTC QLQ-C30) – in Georgian language (Supplement 1).

Methods

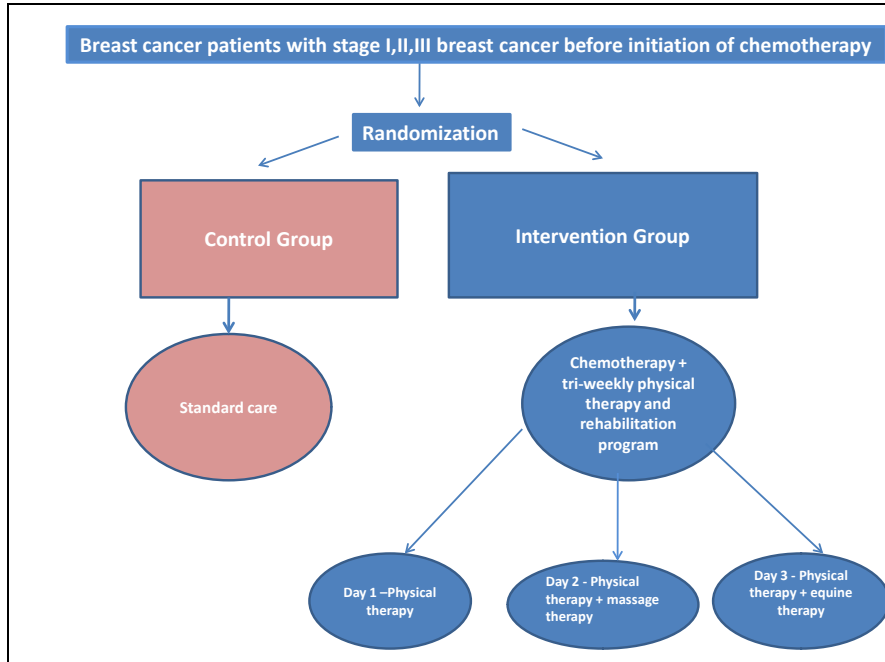
Trial design

This is two-armed, randomized controlled trial to test the efficacy of physical therapy and rehabilitation for improving quality of life of breast cancer patients undergoing adjuvant chemotherapy. The intervention program included physical therapy, massage therapy, equine therapy. Control group received standard care, treatment group received standard care plus intervention.

All patients completed the quality of life questionnaire (EORTC-QLQ-C30) at baseline and at 4 months. All participants randomized to treatment group first received one-on-one consultation with oncologist, Physical Medicine and Rehabilitation (PM&R) physicians and physical therapists. The intervention components include tri-weekly program that included physical therapy, massage therapy and equine therapy. More

details about the flow of the intervention delivery are available in Figure 4.

Figure 4 – Trial Design



The Trial protocol was initially approved by the Institutional Review Board (IRB) at The New Vision University on May 2019. Due to COVID-19 restrictions and required protocol modifications, the recruitment and enrollment period was delayed but resumed in April 2021. All potential participants were asked to provide written informed consent. Participants could withdraw from the study at any time without giving a reason. Participants were informed that they would not be charged for their participation in this study. The primary funding for this study is from the New Vision University.

Eligibility Criteria

All participants were enrolled using the eligibility and exclusion criteria listed in Table 8.

Table 8: Inclusion and exclusion criteria

Inclusion criteria:
• Female breast cancer patients, aged >25, <65;
• receiving AC chemotherapy for adjuvant setting;
• Diagnosed with stage I-III breast cancer;
• Physician approval to start an exercise program;
• Currently sedentary (<60 min. of physical activity per week)
• Able to complete surveys and forms;
• Agree to random assignment to Intervention or control group;
• Can commit to 4 months, three-weekly classes offered;
Exclusion criteria:
• Already receiving chemotherapy;
• Presence of metastatic cancer or concurrent malignancy requiring treatment
• Recent history (past 6 months) of stroke/ MI, atria fibrillation or class 3, 4 heart failure
• Recent joint surgery or conditions limiting physical activity.

Recruitment and Screening Methods

Participants were recruited through the oncology team at the New Vision University Hospital and Todua Clinic. Research staff secured permission from the treating physician prior to approaching the patient. Once this was obtained, staff contacted the patient to ensure eligibility for

enrollment. Additionally, the clinicians were asked to refer patients to staff before initiation of primary cancer treatment. Staff reviewed the electronic medical records to confirm that they were potentially eligible and contact the patient to ensure eligibility for enrollment. The Oncology team clinicians have agreed to assist with identifying breast cancer patients and providing information about the

study, which will then be approached by research staff after review of medical records and with permission from their attending physician. Once the oncologist or referring physician provided approval that the patient is cleared to participate in the study, research staff was able to contact the patient directly, using appropriate scripts. Eligible participants were recruited from November 2019 to April 2022 (Study was halted for a year in 2020 due to COVID pandemic). Thirty-one participants were excluded because they did not meet the inclusion criteria ($n = 21$) or were declined to participate in the study ($n = 10$). After obtaining their consent and performing pretests, the remaining 83 participants were randomly assigned to two groups (group A:43 and group B:40). The block randomization method was used in the study. Randomization was not performed by the researchers but by an external, independent statistician to avoid bias in the research process. An independent statistician who agreed to assist in the study and who was not associated with the practice recorded the information on the data collection forms and then entered it into the computer.

Intervention took place at the New Vision Health Hub rehabilitation center. Intervention group received intervention one week before and 3 times weekly during 4 months of chemotherapy.

Intervention

All patients received an adjuvant Adriamycin-Cyclophosphamide (AC) infusion in the oncology outpatient clinic every 21 days. AC protocol can increase the severity of fatigue by causing loss of appetite, nausea-vomiting and low energy in cancer patients. In addition, chemotherapy-

related symptoms begin to appear after patients receive their first Chemotherapy cycle. Therefore, patients who were planned to receive their first cycles of the AC treatments were included in our study. Women with BC were assigned to either an Intervention group or a control group. Participants in the Intervention group received intervention three times per week. The intervention was stopped 2 weeks after the patients had completed their 4th cycle. Participants in the control group received no intervention other than the usual care. In addition to information about chemotherapy treatment, the treatment group received a one-on-one exercise trainer consult, followed by a modified version of the BEAUTY program, which included three-weekly supervised group exercise (60 min), massage therapy (30 min) and equine therapy. The supervised exercise sessions included light weights or resistance bands plus low-impact aerobic exercise (provided by study), in which movements were explained, demonstrated and modified based on the needs of participants. At the baseline visit, all patients filled the quality of life questionnaire in Georgian language - EORTC – QLQ-C30 and signed the contest form. At the end of intervention, all participants filled the same questionnaire again.

Physical Therapy

The modified BEAUTY program was implemented for intervention group (Table 9). BEAUTY program aims to help with major concerns associated with breast cancer patients such as fatigue, reduced QoL, social anxiety and physical conditioning (Leach H, et al, 2014) (384). Considering there is huge physiological benefits as well major psychological benefits it is important that the physiotherapist promotes the benefits of exercise and ensures that the exercise program is assessable at home or in the community and is specific to the individual. All exercise programs were designed with F.I.T.T principles during breast cancer treatment.

Table 9- Beauty program

Exercise Category	Red Light (easy)	Yellow lights (moderate)	Green Light (hardest)
Aerobic	Heart rate should reach 40%–60% of age-predicted maximum, with a rated perceived exertion of 1–3, for 20–60 minutes	Heart rate should reach 40%–60% of age-predicted maximum, with a rated perceived exertion of 1–3, for 20–60 minutes	Heart rate should reach 40%–60% of age-predicted maximum, with a rated perceived exertion of 1–3, for 20–60 minutes
Resistance	1–2 sets, 8–12 repetitions, 5 exercises	1–3 sets, 8–12 repetitions, 7–8 exercises	2-3 sets, 8-12 repetitions, 14 exercises

F.I.T.T principles during breast cancer treatment - Exercise compliance during cancer treatment is low (Vardar Yağlı N, et al. 2015) (385), numerous factors for this such as lack of availability of services, cost and personal reasons and fatigue are often reasons for this.

- Warm up: 5-10 minutes to raise heart rate
- Aerobic Exercise: Frequency:
- 3 x times per week **Intensity: 50-70% of max. heart rate
- Type: walking cycling aerobic activity
- Time: 30 minutes maintaining as a long term routine
- Resistance Training: Frequency:
- 3 times a week
- Intensity: 12/15 reps of 60 % of 1RM
- Type: Supervised resistance program of major muscle groups

Studies revealed that a vigorous exercise program can improve the quality of life and reduce fatigue for breast cancer patients. It also helps in maintaining a healthy bone health and reducing the risk of developing osteoporosis (CAMPBELL, et al. 2019) (386). The program, which combines resistance and aerobic training, can be beneficial for people who are overweight or obese. People who exercise regularly can improve their quality of life and ward off various cancer-related symptoms. These include fatigue, cognitive impairments, sleep dysfunction, and cardiovascular issues. It has also been shown that treadmill workouts can

protect against the effects of Doxorubicin. Table 10 shows an exercise program designed to help breast cancer patients improve their core stability and flexibility. It includes various exercises and stretches - aerobic exercises, core stability exercises, and some recovery with stretching and myofascial release techniques.

Table 10 – CUIDATE program (Cantarero-Villanueva I, et al ;2012) (387)

CUIDATE program		
Week 1-4		
Material	Small soft ball, mats, and fit-ball	
Endurance program	Unspecific work during sessions	
Exercise Program	Content	Dosage and progression
	(1) Half squat with arm movement	Week 1: Learning proposal. Assessment maximum load Week 2-3: 75% maximum load Increase 5% per week Continue progression between exercises: 2 sets/30 sec pause Week 4: 75% maximum load. Increase number series (3 sets) Medium velocity execution exercises Increase range of joint motion
	(2) Standing rows with leg semiflexion maintained	
	(3) Wall push-ups	
	(4) Abdominal with lower limb movement	
	(5) All fours with hip and knee movement	
	(6) Abdominal with adductor isometric contraction and arm movement	
	(7) Standing hip circumduction	
	(8) Supine on fit-ball with arm movements	
	(9) Superman on fit-ball	
	(10) Oblique partial sit-up	
Week 5-8		
Materials	Fit-ball, elastic band, mats, and small soft ball	
Endurance program	10-25 min of fast working with arms movement two days per week	
Exercise Program	Content	Dosage and progression
	(1) Chest press on fit-ball with elastic band	Week 5: 10-12 repetitions × 2 sets Week 6: 12-15 repetitions × 2 sets Week 7: 10-12 repetitions × 3 sets Week 8: 10-12 repetitions × 2 sets Increase resistance with elastic band and positions that require more body control
	(2) Squat with elastic band	
	(3) Seated rows on fit-ball with elastic band	
	(4) Isometric abdominal sitting on fit-ball with arm and leg movement	
	(5) Biceps curl on fit-ball with elastic band	
	(6) Biceps curl with elastic band and leg semiflexion maintained	
	(7) Leg curl with fit-ball	
	(8) Sit-up with lower limb movement	

Massage Therapy

Although massage is an effective and inexpensive way to relieve tension and improve muscle function, it does not have side effects. It is also safe and can be used for cancer patients. Besides pain, massage can help patients relieve fatigue, depression, and anxiety. For massage therapy the slow-stroke back massage (SSBM) was performed. This technique is an intervention that involves placing a hand on the patient's back. In SSBM - slow, rhythmic and gentle palm strokes are performed, which can help calm patients and stimulate the neuromuscular system. It can also

improve blood circulation and relieve the symptoms of a chronic condition.

1. The patient was asked to lie down on the table where they felt most comfortable.
2. The practitioner warmed up his hands by rubbing them together before starting the massage. Five drops of essential oil were applied to avoid damaging the participant's skin and lubricating the friction surface.
3. The intervention was started from the neck with small circular strokes with thumbs.
4. Surface strokes were made from the skull base to the sacral region with the palm. Then rhythmic strokes were repeated from the sacrum to the skull along the entire spine.
5. Hand strokes were performed with the thumbs along the scapula.
6. Rhythmic movements followed with the thumbs on both sides of the spine from the shoulder to the waist.
7. Then, sweeping strokes were made with the palms of both hands from the neck region to the sacrum.
8. Repeated steps 3 to 7 of the intervention. At the end of the massage, the participant's skin surface was cleaned with a towel.

Equine-assisted Therapy

Equine-assisted therapy provides unique movements to the rider's joints and muscles improving pain, range of motion, and quality of life and has improved outcomes in balance, gait, strength, functional mobility, and spasticity. The EAT intervention, which was provided on the same day of the week and time within the cohorts, included grooming, saddling, and riding the same horse for 1 h each week for 4 months. The horses remained at a walk with two trained and experienced therapeutic riding side-walkers to support the rider. Mounting was assisted by either steps or a ramp at the level of the horse's back allowing participants to sit backwards and swing their right leg over the saddle and horse. All

mounting was supported by two staff members for safety. After mounting, 30 min of riding tasks was performed. Each week progressed to more difficult tasks from riding the horse at a walk around the arena on horseback stretching and learning to communicate with the horse. Human-animal bonding time after riding was provided by allowing the participant's time to groom and give treats to the horse. Participants were monitored for discomfort during the intervention by instructors and not required to perform a protocol task if uncomfortable. To prevent human-animal bond separation anxiety, participants were invited to continue the therapeutic riding at their own cost after the intervention ended.

Quality of life assessment scale

EORTC QLQ-C30 (table 11) was administered to a cohort of breast patients before the first cycle chemotherapy Research and Treatment of Cancer (EORTC) quality of life questionnaire QLQ-C30 was used which was developed by The European Organization for Research and Treatment of Cancer – QL group as a combined assessment system composed of a generic core questionnaire, EORTC QLQ-C30, which evaluates issues common to different cancer sites and treatments, and a range of supplementary modules designed to assess specific issues, according to the type of treatment or disease site, or to dimensions like fatigue (ArrarasUrduaniz JI, et al. 2008) (388). The EORTC study group developed the EORTC QLQ-C36 in the eighties for the specific purpose of monitoring the numerous aspects of QOL in patients. The QLQ-C36 however has since been refined to a more modern version labeled the QLQ-C30 (11). EORTC QLQ C30 is used to calculate patient's Global health status(QL) and it also consists of two subscales : Functional scales and Symptom scales. Functional scales consist of 5 items: Physical functioning (PF), Role functioning (RF), Emotional functioning (EF), Cognitive functioning (CF) , Social functioning (SF) . Symptom scales consists of 9 items: Fatigue (FA), Nausea and vomiting (NV), Pain (PA), Dyspnoea (DY), Insomnia (SL), Appetite loss (AP), Constipation (CO), Diarrhea (DI), Financial difficulties (FI).

Table 11

Scoring the EORTC QLQ-C30 version 3.0

Table 1: Scoring the QLQ-C30 version 3.0

	Scale	Number of items	Item range*	Version 3.0 Item numbers	Function scales
Global health status / QoL					
Global health status/QoL (revised) [†]	QL2	2	6	29, 30	
Functional scales					
Physical functioning (revised) [†]	PF2	5	3	1 to 5	F
Role functioning (revised) [†]	RF2	2	3	6, 7	F
Emotional functioning	EF	4	3	21 to 24	F
Cognitive functioning	CF	2	3	20, 25	F
Social functioning	SF	2	3	26, 27	F
Symptom scales / items					
Fatigue	FA	3	3	10, 12, 18	
Nausea and vomiting	NV	2	3	14, 15	
Pain	PA	2	3	9, 19	
Dyspnoea	DY	1	3	8	
Insomnia	SL	1	3	11	
Appetite loss	AP	1	3	13	
Constipation	CO	1	3	16	
Diarrhoea	DI	1	3	17	
Financial difficulties	FI	1	3	28	

* *Item range* is the difference between the possible maximum and the minimum response to individual items; most items take values from 1 to 4, giving *range* = 3.

[†] (revised) scales are those that have been changed since version 1.0, and their short names are indicated in this manual by a suffix “2” – for example, PF2.

QoL questionnaire was filled before and after the intervention, results were analyzed with statistical methods.

Results

Statistical methods (STATA) were used to analyze the data. We began data analyzes with observational statistics and independent variable analyzes. We had 2 independent variables: age and stage of patients and 4 age groups :Age 0 = 26-35, 1=36-45, 2=46-55, 3=56-65

Descriptive statistics are shown in table 12:

Table 12- descriptive statistics

Stage	Control	Intervention
I	11.4%	6%
II	45.7%	42%
III	42,9%	52%

According to the calculated data we observed that we had a few patients with stage 1 disease, so we decided to unite stages 1 and 2 for better analyses. We came up with simplified model:

Disease stage =0 if disease stage = 1 or 2

Disease stage =1 if disease stage = 3

We decided for this study to use difference/indifference studies (DID) we created 2 statistical models. First model – simple DID model without co variants, second models - DID with co variants.

Before we start running our DID model, we observed treatment group changes before and after intervention/chemotherapy and how control group data changed in pre and post period.

Model 1 simple DID :

$$y = \beta_0 + \beta_1 T + \beta_2 S + \beta_3 (T \cdot S) + \varepsilon$$

T=is a dummy variable for the period= 0 if we are in the pre period and equals 1 when we are post period;

S=Dummy variable for group membership = 0 if it is a control group and =1 If it is treatment group

$$\hat{\beta}_0 = \hat{E}(y | T = 0, S = 0)$$

$$\hat{\beta}_1 = \hat{E}(y | T = 1, S = 0) - \hat{E}(y | T = 0, S = 0)$$

$$\hat{\beta}_2 = \hat{E}(y | T = 0, S = 1) - \hat{E}(y | T = 0, S = 0)$$

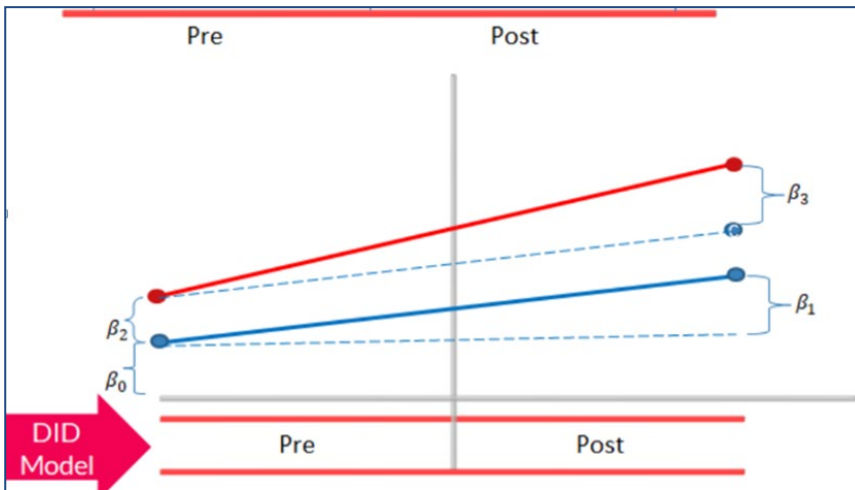
$$\hat{\beta}_3 = [\hat{E}(y | T = 1, S = 1) - \hat{E}(y | T = 0, S = 1)] - [\hat{E}(y | T = 1, S = 0) - \hat{E}(y | T = 0, S = 0)],$$

Beta 1 - How the control group state changed compared to pre-intervention versus post-intervention

Beta 2 – pre-intervention state difference between intervention group vs control group

Beta 3 – measures DID between treatment and control groups

Figure 5 – DID model



We saw the significant difference in observational study which increased our desire to create DID model. We analyze the data further and measured the intervention effects.

Table 13 - observational study

	Treatment Group				Control Group			
	observation (control/treatment)	pre	post	Difference	observation (control/treatment)	Pre	post	Difference
Q L	40/43	45	46.1	1.12	35/35	43.6	23.8	(-19.7)**
P F	40/43	67.5	78	10.4***	35/35	48.76	50.09	1.3
R F	40/43	72.08	81.4	9.31**	35/35	53.3	50	(-3.33)
E F	40/43	62.7	79.7	16.9***	35/35	56.19	61	5.23
C F	40/43	48.1	67.1	18.9***	35/35	37.6	22.38	(-15.23)**
S F	40/43	71.25	80.6	9.37***	35/35	52.85	51.42	(-1,4)
F A	40/43	57.77	57.8	0	35/35	46.66	29,99	(-16.69)**
N	40/43	45.	45	0	35/35	16.	10.	(-6.2)

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V		71	.7			66	46	
P A	40/43	56. 19	60	3.809	35/35	40	24	(- 15)***
D Y	40/43	49. 52	48 .6	(- 0.942)	35/35	32. 5	19. 37	(- 15.96**)
S L	40/43	51. 42	47 .6	(-3.8)	35/35	35. 83	27. 13	(-8.7)
A P	40/43	51. 42	48 .6	(-2.85)	35/35	18. 3	11. 62	(-6.7)
C O	40/43	48. 57	44 .8	(-3.8)	35/35	27. 5	11. 67	(- 15.87)* **
D I	40/43	38. 09	38 .1	0	35/35	15. 8	15. 5	(-0.32)
FI	40/43	51. 42	46 .7	-4.77	35/35	59. 16	53. 48	(-5.67)

Table 14 - Model 1 without co variants (group shows if it is a treatment or intervention group)

Table 15 -Model 2 with co-variants

	QL	PF	RF	EF	CF	SF
b0	43.57***	48.76***	53.3***	56***	37.66**	52.85***
group(B1	1.42	18.73***	18.75***	6.56	10.5**	18.39***

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)						
state (B2)	(-19.76***)	1.33	-3.33	5.23	(-15.23)***	-1.42
DID (B3)	20.88***	9.15*	12.64**	11.7*	34.16***	10.7
	QL	PF	RF	EF	CF	SF
b0	40.19***	50***	59***	53***	39***	63.000***
group(B1)	2.16	15.97***	15.6***	7.03	10.8**	13.42***
state (B2)	(-19.76***)	1.33	(-3.33)	5.23	(-15.23***)	(-1.43)
DID (B3)	22.88***	9.33*	11.6**	12**	35.23***	9.34
Stage	0.49	2.31	0.98	0.62	0.33	1.36
Age	0.94	(-3.26)**	(-3.79)**	0.69	(-0.87)	(-6.05)***

Even though we did not find any difference in some aspects of intervention group during observational study, we saw a significant difference in DID model which showed significant improvement in data. Compared to control group, intervention group showed improved Quality of life (43.57***), improved PF (48.76***), RF (53.3***), EF (56***), CF (37.66**) and SF (52.85***). Another important observation is a fact that age and stage of the disease had no effect on quality of life or affected any aspect of this study, reasons of which has to be further analyzed.

Discussion

Our study proved that physical therapy and rehabilitation can be useful in improving the quality of life of breast cancer patients undergoing chemotherapy.

Physical Functioning

Cancer treatment can lead to a variety of negative effects, such as a reduction in physical function and quality of life. These effects can be seen in various therapies, such as chemotherapy, surgery and radiation (Schmitz KH, et al, 2010, Nadler M, et al, 2017, Schwartz AL, et al. 2007) (389,390,391). A vital function and fitness indicator is aerobic capacity, and it has been shown that during a period of treatment for breast cancer, this capacity has decreased by around 10% to 33%. A third of the survivors have this capacity below what is considered functional independence (Jones LW, et al. 2012, Winters-Stone KM, Dobek J, Bennett JA et al. 2012, Schwartz AL, et al fatigue In Melanoma: A pilot study of exercise and methylphenidate. *Oncology Nursing Forum*. 2002) (392,393,394). A well-designed and progressive exercise program can help prevent or minimize these declines. There is a lot of evidence supporting the benefits of exercise for a variety of self-reported and objectively measured outcomes. It has been shown that exercise during and after cancer treatment can reduce the likelihood of patients dying. It can also help prevent or improve the effects of cancer treatment on various aspects of life, such as quality of life and cardiovascular function (Wolin KY, et al. 2012, Irwin ML, et al. 2011, Irwin ML, et al. 2008) (395,396,397). Our study confirmed the positive effect of exercise on quality of life during chemotherapy.

Positive effects of exercise are observed in various disease states, such as breast, prostate, lung, and colorectal cancer. For instance, the incidence of breast-cancer-related lymphedema varies from 6 to 70% depending on the degree of axillary and radiation therapy. Those who engaged in a vigorous resistance exercise program had a lower risk of developing lymphedema. Men who were treated for prostate cancer had a significant

change in their body composition and skeletal muscle strength. After androgen deprivation therapy, prostate cancer survivors who exercised experienced improved physical function, lower fatigue, and better body composition (Schmitz KH, et al. 2009, Bourke L, et al. 2011, Bourke L, et al 2014, Cormie P, et al. 2015, Galvão DA, et al. 2014) (398,399,400,401,402). Getting enough exercise is very important for cancer patients. Although it is not recommended for everyone, walking 30 minutes a week is a relatively low-impact exercise that can help improve the quality of life for those with cancer. For individuals with a disability, simple exercises such as walking three or four days a week can help improve their mobility and prevent them from experiencing significant declines (Nadler M, et al. 2017) (403). The most common benefits of exercise are improvements in physical function. The results of various studies suggest that exercise can improve the performance of at least one of the physical domains, such as flexibility, strength, and cardio respiratory fitness. They can still maintain their independence and continue to do their daily activities. The reduction in the physical reserve capacity of women with breast cancer is believed to be due to the effects of the treatment on their overall health. It is also believed that exercise can help prevent these patients from developing osteoporosis. There are conflicting reports about the effects of exercise on sexual function and activity. One study found that regular exercise did not affect sexual function, while another found that it did not affect sexual activity. Our study did not analyze effect of exercise on sexuality but the findings of the observational studies suggest that regular physical activity can improve sexual function. Exercise can potentially be a promising intervention for treating sexual dysfunction in patients with this condition (Vear NK, et al. 2020) (404). It is time for us to become advocates for the well-being of cancer survivors by providing them with the necessary resources and support to make informed decisions regarding their health. Unfortunately, many healthcare providers are not aware of the guidelines that are designed to help them implement effective exercise programs (Nadler M, et al. 2017) (405). Moreover, many cancer survivors do not receive the proper information about exercise and its benefits. This is because many healthcare providers do not provide adequate support and resources to help patients make informed decisions regarding their health (Irwin ML, et al. 2011) (406).

After a successful treatment, survivors should be advised to be referred to restorative exercise to improve their quality of life and reduce their risk of developing pain and fatigue. This type of exercise can be performed at a level that is consistent with their level of function. Physical therapy can help patients with severely limited function, such as those with diabetes and other conditions that prevent them from fully participating in their activities. Those who can function without specific deficits, such as those with pain and peripheral neuropathy, can benefit from a cancer exercise program administered by a specialist (Heston AH, et al. 2015) (407). Cancer survivors are immunocompromised, hence they are more prone to experiencing acute side effects during active treatment, which can lead to a negative impact on a person's quality of life and can contribute to the decline in emotional and physical functioning. Although exercise is generally safe during active treatment, survivors still need to learn how to manage their side effects. This can be done through regular exercise programs that are designed to improve their physical abilities. Many studies have shown that regular exercise can improve a person's fatigue. It can also help them manage their depression and anxiety. Oncology professionals must help patients adapt to exercise so that they can achieve the best possible results. This can be done through the guidance of exercise professionals (Schwartz AL, et al. 2001, Schwartz AL, et al. 2000, Wonders KY, et al. 2014, Kneis S, et al., 2016) (408,409,410,411).

The effects of cancer treatment can last for many months or even years following treatment. These include side effects that start during the initial treatment and last for a long time. Some of the common effects of these conditions include fatigue, neuropathy, and pre-mature menopause. To minimize the side effects of cancer treatment, it is important that the survivor makes adjustments to their exercise routine. For instance, while exercise may not prevent lymphedema, precautions should be taken to avoid a flare-up. One of the most effective ways to prevent this condition is by wearing compression sleeves and gloves while exercising (Heston AH, et al. 2015, Schmitz KH, et al. 2009, Schmitz KH, et al. 2009) (412,413,414). About 33% of breast cancer survivors have experienced

fatigue, and this condition continues to be a persistent and chronic issue. Some of the other symptoms that can trigger fatigue include depression and neuropathy. The effects of prolonged exposure to radiation and other chemicals can also increase fatigue levels. Getting active can help decrease fatigue. Although it can be initially hard for cancer survivors to start exercising, they can see improvements in their physical endurance and strength within a couple of months (Bourke L, et al. 2011, Bourke L, et al. 2014, Schwartz AL, et al. 2001, Kushi LH, et al, 2012) (415,416,417,418). Although cardiopulmonary complications can occur during active treatment for various types of cancer, they can become problematic at the later stages of cancer survivorship. For instance, heart failure can be an early sign of cancer that may occur during chemotherapy (Schmitz KH, et al. 2012, Carver JR, et al. 2007) (419,420). Some of the other cardiac complications that can occur are arrhythmia, hypertension, and valvular disease. Radiation therapy or chemotherapy can also have negative effects on the pulmonary function. Breast cancer survivors show significant declines in cardiac function, which can accelerate their aging. In order to reverse these cardiac issues, physical activity can be performed at a low-risk level. Despite the lack of definitive proof, evidence is growing that regular exercise can help improve the cardiac function of cancer survivors.

The effects of cancer therapy can still be seen years after the treatment is completed. This can affect a patient's ability to function properly and exercise. For instance, cardiovascular disease and osteoporosis are examples of late effects of hormonal and chemotherapy therapies that can lead to bone wasting. The effects of cancer treatment on the heart are known to be severe. Compared to individuals without cancer, survivors who have been treated for cancer are 70% more prone to experiencing cardiovascular disease (Schmitz KH, et al. 2012, Christensen JF, et al. 2015, Carver JR, et al. 2007) (421,422,423) . Some of the common conditions that can be associated with these effects include heart failure, stroke, and peripheral vascular disease. Various types of chemotherapy drugs can cause left ventricle dysfunction. These include anthracycline,

alkylation agents, antoxins, and various types of anti-microtubule and anti-protein therapy agents. Radiation therapy or concurrent with cardio toxic therapy can also predispose individuals to myocardial fibrosis, diastolic dysfunction, and heart failure. Patients who received radiation therapy for their cancer usually don't notice the effects of the treatment on their cardiac health for up to two decades. For instance, those who were treated with cardio toxic drugs and mantle field radiation for their cancer were more prone to experiencing a heart attack (Cardinale D, et al. 2010, Hull MC, et al. 2003, Oeffinger KC, et al, 2006) (424,425,426). Early stage breast cancer is known to cause mortality among women. The disease is also known to increase the risk of heart failure and coronary artery disease. Breast cancer survivors who followed exercise guidelines were more likely to reduce their cardiovascular disease risk. A study conducted on almost 3,000 women revealed that those who followed these guidelines had a 23% lower risk of experiencing cardiovascular events (Scott JM, et al. 2016, Jones LW, et al. 2016) (427,428).

Due to the increasing number of studies on exercise oncology, community programs are becoming more prevalent. Many occupational and physical therapists offer cancer exercise programs that are fully reimbursed by insurance in USA or Europe. These programs can be used for various conditions such as pain, fatigue, muscle weakness, and osteoporosis. The goal of these programs is to improve the overall function of people with cancer by preventing or managing the effects of the disease, such as swelling and weakness. The program is led by cancer exercise trainers who are certified by the American College of Sports Medicine (ACSM (Heston AH, et al. 2015) (429)). These individuals have been trained to help cancer survivors adapt to exercise and manage their conditions. Other programs are more structured and can be accessed online. For instance, Restwise™ is an online program that helps cancer survivors understand their symptoms and how hard they can exercise to improve their health (Schwartz AL, et al. 2015) (430). It is important to consider the needs of vulnerable populations, such as those with limited access to care, when it comes to cancer exercise programs. Studies have

shown that African-Americans have a higher death rate and lower survival rate than white individuals. The 5-year survival rate of Native Americans is lower than that of any other group, and they were the only one that didn't see a reduction in cancer mortality during the period 2001 to 2010 (Hughes DC, et al. 2008, Owens B, et al. 2009, Moadel AB, et al. 2007) (431,432,433). This suggests that programs that have shown efficacy may be needed to reach these populations. The program follows the American College of Sports Medicine's (ACSM) guidelines for cancer survivors, and it is culturally tailored to accommodate the needs of people with different cultural background. One of the most important factors that was considered was the training of the individuals who are working with them. They also took into account the various barriers that people face when it comes to cancer treatment and wellness (Bea JW, et al. 2018) (434).

The direction that needs to be explored in the future is the effect of exercise on peripheral neuropathy. Many chemotherapy drugs can cause peripheral neuropathy, which affects about 60% of patients within three months after treatment, and may not improve over time. Although there are various treatments that can help improve the condition, such as exercise, it is not yet known if these can reverse or prevent the damage to the nerves. In addition, long-term cancer survivors who exercise may also experience impaired balance (Wonders KY. 2014) (435). To improve one's aerobic capacity and muscle strength, a prescription should be tailored to address both the physical and mental health of the individual. This can be done through the use of a variety of exercise programs and physical therapy. One simple exercise that can be done at home is to balance on a stable surface. This can help prevent falls and improve one's confidence in moving.

Physical activity and Pain

The current model of care for breast cancer patients focuses on the treatment of the disease, instead of the patient's functional and physical

well-being. In order to improve the quality of care for breast cancer patients, we suggest that the current literature on the rehabilitation of these patients should be updated to include more evidence-based practices. The guidelines should also be designed to use a standardized system to evaluate the effectiveness of various interventions.

Based on the current findings, exercise participation after cancer-related treatments elicits beneficial effects on physical and emotional well-being, lymphedema management, and maintenance of BMD in BCS. Large randomized controlled trials are necessary to determine whether exercise can reduce the risk of cancer recurrence in BCS. Participation in regular exercise, preferably both AE and RE modes, can alleviate some cancer treatment-related side effects and improve survivorship. Although the scientific knowledge supporting participation in exercise is profound, exercise adherence remains a challenge in BCS. In future, health care-supported exercise programs for cancer survivors may be necessary, similar to cardiac rehabilitation exercise programs for cardiac patients, to promote a behavioral change to a more active lifestyle. Most people diagnosed with cancer will experience discomfort at some point in their lives. Even those who have completed therapy can still experience pain. Effective pain management is very important to maintain the quality of life for cancer patients. It is also very challenging to manage due to the varying reactions of patients to different drugs and therapies. According to studies, genetic factors can affect an individual's opioid sensitivity. This means that the dosages of certain drugs can vary widely across people. It is therefore important to consider the various effects of opioid drugs on a person's health. The classification of pain helps physicians make informed decisions regarding the treatment of their patients. This process can also help them identify the various factors that affect the development and maintenance of pain. Nonsteroidal anti-inflammatory drugs, such as ibuprofen and aspirin, are commonly used to treat cancer pain. Acetaminophen, antidepressants, alpha 2 agonists, and NMDA antagonists are also commonly used to treat this condition. Opioids are commonly used to treat cancer pain, especially in more severe cases.

However, there are various alternative therapies that can be used to treat this condition. It is important to note that some patients do not respond well to these drugs. In order to effectively treat cancer pain, a comprehensive evaluation and medication regimen are required. This can be done through a well-defined and organized approach. Results of our study show that exercise may have a role in pain alleviation in breast cancer patients during active phase of treatment.

Based on these assumptions, there is a clear need for a new best practice formulation and new multidisciplinary, multiprofessional guidelines that use a standardized system of evaluating evidence in the rehabilitation of breast cancer patients.

According to both researchers and clinicians, a comprehensive follow-up of cancer-related side effects, including pain, is needed to improve the quality of life for survivors. Besides the treatment of the disease itself, a systematic care pathway is also needed for every cancer patient. This type of care model aims to provide a proactive approach to addressing the pain and disability of patients during cancer treatment. It also involves regular assessment and treatment of these conditions, as well as the development of effective early interventions (Holland, J.C.; et al, 2005, Coccia, P.F.et al.2018. Kvale, E.; et al. 2014, Alfano, C.M.; et al. 2017, Stout, N.L.; et al, 2012) (436,437,438,439,440). For example, early detection and diagnosis of cancer pain are crucial for improving the quality of care for patients. A clear understanding of the pain complaint is a vital step in the clinical decision-making process. In the past few decades, the knowledge about the origin of pain has increased. There has been a paradigm shift regarding the classification of cancer pain (Smart, K.M.; et al. 2011) (441).When a primary cancer is treated with an adjuvant therapy, the tumor is removed, which means that pain is no longer related to the disease. However, in the early stages of the cancer treatment, there are instances of neuropathic pain and nociceptive pain, which are caused by radiotherapy, chemotherapy, or surgery. These short-term side effects can be managed adequately. The initial causes of pain in cancer survivors are

usually resolved in a later stage when the local effects of the treatment are no longer present. However, they can still be triggered by changes in the central nervous system's sensory input. This phenomenon, known as central sensitization, is a type of pain that can be caused by changes in the modulation of pain (Kosek, E.; et al, 2016) (442). For people with cancer, it is important to note that the effects of chemotherapy on the peripheral mechanisms can remain a contributing factor to their pain for a long time following the treatment. In addition, psychosocial factors such as post-mastectomy pain syndrome can also contribute to the pain. It is important that the primary pain mechanism is identified in cancer survivors to effectively manage their pain. However, clinical guidelines on this subject are not yet validated (Nijs, J.; et al. 2016) (443).

Through the clinical pathway, appropriate pain management can be facilitated. There is a wide range of rehabilitation techniques that can be utilized for a variety of physical symptoms following cancer treatment. Unfortunately, many studies did not use pain as an outcome measure. Unfortunately, many people who have cancer do not realize that they have pain, and this often leads to inadequate referral and treatment. Despite the limited research on the effects of rehabilitation techniques on pain, the reviews that have been published suggest that these procedures can help manage pain. Although there are limited studies on the effects of pain on the quality of life following cancer treatment, it is important to consider the various interventions that can be utilized to improve the quality of life. One of the most important factors that can be considered is the introduction of a neuro-science-based approach to pain management. This type of program should be conducted at the start and throughout a rehabilitation program to promote better cognition and pain behavior. In patients with maladaptive behavior and pain beliefs, an educational program is needed to explain the various treatment modalities and their effects on this condition. This will help patients make informed decisions and improve their adherence. Currently, there is not enough evidence supporting the effects of certain mobilization and exercises on the relief of pain following cancer treatment. It is important to further investigate

the role of these interventions in the treatment of neuropathic pain and acute nociceptive pain (De Groef, A.; et al. 2015, Sierla, R.; et al. 2013, Carvalho, A.P.; et al. 2012) (444,445,446).

Although general exercise can provide pain relief, more research is needed to determine the optimal modality and duration of exercise to reduce pain and prevent flare-ups. For instance, in cancer survivors, the modulation of endogenous pain may be impaired. This could affect the response of both general and specific exercise therapy. Although rehabilitation programs are generally safe when it comes to treating cancer, they can still be risky if performed incorrectly. For instance, for patients with hormone therapy-associated arthralgia, regular exercise therapy can help improve their quality of life. It is also important to note that other mind-body interventions such as yoga and Pilates can complement these. Although the effects of exercise on the pain of breast cancer survivors are known to be beneficial, the exact mechanisms by which this effect is achieved are not known. It has been suggested that the reduction of stress and anxiety can be attributed to the enhancement of one's sense of well-being. More evidence has been presented regarding the influence of various emotional and psychosocial factors on pain. Even though cancer treatment is generally safe, it can also trigger anxiety and depression in patients. This is because the fear of the disease coming back can affect their quality of life (Heathcote, L.C.; et al. 2017) (447). As proposed in educational interventions, an effective and biopsychosocial explanation for pain is needed. This concept can be applied to mind-body therapies. They can be utilized to address the psychosocial factors that contribute to pain. It is important to note that these are not exclusively rehabilitative tools. Various forms of mind-body interventions, such as meditation, acupuncture, and mindfulness, are often regarded as complementary to cancer treatment. However, since these do not appear to have bodily movement components, they are not considered to be effective in treating cancer. When developing a rehabilitation program for pain, it is important to consider other co morbidities, such as fatigue. This condition can affect the performance of regular exercise as cancer

treatment can also have detrimental effects on the cardiovascular system (Jones, L.W.; et al. 2009) (448).

Although rehabilitation and pharmacological therapy are commonly used for the treatment of cancer, other disciplines such as massage and psychotherapy are also needed to manage pain. It is important to note that increased stress and anxiety can interfere with the management of pain. Social workers can play a vital role in addressing the issues that affect society's participation. They can also help individuals improve their quality of life and reduce their pain. Some of the lifestyle interventions that have been suggested for cancer survivors include reducing alcohol consumption, improving nutrition, and smoking cessation (Rock, C.L.; et al. 2012) (449). New studies are being conducted on the use of electronic health records (EHRs) in the treatment of cancer. They show that these tools can help improve the quality of life for people with cancer. A review has revealed that there are applications that can help cancer survivors improve their fatigue and pain levels. These include telecoaching programs, which can be useful in helping them stick to a certain exercise program or improve their physical activity. Unfortunately, despite the positive aspects of these programs, researchers are still warning that further studies are needed to confirm their effectiveness (Davis, S.W.; et al. 2017) (450).

Nausea

It is believed that the most common side effects of chemotherapy are nausea and vomiting .It is believed that patients can experience nausea and vomiting up to 24 hours following the use of chemotherapy drugs. They can also continue experiencing these effects for several days. Studies revealed that almost 70% of the patients experienced nausea within the first 24 hours after the chemotherapy. According to our research, physical activity and rehabilitation had a positive effect on frequency of nausea and vomiting. It was also shown that regular breathing exercise can help decrease nausea and improve the functional status of patients. In one

study, all the subjects experienced nausea and vomiting after being given high-emetogenic drugs. The researchers noted that the groups that were given the drugs had similar number of episodes of nausea and vomiting before the treatment (A. Haiderali, et al, 2011, M. Eghbali, et al, 2016, B.B. Bloechl-Daum, et al, 2006, J. Lachaine, et al, 2005, U. Piamjariyakul, et al, 2010, T. Akechi, et al, 2010) (451,452,453,454,455,456).

It has been reported that even though antiemetic drugs can reduce the incidence of nausea, around 30 to 60% of patients experience delayed or acute nausea. In order to reduce the side effects of chemotherapy, various other studies have been conducted on the use of relaxation techniques such as breathing and music (N. Turan, et al,2010) (457). Following the review of the literature on the effects of respiratory exercise on cardiovascular disease (CINV), only one study was found that examined the effects of exercise on the functional status of breast cancer patients. This study, which is the first to look into the effects of breathing exercise on the status of patients with this disease, is believed to have been the first to analyze the issue (A. Suryono, et al, 2020) (458). It has also been reported that cancer patients in various European countries use alternative and complementary medicine at a rate of around 14% to 37%.In Turkey, cancer patients are more likely to use complementary and alternative medicine (CAM) methods than prescribed drugs (N. Uysal,et al, 2016) (459). It has been known that although pharmacological treatment can reduce the nausea and vomiting associated with chemotherapy, it does not eliminate the side effects of this treatment. One of the most common non-pharmacological techniques that can be used to reduce the incidence of this disease is breathing exercise. It was observed that regular breathing exercise can improve the functioning of cancer patients. It is also known that the effects of chemotherapy on the quality of life of patients can vary depending on the degree of nausea and vomiting. The functional status of an individual is evaluated by taking into account their various fields of expertise.

The concept of a functional status is that a person can perform her daily tasks and maintain her well-being. Cohen et al. found that patients who were given chemotherapy experienced significant effects on their daily lives due to nausea and vomiting (M. Ozkan, et al, 2017) (460). According to Glaus et al., about 75% of the individuals who experienced nausea and 50% of those who vomited experienced impaired daily activities. Ortega et al. noted that 45.1% of the patients experienced vomiting, while 31.4% experienced nausea. About 35% of the affected individuals suffered from reduced life functions (A. Glaus, et al, 2004) (461). In one study, Bloechl-Daum and colleagues found that the effects of chemotherapy on the daily lives of cancer patients were not severe. They noted that the mean score of the patients' functional living index was 122.9 before the treatment started. However, after six days, the index decreased to 105.4. Breast cancer patients' doctors should inform them about the side effects of chemotherapy and teach them about the importance of taking part in regular breathing exercises.

Equine Assisted Therapy

Results of our study show that equine assisted therapy may be an important method for breast cancer rehabilitation. The first systemic review to evaluate literature on equine-assisted therapy also showed that the most significant findings of majority of studies were that the quality of life and body composition were positively affected by the horseback riding. The results of one study revealed that the interventions significantly improved the quality of life and the balance, gait, and posture (Beinotti, F., et al, 2013, Frevel, D., et al, 2014, Aranda-Garcia, S., et al, 2015) (462,463,464). The barn environment can be partly attributed to the improvement in therapeutic riding and hippotherapy outcomes. This is because of the interaction between humans and animals. The interventions can improve various aspects of one's well-being and body composition. They can also help decrease the spasticity that can affect one's motor function. One theory states that the horse's high heat can

cause a decrease in various symptoms (Johnson, R. A. et al, 2003, Boswell, S., et al. (2009) (465,466).

Although there is little difference between therapeutic horseback riding and hippotherapy, the results of the studies indicate that the former has a significant effect on the statistical significance of the results. Also, medical supervisions not required for horse exercise.. It's not clear how the medical professional's involvement in the therapy affects the quality of the treatment. There is currently no evidence supporting the need for such professionals to improve their skills in order to provide effective services. The Dynamic System Theory could explain how the feedback mechanism works from the nerve impulses and muscles to the brain, which is involved in hippotherapy (Debusse, D., et al. 2009) (467). Another theory that could be considered is the Motor Learning Theory, which states that learning involves setting targets and performing movements to transform them into muscle commands (Willingham, D. B. et al, 1998) (468). The third theory that could be considered is that of the neuronal group selection theory, which suggests that the environment and genetics can influence the development of motor skills (Granados, A. C. et al, 2011) (469). Various other psychological theories have been proposed. The Attachment Theory explains how equine-assisted therapy can improve a person's psychosocial well-being. According to Bachi and colleagues, horses can provide a sense of mirroring through their non-verbal feedback (Bachi, K., et al. 2012) (470). The ability of horses to provide a sense of autonomy and control over their environment has been regarded as one of the main factors that contributes to the therapeutic outcomes of equine-assisted therapy. The other theories that are related to this phenomenon include the Social Provision Theory, which states that people need reliable and inclusive social interactions.

Promising Directions for Research

Currently, there is limited evidence supporting the effectiveness of rehabilitation programs for patients with cancer. When it comes to

assessing the effects of these interventions on pain, the small to moderate effect sizes are often the result of a combination of interventions. This is a major limitation of our research efforts, as it is difficult to translate the results into meaningful conclusions. A comparative intervention or standard treatment can provide pain relief, but they can also lead to small effect sizes. In clinical trials, non-responders and responders can be identified. For instance, if the intervention is not targeted to a specific pain mechanism, they can be included in the study. This could result in small effect sizes at the group level. In order to avoid this, research should balance the demands of a pragmatic approach with the need for standardized conditions. It is important to diagnose and identify the primary pain source in order to treat it properly. However, the exact clinical guidelines for this procedure are not yet validated (Adriaenssens, N.; et al. 2018) (471). There were many studies that did not explore the link between pain and cancer. It was unclear whether it was a symptom of the disease or a side effect of treatment. Cancer usually spreads through the body, so it is not surprising that pain would be associated with the disease. This paper aims to provide a comprehensive analysis of the various aspects of pain in cancer patients and survivors.

In the future, it should be known that pain is a symptom of cancer when it is diagnosed. This is because the various treatment modalities that are used for the disease, such as hormone therapy and radiotherapy, can have long-term side effects. It is sometimes hard to differentiate between neuropathic or non-neuropathic pain depending on the subtype. Different rehabilitation techniques that are tailored to the specific pain mechanism can lead to larger effect sizes (Kumar, S.P.; et al, 2013) (472).

Besides a diagnosis of a patient's pain condition, a comprehensive assessment is also needed to help design effective rehabilitation programs. According to the IMMAPACT initiative, six core outcome domains should be considered when it comes to developing clinical trials that focus on pain management. Participants are assessed in these domains according to their various dimensions of pain, physical functioning,

emotional functioning, and satisfaction with their treatment. They also report experiencing adverse events and symptoms (Dworkin, R.H.; et al. 2005) (473). In order to understand the concept of pain, it is important that the outcomes include both the impairment and the functioning of the patient. This is because, in order to reduce the intensity of pain, rehabilitation programs should focus on improving the daily functioning of the patient. Although generic outcome measures can be useful in assessing the effects of various interventions on the quality of life, they do not detect subtle changes in the perception of pain. Further studies are needed to determine the role of psychosocial factors in the response to pain and how they can be influenced by rehabilitation programs. It is also important that the rehabilitation programs are designed to sustain the patient's recovery. This is because the longer the patient's recovery, the better it is for the patient. In addition to the high burden patients have, it's also important to consider how the socio-economic impacts of pain are affected by cancer treatment. The number of individuals with long-term leave and reduced working hours following cancer treatment has increased. Low self-efficacy, perceived physical functioning, and pain are some of the factors that can delay a person's return to work (Mehnert, A. et al. 2011, Sun, Y.; Shigaki, et al. 2017) (474,475).

The cost of rehabilitation can be substantial for a health care system. It is therefore important that the various aspects of rehabilitation are analyzed in order to improve the effectiveness of this treatment. New developments in rehabilitation technology can also lead to the development of effective treatment methods for cancer patients. For instance, the effects of virtual reality on the rehabilitation of children with spinal cord injury are promising. It may be beneficial for cancer patients to have a break from their pain to improve their participation and motivation in their treatment (Maggio, M.G.; et al. 2019, Pozeg, P.; et al, 2017, Arane, K.; et al, 2017, Yeo, E.; et al, 2017) (476,477,478,479).

There is now a lot of evidence supporting the use of certain drugs in certain types of cancer, such as breast cancer. However, more trials are

needed in other cancer populations to confirm their effectiveness. For instance, rehabilitation for pain patients in advanced cancer may need to be changed in certain settings.

Conclusion

There are many recommendations and studies about the benefits of exercise for breast cancer survivors. It has been known that regular exercise can improve quality of life and ward off various side effects of treatment. However, there are varying outcomes depending on the level of activity and intensity. Although aerobic fitness can increase a person's chances of survival, a high amount of activity does not necessarily translate into better quality of life. There is evidence supporting the positive effects of exercise on fatigue, and systematic reviews and randomized clinical trials have confirmed this (Adamo R, et al, 2016) (480). It is now up to rehabilitation clinics to integrate the various exercise programs into their daily practice. Although there are numerous studies supporting the benefits of exercise, there are still gaps in the evidence.

Our results showed an improvement in quality of life and symptoms after rehabilitation within the experimental group with improvements significantly better than those in the control group, thus demonstrating the program's benefits. The results of our study therefore encourage the establishment of exercise and rehabilitation programs for breast cancer patients to improve their long-term quality of life and the management of adverse events

Following surgery, rehabilitation should begin immediately. This can be done regardless of the type of operation performed, such as a quadrantectomy or a mastectomy. Patients should aim to regain their strength and control their pain using the range of motion of their upper limb. It is also important to consider the importance of having a correct posture at a later stage. Research has shown that rehabilitation can help prevent or minimize the effects of breast cancer treatment. Active

exercises and multi-factorial physical therapy can help patients recover faster and improve their quality of life after surgery. The increasing survival rate following breast cancer surgery has prompted the need for more effective rehabilitation programs for both short and long-term follow-up. This is especially true in the upper limb, as there is a need for standardized protocols. According to the literature, the prevalence of shoulder pain has increased significantly over the years. Muscle strength and range of motion also decreased (De Groef A, et al. 2015, Lee TS, et al. 2008, Haddad CA, et al. 2013, Testa A, et al. 2014) (481,482,483,484). The use of rehabilitation techniques should be based on a multidisciplinary approach to managing pain. In order to increase the evidence, large clinical trials are needed to confirm the effectiveness of these procedures. These studies should also include the evaluation of other outcomes related to the patient's pain. Although there is evidence supporting the benefits of exercise for breast cancer survivors, the exact effects of physical activity on cognitive impairment are not well understood. More studies are needed to confirm the effectiveness of exercise on this issue. Numerous interventions and exercise programs are also aimed at improving the quality of life for people with this condition. The methodology used in studies varies significantly. Also, the effectiveness of scientific approaches has to be checked in practice. A number of studies conducted on the effects of physical activity on breast cancer survival and recurrence have found that it can reduce the risk of cancer returning. However, the exact mechanisms by which exercise can prevent cancer recurrence are still unclear. For patients, this doesn't mean that exercise programs are designed to prevent cancer from recurring. Instead, they are designed to improve the quality of life and reduce the side effects of cancer treatment (Do J, et al, 2015) (485).

Although there are various recommendations that are designed to help patients improve their quality of life, therapists should also consider the individual goals of their patients. In addition to being able to provide effective and personalized exercise programs, doctors, nurses, and therapists play a vital role in helping patients prevent cancer from

returning (Loprinzi PD, et al. 2012) (486). Besides being able to provide a personalized exercise program, therapists can also help patients develop a supportive environment. They can additionally help them maintain their level of physical activity by encouraging them to participate in rehabilitation programs. Although the recommendations for exercise for cancer survivors are still based on a specific target, many patients still fail to meet these recommendations. For instance, they should maintain a total of 15 metabolic equivalents per week or 150 minutes of moderate exercise per week. Guidelines for physical activity should also consider the preferences of cancer survivors when it comes to creating programs that are personalized. Having a wide range of options and varying programs is very important for patients (Basen-Engquist K, et al. 2017) (487).

There is a need for more controlled and randomized studies to improve the evidence supporting the use of physical activity in the management of breast cancer. These studies should also look into the biological mechanisms that underlie this benefit. Personalized programs that can help patients improve their lifestyle after breast cancer treatment should be considered as the main approach in rehabilitation. More studies should also be conducted in these clinics as the evidence related to physical activity is most relevant there. Physical activity can be integrated into regular breast cancer care, and it should be adapted to the individual needs of survivors. The rehabilitation guidelines should be adjusted to account for the varying needs of patients. In addition to supporting the use of good evidence, rehabilitation institutions should also encourage the development of new approaches to improve the quality of care.

The number of nausea, retching, and vomiting episodes decreased significantly in the intervention group compared to those in the control group. The results indicated that exercise can help reduce the severity of chemotherapy-induced nausea. Similarly, a study conducted on patients with a type of cancer called nasopharyngeal cancer, Soriano and colleagues discovered that the intensity of nausea before and after a

combination of relaxation and deep breathing was different (A. Suryono, et al. 2020) (488). In another study, Isa, Hayama, and colleagues noted that regular exercise can improve the quality of life for prostate cancer patients. They also found that calming down the patients' anxiety and fatigue levels through deep breathing can help decrease their symptoms of the disease. In a study, Yoo and colleagues noted that imagination and relaxation exercises can help ease the symptoms of chemotherapy-induced nausea in breast cancer patients. In a meta-analysis, Luebbert and colleagues noted that these types of exercises significantly decreased the nausea and vomiting symptoms.

Clinicians should make sure to provide survivors with clear information about exercise, as well as avoid inactivity. They need to know that it is safe and beneficial at any stage of their lives, but they should start slowly. Physical or occupational therapy should be provided to those with specific limitations, while those with fewer restrictions should be directed to programs operated by community-based organizations. It is important to start slowly and steadily. An easy-to-use handout with exercise recommendations from the ACSM can help make the process easier for the survivors.

After a diagnosis, it is important that the survivors start taking part in restorative exercise to improve their quality of life and reduce their risk of experiencing adverse effects from their treatment. This can be done at any point in the progression of their illness. Aside from improving their physical health, exercise can also help them maintain their quality of life and improve their cognitive and emotional well-being.

This study revealed that regular exercise can help decrease the severity of nausea and improve the functional status and general quality of life of breast cancer patients. Our findings support the idea of incorporating rehabilitation methods into the treatment of cancer. As medical professionals, we have a vital role in managing the effects of chemotherapy on cancer patients. In addition to being able to identify

and treat nausea, we also have a responsibility to educate patients about the side effects of the treatment and provide them with training on breathing exercises.

Our findings also support the idea that this equine- assisted therapy is beneficial for breast cancer patients. There should also be studies comparing the various components of horse-assisted therapy, such as hippotherapy, therapeutic riding, and horse exercise. This will help in establishing the intervention's parameters and explaining the cost-effectiveness. The results of studies should not be taken lightly, and they should be treated with caution. For instance, the current evidence should be used as the basis for future studies. According to studies, there is a need to develop effective methods to help women manage their symptoms of premature menopause and other related conditions.

Clinical Implications

As the overall treatment of cancer improves, a new challenge arises which comes in the shape of cancer rehabilitation which runs alongside or after the treatment of cancer. Thus, cancer rehabilitation must be considered a multidisciplinary field, with doctors, therapists, and social workers, along with several others being involved depending on the needs of the patient. According to our data rehabilitation techniques such as manual therapy, equine assisted therapy and exercise therapy can be safely and effectively used during breast cancer treatment.

- Rehabilitation needs to be started as early as possible, in order to avoid toxic side effects of to treatment;
- Rehabilitation strategy needs to be planned out and executed by multidisciplinary team, including oncologist, rehabilitation specialist, surgeon, radiation oncologist, radiation oncologist, occupational specialist;
- Rehabilitation needs to be conducted by experienced personal;
- It is important for oncologists to highlight the importance of rehabilitation to their patients;

ბოლო კვირის განმავლობაში:	სრულებით არა	ოდნავ	საკმაოდ	ბლიერად
17. გეონდათ თუ არა ფაღარათი?	1	2	3	4
18. იყავით დაღლილი?	1	2	3	4
19. გიშლიდათ ტკივილი ხელს თქვენს ყოველდღიურ საქმიანობაში?	1	2	3	4
20. გეონდათ საგნებზე კონცენტრაციის პრობლემა, როგორც არის გაზეთის კითხვა ან ტელევიზორის ყურება?	1	2	3	4
21. გრძობდით დამაბულობას?	1	2	3	4
22. იყავით შეწუხებული?	1	2	3	4
23. ადვილად ღიზიანდებოდით?	1	2	3	4
24. გრძობდით დეპრესიას?	1	2	3	4
25. გიჭირდათ თუ არა რამის დამახსოვრება?	1	2	3	4
26. გიშლიდათ ხელს თქვენი ფიზიკური მდგომარეობა ან სამედიცინო მკურნალობა თქვენს <u>დაცხურ</u> ცხოვრებაში?	1	2	3	4
27. გიშლიდათ ხელს თქვენი ფიზიკური მდგომარეობა ან სამედიცინო მკურნალობა თქვენს <u>სოციალურ</u> აქტივობაში?	1	2	3	4
28. იწვევდა თუ არა თქვენი ფიზიკური მდგომარეობა ან სამედიცინო მკურნალობა ფინანსურ სირთულეს?	1	2	3	4

შემდეგი კითხვებისათვის, გთხოვთ, შემოხაზოთ ნომერი 1-დან 7-მდე, რომელიც საუკეთესოდ შეესაბამება თქვენს მდგომარეობას.

29. როგორ შეაფასებდით თქვენს კანმრთელობას საერთოდ ბოლო კვირის განმავლობაში?

1 2 3 4 5 6 7

ბალიან ცუდი

შესანიშნავი

30. როგორ შეაფასებდით თქვენი სიცოცხლის ხარისხს საერთოდ ბოლო კვირის განმავლობაში?

1 2 3 4 5 6 7

ბალიან ცუდი

შესანიშნავი

Abbreviations:

QOL – Quality of life;
PF - Physical functioning,
RF - Role functioning,
EF - Emotional functioning,
CF -Cognitive functioning,
SF -Social functioning,
FA- Fatigue,
NV - Nausea and vomiting ,
PA -Pain,
DY - Dyspnoea,
SL -Insomnia,
AP - Appetite loss,
CO - Constipation,
DI - Diarrhea,
FI - Financial difficulties;
CRF -cancer related fatigue;
HR-QOL - health related QOL;
DID -difference/indifference studies
AC -Adriamycin-Cyclophosphamide;
ADL – Daily living;
CRF- Cancer related fatigue;
WHO – World health organization ;
TENS – Transcutaneous electrical nerve stimulation;
RCT - randomized controlled trial;
EHRs- electronic health records;
ETH- Hormonal hormone therapy;
CAM - complementary and alternative medicine;
T-Ra - tumor necrosis factor alpha;
ACS -American Cancer Society;
NCCN – National Comprehensive Cancer Network;
CRCI - cancer-related cognitive impairment;
RTH –Radiation Therapy

BMT- blood and marrow transplant;
EORTC - European Organization for Research and Treatment of Cancer;
EAET -Emotional Awareness and Expression Therapy;
NICE - National Institute of Health and Care Excellence;
SAN- Spinal accessory nerve
MLT - Lymphedema treatment
BE – Breathing exercise
AIDP -Acute inflammatory demyelinating polyradiculoneuropathy
EAT - Equine-Assisted Therapy
MLT-manual lymphedema treatment.

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