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Sexuality and Menopause: Unique Issues in Gynecologic Cancer

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ABSTRACT

Objective: To provide current evidence on treatment- and disease-related sexual health concerns of women with gynecologic cancers.
Data Sources: Literature from 2006–2017 from MEDLINE, and PubMed databases.
Conclusion: There are both physiologic and psychosocial sexual health sequelae among women treated for gynecologic cancer, including induced menopause. The management of symptoms requires communication between provider and patient because the effects can be long lasting and directly affect the patient's quality of life.
Implications for Nursing Practice: Assessment of and communication about potential sexual health changes should begin at the time of diagnosis of gynecologic malignancies and continue through survivorship.

Gynecologic cancers, consisting of cervical, primary peritoneal/ovarian/fallopian tube, uterine/endometrial, vaginal, vulvar, and more rarely gestational trophoblastic disease-related malignancies, are anticipated to result in over 110,000 new cancer cases and over 32,000 cancer deaths in 2018.[1] Uterine cancer is estimated to be the fourth leading cause of cancer, and ovarian and uterine cancers to be the fifth and sixth leading causes of death, respectively, among women in the United States.[1] The treatment for gynecologic cancer generally includes surgery, chemotherapy, radiation, or a combination of these modalities. Patients are typically followed for 5 years following the completion of treatment when at that time they enter the survivorship phase of cancer diagnosis. With the current advances in treatment of gynecologic cancer, more women are entering the survivorship setting than ever before.

Sexual function and psychosexual well-being are receiving more attention in research and clinical practice as the number of cancer survivors increases.[2] Thousands of women are living with either active disease or a history of gynecologic cancers, which can result in multifactorial sexual sequelae, including but not limited to challenges with sexual interest and arousal, orgasm, genito-pelvic pain, and induced menopause.[3] Approximately 50% of women with gynecologic cancer are estimated to experience acute or chronic sexual health dysfunction.[4] Vast amount of evidence exists showing that cancer dramatically impacts a woman's sexuality, sexual functioning, intimate relationships, and sense of self.[5] Psychological variables, such as depression, anxiety, body image, and the ability to "feel like a woman" are correlated with levels of sexual functioning.[6] The optimal time to address sexual function and concerns about sexuality is with diagnosis and the initiation of treatment. Comprehension of baseline sexual function, role of psychological supports, and available treatment options could attenuate the heavy burden of decreased sexual function.[7]

Sexual dysfunction is one of the most common and distressing quality-of-life issues facing female cancer survivors, yet it is rarely discussed between cancer patients and survivors and their providers.[8–10] Although an important quality-of-life issue, patients are not consistently questioned about this subject during cancer treatment visits or examinations. This is further complicated by diverse religious, political, and philosophical perspectives on sexuality.[11] These challenges are present both for oncologists and primary care providers who report limitations, including lack of training in sexual health and the belief that there are no effective treatments for sexual dysfunction, as well as discomfort with sexual health conversations.[8–10] Years of clinical experience, provider age, a history of training regarding sexual dysfunction, and an international setting of practice can affect providers' opinions and practices toward sexual issues of patients.[12] For patients who endure the challenges of managing cancer treatment, the additional loss of sexuality and intimacy can add a profound burden that is often magnified by the lack of discussion about this problem.[13]

The American Society of Clinical Oncology recommends initiating discussion of sexual health at the time of diagnosis and readdressing it throughout treatment and into survivorship.[14] A conversation initiated by the health care provider opens the door for the patient to feel more comfortable discussing the topic of sexuality and sexual health issues. Sexual dysfunction in gynecologic cancer survivors is often multifactorial

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Table 1
Physiologic and psychological effects by cancer type.[2]

Uterine Cancer	Cervical Cancer	Ovarian Cancer	Vulvar Cancer
• Depression • Irritability • Lymphedema • Radiation changes • Shortened vagina • Vaginal atrophy • Vasomotor symptoms	• Body image disturbance • Cervix associated with sexual function • Depression • Early menopause • Fertility issues • Incompetent cervix leading to premature labor • Irritability • Lymphedema • Radiation changes • Sexual dysfunction • Vasomotor symptoms	• Body image disturbance • Depression • Early menopause • Infertility • Irritability • Vaginal atrophy • Vasomotor symptoms	• Body image disturbance • Depression • Removal of clitoris or labia can have physiologic and psychologic effects • Sexual dysfunction • Vulvar pain

Data from Carter et al[2] and Bennett et al.[7]

and best managed using a multidisciplinary approach.[15] This multidisciplinary approach often includes physicians, advanced practice providers, nurses, sexual health behavioral counselors, as well as oncology fertility specialists. In areas where there are limited resources, a one-on-one conversation initiated by the physician and with the patient can set the tone for further discussion and possible interventions.[9] Understanding the potential sexual health sequelae of gynecologic cancers is pivotal to supporting informed conversations between patients and providers. This article presents an evidence-based overview of potential sexual sequelae of gynecologic cancer (Table 1[2,7]) and its treatment, as well as recommendations for patient education and interventions (Table 2[7,14–17]).

The Sexual Health Sequelae of Gynecologic Cancer and its Treatment

Menopause

Treatment-induced menopause is associated with cancer treatment, particularly in the presence of gynecologic malignancies.[16] To understand issues of sexuality and menopause, one must understand the menopausal process and how it can have varying effects on women. Natural menopause is recognized following 12 consecutive months without a menstrual cycle, and typically occurs at approximately 52 years of age. Primary ovarian insufficiency is characterized by a decrease in the number of oocytes caused by follicular atresia that can lead to the decline and subsequent cessation of ovarian function, including estrogen and progesterone production. Primary ovarian insufficiency can result from pelvic surgery, radiation, or chemotherapy,[17] which are common treatment modalities for gynecologic cancer.

Symptoms of menopause encompass vasomotor effects such as hot flashes and night sweats; hormonal issues such as low testosterone, progesterone, and estrogen; physiologic effects such as vaginal dryness and painful intercourse; sleep disturbances; as well as uncomfortable urinary symptoms. There are also psychological effects such as increased irritability, body image disturbance, and depression. These short- and long-term symptoms commonly affect a woman's quality of life.[17]

Early menopause, typically referred to as menopause before the age of 40, has been associated with the treatment of certain gynecologic cancers, including uterine, cervical, and ovarian cancer.[17] Menopausal symptoms triggered by cancer treatment can be more abrupt, intense, and/or prolonged than those of natural menopause.[2] The incidence of early menopause can have devastating effects on young women, both from a sexual health standpoint to psychological effects such as body image disorders to even the feeling of inadequacy from not being able to bear children.[18] Intimate relationships can be profoundly affected, perhaps even more so for those in sexual minorities for whom additional barriers to communication and sexual health discussion have been identified.[19]

Treatment and symptom management of menopausal symptoms

Treatment and symptom management include hormone replacement therapy (HRT), nonhormonal medications, and behavioral interventions. The evidence and indications for each category are presented below.

Hormone replacement therapy. HRT is an effective evidence-based treatment for vasomotor symptoms resulting from cancer treatment. However, its use has varied given concerns regarding results of the Women's Health Initiative in 2002,[13,20] which suggested an increased

Table 2
Treatment for menopausal and cancer treatment-related symptoms.[2]

Psychological Effects	Vaginal Atrophy	Vasomotor Symptoms	Radiation Effects	Sleep Disturbance
• Mind-body therapy • Psychotherapy • Sexual behavioral counseling	• Coconut or olive oil as lubricant • Estrogen cream such as Premarin or Estrace cream • Femring or Estring vaginal estrogen ring • SERM such as Osphena • Use of polycarbophil vaginal moisturizers such as Replens • Use of water-based lubricants • Vagifem vaginal tablets	• Acupuncture • Gabapentin, clonidine • HRT • Low-dose oral contraceptives • Removal of caffeine and alcohol from diet • SSRIs such as Effexor, Prozac, Lexapro, or Paxil • Bellergal (ergotamine-belladonna-phenobarb)	• Vaginal dilator to be used 2 to 3 times weekly to prevent vaginal agglutination • Vaginal water-based lubricants with intercourse	• Avoidance of caffeine in the evening hours • Establishing a sleep hygiene routine • Melatonin 1–5 mg at bedtime • Mind-body therapy

Data from references[7,14–17].
Products: Premarin (Pfizer, New York, NY); Estrace (Allergan, Madison, NJ); Femring (Allergan); Estring (Pfizer); (Osphena; Duchesnay USA, Rosemont, PA); Replens (LDS Consumer Products, Cedar Rapids, IA); Vagifem (Novo Nordisk, Plainsboro, NJ).
Abbreviations: HRT, hormone replacement therapy; SERM, selective estrogen receptor modulator; SSRIs, selective serotonin reuptake inhibitors.

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risk of heart disease/heart attack, stroke, and breast cancer in women who received hormone replacement. The dramatic decrease in the use of HRT since 2002 in healthy women is even more marked in women who have already been treated for gynecologic cancer. Despite limitations of retrospective and prospective observational studies and the need for more randomized trials, current evidence suggests that short-term HRT does not appear to have an adverse effect on oncologic outcomes in most gynecologic cancer survivors and improves quality of life.[20] The American Society of Clinical Oncology recommends the use of hormonal therapy for the treatment of vasomotor symptoms with the exception of hormone-sensitive breast cancer, for whom such treatment is contraindicated.[14] Recommended treatment includes vaginal creams (17β-estradiol, conjugated equine estrogen), vaginal rings (17β-estradiol) and vaginal tablets (estradiol hemihydrate).[21]

The decision whether or not to use HRT should be part of a comprehensive health assessment including lifestyle, diet, exercise, smoking, and alcohol.[13] Overall, symptom and survival outcomes vary by primary gynecologic malignancy.[16] The American College of Obstetricians and Gynecologists Committee of Gynecologic Practice recommends that the decision to use HRT should be evaluated with each patient and determined based on individual risk-benefit analysis.[21]

Nonhormonal medications. Antidepressants, including selective serotonin reuptake inhibitors and anticonvulsants are the primary classes of nonhormonal drugs used to manage menopausal symptoms in women with cancer. It is important to note that while several agents are used off-label for symptom management in this population, to date only paroxetine has a US Food and Drug Administration-approved indication for the treatment of vasomotor symptoms of menopause.[16] selective serotonin reuptake inhibitors, including venlafaxine and paroxetine, have demonstrated efficacy in reducing vasomotor-associated symptoms, specifically hot flashes.[16,22] Gabapentin, used primarily for the treatment of seizures and neuropathic pain, has also been effective in the relief of hot flashes, with similar outcomes using pregabalin, though both have been associated with sedation and dizziness. Clonidine, an antihypertensive, has also shown promise in controlling hot flashes, as have ergotamine-phenobarb-belladon and methyldopa, though their side effect profiles generally outweigh the benefit of prescribing these agents.[16] The pineal hormone melatonin plays an important role in the regulation of the circadian sleep/wake cycle, mood, and perhaps immune functions, carcinogenesis, and reproduction.[22] Insomnia and sleep disturbance has long been a symptom of menopausal women, associated with decrease in hormone levels such as estrogen and melatonin, and has a direct effect on quality of life. Limited data suggest that the use of melatonin in low doses of 1 to 5 mg nightly has been effective in the aid of sleep disturbances.[22]

Behavioral interventions. Behavioral interventions include lowering room temperature, using fans to circulate air, dressing in layers to allow for removal of outer clothing as vasomotor symptoms occur, and moderating dietary contributors such as alcohol, spicy foods, and caffeine. Nutritional supplements, including herbal supplements such as black cohosh, have demonstrated mixed efficacy in reducing hot flashes. Because of potential contraindication with other treatments, use should be discussed with a provider prior to initiation.[16] Clinical hypnosis has also shown effectiveness with a 74% reduction in hot flashes among individuals undergoing five weekly sessions.[23]

Sexuality

Sexuality is a central aspect of being human throughout life and encompasses sex, gender identities and roles, sexual orientation, eroticism, pleasure, intimacy, and reproduction.[24] At least 50% of individuals treated for reproductive malignancies report sexual dysfunction,[25] with 18.2% of women with cancer reporting dissatisfaction with sexual function as compared with healthy controls.[26] Sexual dysfunction is often categorized in three areas: physical (eg, vaginal dryness), psychological/emotional (eg, decreased sexual interest), and interpersonal (eg, loss of intimacy).[9,27] Sexual sequelae of cancer treatment can be both acute and chronic, and therefore requires early and frequent assessment from time of diagnosis through survivorship.[27]

Physical Sequelae

Vaginal atrophy. The treatment of gynecologic malignancy is associated with genito-pelvic pain and painful intercourse, and many of these symptoms can arise from alterations in vaginal health from surgery, radiation, and chemotherapy causing vaginal shortening, stenosis, atrophy, and dryness.[28] Vaginal atrophy, often resulting from pelvic irradiation or chemotherapy, is a condition in which the vaginal tissues become dry, thin, and inflamed, resulting in itching, burning, and painful intercourse.[29] Atrophy may also contribute to genitourinary symptoms including burning during urination, urinary urgency, or incontinence.[29] Patients who have undergone radiation therapy are often given vaginal dilators or encouraged to have intercourse at least twice weekly to maintain vaginal length and keep the vagina from developing agglutination, which could preclude early diagnosis of a cancer recurrence.

Water-based lubricants are often recommended to alleviate discomfort with intercourse caused by vaginal dryness. Vaginal moisturizers such as Replens (LDS Consumer Products, Cedar Rapids, IA) can be used several times weekly to aid in vaginal dryness. Replens is a polycarbophil-based vaginal moisturizer that binds to vaginal epithelium, hydrating the vaginal cells. Ospemifene (Osphena; Duchesnay USA, Rosemont, PA) is currently the only US Food and Drug Administration-approved, nonestrogen, oral pill for moderate to severe dyspareunia caused by vulvovaginal atrophy in postmenopausal women.[28] Vaginal estrogen creams such as Estrace (Allergan, Madison, NJ) or Premarin (Pfizer, New York, NY) or the vaginal ring known as Femring (Allergan) and Estring (Pfizer) have also been used to give localized low doses of estrogen directly to the vaginal tissue, which can reduce pain and frequent infections.

Female orgasmic disorder. Orgasmic disorder is defined as compromised orgasmic frequency, intensity, timing, or pleasure.[30] Cancer treatment, including radical hysterectomy, have been associated with decreased frequency and intensity of orgasm.[18] Treatment of orgasmic disorder may include psychotherapy, which may be cognitive behavioral, sensate, or mindfulness focused.[30] In addition, physiologic treatments, including physical therapy to improve pelvic floor tone,[18] and medication-based management that may include vaginal or rectal injections of diazepam or baclofen, or intramuscular injections of onabotulimnum toxin A, may be indicated.[30] Treatment should be consistent with the underlying pathophysiologic or psychological factors.

Case Study No. 1

S.S. is a 46-year-old woman being followed for diagnosis of squamous cell carcinoma of the cervix, stage IB1. She was initially diagnosed with cervical cancer following a cervical biopsy for moderate abnormal vaginal bleeding with evidence of cervical tumor. With staging imaging she was found to have a positive retroperitoneal lymph node. She underwent 6 weeks of extended field pelvic radiation with boost to the lymph nodes. She also received six cycles of concurrent weekly cisplatin chemotherapy. Once therapy was completed the patient was given an appropriate-sized vaginal dilator with instruction to use the dilator twice weekly or if not having sexual intercourse at least twice weekly. She was advised that the use of

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a vaginal dilator or sexual intercourse is important to avoid vaginal agglutination following treatment for cervical cancer. At a follow-up visit approximately 6 months following completion of treatment, she complained of pink vaginal spotting with intercourse. She voiced that she had been using the vaginal dilator twice weekly but was afraid to insert too deeply. Her spouse voiced concern that he was afraid of hurting her during intercourse. There were no vaginal or cervical abnormalities noted on exam.

Plan:

1. The patient was reassured of normal vaginal examination.
2. The patient and her spouse were reassured that mild vaginal spotting is to be expected in the first months and up to 1 year following completion of radiation therapy and advised to continue use of the vaginal dilator or to have sexual intercourse at least twice weekly.
3. Use of the vaginal dilator was discussed in detail. She was advised to use lubrication, inserting the dilator as far as comfortable within the vagina, and to leave in place for at least 10–15 minutes with each use.
4. She was encouraged to use water-based lubricants with intercourse for vaginal dryness.

Psychological/Emotional Sequelae

Sexual interest/arousal. Sexual interest and arousal may be caused both by cancer treatment and its psychoemotional sequelae. In additional to treatment-related causes of decreased interest and arousal, such a tamoxifen, the distress caused by the cancer experience itself can reduce sexual interest.[18] Female sexual interest/arousal disorder includes reduced interest in or initiation of sexual activity, reduced sexual thoughts or fantasies or response to sexual cues, and reduced sexual excitement, pleasure, or physical genital sensation during sexual activity.[28] As with female orgasmic disorder, cognitive behavioral therapy may be effective in addressing this loss of interest and arousal.[28] Flibanserin is approved by the US Food and Drug Administration for the treatment of hypoactive sexual desire disorder but should be used with care given black box side effects including hypotension and lack of evidence specifically in women with cancer.[28]

Body image distress. Body image distress is a well-defined psychosocial issue encompassing an individual's perceptions, feelings, thoughts, and behaviors associated with the individual's body and functioning.[31] Body image distress related to treatment-induced hair loss, weight gain or loss, and lowered self-esteem can all affect sexual well-being in women with cancer.[31,32] Evidence-based interventions include cognitive behavioral therapy, psychosexual counseling, expressive-support therapy, educational interventions to improve self-efficacy, cosmesis-focused interventions, and sensate and physical fitness interventions.[31] It is recommend that body image concerns be discussed with every patient at each encounter because these concerns can emerge and change over time. Indications of body image distress include: preoccupation with appearance changes, difficulties with viewing oneself, avoidance of social situations, significant engagement in appearance-fixing behaviors, and persistent distress because of appearance.[31] Fingeret et al[31] suggest using *The Three C's* approach at each patient encounter: stressing that body image difficulties are *common* during and after treatment; asking patients about specific body image *concerns,* and asking patients about *consequences* of body image difficulties.

Interpersonal sequelae

For individuals with sexual partners during and following their cancer diagnosis, several variables can impact sexual well-being. These include changes in relationship roles if the partner becomes a caregiver, viewing the individual as a cancer patient and not a sexual partner, or partner abandonment, both of which can result in the loss of sex and intimacy for the individual with cancer.[32] Changes in sexual well-being are prevalent not only for the patient but for their partner, with 84% of partners of an individual with a cancer of the reproductive organs reporting changes in sex and intimacy.[33] When addressing sexual well-being it is pivotal to evaluate the patient's preference for partner involvement in discussions and interventions.[14] If the patient identifies a partner and expresses preference for their involvement, interventions that produce stronger results tend to be couple-focused and include treatment components that (1) educate both partners about the woman's diagnosis and treatments, (2) promote the couple's mutual coping and support processes, and (3) include specific sexual therapy techniques to address sexual and body-image difficulties.[34] Sexuality and sexual preferences should never be assumed in the management of sexual side effects, and a safe therapeutic relationship should be established between patient and provider in which the patient should be offered the opportunity to identify sexual preferences and ask questions about sexual considerations related to cancer treatment. Ensuring a nondiscriminatory clinical environment with culturally competent staff and providers who are educated about the needs of sexual minority patients can improve access to appropriate care.[35]

Provider Considerations

In discussing with women the concerns regarding the sequelae of undergoing treatment for gynecologic cancer, issues are revealed that are both physical and mental, visible and invisible, objective and subjective.[36] Despite the prominence of these concerns among patients, evidence consistently suggests that providers do not routinely evaluate, discuss, and make recommendations for sexual health outcomes of cancer and its treatment, and that female cancer survivors may be particularly underserved.[37] Stead et al[38] demonstrated that health professionals do not address sexuality issues with patients and physicians in their study, and were both uncomfortable discussing sex and lacked knowledge about the sexual problems that cancer can cause. A survey in 2007 of gynecologic oncologists revealed that more than 40% did not discuss sexual health issues with their patients and 50% stated that they had inadequate time to address sexual health issues.[39] Sexual functioning and sexual health are an integral part of quality of life and should be addressed at the time of diagnosis, during treatment, and well into the survivorship period of the cancer diagnosis.[14,28]

Nurses in diverse roles are uniquely positioned to discuss sexual health with patients. Yet like other interprofessional health care providers, nurses rarely ask patients about sexual health concerns, and do not routinely share sexual health outcomes of cancer treatment with patients.[40] Recommendations for interprofessional health care providers include integrating discussion of sexual well-being, concerns, and sequelae of treatment from the time of diagnosis, and continually throughout treatment and into survivorship because these needs may change.[9,14,37] Utilizing printed materials that can be readily distributed, such as tip sheets, may help to begin the process of addressing sexual concerns in female cancer patients.[8,37]

The sexual health needs of specialty populations should also be addressed. These include lesbian, bisexual, queer, and transgender individuals[35]; medically underserved populations[41]; and adolescents and young adults[42,43]; each of whom may have unique sexual health, needs, and concerns. It is important that providers address sexuality and quality-of-life issues for all populations they serve.

Utilization of evidence-based instrumentation and communication tools for sexual health assessment is recommended to guide conversations between patients and providers.[9,37] One such example is the well-established PLISSIT model (Fig. 1). The PLISSIT model provides a safe, tolerant, and therapeutic environment for the discussion of sexual concerns and, if necessary, promotes a seamless and efficient referral to an appropriate specialist.[11,44] This basic model can be used by

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The PLISSIT MODEL

- **P**ermission – Obtain permission from the client to initiate sexual discussion
- **L**imited **I**nformation – Provide the limited information needed to function sexually
- **S**pecific **S**uggestions – Give specific suggestions for the client to proceed with sexual relations
- **I**ntensive **T**herapy – Provide intensive therapy surrounding the issues of sexuality for the client

Fig. 1. The PLISSIT model.[11,44]

nurses, physicians, psychologists, social workers, and case managers to communicate with and develop interventions for the patient's needs.

Case Study No. 2

C.S. is a 22-year-old nulligravida woman recently diagnosed with bilateral ovarian masses, suspicious for malignancy. CA125 is elevated at 659. She has peritoneal carcinomatosis noted on imaging with moderate pelvic ascites. The plan is to proceed with cytoreductive surgery. If the ovary proves to be malignant on frozen section, a complete tumor debulking surgery will be performed, including bilateral salpingo-oophorectomy, total abdominal hysterectomy, omentectomy, as well as pelvic and para-aortic lymph node dissection. At the time of initial consultation, fertility concerns were addressed. The possible effects of early surgical menopause were considered and discussed with the patient as well.

Plan:

1. Patient was referred to an Onco-Fertility specialist to discuss the effects of surgery and treatment on future fertility. Options for fertility preservation to be discussed including possible egg retrieval.
2. Patient was given educational information on early menopause, including symptoms to expect, symptom relief options, and likely effects on sexual health and well-being.
3. Patient given the opportunity to ask questions and to explore her feelings regarding the potential effects on sexual health.

Conclusion

Gynecologic cancer affects women of varying ages, backgrounds, marital status, as well as sexual orientation. The issue of sexuality and sexual dysfunction is often lost in the midst of a gynecologic cancer diagnosis, with initial concerns focused on the diagnosis itself, preparation for treatment, and coping with the disease process. The most common issues include lack of sexual desire, pain with intercourse, anxiety, loss of sensation in the genital area, as well as the inability to achieve orgasm. For patients' emotional and physical health, it is important to maintain a sense of sexuality and intimacy because it can provide stress relief, psychological relief, as well as a feeling of deep emotional support from their partner. Patients should receive counseling before treatment for gynecologic cancer to address fears, myths, and what to expect with regard to their sexual function, which should include a partner at the patient's discretion. Providers, including nurses, should evaluate their own comfort level, biases, and perceptions with and of sexual health and utilize evidence-based tools to guide conversations with patients, referring to specialty counselors or interprofessional teams to further address sexual health concerns. Ultimately, sexual health is an integral part of each person and therefore requires timely, evidence-based assessment and intervention to promote well-being during and following cancer care.

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