Sexual Health Issues in Men With Cancer

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An Undertreated Problem

While the cancer patient may be affected by sexual dysfunction throughout the entire course of the disease, from the first stage of diagnosis through treatment and cure or progressive disease, sexual health is largely underevaluated and undertreated. Incrocci et al demonstrated a significant decline in patients' self-reported sexual activity-attributed to decreased sexual desire and interest, erectile dysfunction, or a partner's loss of sexual desire-among men diagnosed with localized prostate cancer awaiting definitive treatment.[2] Despite the use of questionnaires 4 to 9 weeks after the diagnosis was made and treatment modality determined (baseline sexual function being based on patient recall), this innovative study emphasizes the impact of the diagnosis of cancer itself on sexual function. The authors concluded that sexual health should be discussed with cancer patients early in the course of treatment, as part of a comprehensive oncologic approach. Sexual problems should be anticipated and patients should be actively screened as they are unlikely to initiate discussion on sexual issues, believing that it is inappropriate to address sexual health when curing cancer should be the main concern. Even if sexual health issues are not present, early discussion will legitimize raising sexual issues later in the course of the treatment or the disease.

Litwin et al compared health-related quality of life (HRQOL) as assessed by the physician and as reported by prostate cancer patients, and demonstrated a gross underestimation of the prevalence of symptoms by clinicians.[3] In fact, they found that underestimation of all domains of quality of life including sexual function (libido and ED) was the rule when reported by the urologist. Ananth et al demonstrated that sexual dysfunction is more profound in patients with advanced cancer receiving palliative care, affecting the frequency of sexual relations and sexual satisfaction. Notwithstanding, cancer patients attending either palliative care or general oncology clinics were more willing to discuss their sexual lives with a professional, compared to healthy controls.[4] With currently available treatment modalities (as curing cancer or achieving a long-term remission is not uncommon), patients may face sexual ill health and its burden on quality of life long after cancer treatment has been completed.

The discomfort level that clinicians exhibit in the evaluation and treatment of sexual health issues is not confined to the cancer setting. By some estimates, only 14% to 35% of patients ever get asked about sexual health by the family physician.[5] This problem is deep-seated and rooted in the inadequate training that medical students and residents receive in sexual health evaluation and management.

Etiology of Sexual Dysfunction in Cancer Patients

Cancer-related sexual dysfunction may involve several different components, and an understanding of the underlying etiologies is essential to tailoring the appropriate treatment to the individual patient.

Psychological Factors
In the early stages of cancer diagnosis and treatment, patients may confront feelings of depression, fear of death or of treatment consequences, apprehension of imminent erectile dysfunction, deterioration of self-esteem, or impairment of a long-lasting emotional and sexual balance with their spouse.[6,7] Both patient and spouse may experience difficulties in discussing sexual relationship issues, feeling that it is not appropriate when confronting cancer. Libido is adversely affected from the initial steps of diagnosis and treatment planning, and sexually oriented thoughts and desire, if they exist, may result in feelings of guilt and further suppression of sexuality. Cancer treatment, especially if it leads to changes in physical appearance (eg, alopecia, stomas), may exert further psychological stress with impairment of body image and loss of one’s perceived sexual attractiveness.[6]

Treatment-related erectile dysfunction may perpetuate loss of self-esteem and sense of manhood if left untreated, and early comprehensive diagnosis and intervention of sexual dysfunction is the goal. Patients may experience fears-often unrealistic-of potential harm to themselves or their partner during sexual activity, especially when cancer treatment is ongoing. Patients should be encouraged to discuss their fears and other sexual issues with their partners and with professionals and to resume sexual activity soon after cancer treatment, if feasible.

Physical Symptoms
Cancer is accompanied by physical symptoms, which may adversely affect sexual function. General symptoms include fatigue, gastrointestinal symptoms (nausea, diarrhea), urinary tract symptoms, sleep disorders, and pain.[8] Surgical treatment, chemotherapy, radiation therapy, combined-modality treatment, and biologic and hormonal therapies may all exacerbate physical symptoms. Uncontrolled symptoms impair all aspects of sexual function including sexual interest, sexual desire, and erectile function and cannot be left untreated if sexual dysfunction is to be successfully managed.

Drug-Induced Sexual Dysfunction
While physical symptoms may induce sexual dysfunction in cancer patients, symptom control may be further complicated by the adverse effect of drugs on sexual function. Chronic opioid consumption to control pain in cancer patients has been demonstrated to induce hypogonadism in males and further exacerbate depression, fatigue, and sexual ill health.[9,10] Treatment of depression and anxiety in cancer patients with psychotropic drugs may further impair sexual function by adverse effects on libido, erection, ejaculation, and orgasmic function.[11] Selective serotonin-reuptake inhibitors (SSRIs) also have been reported to decrease libido in up to 40% of patients. SSRIs and tricyclic antidepressants (TCAs) have been shown to impair orgasmic function; indeed, they are used in clinical practice to treat premature ejaculation. The TCA amitriptyline has also been shown to decrease nocturnal penile tumescence; however, this effect has not been demonstrated with other TCAs.[11] Drug-induced sexual dysfunction can be treated with careful selection of "sex-friendly" drugs, careful dose adjustment, and drug holidays.

Altered Genitourinary Tract Structure and Function
Cancers involving the genitourinary tract and their treatment may lead to structural and functional alterations and consequently have an impact on sexual function and pleasure associated with sexual activity. Anejaculation following retroperitoneal lymph node dissection (RPLND) for testicular cancer is a major concern for young patients who desire paternity after successful cancer treatment. All patients experience anejaculation following radical prostatectomy, and up to 74% describe orgasmic dysfunction manifested as decreased or absent orgasm.[12,13] Involuntary loss of urine has also been described by patients after radical prostatectomy and occurs in 93% of patients within the first year after radical prostatectomy.[13]

Patients with urologic cancer may suffer penile deformities as a consequence of penile skin or distal urethral tumors and their treatment- either surgery (penectomy, urethrectomy) or local irradiation, which may cause penile fibrosis and resultant deformity.[14] However, penile deformities occur not only as a consequence of treatment for penile cancer: Radiotherapy for other pelvic tumors that includes the genitalia may cause local penile or genital skin reactions, temporarily precluding sexual activity or permanent changes in penile sensation.

Moreover, penile structural changes have been described after surgical treatment of prostate cancer. In a prospective study, Savoie et al recently confirmed previously reported data describing penile shortening of 0.5 to 5 cm in two-thirds of patients undergoing radical prostatectomy. However, to what extent these anatomic changes (without accompanying ED) affect sexual function is not clear.[15,16] The impact of other extensive pelvic operations or of pelvic irradiation on penile length has not been described thus far. However, it cannot be presumed to be nonexistent in light of the vascular insults and resultant fibrosis following application of these treatment modalities.

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Endocrine Dysfunction
Hypogonadism in cancer patients undergoing treatment and cancer survivors is a well-recognized cause of decreased libido, ED, and sexual dysfunction. Hypogonadism may be encountered among prostate cancer patients receiving androgen deprivation therapy adjuvant to definitive radiotherapy or for recurrent disease after failed definitive treatment.[17,18] Bilateral orchiectomy for bilateral testicular tumors leads ultimately to severe hypogonadism and requires hormonal replacement therapy. Although bilaterality of testis cancer is relatively rare and occurs in only 1% of testis cancer patients, the risk of hypogonadism is markedly increased among survivors of testicular cancer even after unilateral orchiectomy, and even without chemotherapy.[19,20] This risk is further increased with increased treatment intensity.

Hypogonadism and Leydig cell dysfunction, transient or permanent, has also been described in patients with hematologic malignancies undergoing intensive chemotherapy and bone marrow transplantation, with or without whole-body irradiation.[21,22] Sexual dysfunction and ED in these patients may also involve psychological, vascular, or other factors. Treatment-related hypogonadism may also be caused by chronic opioid use and radiotherapy to the base of the skull.[10,23] Primary testicular failure (primary hypogonadism) and depression of gonadotrophin secretion axis (secondary hypogonadism) have also been described in chronic and acute illnesses, including cancer. The exact underlying pathophysiologic mechanism of this endocrine insufficiency is poorly understood. However, hypogonadism may worsen with weight loss and disease progression.[24]

Neurogenic Sexual Dysfunction
Normal sexual function requires intact neurologic pathways. Neural pathways involved in sexual function originate in S2-S4 nerve roots and include the superior hypogastric plexus, inferior hypogastric plexus, pudendal nerve, cavernosal nerve, and pelvic splanchnic nerves.[25] Although the most commonly studied form of neurogenic sexual dysfunction in cancer patients is ED following insult to the neurovascular bundles that travel along the dorsolateral aspect of the prostate in radical prostatectomy or radical cystectomy, erectile function is not the sole component of surgical treatment-related neurogenic sexual dysfunction. Normal sexual function incorporates sensory, motor (eg, pudendal nerve to bulbospongiosus and ischiocavernosus muscles), sympathetic, and parasympathetic activities to achieve erection, ejaculation, and orgasm.

While neural structures involved in the conduction of sympathetic activity may be disrupted during RPLND for testicular cancer, resulting in impaired ejaculation, erection is usually preserved. Extensive pelvic surgery for rectal cancer may damage all the previously described neural structures, leading to impairment of ejaculation, erection, and orgasm.[25] With advances in surgical techniques and the advent of nerve-sparing surgery for prostate cancer, bladder cancer, and testicular cancer, surgery-induced neural damage and resultant neurogenic sexual dysfunction can be minimized.

Vasculogenic Sexual Dysfunction
Cancer treatment-related vascular damage impairs erectile function, while other domains of sexual health are not known to be affected. Upon sexual stimulation, an adequate arterial blood inflow and a competent veno-occlusive mechanism are required to achieve functional erection, both of which may be adversely affected by cancer-related treatment.

Vasculogenic ED notoriously occurs following pelvic radiotherapy. Radiation has been shown to induce endothelial proliferation, fibroblast proliferation, collagen deposition, and microvascular fibrosis accelerating existing arteriosclerosis and atherosclerosis, leading to occlusive vascular disease.[26,27] Pelvic arteriography after pelvic radiotherapy demonstrates bilateral narrowing of the internal iliac arteries and tortuosity and occlusions of the internal pudendal and penile arteries.[28] Following radiotherapy, months to years may elapse before clinical ED is evident.

Vasculogenic ED-in particular, venous leak (deficient penile valve function)-has been reported to occur not only following radiotherapy, but also as a consequence of cavernous nerve injury during pelvic surgery. This results in corporal fibrosis, erectile tissue apoptosis, and disruption of the penile venoocclusive mechanism.[29,30]

Erectile Dysfunction
Erection is a complex physiologic event that requires an intact psychological, endocrine, vascular, and neural function. ED in cancer patients may be psychogenic or organic, associated with the disease itself or with cancer treatment, as previously described. A functional erection plays a pivotal role in satisfactory sexual function, and ED treatment should be tailored to the etiology of an individual patient’s dysfunction as well as his (and the couple’s) goals and expectations. For example, neurogenic ED following extensive pelvic surgery, with disruption of the neural pathways, may be difficult to treat and responds poorly to oral drugs. With the widespread use
phosphodiesterase (PDE)-5 inhibitors and their revolutionary role in the treatment of ED, we tend to forget that there are additional treatment modalities that do not require intact neural pathways and can be beneficial in cancer patients who do not respond to PDE-5 inhibitors. These patients should be treated in a sexual medicine center affiliated with a comprehensive cancer care center, for consideration of other treatment modalities, such as intraurethral suppositories, intracavernosal injections, or penile prosthesis.

The technical success of these treatment modalities is high. However, patient and spouse satisfaction relies on specific tailoring of the treatment as well as patient and spouse education. Although intact erectile function sufficient for penetration is the cornerstone of sexual function, and loss of erectile function is a major concern for cancer patients, being capable of having an erection is not synonymous with having a satisfactory sex life. Moreover, individuals who are unable to achieve erections due to treatment failure or are unwilling to undergo treatment can still enjoy noncoital sexual activity if properly counseled.[6,7]

Prostate Cancer and Sexual Dysfunction

Prostate cancer is the most prevalent cancer in men, with a lifetime probability of developing prostate cancer of approximately 18% and a lifetime probability of dying of prostate cancer of 3%. Treatment modalities for localized prostate cancer include watchful waiting (for selected patients), radical prostatectomy, external-beam radiotherapy, and brachytherapy.

Androgen-deprivation hormonal therapy is used as a neoadjuvant treatment with radiotherapy or for systemic disease, and chemotherapy may be added for advanced disease.

All of these treatment modalities, excluding watchful waiting, adversely affect sexual function and HRQOL.[32] Types of sexual dysfunction after treatment for prostate cancer include decreased interest in and frequency of sexual activity, decreased enjoyment of sexual activity, decreased sexual confidence and masculine self-esteem, orgasmic dysfunction (painful orgasm, decreased intensity of orgasm, difficulty in reaching orgasm), decreased ability to satisfy the sexual partner, anejaculation, hematospermia, and ED.[32-35]

ED is the most reported adverse outcome of prostate cancer. Nevertheless, its measurement is complex and there is no agreed upon method, although there are a number of validated instruments that can be used.[36] It is agreed, however, that sexual dysfunction should be patient-reported, not physician-reported, and that all domains should be addressed, in addition to the impact of the dysfunction on quality of life.[3,36] The timing of sexual dysfunction assessment plays a pivotal role, as the time course of the onset of ED and its interval differ across different treatment modalities.[37-39]

Most published data describe sexual dysfunction, ED, and HRQOL after a variety of treatments for clinically localized prostate cancer in pretreatment-potent individuals (Table 1).[28,33,34,39,40-45] ED after treatment for localized prostate cancer has been shown to be associated with poor HRQOL, regardless of treatment modality.[35,40] Patients with disease progression after potentially curative local therapy report significantly lower sexual function HRQOL compared with progression-free patients.[32]
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Results also differ according to the patient population assessed; patient age; pretreatment erectile function; radiation technique, field, and dose; surgeon’s experience, technique, and preservation of the neurovascular bundles; and the use of combined treatment (EBRT plus neoadjuvant hormonal therapy, brachytherapy plus EBRT).[28,34,41] Response to sildenafil (Viagra) treatment varies by treatment modality and is reported to be 29% to 90% for radical prostatectomy, 66% to 78% for EBRT, and 78% to 81% for brachytherapy.[46-48]

Bladder Cancer and Sexual Dysfunction

In 2005, 63,210 new cases of bladder cancer were diagnosed, 47,010 of which occurred among males.[1] Although bladder cancer is fourth in prevalence among male cancers (7% of all male cancers), the literature on sexual health and bladder cancer is scarce. Superficial bladder tumors tend to recur, and their treatment involves repeated cystoscopic resection, bacillus Calmette-Guérin (BCG [TICE BCG, TheraCys]) instillations as needed, and frequent cystoscopic surveillance. In cases of invasive tumors or failure to control superficial disease, the treatment of choice is radical cystoprostatectomy with urinary diversion noncontinent (ileal conduit), continent cutaneous (continent pouch), or continent orthotopic (neobladder). Chemotherapy may be added as neoadjuvant or adjuvant therapy, or for advanced disease. Radiotherapy is also used either in combination with chemotherapy as a part of bladder preservation protocols for invasive disease, or to palliate patients with uncontrolled hematuria. All of these treatment modalities take their toll on male sexual function. Treatment for superficial disease may induce dysuria or genital pain, and may have psychological impact, as described earlier. Radical cystoprostatectomy may affect body image (especially in the case of stoma formation) in addition to sequelae as described after radical prostatectomy. Damage to pelvic neural structures in radical cystoprostatectomy is extensive, and even with nerve-sparing surgical techniques, the overall incidence of ED is 47% to 64% (38% among young patients and up to 80% in older patients).[49,50] No data have been reported regarding the efficacy of PDE-5 inhibitors for ED after...
radical cystectomy. However, in our clinical experience, these agents are relatively ineffective unless deliberate nerve-sparing has been performed. Oral agent failures should be treated with intracavernosal therapy in patients desiring functional erections.

Testicular Cancer and Sexual Dysfunction

Testicular cancer is the most prevalent malignancy among men aged 20 to 34, and sexual dysfunction has a profound impact on patients in this age group, not uncommonly before consistent sexual relations are established.[51] Treatment modalities include orchiectomy followed by watchful waiting, RPLND, and/or cisplatin-based chemotherapy. The effect of orchiectomy alone on sexuality in testicular cancer patients has not been adequately studied. However, its effect on self-body-image, sexual confidence, and sexual activity should not be overlooked. Jonker-Pool et al, in a meta-analysis of sexual function studies encompassing 2,786 testicular cancer patients, found that the adverse effects of testicular cancer treatment (RPLND, chemotherapy, or radiation) include decreased libido and loss of desire (20%), decreased arousal (12%), ED (11.5%), orgasmic dysfunction (20%), ejaculatory disorders (44%), decrease in sexual activity (24%) and sexual dissatisfaction (19%).[52]

Stratified by treatment modality, ED was most common after radiotherapy (25%), and ejaculation disorders were most frequently encountered after RPLND with or without chemotherapy (62% to 81%) but were also reported after radiotherapy (40%).[52] With modern surgical techniques and the introduction of nerve-sparing RPLND with preservation of the postganglionic fibers of the para-aortic lumbar sympathetic nerves, postoperative anejaculation is uncommon (2% to 7% after primary RPLND and 11% after postchemotherapy RPLND).[53-55] Given that in certain clinical circumstances several equally effective treatment options regarding cancer control are available, issues of sexual dysfunction, as well as other complications, should be considered.

Penile Cancer and Sexual Dysfunction

Penile cancer is an uncommon malignancy; treatment options include total or partial penectomy for local tumor control and inguinal lymph node dissection and radiotherapy for regional disease. Local control can be achieved with organ-sparing surgery or laser treatment in highly select patients, allowing for improved cosmetic, functional, and psychosexual outcome.[56,57] Due to the rarity of penile cancer, well-designed, large population-based studies are not available and data regarding sexual outcome are limited. Penile cancer itself impairs sexual function, and after total penectomy, the inability to achieve orgasm, either by intercourse or by self-stimulation, is an obvious result. After partial penectomy, however, even if the penis is considerably shorter, penetration, ejaculation, and orgasm are possible.[58] Conservative laser treatment is aimed at minimizing sexual dysfunction, although patients still experience decreased sexual desire (17%), ED (22%), sexual dissatisfaction (28%), ejaculatory dysfunction, and dyspareunia.[59] The desire and the ability to resume sexual activity after treatment for penile cancer may be accounted for by strong psychological adaptation mechanisms, emphasizing the significant role of sexual function among cancer survivors.

Summary

With advances in medical and surgical oncology allowing for better cancer control and longer survival, issues of HRQOL in cancer survivors must be considered. Sexual dysfunction should be evaluated, diagnosed, and treated as a part of comprehensive cancer care in all cancer patients and along the entire course of cancer diagnosis, treatment, and posttreatment survival. During the past decade, cancer treatment-related sexual morbidity has been minimized and new interventions for sexual dysfunction have become available. Clinicians should not let lack of knowledge, emotional barriers, or time constraints impede the evaluation and treatment of sexual dysfunction in their cancer patients.

Disclosures:
The author(s) have no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article.

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