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Review

Sexual Disorders in Breast Cancer Survivors

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Abstract

Breast cancer survivors (BCS) often experience sexual desire, interest, arousal, orgasm, and genitopelvic pain. Sexual difficulties are underdiagnosed and undertreated in BCS, despite their prevalence. This study sought to look into the primary studies that intervene on sexual dysfunction in BCS. In the absence of RCTs, observational studies on vaginal therapies were included. Regular and prolonged use of vaginal moisturizers has been demonstrated to reduce vaginal dryness, dyspareunia, and sexual discontentment. Diverse aspects of sexual health were consistently improved by sexual dysfunction educational and counseling therapy. Physical activity, transdermal testosterone, and hot flash therapy did not consistently improve sexual health. Regarding vaginal lubricants, vibrators, dilators, pelvic floor therapy, flibanserin, and ospemifene, no BCS-specific information was available. The evidence quality for these studies varied between high and poor. Due to the low efficacy of each of the treatments with BCS data, clinical studies are necessary to investigate new approaches in order to provide evidence-based therapy recommendations and improve sexual function in BCS.

Keywords: Breast cancer, chemotheraphy, hormonotheraphy, menopause, sexual dysfunction

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Breast cancer (BC) is the most frequent cancer in women across the world.[1, 2] In 2020, more than two million women will be diagnosed with BC.[1] Furthermore, one-eighth of all women will be diagnosed with BC throughout their lifetime.[2] Patients' life expectancy has grown in recent years as a result of advancements in cancer therapy.[1] This condition has resulted in new health issues for breast cancer survivors (BCS). As a result, there is a need to concentrate not just on patients' survival, but also on their long-term quality of life.

There is proof that BCS has the highest rates of disability-adjusted life years (DALY) loss among all forms of cancer.[3] The most important factor leading to this high DALY rate is sexual dysfunction (SD).[4, 5] The DALY index is a reliable health metric and status indicator that assesses the impact of medical interventions on patients' quality of life. The World Health Organization defines sexual health as "a positive and respectful attitude toward sexuality and sexual relationships, as well as the ability to enjoy pleasurable and safe sexual experiences free of compulsion, discrimination, and violence".[6] Sexual function includes sexual activity that is pain- and discomfort-free, as well as a sexual response in which desire, arousal, and orgasm are experienced without psychological difficulties.[7]

Sexual dysfunction might well be diagnosed according to psychiatric criteria when women demonstrate persistent (minimum six months) symptoms that cause significant personal suffering and a significant deterioration in their sexual life.[8-10] According to the symptoms, SD is divided into three categories: female sexual desire arousal disorder, orgasmic and penetration disorder, and genitopelvic pain. To complete this definition, it is important to mention that SD extends beyond physical symptoms and has significant implications for patients' mental and sexual well-being.

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The frequency of SD in breast cancer survivors varies from 40% to 83%, which is much higher than in healthy women. [10-12] As patients' survival improves, their symptoms worsen and their sense of well-being decreases.[10, 11, 13-15] Arousal or arousal difficulties, lower sexual attraction, poor lubrication, and penetration pain are the chief symptoms of SD identified by BC patients.[7, 11, 15]

Despite the fact that SD is a prevalent issue among BC patients, it is generally neglected in clinical practice. Because healthcare professionals are typically uncomfortable addressing sexual issues with patients.[16-18] In addition, oncologists are rarely trained in this field.[17, 19] Secondly, patients are frequently embarrassed to discuss sexual difficulties during BC-related visits.[20] As a result, BC patients are seldom offered sexual therapy, and sexual dysfunction is rarely considered.[13, 18] In these women, SD is still underdiagnosed and inadequately treated.[21]

The purpose of this study is to determine the prevalence of sexual dysfunction among BCS patients. This study also aims to examine treatment interventions that can minimize SD in BCS patients and highlight their significance in clinical practice. In this study, prospective randomized controlled studies, observational studies and retrospective studies evaluating SD in breast cancer survivors were reviewed. Other studies involving cancer types other than breast cancer were not included in this review.

Reasons for Sexual Problems in People with Breast Cancer

SD in breast cancer survivors cannot be explained by a single cause. Many different mechanisms play a role in the development of SD. Chief among these is the suppression of ovarian functions secondary to oncological treatment. Another factor is the patient and the patient's partner related psychological factors. A third factor is surgery and the decrease in organ functions secondary to surgery.

The procedure immediately affects body image, particularly in women who have undergone a mastectomy. This shift is exacerbated by the fact that breasts are regarded symbols of sexuality and sexual identity, as well as one of the most significant erogenous areas of the female body.[11, 22, 23] In addition to possessing a sexual organ, the woman's sense of psychological inadequacy plays a role in the process. As a result, surgery increases sexual dysfunction at the initiation of breast cancer therapy. Additionally, radiation treatment might produce changes in the breast, such as pain, discomfort, skin sores, or loss of flexibility.

Chemotherapy is a frequently preferred treatment method in breast cancer patients, and approximately three-quarters of patients with breast cancer are treated with chemotherapy.[24] Doxorubucin, taxanes, and especially cyclophosphamide, which is one of the frequently used chemotherapy agents, suppress ovarian functions. In addition, chemotherapy causes skin changes, hair loss, mucosal damage and bleeding disorders. For these reasons, it can be said that chemotherapy causes sexual dysfunction in many different ways. For example, liposomal doxorubucin has significant vaginal and rectal mucositis-forming effects.[25] Therefore, in patients receiving liposomal doxorubucin treatment, the patient should be informed about mucositis and information on SD should be given. Endocrine treatment, in addition to chemotherapy, is a typical therapeutic technique. Adjuvant treatment with tamoxifen and gonadotropin-releasing hormone (GnRH) agonists is used in patients with hormone-positive breast cancer. GnRH agonists suppress the patient's ovarian functions, decrease desire, and make effective sexual interaction difficult.

Intensive therapy, such as surgery, radiotherapy, chemotherapy and hormone therapy, has many side effects as we mentioned. But perhaps the key point in this process is the psychological fatigue caused by the disease, which lasts from the moment of diagnosis to the end of treatment. As a matter of fact, breast cancer treatment takes a relatively long time and the patient cannot fully recover psychologically due to the fear of recurrence.[26, 27] For this reason, it is of great importance to provide psychological support to the patient from the moment of diagnosis and to discuss sexual function disorders without hesitation.

There is scientific proof that women with SD have worse mental health.[13,14,21] Patients with SD feel embarrassed about their bodies, ugly, unloved, and refused by their partners.[14,19,21,45] There have also been changes in how people feel about their sexual selves.[14,15,21,22] Both the diagnosis of BC and SD might act as potential stresses for women, leading to a decline in their overall health and perhaps having a negative impact on the effectiveness of BC therapies and disease progression.[46] The mere fact of having BC may result in mental health deficits such as sadness, anxiety, or emotional discomfort.[11,13,14,21,30] SD may impact BCS partners as well. Partners may modify their attitudes during sexual encounters in order to prevent physical injury to women with SD.[14,45]

Evaluation of Sexual Dysfunction

Numerous scales have been used in the literature to assess the sexual function of patients based on the available data. [7, 28-30] Several research groups have developed and published new or modified versions of existing measures to assess sexual function in the BCS.[23] In addition, no validated scale exists to measure SD in patients with BCS.[23]

Although adaptations of many indices have been developed, the most accepted index today is the Female Sexual

Function Index (FSFI).[7] A recent systemic review of the optimal scale to assess SD concluded that the Arizona Sexual Experience Scale (ASEX) and Female Sexual Function Index (FSFI) were the most appropriate scales to use in the BCS.[7, 23, 30] The Female Sexual Dysfunction Index assesses the regions of desire, arousal, lubrication, orgasm, pleasure, and pain. Validation testing on women ranging in age from 21 to 70 revealed that each subscale had excellent internal consistency.[26] The Arizona Sexual Experiences Scale (ASEX) is a five-item rating scale that evaluates sex desire, arousal, vaginal lubrication/penile erection, capacity to achieve orgasm, and orgasm pleasure.[30]

Although the number of studies on SD is quite limited, FSFI has been used in most of them. A total of 201 patients were included in a study of young breast cancer patients in China.[10] Total mastectomy, endocrine therapy and chemotherapy were found to be independently associated with SD. In this study, the incidence of SD was found to be 83% in patients. In another study published in 2019, the relationship between the treatments received by breast cancer patients and SD was evaluated with FSFI.[22] While 278 of 600 patients were sexually active, it was found that aromatase inhibitors were the most common treatment for SD in these patients. In another observational study conducted in Denmark, the FSFI questionnaire was administered to 227 sexually active BCS patients.[31] While SD was detected in 139 (58%) of the patients, it was reported that the biggest complaint of the patients was vaginal dryness and psychosocial reasons. As a result, SD is frequently detected in BCSs and is overlooked. The FSFI is a simple questionnaire and has shown its effectiveness in many observational studies. Therefore, the frequent use of FSFI in BCS patients and the recommendation of treatment in patients with SD are of great importance.

Treatment in Patients with SD

Recently, a number of therapies have been recommended to control SD in BCS. However, a standard therapy for addressing SD in BC survivors has not yet been developed. There are both medical and non-medical treatments available as treatment options. This chapter will focus on these therapies.

Topical therapies for SD include vaginal application items such as moisturizers and lubricants. Polycarbopyl-based moisturizer,[32, 33] compounded testosterone cream,[34, 35] pH-balanced lactic acid gel,[36] and vaginal estrogens[37] were all tested. Evidence shows that certain SD symptoms, particularly discomfort during penetration and vaginal dryness, improve with local therapies. Although vaginal estrogens have been demonstrated to increase sexual performance more successfully than moisturizers, they have also been shown to have systemic absorption.[38] Furthermore, information from studies in healthy women and women with other causes of sexual dysfunction suggests that using vaginal vibrators improves numerous aspects of patients' sexual function, notably desire, arousal, lubrication, orgasm, and pain and is a valuable tool for anorgasmia.[39, 40] The usage of a vaginal vibrator might even help with genitopelvic discomfort and dyspareunia.[40, 41] Despite the possible utility of vibrator stimulation as an SD treatment, no trials with BC patients have been undertaken to yet. In a meta-analysis evaluating local treatments, no clinical studies were identified with lubricants, DHEA, vibrators and dilators.[42] Polycarbopyl-based moisturizer has been shown to improve complaints such as dryness, but its effectiveness has been found to be lower than estrogen-based creams.[43] As mentioned above, estrogen-based creams have been found to increase serum estrogen levels.[44] The effectiveness of vaginal compounded testosterone, another local treatment, was tested in two different studies.[45, 46] After four weeks of treatment, there was a decrease in SD symptoms according to FSFI in patients using vaginal compounded testosterone. In addition, it was observed that this treatment did not have an effect on increasing serum estrogen levels.

To increase sexual function, systemic androgens, antidepressants, ospemifene, and flibanserin might well be administered. There are no clinical data on ospemifene or flibanserin in the published literature. There are few clinical research on antidepressants and androgens. In the single trial, including the daily application of testosterone cream on the skin for one month, testosterone in BCS did not increase sexual desire, pleasure, or function compared to a placebo cream.[47] Consistent with earlier studies in women without a history of breast cancer, the use of testosterone cream did not lead to an increase in serum estradiol levels.[48-50] Two further trials comprising 115 people explored whether sexual function improved with venlafaxine, clonidine, or bupropion in relation to hot flashes as the main outcome.[51, 52] There was no change in sexual function between women treated with venlafaxine, clonidine, bupropion, or placebo.[52] In conclusion, there is no known systemic medication that provides an advantage over a placebo in resolving SD in BCS.

The effects of physical exercise treatments on hot flashes, lymphedema, physical strength, and sexual function were studied in three randomized clinical studies. All patients in these trials have completed primary therapy for breast cancer. No research have been conducted on pelvic floor physical therapy. As judged by the FSFI Questionnaire, a home-based, self-administered exercise program did not enhance sexual habit, frequency, or discomfort in over four hundred BCSs. At six months, cognitive behavioral treatment with or without exercise had a minor impact on the

improvement of sexual health habits. More than one year of strength training was related with a modest change in self-perceptions of appearance and sexuality in a second study with 295 individuals.[53] In around 200 cancer survivors, general physical exercise did not alter the occurrence of sexual issues.

Educational therapies and counseling have been examined in a number of studies as a therapy for SD in BCS. The impact of sexual therapy on SD during medical visits was studied. SD symptoms have been shown to reduce after educational therapies that highlight sexual characteristics of BC.[54, 55] Couple sex therapy, which has been shown to enhance communication in many aspects of SD and cancer, has also been shown to improve SD.[56, 57] As a result, it seems that SD does not improve when psychological treatments are not focused on sexual issues.[58, 59]

Discussion

Advances in breast cancer treatment have allowed patients to survive longer. Long-term health problems connected with the identification and treatment of BCSs have emerged as a result of longer survival. BCS patients should be continuously monitored for quality of life and psychological issues, as well as for malignant disease. SD is a BCS complication that is usually neglected. In addition to its common occurrence, SD frequently remains unresolved since it is rarely questioned. This topic is not well addressed during oncology visits, and it is regarded as taboo. On the contrary, it is necessary to inform patients about sexuality before treatment and to offer them medical and psychosocial treatment for any SD that may develop.

It is not possible to make a single decision about sexuality by melting all patients in a single pot. As a result, some specific scales for assessing the quality of sexual life are required. FSFI has been the most widely accepted scale among these, and most studies in the literature have been done with FSFI.[7] In various studies, FSFI and SD were evaluated in BCS, and the prevalence of SD was found to be between 40% and 83%.[10] The differences in these rates between studies can be explained by the level of education, the use of different treatment modalities, and different socioeconomic conditions. As a result, physicians conducting studies in different countries to evaluate the patient population they serve would be inaccurate. Perhaps in oncology practice, periodic use of FSFI with BCS may be a standard approach. In this way, they will be able to determine the incidence of SD in their own patients, and they will have a chance to treat SD-related problems earlier. In this way, oncologists will be able to increase the patient's treatment compliance and be able to treat the patient's psychological and social problems early.

Although SD is not usually questioned in BCS, it is expected to be common. Because almost all of the patients have lost an organ that directly affects female sexuality and sexual activity. On the other hand, patients are under the great psychological stress of being diagnosed with cancer. In addition, the deterioration of the external appearance can bring about a feeling of inadequacy in the BCS. In a study, the most common causes of SD in BCS patients were found to be fear of cancer recurrence and low self-confidence.[17] Additionally, many women do not find themselves attractive and feel that their partner does not desire them. Furthermore, during sexual activity, the patient's anxiety about SD may make it difficult for him or her to be shy, express desire, arousal, bond with the partner, and enjoy sexual intercourse.[23] All these factors put the patient in a vicious circle and increase SD even more.

Moreover, cancer treatments (surgery, chemotherapy, radiation therapy, endocrine therapy) have a negative impact on the sexual life of women, manifesting as physical symptoms such as fatigue, joint pain, penetration pain, decreased libido, and difficulty arousing. Despite the prevalence and severity of SD, there are currently no clear, standard therapeutic approaches for these patients. Given the multifactorial nature of SD and its impact on a variety of aspects of patients' quality of life, pharmacological and psychological strategies can be combined to provide appropriate treatment options. The use of vaginal moisturizers should be considered in conjunction with sexually-focused psychological therapy. In addition, the incorporation of mechanical stimuli (vibrators, dilators) in local therapy might have been advantageous, but it is not widely used and should be a future research focus.

In conclusion, SD in BCS is a common and often underestimated clinical problem. Patients should be informed before oncological treatments and further questioned afterwards. Efforts should be made to eliminate SD problems in these patients with current local treatment agents, physical exercises, or psychological counseling. There is a need for additional studies in which the efficacy of combination therapies will be evaluated and treatment efficacy will be presented.

Disclosures

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