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Clinical Expert Series CME

Sexual Health in Women Affected by Gynecologic or Breast Cancer

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Sexual health problems are prevalent among women affected by gynecologic or breast cancer. It is important to understand the effects cancer treatment can have on sexual health and to have the tools necessary to identify and treat sexual health problems. This Clinical Expert Series discusses practical methods for routinely screening for sexual dysfunction and reviews sexual health treatment options for women affected by cancer. We review the limitations of the current literature in addressing sexual health problems among sexually and gender minoritized communities. Finally, we discuss appropriate timing of referrals to sexual health experts, physical therapists, and sex therapists. Multiple resources available for both patients and clinicians are included.

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In the United States, one in three women will be diagnosed with cancer during their lifetime.[1] With the significant advances in cancer treatment modalities, there has been an overall decline in cancer-related deaths, and patients are living longer during and after cancer treatment. According to the National Cancer Institute, in 2019 there were an estimated 16.9 million cancer survivors in the United States, and that number is projected to increase to 22.2 million by 2030.[2] In turn, quality-of-life and survivorship issues have become increasingly important.

Sexual dysfunction is one of the most common consequences experienced by women with cancer during and after treatment.[3–5] Cancer treatment modalities, including surgery, chemotherapy, endocrine therapy, radiation, and targeted therapies, can adversely affect sexual function, which can be further exacerbated by the psychological and interpersonal effects of cancer. The National Comprehensive Cancer Network's (NCCN) survivorship guidelines specifically provide guidance on suggested treatment options and referrals for patients experiencing sexual dysfunction (see the "Screening for Sexual Dysfunction" section). Clinicians caring for people with ovaries and other female reproductive organs, including obstetrician–gynecologists, are a critical part of the interdisciplinary team. Although most people with cancer will experience at least one symptom related to sexual dysfunction, symptoms and their severity can vary depending on cancer type and treatment modality. Specifically, sexual dysfunction has been reported to be as high as 90% among people diagnosed with gynecologic cancer and higher than 70% among those diagnosed with breast cancer.[6–9]

This Clinical Expert Series will review the etiologies of sexual dysfunction and the physical and psychosocial effects of cancer treatment on sexuality specifically in patients diagnosed with primarily gynecologic or breast cancer. Strategies for the evaluation and management of sexual dysfunction are included (Fig. 1).

SEXUAL AND GENDER MINORITIZED COMMUNITIES

Sexual and gender minoritized (SGM) communities include individuals who define their sexuality as other than heterosexual and gender as other than cis-male or cis-female. As such, it is a large umbrella that comprises

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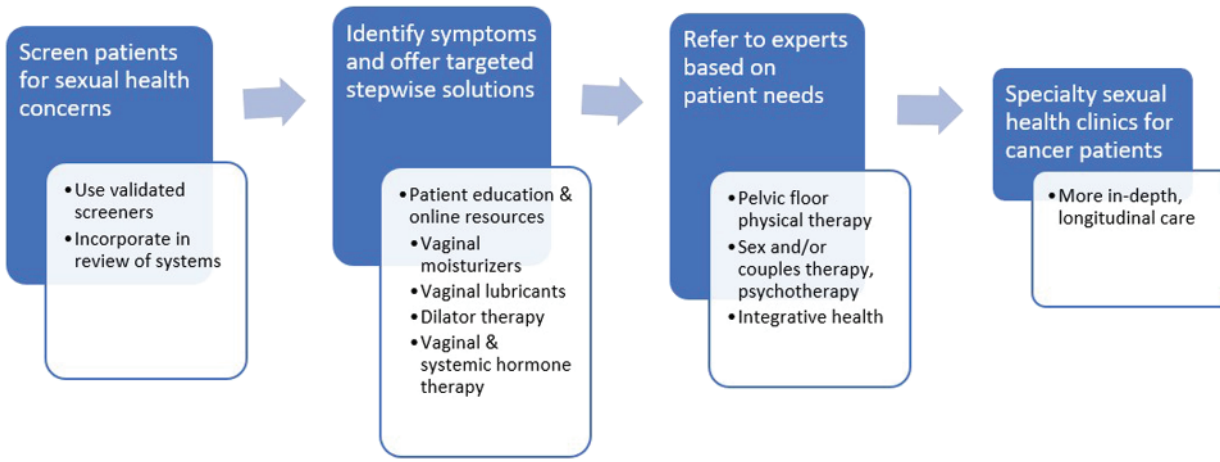

Fig. 1. The approach to sexual health needs among patients with cancer.
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individuals with both similar and very different considerations when it comes to sexual health. Much of the literature on this topic is heteronormative; as such, our understanding of the experiences of patients with cancer and their subsequent survivorship needs, especially as they relate to sexuality, is limited.

Efforts to address the needs of SGM people are underway. The National Academies of Science, Engineering and Mathematics recently called for the routine collection of sexual orientation and gender identity data across National Institutes of Health–sponsored efforts[10]; within oncology, many organizations, including the American Society of Clinical Oncology (ASCO)[11] and the Society of Gynecologic Oncology,[12] are highlighting disparities experienced by SGM people in cancer care.

As they relate specifically to sexual health, the data suggest that the questionnaires used to evaluate sexual function after cancer are not adequate. This was perhaps best illustrated in a study that included cognitive interviews of 27 SGM people gauging their perceptions about the FSFI (Female Sexual Function Index), a commonly used sexual function questionnaire.[13] Volunteers perceived the FSFI as a fairly narrow, heteronormative experience of penile-vaginal intercourse. Issues around emotional closeness, lubrication, and orgasm were all areas that appeared not as important to SGM patients. Therefore, it is unclear which aspects of this clinical expertise series will be applicable to SGM communities and highlights the need for more work in this area.

DEFINITION OF SEXUAL DYSFUNCTION AFFECTING WOMEN WITH CANCER

The *Diagnostic and Statistical Manual of Mental Disorders*, 5th Edition, Text Revision (DSM-5-TR) classifies female sexual dysfunction into three broad categories: sexual desire and arousal disorders, orgasmic disorders, and sexual pain disorders. In the DSM-5-TR version, the key differences from the DSM-5 are that sexual aversion disorder is no longer considered a classification, desire and arousal disorders are grouped together, and dyspareunia and vaginismus are grouped together.[14] However, in practice, sexual health among women diagnosed with cancer is often more complex than the DSM-5-TR classifications. For example, the role of intimacy, discussed in further detail below, plays a large part in sexual health and is crucial when addressing sexual health problems, yet it is not included in the DSM criteria.

UNDERSTANDING THE IMPORTANCE OF INTIMACY

Intimacy is an inherent part of sexuality that includes both physical and emotional components. It is not synonymous with sexual activity, including penetrative intercourse. Yet, its importance in the sexual lives of people after cancer often is unaddressed because of the emphasis of oncologists and other medical clinicians on coital relationships, which often assumes penile-vaginal intercourse, itself a heteronormative construct that negates the importance of intimacy itself.[15] Basson goes so far as to illustrate that intimacy is experienced separately from stimulation, arousal, desire, and satisfaction, which explains more fully that it can be experienced as a distinct experience that does not rely on sexual intercourse.[15]

Perz et al[16] conducted a methodologic study around the constructs of sex and intimacy that involved interviews with health care professionals in oncology and people with cancer and their partners.

They found that both men and women adapt sexually to their cancers and that, for both, maintaining closeness becomes more important than navigating sexual intercourse.

CANCER TREATMENTS LEADING TO CHANGES IN SEXUAL FUNCTION

Sexual function problems among women living with or surviving cancer are common, with the highest prevalence in women with gynecologic cancers (78%).[17] Sexual health may be affected by cancer and its treatments, including surgery, chemotherapy, radiation, immunotherapy, and hormonal therapy. However, the psychosocial and mental health effects of cancer can also affect sexual function. Sexual challenges can present in various ways depending on the type of treatment, sexual health before cancer diagnosis, coexisting urinary or gastrointestinal disorders, coexisting medical comorbidities, anxiety or depression, cultural concerns, and history of trauma.

Despite being highly prevalent, sexual health problems often are not adequately addressed, particularly in gynecologic and breast cancer survivors.[18–20] The majority of gynecologic cancer survivors believe that physicians should regularly ask about sexual issues.[18] Understanding the effects that a cancer diagnosis can have on sexual health and the potential negative effects of surgeries, radiation therapy, and systemic therapy is the first step to addressing the issues.

Sexual Dysfunction After Surgery

Patients with gynecologic and breast malignancies often will undergo surgery as part of their treatment, which may negatively affect sexual health and quality of life.

Radical Hysterectomy

Radical hysterectomy is the standard treatment for early-stage cervical cancer and is performed occasionally for endometrial and ovarian cancers. In the short-term, patients may experience difficulty with orgasm, vaginal shortening, dyspareunia, lymphedema, genital numbness, and sexual dissatisfaction after radical hysterectomy.[21,22] In the long-term, patients can have a lack of sexual interest, lymphedema, genital numbness, and insufficient vaginal lubrication.[23,24] Additionally, radical hysterectomy can affect bowel and bladder function, with indirect negative effects on sexual function.[24] Disruption of the hypogastric and splanchnic nerve plexuses during surgery may be the cause; nerve-sparing radical hysterectomy has shown improvements in short-term and long-term bowel and bladder function, as well as improved sexual function, with similar oncologic outcomes when compared with traditional radical hysterectomy.[25]

Oophorectomy

The removal of the ovaries at the time of surgery for ovarian and endometrial cancer can cause hormonal changes resulting in sexual health and menopausal symptoms, even if the patient is postmenopausal at the time of surgery.[26] The changes in hormones can lead to decreased sexual desire.[27] Premenopausal patients with ovarian cancer who undergo oophorectomy are at highest risk for abrupt and severe onset of menopausal symptoms and experience less sexual pleasure than postmenopausal patients.[28]

Vulvectomy With and Without Lymphadenectomy

Vulvar surgery has been associated with problems with sexual function and psychological sequlae.[29,30] The vulva, which includes the clitoris and the labia, is a sexual organ. The removal of a portion of the vulva can affect body image and lead to pain with intercourse.[31–33] The anatomical changes that might occur because of surgery include vaginal narrowing, numbness along the scar, removal of the clitoris, and change in tissue quality.[31] A study by Gunther et al reported that patients who were not sexually active after radical vulvectomy cited genital complications from their surgery as the reason for abstinence.[34] Data are conflicting regarding whether more extensive vulvar excisions are associated with poorer sexual function. Resection or laser of the clitoris is associated with significantly more problems with arousal compared with vulvectomy in patients in whom the clitoris was spared.[18,34,35]

Traditionally, complete groin dissections have been part of the surgical management for many vulvar cancers and carry a 30% risk of lymphedema.[36] Lymphedema is associated with a decreased quality of life and sexual function; thus, it is important to identify lymphedema symptoms early and begin treatment in a timely fashion.[37]

Breast Surgery

The breast itself is a sexual organ and often is important for sexual stimulation, arousal, and a positive body image. Surgery for breast cancer is associated with detrimental effects across multiple domains of sexuality, also coined "breast-specific sensuality."[38–40] Gass and colleagues conducted a survey using a convenience sample of women in follow-up after breast cancer treatment. Regardless of surgical

procedure, 80–90% of patients reported that the chest or breast was important for sex and intimacy. After surgery, the importance of the chest or breast for sex and intimacy decreased to 74% in patients who underwent lumpectomy, 77% in those who underwent mastectomy with reconstruction, and 47% in those who underwent mastectomy without reconstruction.

Sexual Dysfunction After Radiation Therapy

Radiation therapy (RT) to the pelvis is used routinely in cervical, endometrial, and vulvar cancers and is associated with vaginal stenosis, vaginitis, ulceration, scarring and fibrosis, atrophy, and premature menopause leading to problems with sexual function, particularly dyspareunia.[41] When compared with chemotherapy, RT has a greater negative effect on body image, sexual dysfunction, and loss of sexual interest due to poor self-esteem.[42]

Vaginal stenosis is a subacute-to-"late" effect of RT that can occur weeks to months after treatment. The incidence of vaginal stenosis increases over time and can result in permanent vaginal changes, including adhesion formation and vaginal shortening.[43–46] The secondary effects of RT are related to repair mechanisms in the irradiated tissue, which can lead to vaginal wall thickening and subsequent narrowing of the vaginal canal. Late effects may continue up to 20 years after RT but typically do not worsen or develop until after 5 years.[47]

Sexual Dysfunction After Chemotherapy

Patients with gynecologic malignancies often will receive chemotherapy, as will select patients treated for breast cancer. Whether it is neoadjuvant, adjuvant, sensitizing, or in the recurrent setting, chemotherapy is associated with high rates of sexual dysfunction.[48,49] However, there have been few studies to date examining sexual function problems while women are actively receiving chemotherapy.[50,51] A study by Kulkarni et al[48] evaluated sexual function among women receiving systemic therapy for gynecologic cancers in the upfront or recurrent setting. They found that only 49% of patients surveyed were sexually active in the prior year and just 24% in the prior month. Additionally, sexual dysfunction was prevalent among both groups, including 62% of patients in the upfront treatment group and 72% of those in the recurrent treatment group. Despite the high rates of sexual inactivity and sexual dysfunction, the majority of patients (67%) had a desire for sexual activity in the future.

Buković et al investigated sexual function among three groups: those with early-stage ovarian cancer having surgery alone, those having both surgery and chemotherapy, and those with advanced ovarian cancer receiving chemotherapy only.[49] They found that sexual satisfaction decreased in all patients after treatment but was more pronounced in the groups receiving chemotherapy.

HOW TO ADDRESS SEXUAL HEALTH AMONG WOMEN WITH CANCER

There are multiple steps needed to adequately address sexual health problems among women with cancer (Fig. 1). The first step in addressing sexual health among women with cancer or in remission is to screen.

SCREENING FOR SEXUAL DYSFUNCTION

Cancer Care Ontario issued guidelines recommending that sexual health be addressed by the health care team at the time of diagnosis and reassessed at designated follow-up intervals. These guidelines have been endorsed by ASCO.[47,52] Yet, the majority of patients with cancer have not been asked about sexual dysfunction during their cancer care.[4,52,53] Barriers to discussion are both patient- and clinician-driven. For patients, there may be fear or misperception that the discussion will be uncomfortable for their care team, that their concerns will be dismissed, that are no adequate treatments, or that this is just an expected consequence of cancer and its treatment. Further, many patients feel that the topic should be initiated by their clinician.[4,54,55] Reasons that many clinicians fail to discuss sexual health include lack of time, lack of comfort with or training on the topic, and a perceived lack of resources.[56] Further, clinicians may incorrectly assume that the topic is not of importance to a patient based on their age or marital or cancer status.

One way to overcome these barriers is through standardized, routine screening for sexual dysfunction among all patients with cancer. Routine assessment is supported by the NCCN's Clinical Practice Guidelines in Oncology for Survivorship, which state, "At regular intervals, female cancer survivors should be asked about their sexual function, including their sexual functioning before cancer treatment, their present activity, and how cancer treatment has affected their sexual functioning and intimacy."[57]

We advocate for addressing sexual health throughout a patient's cancer treatment as opposed to only during survivorship. Some patients may be receiving treatment for recurrent disease or receiving maintenance therapy for years and may have sexual health problems that may be missed if left to the survivorship period.[48] Universal screening can occur through a standardized review of systems or with

the use of screening tools. Self-administered screeners completed ahead of or at the start of a visit are efficient, allowing clinicians to focus their limited time during clinical visits to those individuals who screen positive for sexual dysfunction.

A number of tools exist to assess for sexual dysfunction (Table 1), many of which have been validated among populations of patients with cancer, including[58]: the Brief Sexual Symptom Checklist for Women as a primary screening tool, the ASEX (Arizona Sexual Experience Scale), and the FSFI.[59] Additional options include the single-item screener from the National Institutes of Health's PROMIS (Patient-Reported Outcomes Measurement Information System) group and the Scientific Network on Female Sexual Health and Cancer, the Sexual Function Questionnaire,[60] and the Sexual Function and Satisfaction measure developed by the PROMIS Network.[61] The FSFI includes 19 questions and assesses six domains of sexual function, including desire, subjective arousal, lubrication, orgasm, satisfaction, and pain or discomfort. The PROMIS SexFS Version 2.0 Survey assesses interest in sexual activity, lubrication, vaginal discomfort, clitoral discomfort, labial discomfort, orgasm ability, and orgasm pleasure over the previous 30 days. In practice, these tools are lengthy and cumbersome, originally designed for research purposes, and less user-friendly for patients to complete and clinicians to review in the clinical setting. They may also be perceived as heteronormative by those who are gay, lesbian, or transgender. More recently, brief checklists and single-question screeners have been developed.

The Sexual Symptom Checklist for Women after Cancer[6] (Fig. 2) and the Single-Item Screener for self-reporting sexual problems[62] (Fig. 3) are two brief screeners that have been studied among female patients with cancer and offer a simple and quick way to assess for sexual health problems in a busy clinical setting (Table 1). Most importantly, no matter how or when sexual health is assessed, it is important to ensure that the topic is inclusive of individuals' cultural and religious backgrounds as well as sexual orientation.

TREATMENT CHOICES FOR SEXUAL DYSFUNCTION

Moisturizers

Vaginal moisturizers are recommended by Cancer Care Ontario in the management of vaginal atrophy for daily comfort and for pelvic examinations.[47,63] The American Society of Clinical Oncology recommends that vaginal moisturizers be used to improve vulvovaginal tissue quality and that they may need to be applied three to five times per week in the vagina, at the vaginal opening, and on the external folds of the vulva for symptom relief.[63]

Vaginal moisturizers are intended to be used for long-term relief of vaginal dryness, as opposed to lubricants, which are discussed below.[64] Vaginal moisturizers are classified as class IIa medical devices by the Medicines and Healthcare products Regulatory Agency based on the duration of use. There are many commercially available vaginal moisturizers that can be used.[65,66] There is only a small number of studies evaluating their use, but, due to their low risk, we often recommend plant-based oils given their natural formulation free of additives and preservatives that may cause irritation.[67,68] These include pure coconut oil and olive oil. There are some concerns that plant-

Table 1. Sexual Health Screening Tools

Tool	Reference No.	No. of Questions	Use in Patients With Cancer
Brief Sexual Symptom Checklist for Women*	120	4	
Single-Item Screener for Self-Reported Sexual Problems	62	1	
FSFI†	59	19	Validated in patients with breast cancer
ASEX†	121	5	Validated in patients with breast cancer
Sexual Function Questionnaire	122	28	
(PROMIS) Sexual Function and Satisfaction measure	123	81	Validated in general cancer population

FSFI, Female Sexual Function Index; ASEX, Arizona Sexual Experience Scale; PROMIS, Patient-Reported Outcomes Measurement Information System.
* Adapted for use in female patients with cancer.
† Validated and used in patients with cancer.

Brief Sexual Symptom Checklist for Women (BSSC-W)*

Please answer the following questions about your overall sexual funciton

1. Are you satisfied with your sexual funciton?
   __ Yes __ No
   If No, please continue.
2. How long have you been dissatisfied with your sexual funciton?
   _____
3a. The problem(s) with your sexual funciton is: (mark one or more)
   __ 1 Problem with little or no interest in sex
   __ 2 Problem with decreased genital sensation (feeling)
   __ 3 Problem with decreased vaginal lubcrication (dryness)
   __ 4 Problem reaching orgasm
   __ 5 Problem with pain during sex
   __ 6 Other:
3b. Which problem is most bothersome (circle) 1 2 3 4 5
4. Would you like to talk about it with your doctor?
   __ Yes __ No

Fig. 2. Brief sexual symptom checklist for women. Reprinted from Huffman LB, Hartenbach EM, Carter J, Rash JK, Kushner DM. Maintaining sexual health throughout gynecologic cancer survivorship: a comprehensive review and clinical guide. Gynecol Oncol 2016;140(2):359–68. doi: 10.1016/j.ygyno.2015.11.010. Copyright 2015, with permission from Elsevier *and* *reprinted with permission from Hatzichristou D, Rosen RC, Derogatis LR, Low WY, Meuleman EJ, Sadovsky R, Symonds T. Recommendations for the clinical evaluation of men and women with sexual dysfunction. J Sex Med 2010;7(1 Pt 2):337–48. doi: 10.1111/j.1743–6109.2009.01619.x.

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based oils used vaginally may be associated with increased risk of urinary tract infections, but data are limited. We recommend the use of moisturizers five times per week with applicator if desired and 1 hour before planned penetrative activities. We also tell patients to avoid douching or other products marketed as vaginal washes because they can alter the vaginal microbiome, leading to more vulvovaginal discomfort.

Vaginal estrogen, discussed further below, can be considered when symptoms do not respond to nonhormonal approaches.

Lubricants

Lubricants differ from moisturizers in that they are intended to provide short-term relief of vaginal dryness and discomfort during sexual activity.[69] There are numerous commercially available lubricants, which can be water-, silicone-, mineral oil–, or plant oil–based. Lubricants can be applied to the vagina, vulva, penis, or sex toy before and during sexual activity. There are advantages to each type of lubricant. Water-based lubricants are nonstaining and are associated with less irritation compared with silicone-based lubricants.[70] However, they typically do not last as long as silicone- and oil-based lubricants and may require reapplication during sexual activities. Mineral oil– and plant oil–based lubricants typically last longer and result in less irritation. It is important to counsel patients on the possibility of urinary tract infections and condom ineffectiveness with plant oil–based lubricants. Additionally, we recommend avoiding lubricants with flavors, scents, and warming effects, because they can cause irritation.

Dilator Therapy

Vaginal dilator therapy is used frequently to prevent vaginal stenosis after RT, which is associated with decreased sexual function. Quinn et al performed a prospective study evaluating vaginal length and sexual function in women using vaginal dilators after RT (external beam or brachytherapy). They found that dilator use was associated with maintenance of vaginal length for all patients and improvement in sexual function.[71] Multiple studies have shown similar improvement in sexual function and decreased vaginal stenosis with dilator use among women who received RT, but there are some conflicting results.[71,72]

Single-item Screener for Self-Reported Sexual Problems**

In the past 12 months, has there ever been a period of 3 months or more when you had any of the following problems or concerns? Check all that apply.

- You wanted to feel more interest in sexual activity
- You had difficulty with erections (penis getting or staying hard) – MEN ONLY
- Your vagina felt too dry – WOMEN ONLY
- You had pain during or after sexual activity
- You had difficulty having an orgasm
- You felt anxious about sexual activity
- You did not enjoy sexual activity
- Some other sexual problem or concern
- No sexual problems or concerns

Fig. 3. Single-item screener for self-reported sexual problems. **Proposed by the PROMIS group and the Scientific Network on Female Sexual Health and Cancer. Reprinted from Huffman LB, Hartenbach EM, Carter J, Rash JK, Kushner DM. Maintaining sexual health throughout gynecologic cancer survivorship: a comprehensive review and clinical guide. Gynecol Oncol 2016;140(2):359–68. doi: 10.1016/j.ygyno.2015.11.010. Copyright 2015, with permission from Elsevier, *and* reprinted with permission from Flynn KE, Lindau ST, Lin L, Reese JB, Jeffery DD, Carter J, Baron SR, Abramsohn E, Weinfurt KP. Development and validation of a single-item screener for self-reporting sexual problems in U.S. adults. J Gen Intern Med 2015;30(10):1468–75. doi: 10.1007/s11606-015-3333-3.

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Vaginal dilators can also be of benefit in women who have not had pelvic RT, for the management of vaginismus, vaginal stenosis, and dyspareunia, and can be offered to anyone having pain with examinations or sexual activity.[47,63] Future studies evaluating the role of vaginal dilators in improving dyspareunia specifically among patients with cancer without prior pelvic RT are warranted. However, the risks associated with dilator therapy are low and should be considered in women with dyspareunia who have not received RT.

Dilator therapy to prevent or treat vaginal stenosis is most efficacious when initiated early and used regularly, regardless of a patient's sexual activity or orientation.[47] Ideally, dilators should be used at least three times per week to prevent vaginal stenosis and continued for a long as possible to see sustained benefits.[63] We often advise patients to attempt daily dilator use so that, if a day or two is missed, they have used the dilator at least three times per week. We typically recommend using the dilator at the same time each day so that it becomes part of a daily routine. We recommend inserting a size that is comfortable after applying a lubricant or moisturizer of choice and leaving the dilator in for at least 5 minutes and up to 20 minutes. Once the initial dilator size can be inserted comfortably for a week, we recommend increasing to a larger size. Mild vaginal bleeding or spotting is common with dilator use and can be minimized with liberal use of moisturizers or lubricants. Providing clear counseling and anticipatory guidance about expectations will help promote dilator adherence and improve outcomes.

Lidocaine

For women with persistent introital pain and dyspareunia, topical lidocaine can be offered.[47] One study found that, in women with a history of breast cancer who had pain limited to the vaginal opening (vestibule), 4% aqueous lidocaine applied just before vaginal penetration or tampon insertion decreased pain during intercourse or tampon use. Furthermore, 85% of women were able to resume comfortable penetrative sex.[73] People with associated vaginismus did not benefit from this intervention.

Hormone Therapy in Women with Gynecologic and Breast Cancers

Hormone therapy (HT) is an effective treatment option for women experiencing vasomotor symptoms and genitourinary systems of menopause, which may contribute to sexual dysfunction. In this section, we review the data regarding the risks and benefits of vaginal and systemic HT based on cancer type for the treatment of sexual dysfunction symptoms.

Low-dose vaginal estrogen is the most effective treatment option for moderate-to-severe genitourinary systems of menopause, with few side effects or risks given that it acts locally and has minimal systemic absorption.[47,74,75] The goal of vaginal estrogen is to restore the vaginal microenvironment and the naturally acidic pH, thereby improving elasticity of the vaginal epithelium, blood flow, and vaginal secretions. This in turn reduces vaginal dryness and dyspareunia and may also improve urinary symptoms caused by a low-estrogen state.[76,77]

In terms of systemic HT, much of the short-term and long-term safety data has been studied in the general population and extrapolated to patients with cancer. Adverse events that have been attributed to HT include coronary artery disease, stroke, venous thromboembolism, dementia, and increased risk of breast cancer. The North American Menopause Society recommends taking an individualized approach to the use of HT for the treatment of menopausal symptoms, with a focus on maximizing benefits while minimizing risks, and reassessing the need for continued HT periodically.[74] Specifically, they state that individuals younger than age 60 years who are within 10 years of menopause have a favorable risk–benefit profile for HT treatment of vasomotor symptoms, including benefits of bone health, whereas those older than age 60 years or more than 10 years from menopause are at higher risk of experiencing one or more of the above-mentioned adverse events.

Although many patients with gynecologic cancers are postmenopausal, depending on the primary cancer site, a proportion of patients are diagnosed before menopause. For example, a greater number of young patients are diagnosed with cervical cancer compared with other disease sites, with a median age of 50 years at time of diagnosis, and more than 50% are premenopausal.[78] Among patients with endometrial cancer, up to 25% are premenopausal at diagnosis; 40% of patients with ovarian cancer are between age 30 and 60 years.[79] Approximately 30% of new female breast cancers are diagnosed in women younger than age 54 years.[80] Premenopausal and perimenopausal patients are at risk of experiencing more severe menopause symptoms associated with cancer treatments, including oophorectomy and exposure to chemotherapy and pelvic radiation, compared with natural menopause.

Historically, there has been hesitancy to offer HT to patients with a history of gynecologic or breast

cancer given the theoretical concern for stimulating cancer cells that may be hormonally receptive, leading to cancer recurrence.[81] Unfortunately, there is limited high-quality data in the form of large randomized controlled trials (RCTs) among patients with gynecologic cancer, but data do exist in the form of smaller RCTs and observational and retrospective studies to help guide shared decision making between patients and clinicians based on cancer type.[82,83]

The Women's Health Initiative (WHI) was the largest series of RCTs investigating the risks and benefits of HT among women in the general population aged 50–79 years.[84] Although patients with cancer were not included in the original WHI studies, it is worth considering how the WHI results affect our decisions to offer HT to this population.

Ultimately, research assessing the safety of HT among patients with a cancer history remains limited; thus, the guidance here is based on available research coupled with clinical experience. We recommend shared decision making when discussing HT with women with a known history of gynecologic or breast cancer. Although risks exist, they are rare for most patients, especially if HT is used for the shortest time and at lowest dose indicated. Below we discuss our practice in regard to HT for women with gynecologic or breast cancer.

Endometrial Cancer

The majority of endometrial carcinomas are endometrioid histology, which are estrogen-dependent and most often low-grade. The standard definitive treatment for early-stage endometrial cancer is total hysterectomy and bilateral salpingo-oophorectomy (BSO) with lymph node evaluation. Although the cancer is estrogen-dependent, there are no existing data to suggest that systemic HT in the form of estrogen increases the risk of recurrence or affects overall survival for patients with low-grade, early-stage endometrial cancer. This has been evaluated in eight studies,[85–87] including a randomized, double-blind, placebo-controlled study evaluating recurrence risk and overall survival among patients with stage I or II endometrial cancer randomized to oral estrogen compared with placebo.[88] This Gynecologic Oncology Group study was closed early due to inability to meet enrollment targets, which they attributed to the release of the WHI study results. The authors stated that they could not, "conclusively refute or support the safety of exogenous estrogen." The median follow-up of patients who enrolled was 32 months, and cancer recurrence was 2% in the HT group and 1.6% in the control group.

Data for HT use among patients with high-risk endometrial cancer, either advanced-stage or high-grade histology, are even more limited. Although some of the cited studies included nonendometrioid histology, the numbers are small, limiting the conclusions.

Separate from endometrial carcinomas is the heterogenous group of uterine sarcomas. Leiomyosarcomas are not considered to be hormonally driven; thus, the ovaries are often preserved in younger patients. However, data are lacking on the safety of HT for patients in this group who undergo BSO. On the other hand, endometrial stromal sarcomas commonly overexpress estrogen and progesterone receptors; thus, HT is contraindicated in these patients given concern for stimulation of residual tumor cells.[89] Based on the available data, the Society of Gynecologic Oncology's Clinical Practice Committee states that HT can be considered for patients with early-stage, low-risk endometrial cancer who have severe menopausal symptoms not otherwise relieved by alternative therapies.[90]

Ovarian Cancer

Among patients with epithelial ovarian cancer, a handful of studies have examined the risk of recurrence and overall survival in patients who received HT after cancer treatment. Although it is difficult to synthesize the existing literature due to heterogeneity in study designs and methodologies among studies, two meta-analyses resulted in the overarching consensus that HT use after epithelial ovarian cancer treatment did not significantly increase the risk of recurrence or affect overall survival when compared with placebo in patients with epithelial ovarian cancer.[81,91,92] Unfortunately the data are even more limited for germ cell, sex cord stromal, and borderline tumors. Germ cell tumors commonly affect girls and young women between age 10 and 30 years. These patients often require adjuvant chemotherapy with bleomycin, etoposide, and cisplatin, which can lead to premature ovarian failure. For these patients, HT may be beneficial, and there are no data to suggest an increased risk of cancer recurrence. However, sex cord stromal tumors, most commonly granulosa cell tumors, are hormonally dependent; thus, we recommend avoiding HT use in these patients.[83]

Lastly, a subset of women with *BRCA1* or *BRCA2* pathogenic variants are at higher risk for breast and ovarian cancer. Risk-reducing BSO is the most effective way to reduce the risk of ovarian cancer. This procedure is recommended for women between the ages of 35 and 45 years once childbearing is complete.

For women who have undergone risk-reducing BSO, HT is recommended for all premenopausal women and all women with menopausal symptoms. Hormone therapy has not been shown to increase the risk of breast cancer in this population.[93]

Cervical Cancer

Cervical cancers, both squamous cell and adenocarcinoma, are not thought to be hormonally driven. For young women not pursuing fertility-sparing treatment, the standard treatment options are radical or simple hysterectomy with possible BSO and lymph node evaluation for early-stage cancer or primary chemoradiation for locally advanced cancer. Both treatments may result in premature menopausal symptoms. It is reasonable for patients with early-stage squamous cell carcinoma of the cervix to consider ovarian preservation at the time of surgery, because the risk of ovarian metastases is low.[94] Although estrogen and progesterone receptors are in the cervix, there does not seem to be any prognostic significance nor increased risk of cancer recurrence with HT use, particularly in adenocarcinoma.[95]

In a prospective study of 120 women with stage I–II cervical cancer treated with surgery or RT, there was no difference in recurrence rates or overall survival between patients treated with HT compared with placebo.[96] Given the potentially significant and long-term sequalae related to estrogen deprivation in young survivors of cervical cancer, the NCCN recommends that HT be considered in this population, particularly premenopausal patients. For patients who received radiation with an intact uterus, the amount of radiation likely will have caused irreversible endometrial ablation; nevertheless, it is recommended to use a combined estrogen–progesterone formulation.[97]

Breast Cancer

Systemic HT generally is not recommended for individuals with a history of breast cancer due to concerns about increased risk of cancer recurrence. This is based on the results of two RCTs and data from observational and retrospective studies with inconsistent conclusions.[98–100] For survivors of breast cancer, our approach to sexual dysfunction is to begin with lifestyle changes and nonhormonal medications to manage vasomotor symptoms, coupled first with nonhormonal moisturizers and lubricants for vulvovaginal symptoms. If symptoms persist, low-dose vaginal estrogen can be initiated, even among women with hormone-sensitive breast and endometrial cancers after shared decision making between patient and clinician about the potential risks, particularly in patients with breast cancer who are receiving aromatase inhibitor therapy.[74,101] However, communication between sexual health and oncology clinicians is critical given the lack of level 1 data to inform the safety of estrogen in people taking aromatase inhibitors and in light of lower-quality data that suggest an association between vaginal estrogen and recurrence in these patients.[102]

Laser

Although laser procedures, commonly referred to as "vaginal rejuvenation," may be offered, we do not routinely recommend them to our patients without clinical trial data. Our practice is supported by the International Society for the Study of Vulvovaginal Disease.[103] If a patient is interested in a laser procedure, consideration of enrollment in a clinical trial may be useful in the absence of data, to provide future information to improve decision making.

EXPERT REFERRALS FOR THE MANAGEMENT OF SEXUAL DYSFUNCTION

Pelvic Floor Physical Therapy

Many forms of cancer treatment as described earlier can lead to pelvic floor symptoms that affect sexual function, such as vaginal stenosis, vaginal dryness and impaired tissue elasticity, and increased pelvic floor muscle tone and contractility dysfunction. These physical symptoms can lead to psychological sequelae that can worsen both the pain and the anxiety related to the fear of pain.[104] The Cancer Care Ontario guidelines, endorsed by ASCO, recommend that pelvic floor physical therapy be offered to women with dyspareunia or other pelvic floor issues as a first-line treatment; timely referral is critical.[41,95,101,102] Pelvic floor physical therapy includes massage, pelvic floor strengthening, and relaxation exercises. These exercises can help to improve blood flow, tensile strength, and flexibility of the pelvic floor tissues. Women with optimum strength in their pelvic floor muscles can have improved arousal and orgasm and decreased pain.[103]

In a systematic review of five RCTs and two retrospective studies, Brennan et al found moderate-level evidence that conservative pelvic floor muscle interventions may improve the sexual health and quality of life of patients with gynecologic cancer.[104] In a multicenter prospective study, Cyr et al[105] demonstrated the feasibility of multimodal pelvic floor physical therapy for survivors of gynecologic cancer who have painful sexual intercourse, with an adherence rate of 88% with significant improvements in pain, sexual function, pelvic floor dysfunction

symptoms, and quality of life. Long-term follow-up of this cohort supported that both physical and psychological improvements were sustained at 1 year.[106]

Not all centers have access to physical therapists with expertise in pelvic floor physical therapy (Table 2). In this situation, we recommend discussing self-directed pelvic floor exercises, with consideration of vaginal dilator therapy as a start.[107]

Problems Surrounding Desire and the Role of Psychosocial Counseling

Sexual desire is a key component of the sexual response cycle that can be spontaneous or responsive to sexual stimuli. For many females, spontaneous desire is uncommon except in new relationships.[15] For patients with cancer, issues with desire can stem from physical or hormonal changes after surgery, radiation, or systemic therapies such as chemotherapy and hormonal therapy. Desire can also be negatively affected by emotional and psychological factors including stress, anxiety, and depression, which are highly prevalent among patients with cancer. Additionally, medical comorbidities and their associated medications may affect libido. For example, selective serotonin reuptake inhibitors and selective serotonin-norepinephrine reuptake inhibitors used to treat anxiety and depression and calcium channel blockers commonly used to treat hypertension have been shown to cause adverse sexual side effects.

Female sexual interest and arousal disorder (also referred to as hypoactive sexual desire disorder and female sexual arousal disorder) is defined as patients reporting low desire for at least 6 months that is associated with significant distress and cannot be attributed to another diagnosis. It affects approximately 10% of women in the United States.[108] Addressing decreased libido often requires a multimodal approach. Psychotherapy for both individuals and couples can be helpful in addressing emotional and interpersonal difficulties that may be contributing. Psychologists and licensed social workers with expertise in couples therapy as well as trained sex therapists can be especially helpful, incorporating cognitive behavioral therapy and mindfulness-based exercises that have been shown to improve perceptions of arousal and sexual satisfaction despite physical impairments.[109–111]

The American Society of Clinical Oncology recommends that psychosocial counseling be offered to women with cancer and body image issues. The majority of studies found an improvement in body image after some type of counseling; at least six sessions appeared to have the greatest effects. However, the expert panel did not recommend a specific number of sessions. If a woman is partnered, couples-based interventions are more effective compared with usual care.[112,113]

In 2015, the U.S. Food and Drug Administration approved flibanserin (Addyi), a serotonin receptor agonist–antagonist, for use in premenopausal women with hypoactive sexual desire disorder.[114,115] It was subsequently studied in naturally postmenopausal patients compared with placebo and was found to have similar efficacy to that seen in the studies with premenopausal women; however, it is not approved by the U.S. Food and Drug Administration for this group.[116] Furthermore, until recently, the drug had not been studied in patients with cancer. Goldfarb

Table 2. Patient and Clinician Sexual Health Resources

Resource	Website
American Cancer Society, How Cancer and Cancer Treatment Can Affect Sexuality	https://www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/how-cancer-affects-sexuality.html
National Comprehensive Cancer Network, Survivorship: Late Effects/Long-Term Psychosocial and Physical Problems: Sexual Health	https://www.nccn.org/patients/guidelines/content/PDF/survivorship-crl-patient.pdf
Scientific Network on Female Sexual Health and Cancer	https://www.cancersexnetwork.org/
International Society for the Study of Women's Sexual Health	https://www.isswsh.org/
North American Menopause Society	https://www.menopause.org/
Topic-specific resources	
Pelvic floor physical therapy	
Academy of Pelvic Health Physical Therapy: Find a PT	https://ptl.womenshealthapta.org/
Sex therapy	
American Association of Sexuality Educators, Counselors, and Therapists	https://www.aasect.org/referral-directory

et al reported at the ASCO 2023 annual meeting that flibanserin improved libido, arousal, lubrication, sexual satisfaction and confidence, and climax among women with breast cancer on endocrine therapy who had decreased libido.[117] However, this was a small study, including fewer than 50 women, and treatment was not compared with placebo.

SEXUAL HEALTH CLINICS

There are a growing number of programs in the United States that focus specifically on evaluation and treatment of people with gynecologic and breast cancer and sexual health problems, aiming to improving sexual outcomes in this population. Carter et al describe one such program, which assessed sexual outcomes in 175 female cancer survivors. They found a high adherence to recommendations for patients attending this clinic and significant improvement in vaginal symptoms, sexual function, and increased sexual activity.[118] Seaborne et al also conducted a retrospective survey-based evaluation of their multidisciplinary clinic, with nearly 90% of their 113 predominately postmenopausal (68%) women with breast (57%) and gynecologic cancers (32%) indicating that the service was at least somewhat helpful and that their sexual symptoms improved.[119] Most of these clinics are staffed by physicians or advanced practice professionals trained in sexual medicine or gynecology, a psychologist with sex therapy expertise, or both. The addition of physical therapists, when available, is valuable.

CONCLUSIONS

Sexual health problems are prevalent among women living with cancer and survivors and can greatly affect their quality of life. It is important to understand the negative effects cancer treatment can have on sexual health and to screen for sexual health problems. Identifying sexual health resources and experts in your area is a critical step in being able to effectively and efficiently address patient concerns related to sexual health. If you do not have sexual health experts in your area to refer to, there are multiple resources available for both patients and clinicians (Table 2).

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