Oncosexology
Sexual Issues in the Male Cancer Survivor

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KEYWORDS

• Oncosexology • Cancer • Sexual dysfunction • Erectile dysfunction • Prostate cancer
• Testosterone deficiency • Peyronie's disease • Ejaculatory dysfunction

KEY POINTS

- Cancer and its associated treatments often have a negative impact on the sexual function of patients and their partners.
- Pelvic malignancies, such as prostate, bladder, or colorectal cancer, have the most significant impact on the sexual function of male cancer survivors.
- Sexual dysfunction associated with pelvic cancer treatments include erectile dysfunction, testosterone deficiency, ejaculatory dysfunction, orgasmic dysfunction, sexual incontinence, and penile shortening.

INTRODUCTION

Oncosexology is a relatively new term that refers to a multidisciplinary field addressing sexual issues in patients with cancer .[1] Physicians, nurses, psychologists, and other health care providers can all be involved in the field of oncosexology. An oncosexologist can be any of these practitioners who focus on the sexual function of patients with cancer . This discipline has developed out of a need to adequately address sexual concerns in oncology patients. Cancer remains a significant health burden in the United States, with almost 2 million new cases and more than 600,000 cancer deaths anticipated. There is a need for specialists to help cancer survivors and their partners navigate changes to sexuality related to the diagnosis and treatment of cancer.

Monitoring for patient cancer-related distress is an American College of Surgeons cancer hospital accreditation standard in the United States.[2] Although this focus on distress is warranted, the follow through for patients who express distress is suboptimal; only approximately one-third of patients referred for distress symptoms actually obtain the desired assistance. There are many barriers to access, including time restraints, patient beliefs, logistical issues, and variability in insurance/financial issues.[2] A proposed model to address this gap in care is to identify distress and patient needs, offer support within the oncology team as appropriate, and/or refer out as needed. The oncology team should then help the patient navigate barriers to care and continue to monitor and address patient distress.[2]

The management of distress in general needs to be improved in oncology patients. Distress related to sexual issues is a particularly sensitive and important aspect of oncology-related distress. Cancer and its treatments can have direct and indirect impact on sexual function and satisfaction. Absence of sexual experience can be a source of distress. Sexual expression may also be a form of coping with distressing life circumstances and its absence can compound other forms of cancer-related distress.[3]

Historically, health care providers have not adequately discussed sexual issues with patients

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with cancer . This is of major concern, given the significant impact of cancer and cancer treatments on sexual functioning. It is estimated that 40% to 100% of patients with cancer experience perturbations in sexual functioning. Patients with pelvic cancers tend to have greater risks with respect to sexual dysfunctions.[4] Despite this, many patients with cancer are not counseled on sexual side effects. A study of nearly 500 patients with colorectal cancer (CRC) found that only 16% of patients said that their medical team discussed sexual concerns with them.[5] Among patients with prostate cancer (PCA), few report being counseled on penile length loss, Peyronie disease (PD), and/or anejaculation after prostate cancer treatment such as radical prostatectomy (RP).[6]

Self-identified oncosexologists tend to be more engaged and inquisitive regarding a patient's experience of sexual distress during or after treatment. However, even among these providers, up to 10% may not address sexual issues with patients. A survey of self-reported oncosexology providers who attended a "Cancer, Sexuality and Fertility" meeting demonstrated that only 90% endorsed discussing sexuality with patients. Almost 7% of these practitioners noted they felt uncomfortable discussing sexual concerns with patients, and most had no experience discussing sexuality with adolescent patients.[4]

Fortunately, research has shown that training practitioners can improve their handling of oncosexology issues. A review of these interventions evaluated 7 studies that aimed to improve sexual health knowledge of providers and increase their comfort level with these discussions. Interventions included either face-to-face workshops or lectures or online video-based training. Endpoints were assessed anywhere from 3 weeks to 16 months after the interventions and included self-reported questionnaires that ranged from sexual health knowledge and attitudes to frequency discussing the topic, and provider comfort level. Many studies showed that with training of health care providers, there may be a durable improvement in their knowledge and comfort level regarding sexual concerns. This has the end result of an increase in the frequency with which providers discuss sex with patients.[7] Increasing these conversations is vital, as it has been shown to improve sexual function in patients with cancer . Of patients with hematologic cancer status-post stem cell transplantation, those who had been counseled on sexual side effects had fewer sexual problems at 3 years after treatment ($r = -0.43$, $P = .02$).[8]

These data demonstrate a clear need to expand the field of oncosexology and better counsel patients with cancer on the sexual impact of their disease and treatments. Sexual functioning should be discussed to assess baseline symptoms and in the context of the impact of various treatment options.[3] This article discusses sexual issues in male patients with cancer , with a specific focus on men with prostate malignancies, as these men are at high risk for sexual dysfunction (**Box 1**). Readers interested in oncosexology in women are referred to the Mindy Goldman and Mary Kathryn Abel's article, "Oncology Survivorship and Sexual Wellness for Women," elsewhere in this issue.

IMPACT OF CANCER DIAGNOSIS ON SEXUAL FUNCTION

Any cancer diagnosis can affect patients' sexual function, and cancer treatments often compound this issue. A survey of 2500 patients with cancer demonstrated that 44% of patients endorsed sexual symptoms. More than half of patients answered that they had unmet informational needs. Of these patients seeking information, 50% sought information of the impact of cancer on their spouse or their relationship. Patients with sexual side effects were 2 times more likely to have questions on the impact of cancer on their relationship (odds ratio [OR] 2.05, 95% confidence interval [CI] 1.54–2.72).[9] Clearly, sexual side effects of cancer and its treatments are common and leads to patient concern about their relationships.

The impact of PCA on sexual function can be profound. Analysis of almost 60,000 patients with PCA in the United Kingdom showed that 81% of these men had sexual issues related to their cancer and treatment. Surprisingly, 55.8% of them had not received any treatment for these sexual issues.[10] Clearly there is a high burden of unmet needs in this population.

Couples-based intervention may be particularly helpful for men and their partners who are struggling with cancer-related sexual issues. A randomized trial in 189 post-RP patients with PCA and their female partners compared "usual care" (ie, printed education materials and standard medical care) to peer support or nurse support (ie, phone calls for support or counseling from either peers or nurses, respectively, as well as written and audiovisual materials) over a 5-year span. There was clear benefit to both experimental arms compared with control for men adhering to erectile dysfunction (ED) treatment. At time points of 2, 3, 4, and 5 years post-RP, the men in the treatment arms reported higher overall use of ED treatments, to include phosphodiesterase 5 inhibitors (PDE5i), intracavernosal injections (ICI), or vacuum erection

Box 1
Sexual conditions associated with prostate cancer treatment

- Erectile dysfunction
- Orgasmic dysfunction
  - Anorgasmia
  - Dysorgasmia
  - Delayed orgasm
  - Change in orgasm intensity
- Ejaculatory dysfunction
  - Anejaculation
  - Decreased volume
  - Premature ejaculation
- Sexual incontinence
  - Arousal incontinence
  - Climacturia
- Low libido
- Loss of penile length
- Peyronie's disease

devices (VED) (P<.05 for both groups compared with control).[11] At 2 years, 61% of the usual care group used ED treatments compared with 89% in peer and 88% in nurse support groups; at 3 years, this was 55% in usual care versus 80% in peer support and 81% in nurse support. This trend continued at 4 years, with 47% of usual care and 87% and 79% of peer and nurse support, respectively, using ED treatments. Similar results were seen at year 5, with 54% of usual care, 87% of peer support, and 80% of nurse support patients using ED treatments.[11] Interestingly, although the support groups used more ED treatment, there was no difference in sexual satisfaction and function, as measured by the International Index of Erectile Function (IIEF), among the 3 groups.[11]

IMPACT OF MALE SEXUAL DYSFUNCTION ON PARTNERS

Sexual well-being in patients with cancer is often overlooked; the sexual well-being of partners of patients with cancer is similarly poorly understood and often neglected. The unmet needs and stressors facing the partners of patients with cancer can have a negative effect on both members of the dyad.[12] A survey of 113 female partners of patients with PCA noted key themes of coping with changes to their relationship and the emotional distress of dealing with their partners' illness. Women had a range of responses, from complaining of inconvenience due to changes in sex life to lamenting the complete loss of their sexual relationship.[13] The impact on partners is further demonstrated with quantitative data. Eighty-eight pairs of patients with PCA and their partners were surveyed at 6 and 12 months after PCA diagnosis. At 6 months, 51% of partners noted a very or somewhat negative impact on their sexual relationship, and this increased to 71% at 12 months. The overall relationship suffered as well, with 10% of partners noting a very or somewhat negative impact at 6 months, which increased to 14% at 12 months postdiagnosis.[14]

The impact on partners is less well studied in gay or bisexual men. A review of PCA in this population noted unique challenges. A firmer erection is needed for insertive anal intercourse, and thus the sexual role of the patient may be changed. Fewer than half of insertive partners are able to always remain insertive postoperatively. Similarly, due to discomfort or lack of pleasure postoperatively, receptive partners may also change their sexual roles. As not all gay or bisexual men are versatile (acting as insertive and receptive partner), this can impact the couples' sexual relationship.[15] Clearly, patients and their partners (regardless of sexual orientation) need resources to help mitigate this decline in their sexual and overall relationship.

PELVIC MALIGNANCIES

Pelvic malignancies, such as PCA, CRC, or bladder cancer (BCA), arguably have the most significant impact on sexual function and have been the best studied with respect to oncosexology. Although this article focuses on PCA, some general guidance on management of other pelvic malignancies can be derived from these data.

ERECTILE DYSFUNCTION

ED is multifactorial in patients with cancer . Psychological issues, such as anxiety, depression, or relationship stressors can contribute to ED in all male patients with cancer .[6] Although clearly all patients with cancer are at increased risk, arguably no oncology patients are more at risk for ED than men with PCA.

The rate of ED after an RP is difficult to compare given that many studies do not mention how ED was defined or the timepoint it was defined. Patient populations also vary between studies. The published literature thus has a broad

range of 6% to 68%.[16] From a purely function perspective, erectile function (EF) recovery can be conceptualized as the ability to achieve and maintain an erection that allows for satisfying sexual activity. Using this definition, rates of satisfactory EF at 12 months post-RP can be anywhere from 25% to 77%.[16] The International Consultation for Sexual Medicine (ICSM) recommends that researchers use validated instruments[16] for future studies to allow for comparisons between series and to provide patients with more realistic expectations.

ED is also common in men after a radical cystoprostatectomy (CP), with ED rates as high as 94% in the literature and up to half of patients being sexually inactive postoperatively.[3] Likewise, ED is high in patients with CRC. Unsurprisingly, this is higher in patients with rectal compared with colon cancer. Eighty-six percent of all patients with rectal cancer endorse sexual dysfunction compared with 39% of patients with colon cancer .[3]

Factors predicting EF recovery include younger age, bilateral nerve-sparing surgery, and better preoperative EF.[16] A common practice in men after RP or radiation therapy (RT) for PCA is a program referred to as penile rehabilitation. Penile rehabilitation is nonspecific, but is broadly intended to enhance recovery of penile erections after cancer treatment. Penile rehabilitation protocols vary widely, but typically include routine or even daily dosing of PDE5i, which can be given in a low dose daily and/or on demand dosing to enhance erections. Rehab ICI or VED is used by many.[6]

Existing data on penile rehabilitation comes from varied sources using different protocols and outcome measures and is hence difficult to compare. The ICSM is unable to recommend a specific rehabilitation protocol as optimal after PCA treatment.[6] Furthermore, the American Urological Association (AUA) guidelines on ED concluded, based on a review of all randomized placebo-controlled studies of PDE5I for rehabilitation after RP, that there is no evidence that PDE5I-based penile rehabilitation protocol leads to improved recovery of spontaneous erection function.[17]

PDE5I-based penile rehabilitation remains generally safe, and it is our practice that men take a low-dose PDE5i daily, with at least 1 full dose each week to try to achieve an erection. If men are unable to achieve an erection satisfactory for penetration with the full dose PDE5i by 6 weeks postoperatively, then they remain on the low dose daily and perform ICI at least once a week to induce an erection.

Ejaculatory Dysfunction

Although ED is arguably the most common sexual change in male patients with cancer , there are numerous other changes that can occur in these men. This includes ejaculatory dysfunction, which comprises anejaculation, change in ejaculate volume, and premature ejaculation.

Anejaculation refers to the absence of antegrade ejaculate efflux at the time of orgasm. This can be due to failure of emission, where ejaculate is not released, or retrograde ejaculation, where the ejaculate travels backwards into the bladder due to bladder neck dysfunction. Anejaculation is universal after RP, as surgery involves removal of the organs responsible for production of more than 95% of the content of semen. This should be discussed with all patients preoperatively, as natural conception is no longer be possible.[6] Aside from effects on fertility, anejaculation can have a significant impact on men, as it can affect body image and feelings of masculinity. There is also thought that the absence of ejaculate may reduce orgasmic intensity.[6]

Anejaculation can also occur with prostate RT but to a lesser degree. This has been noted in 11% of men undergoing prostate external beam RT (EBRT)[18] and approximately 19% of men undergoing brachytherapy. Of those men who maintained ejaculation, almost all (85%) reported reduced ejaculate volume. Interestingly, the addition of androgen deprivation therapy (ADT) did not affect ejaculatory function ($P>.05$).[19] Another study evaluated 364 men who had RT, including EBRT, and brachytherapy $\pm$ ADT. Men were followed for a mean of 6.0 ± 4.5 years. Anejaculation was seen in 16% of men at 1 year, 69% at 3 years, and 89% at 5 years. At their last visit, 72% of men reported anejaculation. Variables associated with greater risk for anejaculation included age older than 65 years (OR 2.8; 95% CI 1.8–4.2; $P<.01$), baseline prostate volume <40 g (OR 1.8; 95% CI 1.3–6.1; $P<.01$), use of ADT (OR 2.2; 95% CI 1.9–9.8; $P<.01$) and a total RT dose of greater than 100 Gy (OR 1.6; 95% CI 1.4–7.2; $P<.05$).[20]

Premature ejaculation (PE) is common in patients with cancer, although there is no specific organic mechanism through which cancer or its treatments leads to PE. In general, the rates of PE are difficult to establish, given various definitions used. This can range in the literature from 3% when using a strict definition of chronic and consistent intravaginal ejaculatory latency time of less than 1 minute coupled with absence of sense of control and personal bother to 78% in men reporting any history of ejaculating before they wished to do so.[21] The data are limited when

specifically evaluating men with cancer. An assessment was conducted in 1202 men newly diagnosed with PCA who were referred to urology for treatment discussion. PE was diagnosed by physicians using the PE Diagnostic Tool, which is based on Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) criteria for PE and hence lack a robust time-based criterion. The rates were high at 63.7% for PE and 66.2% for ED (as measured by the IIEF-5).[22] Predictors of PE included IIEF-5 scores (β 0.58 [0.03], $P = .007$), which suggests that these 2 disorders are associated.[22] These data support the notion that acquired PE is strongly linked to ED; the estimated prevalence for clinical PE may be artificially elevated in this study, as the DSM-IV-TR definition is outdated and does not include essential time-based criteria.

Orgasmic Dysfunction

Many men after PCA treatment notice some form of orgasmic dysfunction, such as change in orgasm intensity, inability to reach orgasm (anorgasmia), delayed orgasm, or pain with orgasm (dysorgasmia). Changes in orgasm intensity may be psychological or physical and related to changes in pelvic floor muscle contraction and/or ejaculation; data on this topic are sparse.[6] Dysorgasmia is poorly understood. The etiology is proposed to be from spasms of pelvic floor musculature or issues at the vesicourethral anastomosis. Many patients experience a reduction in symptoms after treatment with an alpha blocker such as tamsulosin.[6]

In a series of more than 250 men post-RP, 5% had complete anorgasmia, whereas 57% had delayed orgasm; 60% noted a decrease in orgasm intensity, and 10% had dysorgasmia.[23] Orgasmic dysfunction has also been studied in men post-RT for PCA. A survey of more than 100 men status-post EBRT ± ADT noted common orgasmic changes in these men; 15% reported dysorgasmia, 24% had anorgasmia, 40% reported delayed ejaculation, and 44% reported decreased orgasmic intensity.[18] In men status-post brachytherapy ± ADT, 30% had dysorgasmia and 10% anorgasmia. Interestingly, ADT did not increase the risk of orgasmic dysfunction in these men ($P>.05$).[19]

Sexual Incontinence

Sexual incontinence is composed of arousal incontinence (ie, urine leakage with foreplay or arousal) and climacturia (ie, orgasm-associated incontinence). These conditions are not as well studied as other sexual changes in patients with PCA , but they are known to occur after RP and to a lesser extent RT.[18,23] The RP literature is more robust, with multiple studies describing sexual incontinence postoperatively.

With regard to climacturia, the rate ranges from 20% to 93% based on the definition used.[23–29] For example, Choi and colleagues[25] report the lowest end of the spectrum at 20% of men post-RP, but they used a definition of 3 or more episodes of climacturia. Conversely, Barnas and colleagues[29] reported a 93% rate of climacturia, as defined by ≥1 episode. However, this study design was a retrospective survey with a 68% response rate, which could have introduced bias and thus contributed to these higher rates.

Data on arousal incontinence (AI) is limited, but this entity has been described in 38% of post-RP men without diurnal incontinence and in 82% of men undergoing a sling or artificial sphincter placement for stress urinary incontinence post-RP.[30,31] A larger series of prostatectomy patients noted 49% of men endorsed experiencing AI after their surgery.[32]

In a series of more than 250 sexually active men post-RP, 38% endorsed sexual incontinence when surveyed between 3 to 36 months postoperative; 29% of men reported AI and 27% had climacturia (there was overlap between these groups). On multivariate analysis of predictors of sexual incontinence, the only significant factor was more severe stress urinary incontinence (SUI) as measured by the International Consultation on Incontinence Questionnaire (OR 1.17; 95% CI 1.10–1.25; $P<.0001$).[23]

When specifically evaluating AI, more severe SUI was still a predictor. A total of 226 men post-RP were queried on AI. At a mean of 18.3 ± 5.5 months after surgery, 49% of men endorsed experiencing AI at some point during their recovery. On multivariate analysis of predictors of AI, worsening SUI, as measured by increasing pads per day (OR 1.55; 95% CI 1.12–2.13; $P = .01$) and the absence of hypertension (hypertension OR 0.44; 95% CI 0.25–0.80; $P = .01$), was associated with AI.[32]

The available evidence suggests against a close link between climacturia and SUI. A study evaluating predictors of climacturia showed that none of the factors analyzed, such as age, time since surgery, urinary flow rate, stress incontinence (as defined as >1 pad per day), or urinary symptoms as measured by the International Prostate Symptom Score, were associated with climacuturia.[26] There are some data to suggest a link between functional urethral length and climacturia. A small functional urodynamics study showed men with climacturia post-RP had shorter functional urethral length at 20.3 ± 4.03 mm compared with controls at 35.2 ± 4.81 mm ($P = .02$).[33]

Strategies to manage sexual incontinence include limiting fluid intake, urinating before sexual activity, and/or using condoms.[34] We have also recommended use of a variable tension penile loop worn at the base of the penis, as this has been shown to eliminate climacturia in almost half of patients and improved symptoms in the remaining paitients.[35] This band may be less useful in patients with AI, as it can be more difficult to predict arousal.

Peyronie Disease

One of the most underrecognized sexual change associated with PCA treatment is PD. PD is characterized by penile deformity, such as curvature, waisting, or indentation, and can be associated with penile pain. In a group of more than 250 men post-RP, 10% noted a new penile curvature postoperatively.[23] A larger series evaluated more than 1000 men post-RP at a mean time of 13.9 $\pm$ 0.7 months after surgery and found that 15.9% had new-onset PD postoperatively. On multivariate analysis for incident PD in these men, younger age (per 5 years) and white race (compared with nonwhite) were both associated with higher risk (OR 1.28; 95% CI 1.24–1.32 and OR 4.08; 95% CI 1.73–9.58, respectively).[36] Although the data are even more limited with RT, a series of more than 100 men status-post RT $\pm$ ADT noted that 12% endorsed new penile curvature and 6% had penile pain.[18] More research is needed to fully elucidate the rates of PD in patients with PCA after RT and RP.

Penile Shortening

Penile length loss is common after PCA treatment and has been linked to treatment regret.[37] Proposed etiologies include sympathetic hyperinnervation or structural changes, such as fibrosis or collagenization from cavernous nerve injury or cavernosal hypoxia.[38] Men post-RP have been noted to endorse subjective length loss, but there are limited data on objective measurements. With regard to subjective report, a series of more than 250 men post-RP showed that almost half (47%) reported >1 cm length loss.[23] On multivariate analysis, risks of self-reported penile shortening included ED (Erectile Hardness Score < 3 with OR 1.81; 95% CI 1.07–3.10) and increasing body mass index (BMI) calculated by self-reported height and weight (OR 1.10; 95% CI 1.02–1.19; P = .01). The only protective factor was unilateral or bilateral nerve-sparing surgery (OR 0.32; 95% CI 0.16–0.95; P = .0005) compared with bilateral non–nerve-sparing.[23]

Although subjective length loss is common, objective data indicate that penile length loss is less common than self-report would indicate. This could, however, be in part due to differing measuring techniques. The most common way to measure stretched flaccid length it to place axial traction on the penis and measure from coronal sulcus to penopubic junction.[39] This can underestimate penile length by up to 23% depending on the amount of traction and whether the suprapubic fat pad is compressed or not.[39]

One study used a single evaluator and measured stretched flaccid length from pubic bone to coronal sulcus preoperatively and then at 2 and 6 months post-RP.[40] EF was measured via the IIEF erectile function domain (EFD). Men were recommended for a penile rehabilitation protocol of a low dose of sildenafil nightly and a full dose twice a week to induce an erection. The men were separated based on PDE5i compliance into a group who "always" took the PDE5i compared with those in all other frequencies of compliance, from never to frequently. At 6 months, fewer of the compliant patients had length loss at 25% compared with the men with less frequent PDE5i use at 52% (P = .03).[40] The PDE5i-compliant patients had no penile length loss at 6 months (difference of +1 $\pm$ 6.7 mm, P = .37), whereas the noncompliant group experienced length loss (-4.4 ± 16.6 mm, P<.002).[40] On multivariate analysis of stretched flaccid penile length loss, both "always" using PDE5i and EFD score at 6 months were associated with less length loss ($\beta = -0.54$, P = .002 and $\beta = -0.35$, P = .05, respectively).[40]

Although less well described, there are also data indicating penile length loss after radical CP for BCA. A series of 151 men post-CP evaluated EF via the IIEF-5 and asked subjective questions on perceived penile length. At a median follow-up of 28 months, these men had severe ED with a mean IIEF-5 of 3. More than half reported penile length loss, and of those, 55% reported a loss of greater than 1 inch.[41] On multivariate analysis of predictors of length loss, severe ED (defined as IIEF-5 score 1–7) and higher BMI were associated with length loss (OR 3.712; 95% CI 1.43–9.64; P = .0071 and OR 1.198; 95% CI 1.38–10.53; P = .006, respectively).[41]

Surgery is not the only cause of penile length loss in patients with cancer . A survey of more than 100 men who had EBRT $\pm$ ADT 3 months to 5 years prior inquired about subjective length loss; 44% endorsed penile length loss of >1 cm.[18] Factors analyzed included not receiving ADT, the duration of ADT, cancer tumor stage, BMI, Charlson comorbidity index, and ED

(as measured by an erectile hardness scale score of 1 or 2) On logistic regression analysis, none of the factor analyses predicted length loss.[18] A series of 47 men had 9 months of ADT and 70 Gr of RT. Flaccid length was measured at baseline and then every 3 months for 18 months. Flaccid penile length decreased from 14.20 ± 1.10 cm at baseline to 8.60 ± 1.06 cm at 18 months (P<.001).[42] These studies are limited in that there are no data on RT alone.

A large series of almost 950 men treated with RT for biochemical recurrence after PCA treatment had an overall subjective rate of penile shortening of 2.63%. Interestingly, length loss was reported by no patients in the RT alone group compared with 2.67% in the RT plus ADT group (P = .016).[43] This suggests that ADT as opposed to RT is what leads to penile length loss in these men. This is supported by a study of men who received ADT as primary continuous therapy for PCA. Thirty-nine men had stretched flaccid length measured at baseline and then every 3 months for 24 months. Results showed a steady decline in penile length that stabilized by 15 months after initiation of ADT. The mean length went from 10.76 ± 1.92 cm pre-ADT to 8.05 cm ± 1.36 after 24 months of treatment (P<.001).[44]

Although penile length loss is clearly common after PCA treatment, there are data to suggest that this can be reduced. As mentioned previously, daily PDE5i use was associated with preserved length in RP patients compared with those with less frequent use.[40] VEDs have also been investigated for penile length preservation. A review article summarized that penile shortening and loss of girth was reported in 45% to 71% of men post-RP who did not use a VED compared with 3.5% to 27% of men who used VED (no P-value provided).[45] Existing data are hampered by the absence of randomization, blinding, and control interventions, so these conclusions should be interpreted with caution; better designed studies are required.

TESTICULAR CANCER

Patients with testicular cancer (TCA) can experience significant changes in their sexual health, from erectile and ejaculatory dysfunction to testosterone deficiency (TD). These changes can be psychologically devastating, as most patients with TCA are young and may not be in stable supportive relationships.

Ejaculatory Dysfunction

Ejaculatory dysfunction is common in men with TCA after retroperitoneal lymph node dissection (RPLND) due to damage to lumbar sympathetic nerves. Up to 50% of patients with TCA have ejaculatory dysfunction.[3] With newer nerve-sparing techniques (when possible from an oncologic perspective), there is less risk of anejaculation in these men.[46] Both a modified unilateral template or a nerve-sparing technique have been shown to preserve antegrade ejaculation in many men. For primary RPLND, the rates of preserved ejaculation range from 75% to 100% and 25% to 100% for post-chemo RPLND.[46] Given that many men with TCA are young, the risk of anejaculation and its implications on fertility should be discussed before RPLND.

Testosterone Deficiency

Men with TCA are at risk for TD; this may be the result of treatments but could also be attributable to testicular dysgenesis syndrome. Testicular dysgenesis is a putative syndrome that involves endocrine disruption during fetal development, leading to a constellation of symptoms to include hypospadias, cryptorchidism, infertility, and TCA.[47] The fact that many men with TCA have preexisting TD and/or impaired spermatogenesis in non–cancer-containing testicle supports this notion.[47] One series showed that 5% of patients with TCA had TD before orchiectomy, increasing to 16% when assessed at 1-month post-orchiectomy.[48] This suggests that these men are predisposed to TD, and that further loss of testicular tissue exacerbates the issue.

Treatment for TCA clearly compounds the risk of TD. For example, data on men with TCA has shown that chemotherapy has a clear dose-response relationship with TD due to the gonadotoxicty.[49] Retroperitoneal radiation for metastatic disease can also lead to TD due to scatter to the testes.[50] An abdominal radiation dose of 30 Gy is associated with a 0.09 to 0.32 Gy to the testes, which leads to a slightly increased risk of TD due to Leydig cell damage.[50]

In an elegant meta-analysis, rates of TD were assessed in standard chemotherapy, nonconventional chemotherapy (essentially high-dose) and RT as compared with orchiectomy alone.[49] The lowest risk of TD was with RT (OR 1.6; 95% CI 1.0–2.4; P = .03). This was followed by conventional chemotherapy regimens, which had an OR of 1.8 (95% CI 1.3–2.5; P = .0007). The highest risk of TD was with nonconventional chemotherapy (OR 3.1; 95% CI 2.0–4.8; P<.001).[49]

Low Libido

Libido, or sex drive, is another form of sexual dysfunction that is multifactorial and can have

organic as well as psychological components. Although this can happen to any patient with cancer, the effects are often more noticeable in younger patients (such as men with TCA), as these patients often have a higher pre-illness libido.

One study evaluated 129 consecutive patients with TCA 3 to 5 years after treatment compared with 916 age-matched controls. Sexual dysfunction was self-reported using epidemiologic study questions. After controlling for comorbidities, patients with TCA were more likely to have low libido (OR 6.7; 95% CI 2.1–21) compared with controls.[51]

Another study followed patients longitudinally. They used a Dutch questionnaire on sexual function and administered it to patients with TCA post-orchiectomy but preradiation, and then again 3 and 6 months after radiation[52]; 23% of the patients reported a decrease in sexual interest. Many men endorsed body image issues due to testicular loss, and in 13% of men, this led to concern about having sexual relations with their partners.[52]

TD is thought to be an etiology of impairment of sexual desire. Testosterone has a clear link to libido, and thus this can be affected with systemic illness, CT, or abdominal/pelvic RT, as these can all lead to TD. The general link between TD and libido was evaluated in a study of 400 healthy men aged 20 to 50 years. These men all received 16 weeks of ADT and either testosterone gel in concentrations of 1.25 g, 2.5 g, 5g, or 10g daily or a placebo gel. Results showed a stepwise decrease in libido as testosterone replacement decreased. This demonstrates how sex drive is intricately linked to testosterone levels.[53]

However, low libido is multifactorial and there are additional factors at play, especially in patients with cancer . In the aforementioned study of patients with TCA versus controls, TD, as defined by a luteinizing hormone (LH) level greater than 10 IU/L or testosterone less than 10 nmol/L (288 ng/dL) was not associated with low libido (OR 1.2; 95% CI 0.11–14).[51] Another study evaluated men with bilateral orchiectomies who were on intramuscular testosterone every 3 weeks. They were evaluated with laboratory tests and questionnaires 1 day after injection, mid-cycle, and just before injection.[54] With respect to libido, men were asked to grade it from a scale of 1 to 10 with 1 being absent and 10 being very strong. Three of 7 patients reported low libido before injection; however, their testosterone levels were no different from men who did not complain of low libido.[54] This demonstrates the multifactorial nature of this condition and suggests that some men may be more sensitive to changes in testosterone and its impact on libido.

Erectile Dysfunction

Patients with TCA are at risk for ED given the frequency of TD in this population. In general, there is a clear link between TD and ED. In the aforementioned study with young men receiving ADT and then testosterone gel versus placebo, results show a link between ED and testosterone, but only at subphysiologic levels of testosterone. A decline in EF was only seen in the men on placebo or on the lowest testosterone dose of 1.25 g daily, but the men on 2.5 to 10 g daily did not experience a change in their erections ($P<.05$).[53] Normal EF is testosterone-dependent, but only at lower levels. Hence, men undergoing cancer treatment may be at higher risk for hormone-deficiency–related ED because many cancer treatments may lead to TD.

Patients with TCA can also be at risk for ED independent of their testosterone levels. In the aforementioned study on patients with TCA versus controls, the patient with cancer had higher rates of ED (OR 3.8; 95% CI 1.4–10).[51] However, ED was not associated with TD (OR 1.1; 95% CI 0.26–4.5).[51]

HEMATOLOGIC MALIGNANCIES

Patients with hematologic malignancies, especially those undergoing stem cell transplantation (SCT), are at high risk for sexual dysfunction. These patients require high-dose chemotherapy, usually involving alkylating agents, which are highly gonadotoxic. Total body irradiation (TBI) can also damage the testes and penis, thus further contributing to sexual dysfunction.[55] Patients with an allogeneic SCT will typically require immunosuppressants, which can further worsen hormonal status and sexual function.[55] This section focuses on TD, ED, and low libido in these men.

Testosterone Deficiency

The etiology of TD in men undergoing SCT is multifactorial and can include chemotherapy, TBI, and chronic corticosteroids.[55] In a series of 16 men status-post SCT, 88% had elevated follicle-stimulating hormone and 47% elevated LH; 38% of these men had low testosterone.[56] The impact of these specific hormonal perturbations on sexual function remains ambiguous.

Erectile Dysfunction and Low Libido

ED in patients with hematological malignancy may be multifactorial, related to TD, autonomic neuropathy from chemotherapy, TBI, and/or psychogenic causes.[3,55] A case-control series of men undergoing SCT evaluated patients pretransplantation,

6 months after, and 1, 2, 3, and 5 years post-SCT and compared their results at 5 years with age-matched controls (eg, siblings or friends of the patients or community-based volunteers).[57] One hundred percent of controls had been sexually active in the past month compared with 82% of patients ($P = .04$). Sexual function was assessed via the Sexual Function Questionnaire, and the sexual function mean score was slightly lower in patients (3.2 ± 1.0) compared with controls (3.7 ± 0.6); $P = .01$.[57] Forty-six percent of male patients had at least 1 sexual complaint compared with 21% in male controls ($P = .05$). Delayed ejaculation was the most common sexual complaint (27% of men), but ED was also common, with problems achieving erection in 23% and problems maintaining erection in 23%. These rates were lower in controls, with only 3% having delayed ejaculation, 6% had difficulty achieving erection, and 9% had difficulty maintaining an erection.[57]

In the aforementioned study of hormone changes after SCT, TD was a significant predictor of low libido ($P = .008$).[56] A decrease in sex drive and sexual activity is common after SCT. Of 34 men after SCT for leukemia, 56% noted a decreased interest in sex, 59% decreased sexual pleasure, and 62% had decline in sexual activity based on answers to study-specific, single-item questions.[58] When followed longitudinally, it is clear that these problems persist for years after SCT. At 5 years post-SCT, 23% of men noted low libido. Of men who were not sexually active, low libido was one of the most common reasons cited for lack of sexual activity.[57]

Although not evaluating ED or libido per se, a longitudinal study evaluated sexual activity in patients post-SCT, which can be considered a surrogate for sexual dysfunction. Patients were interviewed pretransplantation and then 6 months and 1 and 3 years afterward. Pretransplant men were most concerned with lack of sexual interest (46%), but this shifted to concern regarding body appearance in 61% of men at 3 years.[8] Of 90 men who were sexually active pretransplant, only 18 were active at 1 and 3 years after treatment.[8]

RECOMMENDATIONS

The aforementioned data demonstrate the breadth and prevalence of aspects of sexual dysfunction seen in male patients with cancer . A diagnosis of cancer itself can lead to various sexual side effects. This is further compounded by various treatments, such as chemotherapy, radiation, surgery, and ADT. We recommend a discussion of sexual functioning be initiated by providers early on in the process, typically following the initial cancer diagnosis. The impact of all oncologic treatment modalities on sexual functioning also should be discussed. Patient and partner goals need to be addressed, as this may impact treatment decisions. Throughout the treatment and recovery process, men should be routinely queried about the presence of sexual dysfunction and have a thorough discussion of their treatment options.

With regard to radical pelvic surgery or radiation, we recommend all men with any possible interest in future sexual function undergo a penile rehabilitation program. As mentioned previously, at our institution, this involves a low-dose PDE5i daily with 1 full treatment dose at least once a week. Any patient who is not able to achieve a penetration-hardness erection by 6 weeks is taught to perform ICI weekly in lieu of the test dose.

Any patient undergoing chemotherapy or TBI needs to be counseled on the risk of TD. They should be regularly screened for symptoms. If there is clinical concern for TD based on signs or symptoms, they should have 2 early morning testosterone labs as per the AUA guidelines.[59] If their testosterone is low in the context of signs and symptoms, testosterone therapy should be offered.

SUMMARY

In summation, the emerging field of oncosexology focuses on the sexual consequences of cancer and its treatments. As many patients are not being appropriately counseled on sexual consequences, it is imperative that health care practitioners provide adequate information on the sexual dysfunction associated with cancer treatment. Although pelvic cancer, especially genitourinary malignancy, has higher risk of sexual dysfunction, these changes can occur in all patients with cancer . The etiology is often multifactorial, with psychological and organic components at play. TD from chronic illness, CT, RT, or ADT can contribute to ED, low libido, and ejaculatory and orgasmic dysfunction. Pelvic surgery or RT can remove or damage the ejaculatory apparatus, as well as the cavernous nerves responsible for normal EF. With appropriate treatment and counseling, oncosexologists can help patients to navigate these sexual changes.

CLINICS CARE POINTS

- Health care providers need to discuss sexual issues with patients with cancer, including potential adverse effects of all treatment options.

- Many patients with cancer endorse sexual dysfunction and associated unmet informational and/or treatment needs.
- Pelvic malignancies, such as prostate, bladder, or colorectal cancer, have high rates of sexual dysfunction.
- Sexual dysfunction in male patients with cancer include ED, ejaculatory dysfunction, orgasmic dysfunction, PD, low libido, TD, and penile shortening.
- Penile rehabilitation is recommended after pelvic cancer treatment; however, there are no data to suggest the superiority of one rehabilitation protocol over another.

DISCLOSURE

The authors have nothing to disclose.

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