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VIEWPOINT
Breast

Breast Cancer Survivorship: Understanding Breast Tissues' Potentiating Role in Precipitating Deviations from Baseline Sexual Function Post Oncologic Resection

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In recent decades, notable progress in diagnostic modalities, pharmacotherapeutics, and operative treatments has resulted in declining rates of breast cancer mortality, thereby increasing breast cancer survivorship.[1] As conventional patient outcomes (eg, complications, morality) improve, focus has shifted toward merging patients' perception of their health, by assessing patient-reported outcomes [eg, health-related quality-of-life (QoL), patient satisfaction], with traditional clinical outcomes, contributing to the advancement of person-focused care. The BREAST-Q, a validated patient-reported survey examining three QoL domains (eg, psychosocial, physical, and sexual well-being) in women undergoing breast surgery, is an example of such patient-reported outcomes assessment instruments.[2] Historically, sexual well-being, defined as the complex, dynamic biopsychosocial identity that is unique to each individual, following breast cancer treatment has been insufficiently addressed by medical practitioners. Understanding sexual well-being necessitates a granular approach and continual assessment by clinicians to further characterize all the contributing factors affecting an individual's sexual well-being.

Deviations from an individual's baseline sexual function is a significant, multifactorial postoncologic treatment-related morbidity that directly impacts the health status of breast cancer survivors. Deviations may be attributed to psychologic, biologic, iatrogenic, and/or interpersonal factors. [MOU1] For example, the effects of oncologic treatments, including chemotherapy, radiotherapy, and surgery, may cause iatrogenic-induced sexual dysfunction (Table 1). Estrogen deprivation secondary to oncologic pharmacotherapy catalyzes iatrogenic-induced menopause (eg, vaginal dryness, dyspareunia, reduced libido), potentiating deviations from baseline sexual function, ultimately affecting overall sexual health.[3] Given that patients are often concurrently exposed to several aforementioned factors, it is difficult to isolate the specific effects of individual factors on sexual well-being.

Although oncologic and reconstructive surgery is concerned with achieving curative treatment while retaining/restoring form and function, breast cancer surgery primarily focuses on treatment and restoring form. However, recent literature examining how postoperative breast sensation impacts sexual well-being demonstrates the paradigm shift toward retaining/restoring patients' functional outcomes.[4] Previous research investigating sexual well-being in breast cancer survivors characterizes the impacts of pharmacotherapy, surgical intervention type (eg, BCS versus mastectomy), breast reconstruction status/type/timing, and other psychosocial factors on sexual well-being (Table 2). Although significant evidence has illuminated the role of pharmacotherapy and psychosocial factors on sexual well-being, limited literature exists examining how resection of molecularly active breast tissue modifies baseline, physiologic sexual function/well-being.[5]

Recent evidence suggests that individuals undergoing less-invasive breast cancer resections may retain better function outcomes, improving overarching sexual well-being following treatment.[4] Although researchers characterize these findings to denote that larger resections of breast tissue influence sexual well-being secondary to adversely impacted self-esteem/image,[4] these findings are limited in scope, overlooking the fact that native breast tissue itself may have a direct impact on sexual well-being. Our understanding of the physiologic and molecular processes performed by breast tissue in relation to maintaining baseline sexual well-being is unspecified. Although psychosocial factors have been documented as contributing significantly to sexual well-being, it is important not to overlook the possible biologic and molecular underpinnings that may be exacerbating this morbidity.

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Table 1. Common Oncologic Treatment Modalities for Breast Cancer and Their Side Effects

Breast Cancer Treatment Modality	Examples of Treatment Modalities	Treatment-related Adverse Effects
Surgical intervention	Lumpectomy (unilateral versus bilateral), oncoplastic breast surgery, mastectomy (unilateral versus bilateral, nipple sparing versus skin sparing, partial versus modified radical versus radical; with immediate breast reconstruction versus delayed breast reconstruction versus no breast reconstruction, sentinel lymph node biopsy, and/or axillary lymph node dissection	Disfigurement and/or total removal of erogenous breast tissue, loss of sensory innervation, lymphedema
Radiation therapy (radiotherapy)	External beam radiation (whole breast radiation, accelerated partial breast radiation, proton beam radiation) and internal radiation (seed brachytherapy). Implemented as a part of breast conservation therapy (BCT) (eg, lumpectomy followed by whole breast radiation) and postmastectomy.	Skin fibrosis and wound healing issues, pain, discoloration, iatrogenic menopause, changes in sensation
Chemotherapy	Docetaxel, cyclophosphamide, doxorubicin, paclitaxel, methotrexate, fluorouracil, carboplatin, etc. Therapies are often utilized in combination as a treatment regimen (eg, doxorubicin and cyclophosphamide [AC], docetaxel and cyclophosphamide [TC], etc)	Hair loss, gastrointestinal distress, mucosal ulcerations and bleeding, cardiac effects, fatigue, easy bruising, numbness and tingling
Hormone therapy	Selective estrogen receptor modulators (SERMs; eg, Tamoxifen, Raloxifene, Clomiphene); aromatase inhibitors (AI; eg, Anastrozole, Letrozole, Exemestane); Gonadotropin releasing hormone agonists (GnRHa; eg, Goserelin, Leuprolide)	Vaginal dryness, hot flashes, reduced libido, menopause, headaches
Immunotherapy and molecular targeted therapy	Pembrolizumab, dostarlimab-gxly	Infusion reaction (fever, chills, gastrointestinal distress, fatigue, skin rash

Table created with data from *JAMA*. 2019;321:288–300.[6]

Table 2. Prior Literature Assessing Sexual Well-being after Breast Cancer Postoncologic Treatment

Author, Year, Origin, & Source	Title	Study Design & Sample	Summary of Findings Related to Sexual Health/Function
Alder et al., 2008[7] Switzerland *The Journal of Sexual Medicine*	Sexual dysfunction after premenopausal stage I and II breast cancer: do androgens play a role?	Retrospective study 29 patients with premenopausal breast cancer, stage 1 & 2, terminated adjuvant therapy.	Chemotherapeutics causes sexual dysfunction, affecting arousal, lubrication, and pain
Aerts et al, 2014[8] Belgium *The Breast*	Sexual functioning in women after mastectomy versus breast conserving therapy for early-stage breast cancer: A prospective controlled study	Prospective control study 149 women with breast cancer and 149 age matched controls were enrolled. Experimental group evaluated before surgery (n = 149), 6 months postsurgery (n = 129), and 1-year postsurgery (n = 114)	Individuals receiving BCS had decreased rates of sexual dysfunction and greater sexual adjustment postsurgery compared with women undergoing mastectomy
Whelan et al, 2010[9] Canada *The New England Journal of Medicine*	Long-term results of hypofractionated radiation therapy for breast cancer	Randomized control clinical trial 1234 patients enrolled in the trial. Control group (n = 612). Experimental hypofractionated-radiation group (n = 622)	Both accelerated, hypofractionated and standard radiation therapy regimens resulted in a worse cosmesis outcome over time
Broeckel et al, 2002[10] United States *Breast Cancer Research and Treatment*	Sexual functioning in long-term breast cancer survivors treated with adjuvant chemotherapy	Retrospective study 119 participants. Control group; individuals without breast cancer (n = 61). Experimental group; individuals with a history of breast cancer treated with neoadjuvant chemotherapy (n = 58)	Compared with control, survivors of breast cancer treated with chemotherapeutics reported higher rates of sexual dysfunction, including low libido, anorgasmia, and vaginal atrophy

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