Addressing the Sexual Health Concerns of Women with Gynecologic Cancer: Guidance for Primary Care Physicians

Devin T. Miller, MD, Eve Overton, BA, and Elena S. Ratner, MD

ABSTRACT
• Objective: To review the sexual health concerns of women with gynecologic cancer and provide guidance for primary care physicians.
• Methods: Review of the literature.
• Results: Issues of sexuality and intimacy are known to significantly impact the quality of life of patients following diagnosis and treatment of gynecologic cancers. At the time of diagnosis, women should be informed of the potential physiologic, hormonal, and psychosocial effects of gynecologic cancer on sexuality. Many providers fail to address these issues given time constraints and patients’ trepidation in alerting their providers to their concerns. While systemic hormone therapy directly addresses these symptoms, its use remains controversial due to potential cancer recurrence risks. Thus, treatment centers around therapeutic alternatives. For vasomotor symptoms, selective serotonin reuptake inhibitors have shown effectiveness and are typically well tolerated, and antiepileptics such as gabapentin have shown promise. There is promising but limited data employing pelvic floor physical therapy as a tool to aid in addressing pelvic floor symptoms. Psychological care and the involvement of the partner are also part of managing the sexual health concerns of these patients.
• Conclusion: Sexual morbidity is a distressing and undertreated problem among gynecologic cancer survivors. Successful treatment requires the provider’s appreciation of the problem and willingness to address it.

Issues of sexuality and intimacy are known to significantly impact the lives of patients following diagnosis and treatment of gynecologic cancers. [1,2] Treatment of gynecologic malignancy is highly dependent on pathology and stage, with some patients subject to extensive surgeries, chemotherapy, and radiation treatment, and it is difficult to predict how each individual’s sexual health will be impacted. However, the evidence suggests that at least half of women treated for gynecologic cancer will experience sexual dysfunction [3]. Although the impact of gynecologic cancer and treatment can be profound, providers often do not address their patients’ sexual concerns [4,5], yet most patients have indicated that they would like these issues to be addressed [6].

Female Sexual Dysfunction
Sexual dysfunction is multifactorial and involves physical, social, and psychological dimensions. It is common in the general population, with rates ranging from 25-63% [7]. The DSM-IV [8] defines female sexual dysfunction as a disturbance in or pain during the sexual response, which can be further classified as hypoactive sexual disorder, orgasmic disorder, sexual pain disorder, or sexual arousal disorder [9]. It should be noted that women who have been treated for gynecologic cancers may have a pre-morbid history of sexual dysfunction. Assessment of a woman’s sexual function prior to her cancer diagnosis can help establish which sexuality changes are due to the cancer treatment and may allow the provider to tailor interventions accordingly.

Sexual Dysfunction and Quality of Life
As treatments for gynecologic cancers improve, toxicity of treatment decreases, and survival increases, quality of life for survivors has become an increasingly important health issue. Several studies have examined patient-reported quality of life in short- and long-term cancer survivors and report overall significant alteration

From the Yale School of Medicine, New Haven, CT.
in quality of life over many aspects of health and psychological well-being [10]. It is well established that health-related quality of life and sexual functioning are closely associated [11].

In gynecologic cancer patients, sexual and quality of life outcomes can vary. For example, Kim et al recently compared quality of life and sexual functioning in ovarian cancer survivors with no evidence of disease after primary treatment and a cohort of health women. Sexuality, both in terms of desire, arousal, lubrication, orgasm, satisfaction, and pain and in terms of interest in sex, sexual activity, and enjoyment of sex were similar between the groups; however social functioning deteriorated in cancer patients [12]. Other women report different experiences. Women with a history of vulvar, vaginal, or cervical cancer who may have had extensive pelvic surgery, lymphadenectomy, and radiation treatment to the pelvis typically report greater alterations in quality of life and sexual activity depending on the extent of their treatment [13]. Patients undergoing chemotherapy often report significant changes in quality of life due to the physical symptoms of fatigue, nausea, hair loss, diarrhea, etc. as well as the psychological effects of cancer diagnosis, changes in body image, and poor coping [14]. Sexual side effects are common due to alterations in the HPA axis, direct gonadal toxicity and neuropathies [15].

**Impact of Gynecologic Cancer on Sexuality**

Gynecologic cancer and treatment can alter sexuality through a variety of effects. The impact of anatomical changes may alter a women’s self-esteem, body image, and sense of femininity, resulting in a reluctance to engage in intimate behaviors. Furthermore, if the partnership is disrupted by changes in roles in the household or within the relationship, relationships dynamics may be tested and result in mental distress for the patient, thus effecting sexuality and intimacy.

Surgical or chemical withdrawal of sex hormones, new medications, and postoperative sequelae can contribute to sexual arousal problems. The emotional and psychological components of a cancer diagnosis also can hinder the sexual response [16]. Depression and anxiety, the rates of which increase with cancer diagnosis, can also significantly affect sexual function [17].

Sexual pain is common in this population due to hormonal considerations as well as post-treatment side effects and a frequent cause of sexual dysfunction for these patients. Pelvic radiation may result in adverse physical changes to the vagina including vaginal stenosis, thinning of vaginal mucosa, loss of lubrication, and loss of elasticity [18,19]. A recent review of 20 studies of cervical cancer survivors found that patients were at risk for lack of lubrication and had high rates of dyspareunia [20]. Psychosocial factors have been found to be important predictors of sexual desire and more important than hormones in predicting low sexual desire in middle age [21]. These factors include emotional and physical closeness to the partner, satisfactory communication, and a positive relation to one’s own body [16].

**Effects on Relationships and Partners**

Women whose sexual capacity is compromised may be worried about their partners’ quality of life and overall well-being. Indeed, the partners of women with gynecologic cancer are also impacted by the changes to sexual function and loss of sexuality and intimacy. Hawkins et al found that cessation or decreased frequency of sex and intimacy was reported in 79% of male partners of women affected by cancer. Among partners of the persons with cancer in this study, changes to sexuality were associated with feelings of self-blame, reflection, sadness, anger and lack of sexual fulfillment [22]. Further, male partners of women diagnosed with gynecological cancer often express conflicting emotional states including feeling worried about their significant other’s health, having the desire to engage in sexual activity, and feeling guilty about wanting to increase sexual intimacy. These feelings, in turn, can lead to resentment and withdrawal from their partner and overall relationship discord [23].

Evidence suggests partners of cancer patients greatly benefit from increased social support even years after an apparent cure [24]. Specifically, male partners who take on a new role as caregiver in the relationship experience difficulties with emotional changes, challenges to their masculinity, and new stressors [25]. These new roles and feelings also contribute to changes in sexuality and intimacy in relationships, making support for partners all the more necessary.

**Menopausal Symptoms Following Cancer Treatment**

Gynecologic cancer treatment invariably affects the female hormonal balance, sometimes suddenly with surgical excision of the gonads or via radiation treatment or chemotherapy. It is well known that the sudden withdrawal of estrogen and testosterone, especially in
the premenopausal postoperative population, can lead to significant acute menopausal symptoms. Given the many emotional and physical issues affecting patients during treatment, it can be difficult to delineate what proportion of sexual problems are caused by or enhanced by vasomotor symptoms, sleep disorders, and vaginal atrophy.

In general, premenopausal women who experience abrupt surgical menopause may often have immediate severe symptoms. Many agree that the younger a woman is when going through this process, the more severe her symptoms may be. Although the average age of endometrial cancer diagnosis is 67, approximately 25% of women who are diagnosed are premenopausal, and 5% of cases occur in women under 40. As the obesity epidemic worsens and more women are exposed to higher levels of estrogen at younger ages, it is expected that the number of premenopausal women who are diagnosed will continue to rise. The average age of diagnosis for ovarian cancer is 63, however, there is a large cohort of women diagnosed with borderline and malignant tumors in the premenopausal period [26]. These patients often experience vasomotor symptoms in the hours to days following surgery.

Interventions for Survivors of Gynecologic Cancer with Sexual Dysfunction

Systemic Hormone Therapy

Systemic hormonal therapy to treat menopausal symptoms remains controversial following the release of findings from the Women’s Health Initiative, which showed a number of adverse effects, including an increased risk of breast cancer in healthy postmenopausal women who received systemic hormonal therapy for menopausal symptoms. While views have changed since that time, providers are often reluctant to prescribe hormonal therapy, and patients are reticent to take it, due to fears of cancer recurrence. However, there is no evidence showing hormones negatively influence survival after treatment for epithelial ovarian, squamous cervical, or vulvar cancer [27]. With the exception of endometrial cancer, there is no biological evidence that HRT may increase recurrence risk [28]. Approach to clinical decision making should be individualized, taking into consideration the patients’ symptoms, quality of life, tumor histology, and overall prognosis.

Cervical cancer, vulvar cancer, and vaginal cancer are not considered hormonally responsive tumors. While the data are limited, a study published in 1987 of cervical cancer survivors treated with systemic hormone replacement therapy showed no increase in relapse rates and showed an increase in quality of life [29]. There are no studies regarding systemic HRT in patients with vulvar or vaginal cancer though it is generally accepted they can be treated with HRT. No significant data exists for cervical adenocarcinoma patients, and most oncologists suggest treating these patients the same as those with endometrial cancer primary.

There is limited data on the use of HRT in women with ovarian cancer but available studies do not show any difference in overall or disease-free survival between HRT groups and controls [27,30–32]. Many studies report a significant increase in quality of life with HRT. A 2013 retrospective chart review of 77 patients with epithelial ovarian cancer who received postoperative HRT showed no significant difference in progression-free survival [33].

The most controversy surrounds the use of HRT in patients with endometrial cancer [34]. The only major data available come from the Gynecologic Oncology Group’s truncated study, which was a large prospective randomized controlled trial. Over 1200 women treated for stage I and II endometrial cancer were enrolled between 1997 and 2003, and before the study was terminated these patients were followed for a median of 3 years following initiation of therapy. The recurrence rate of malignancy was low, 2.1, and an insignificant risk of recurrence of 1.27 was noted between with HRT and placebo groups (80% CI, 0.916-1.77) [35]. Women included in this study were between the ages of 26 and 91, and their indications for therapy included vasomotor symptoms, vaginal atrophy, as well as osteoporosis risk and cardiovascular disease risk. Gynecologist oncologists often use estrogen therapy to treat symptomatic women with early stage endometrial cancer given the very low risk of recurrence.

Tibolone is a synthetic steroid with activity on estrogen and progestosterone receptors, and mainly acts as an agonist at estrogen receptors. It is prescribed outside the United States for osteoporosis and is being investigated as treatment for female sexual dysfunction. Efficacy on vasomotor symptoms has been positive thus far. One case-control study confirmed tibolone’s safety for endometrial cancer survivors, with no adverse effects on disease-free or overall survival [36]. One group recently examined tibolone in the setting of breast cancer patients in a prospective randomized controlled trial and reported an increased risk of breast cancer recurrences in women.
receiving tibolone for HT [37]. That study reported no increase in risk of gynecologic cancers and did report favorable outcomes for patients in terms of osteoporosis and vasomotor symptoms.

**Topical Therapy**

Women who are concerned about systemic HRT but who have been treated with radiation in addition to their surgery may be interested in topical estrogen therapy. These women may have vaginal stenosis and atrophic symptoms, and for them topical estrogen therapy can be helpful [38]. Many formulations of topical estrogen are available, including creams, tablets, and rings. Using vaginal estrogens and dilators can be useful to help with eventual resumption of sexual activity once healing has taken place and can help to avoid dyspareunia. Combination topical and systemic therapy can also be useful to relieve symptoms. Women concerned about absorption with topical therapy can be advised that while there is some absorption initially, absorption is reduced as atrophy is improved with treatment.

One recent study examined the use of alpha-tocopherol to reduce acute vaginal complications in women with endometrial and cervical cancer undergoing radiation treatment. The treatment group experienced reduced vaginal toxicity and pain, although vaginal secretion was not significantly different in the 2 groups studied [39]. No adverse effects were noted. This compound has not been studied further but may be beneficial in the future. Some women may prefer to avoid hormones altogether. Over-the-counter vaginal moisturizers and lubricants can be recommended to women to help with intercourse and atrophic symptoms, with or without estrogen therapy.

**Physical Therapy**

Pelvic floor physical therapy has become an increasingly popular modality for treatment of many aspects pelvic floor dysfunction, the symptoms of which include defecatory dysfunction, constipation, bladder dysfunction, painful urination, dyspareunia, pelvic pain, and low back pain [40]. Pelvic floor physical therapy is well studied and utilized frequently for urinary incontinence and pelvic organ prolapse, but is understudied for sexual dysfunction [41,42].

Promising areas of study include educational sessions, cognitive behavioral therapy, vaginal dilator therapy, pelvic floor muscle strengthening and relaxation techniques with biofeedback, stretching and massage [40]. Biofeed-
shown to have efficacy in treating the broader psycho-social concerns of gynecological cancer patients [50,51]. In a recent study Brotto and colleagues randomized 31 survivors of gynecological cancer with self-reported sexual dysfunction to either three 90-minute CBT sessions or a waitlist control. Patients who underwent the intervention reported significant improvements in sexual arousal and desire both immediately post-therapy and at 6-month follow-up while patients in the waitlist arm experienced no significant changes in symptomatology [52].

Psychoeducational interventions are another promising avenue for addressing sexual dysfunction in this population [53]. In a 2008 therapeutic trial, Brotto and colleagues combined elements of CBT with education in 3 one-hour sessions featuring written materials on sexuality and relationships. The intervention enrolled 22 women with early stage gynecologic cancer who met criteria for female sexual arousal disorder. The psychoeducational intervention was associated with positive effect on sexual desire, arousal, orgasm, satisfaction, sexual distress, depression, and overall well-being [16]. Psychoeducation can also be used to augment other therapeutic modalities. Robinson and colleagues used such an intervention to improve adherence to vaginal dilator use in 32 women with early stage endometrial cancer who were being treated with radiotherapy [48].

Some gynecologic cancer patients may have significant alterations in their anatomy and thus penetrative intercourse may not be possible. In patients even without these physical changes, some may prefer to avoid intercourse due to pain or anxiety. Thus patients can have significant benefits from discussing their concerns with a therapist specializing in these issues as many patients are concerned about their ability to engage in intimate behavior. Therapy can assist with the changing sexual relationship and assist the partners in different ways of engaging in intimate acts. It is important to avoid stressing penetrative intercourse as the goal for sexual function with these or any patients with anxiety relating to their disease as there are many ways to engage in mutually pleasurable experiences for both partners, thus removing anxiety about inability to resume vaginal intercourse post-treatment. Discussing this with patients can be challenging but can often reduce anxiety surrounding body image issues following treatment.

Studies have shown that cancer care providers often do not adequately address sexual concerns [54] but that when these concerns are appropriately managed, patient satisfaction and quality of life significantly improve [55]. Several studies have focused on how providers can incorporate the approaches of CBT and psychoeducation to better address the sexual concerns of patients without requiring external psychiatric care [56,57]. Barbera et al have described a successful model in which multidisciplinary care teams provide education and counseling for gynecological cancer patients in a sexuality clinic [58].

Involvement of the partner in interventions has not been well studied; however, involving the partner in psychological therapies to address sexual dysfunction should be beneficial.

**Alternative Therapies for Vasomotor Symptoms**

Gynecologic cancer patients suffering prominent vasomotor symptoms have limited alternatives to hormone therapy. Clinicians must balance potential medication benefit with potential exacerbation of other medical and psychological issues, including sexual dysfunction.

**Antidepressants**

The use of SSRIs and SNRIs for vasomotor symptoms was pioneered by medical oncologists for men with hot flashes secondary to GnRH agonist therapy for prostate cancer and women with breast cancer [59,60]. Limited studies have shown that antidepressant medications do not increase cancer recurrence risk in ovarian cancer patients and are relatively well tolerated [61]. However, these medications are known to have partial efficacy in improving vasomotor symptoms and may worsen sexual symptoms, a well-known side effect of antidepressants. There is variation of the reported rates of sexual dysfunction associated with various antidepressants and clinicians may take the likelihood of sexual side effects into account when prescribing SSRIs or SNRIS [62]. More recently developed SSRIs, such as citalopram and its enantiomer escitalopram, have shown significant improvements in vasomotor symptoms and were better tolerated than venlafaxine and fluoxetine [63,64]. Additionally, limited uncontrolled studies of mirtazapine, a structurally unique SSRI, and bupropion, which acts on dopamine and norepinephrine, have shown significant decreases in
hot flash symptoms and are less associated with sexual side effects than SSRIS/SNRIS [65,66].

Other Agents
Other pharmaceutical options for menopausal vasomotor symptoms include gabapentin and adrenergic agonists. Gabapentin can yield impressive reductions in vasomotor symptoms. A recent double-blind randomized trial in 50 patients revealed a 60% reduction in hot flashes as 12 weeks and an 80% reduction in self-reported composite symptom scores [67]. However, side effects such as palpitations, edema, and fatigue, lead to high study withdrawal rates and limit its widespread clinical use for this indication [68]. Clonidine has been assessed versus venlafaxine in several clinical trials with breast cancer patients. These trials have shown mixed results, with findings of both inferiority and superiority to venlafaxine, but with consistent significant improvement in symptoms over placebo. Side effects, such insomnia, constipation, and dry mouth, occurred but did not lead to higher dropout rates than venlafaxine [69,70].

Long-Term Sexual Outcomes
For women treated for gynecological cancers, alterations in sexual function may persist in the long term. A study following cervical cancer patients managed with radical hysterectomy up to 2 years post treatment showed they had more sexual dysfunction compared with healthy controls, although at rates similar to those who underwent radical hysterectomy for benign disease [71]. A 2007 review of quality of life studies revealed that although ovarian cancer survivors 5 years past diagnosis had excellent overall quality of life, sexual symptoms persisted, with as many as 57% of patients reporting a decline in sexual function due to their cancer [72].

Studies show some differences in outcomes based on treatment modality. A recent review of cervical cancer outcomes revealed that women who received radiotherapy as a component of their treatment have a higher risk of long-term sexual side effects [73]. In contrast, a study assessing endometrial cancer patients 5 years after initial diagnosis between those patients who had received surgery alone and those who had received surgery and vaginal brachytherapy. There was no significant difference in any measures of quality of life and sexual function between these 2 groups [74].

Age appears to play a role in long-term sexual outcomes regardless of diagnosis. Bifulco and colleagues assessed quality of life in survivors of gynecological cancer, comparing women under age 45 to those over 45 after nearly 3 years of survival. After controlling for age and other factors, younger patients were found to have worse sexual activity, including significantly higher rates of poor body image, perceived worse sexual vaginal function, and more severe menopausal symptoms, probably related to the effects of surgical menopause [75].

Despite enduring sexual dysfunction, symptoms tend to improve over time. A cohort study of 103 gynecological cancer patients undergoing radiation therapy were followed for 3 years. Patients were offered standard interventions for sexual dysfunction, including vaginal lubricants, dilators, and menopausal symptomatic therapy, although adherence to these measures was not assessed. Three years after initial therapy, the percentage of sexually active women increased from 21.5% to 44.2% [76]. In the subset of patients who successfully return to sexual activity, outcomes can be comparable to healthy peers. Kim and colleagues compared disease-free sexually active ovarian cancer patients with demographically matched healthy controls on standardized self-report measures. Sexual functioning did not differ between the 2 groups, despite lower social functioning in cancer survivors [12].

Conclusion
Sexuality and intimacy can be greatly affected by the diagnosis and treatment of gynecologic malignancies. It is important to routinely discuss sexuality and sexual functioning with patients from diagnosis onward. Reassuring patients, acknowledging the importance of their concerns, and validating their desire to enjoy improved intimacy should be considered part of the clinician’s role. Valuable information sources that may aid discussions are available on the internet. Oncolink (www.oncolink.org), a large cancer information website maintained by University of Pennsylvania Cancer Center, offers a plethora of information for patients and health care professionals. In addition, the American Cancer Society offers a detailed guide, “Sexuality for the Woman with Cancer” [77]. Treatment is available, and improvement in outcomes is possible. Further prospective studies are needed to clearly delineate risks and benefits of hormone replacement therapy in patients with gynecologic cancers.

Corresponding author: Elena S. Ratner, MD, PO Box 208063, New Haven, CT 06520, elena.ratner@yale.edu.
References