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Sexual dysfunction and infertility as late effects of cancer treatment

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ABSTRACT

Sexual dysfunction is a common consequence of cancer treatment, affecting at least half of men and women treated for pelvic malignancies and over a quarter of people with other types of cancer. Problems are usually linked to damage to nerves, blood vessels, and hormones that underlie normal sexual function. Sexual dysfunction also may be associated with depression, anxiety, relationship conflict, and loss of self-esteem. Innovations in cancer treatment such as robotic surgery or more targeted radiation therapy have not had the anticipated result of reducing sexual dysfunction. Some new and effective cancer treatments, including aromatase inhibitors for breast cancer or chemoradiation for anal cancer also have very severe sexual morbidity. Cancer-related infertility is an issue for younger patients, who comprise a much smaller percentage of total cancer survivors. However, the long-term emotional impact of being unable to have a child after cancer can be extremely distressing. Advances in knowledge about how cancer treatments may damage fertility, as well as newer techniques to preserve fertility, offer hope to patients who have not completed their childbearing at cancer diagnosis. Unfortunately, surveys in industrialised nations confirm that many cancer patients are still not informed about potential changes to their sexual function or fertility, and all modalities of fertility preservation remain underutilised. After cancer treatment, many patients continue to have unmet needs for information about restoring sexual function or becoming a parent. Although more research is needed on optimal clinical practice, current studies suggest a multidisciplinary approach, including both medical and psychosocial treatment options.

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1. Introduction

Reproductive problems are among the most common and distressing consequences of cancer treatment. Infertility caused by cancer treatment only affects a minority of cancer patients, since most are beyond the age of wanting to have a child. Sexual dysfunction is a more universal threat. For most men and women, reproductive problems persist long after cancer treatment. We summarise the mechanisms of damage to reproductive health from cancer treatment and suggest ways to provide information and effective medical and psychosocial interventions to cancer patients and survivors. We also summarise recommendations for research and practice from the authors, who comprised a panel of experts at the first European Organisation for Research and Treatment of Cancer (EORTC) Survivorship Summit.

2. The prevalence of sexual dysfunction related to cancer

Close to two-thirds of cancer survivors in the United States were treated for pelvic or breast tumors [1], with at least a 50% prevalence of long-term, severe sexual dysfunction [2]. The situation is likely to be similar across Europe, given comparable prevalence and types of cancer [3]. Most sexual problems are not caused by the cancer itself, but by toxicities of cancer treatment [2]. Although sexual problems are more distressing for those under age 65 [4-6], and among patients who are sexually active at cancer diagnosis [7-10], sexuality remains important even for many geriatric cancer survivors [11,12]. Damage during cancer treatment to pelvic nerves, blood vessels, and organ structures leads to the highest rates of sexual dysfunction [10,11,13-20], but problems are common even after lung cancer [8,21], haematologic malignancies [22], or head and neck tumors [23]. Rates of sexual problems are close to 33% in survivors of childhood cancer, with women twice as likely as men to report dysfunction [24,25]. People treated for central nervous system tumors in childhood or adolescence may be limited in their adult relationships by learning disabilities and continued dependence on their families of origin [24]. In both men and women, other side effects of cancer treatment can lead to discontinuation of sexual activity, particularly persistent fatigue [26], nausea, or urinary and bowel incontinence [27-29].

2.1. Sexual problems in men

In men, the most common sexual problems are loss of desire for sex and erectile dysfunction (ED) [2]. Less common, but certainly distressing, are changes in the quality of orgasm, difficulties reaching orgasm, and pain with erection or orgasm [29,30]. Despite innovations such as laparoscopic robotic radical prostatectomy, few men recover normal erections after pelvic cancer surgery. Even among men who had excellent erections at baseline and are under age 65, fewer than 25% retain or recover their former erection quality [31-33]. Similarly, techniques to limit damage from radiation therapy have been disappointing, with little evidence of superior erectile function after intensity-modulated radiation

therapy or proton therapy compared to computer guided external beam protocols [34-39], and disappointing long-term results after brachytherapy [20,34,39]. It is clear that a history of prostate cancer is a major predictor of sexual dysfunction, even for men on active surveillance. In the Scandinavian Prostate Cancer Group Study, at 12-year follow-up, 84% of men reported erectile dysfunction after radical prostatectomy, as did 80% on active surveillance, compared to only 43% of matched control men who had not had prostate cancer [40]. In the United States, the 10-year follow-up for the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, revealed that over 95% of men in each prostate cancer treatment group had erection problems, again significantly worse than rates in controls [41]. Another prospective cohort study recently reported that by 15-yr follow-up, 87% of men with localised disease have erectile dysfunction [20].

Men who have surgery for bladder [42] or rectal cancer [14,43], or chemoradiation for anal cancer [44] also have high rates of ED. Sexual problems are not exclusive to men who have treatment to the pelvic organs. Hypogonadism and damage to pelvic nerves may lead to sexual dysfunction after intensive chemotherapy [26,45,46], or in men treated with either pelvic radiotherapy or total body irradiation [39,47,48]. Survivors of testis cancer or lymphoma also may have excess rates of sexual inactivity and low desire [49,50], though evidence remains equivocal [51]. Causes may be multifactorial, including hypogonadism, fatigue, and negative mood [45].

Animal studies suggest that obtaining erections several times a week by using treatments such as phosphodiesterase-5-inhibitors, penile injection therapy, or vacuum erection devices may protect the erectile tissue in the penis from atrophy, allowing better recovery of erections over time. Unfortunately, adherence to such treatments, often called penile rehabilitation, is so poor that it has been difficult to demonstrate clear benefit [52].

2.2. Sexual problems in women

In women the most common sexual problems are vaginal dryness and other genital changes that lead to pain during sexual activity, or loss of sexual desire, usually accompanied by difficulty feeling arousal and pleasure during sex [2]. Cancer treatments that increase the risk of sexual dysfunction for women include any that cause abrupt, premature ovarian failure in women who had not yet begun menopause [53,54]. Women whose combination chemotherapy leads to permanent ovarian failure seem to have a higher risk for sexual problems than those who continue to menstruate or have just a temporary cessation of menses [55,56]. The risk of permanent ovarian failure increases with the woman's age, especially for women over age 35, and with alkylating drugs and higher total doses of chemotherapy. As in men, any pelvic radiation therapy contributes strongly to the risk of sexual dysfunction, from a combination of ovarian failure and direct tissue damage to genital areas in the radiation field [11,19,39,57]. Use of gonadotropin agonists or antagonists to create a temporary state of ovarian failure also causes sexual problems, although the dysfunctions may resolve once hormonal therapy is discontinued [13]. Bilateral oophorectomy increases the prevalence of sexual dysfunction whether per-

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