Radiotherapy for prostate cancer and sexual functioning

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The incidence of erectile dysfunction after radiotherapy for prostate cancer is high. A multifactorial aetiology has to be considered, taking into account pre-treatment erectile function. Patients need to be informed about effective treatments such as sildenafil and intracavernosal injections.

In recent years, the number of patients diagnosed with prostate cancer has greatly increased (Greenlee et al, 2001), as a result of the widespread use of prostate-specific antigen testing and the possibility for cure of early disease. Standard treatments for prostate cancer include surgery (radical prostatectomy), external beam radiotherapy, interstitial radiotherapy (brachytherapy), hormonal therapy and observation. The choice of treatment depends on tumour staging, patient's age and comorbidity, and urologist's and patient's preferences. A commonly under-evaluated aspect is the impact of prostate cancer therapy on patients' future sexual functioning.

The incidence of erectile dysfunction after radiotherapy for prostate cancer reported in the literature varies from 6 to 84% after external beam radiotherapy to 0–61% after brachytherapy. Most of these studies are retrospective, the definition of erectile dysfunction is variable and sexual functioning is frequently assessed by asking only one question. Because of the high incidence of post-radiation erectile dysfunction and the controversial studies published, the literature has been critically reviewed to better understand the possible mechanisms involved in post-radiation erectile dysfunction.

EVALUATION OF ERECTILE DYSFUNCTION

The National Institutes of Health Consensus on erectile dysfunction defined impotence as: the consistent inability to attain and maintain a penile erection sufficient to permit satisfactory sexual activity (National Institutes of Health Consensus Conference, 1993). Furthermore, rigidity of erections, presence of spontaneous daytime erections or morning and night erections are also important issues. The most practical and quickest way to evaluate erectile dysfunction is by using a questionnaire. Patients should not be burdened with too many forms to complete and the testing must be relatively brief, while encompassing the different aspects of sexuality.

More recently an international questionnaire, the International Index of Erectile Function (IIEF), has been introduced (Rosen et al, 1997). The IIEF has been translated and validated in many countries and allows comparisons between different studies, but it has not been specifically developed for cancer patients.

In most of the published studies on radiotherapy for prostate cancer which reported on sexual functioning, authors used the general terms potency or impotence without giving a clear definition. Only in a few articles was a detailed definition provided. The different questionnaires used in the radiotherapy literature were often limited to a few items. In papers from the 1970s and the 1980s, only the rates of potency or impotence were mentioned, without refering to the methodology used for their assessment. Evaluating sexual functioning in an oncology population is different from evaluating it in a healthy population because specific medical, psychological and social factors must be considered. In this patient population both the sequelae of cancer itself and also the consequences of cancer treatment have to be considered.

INCIDENCE OF ERECTILE DYSFUNCTION AFTER RADIOTHERAPY FOR PROSTATE CANCER

Until the 1970s, surgery was the mainstay of treatment for prostate cancer as this was considered to be not very sensitive to radiation damage. Erectile dysfunction was reported in the literature in up to 41% of patients treated with

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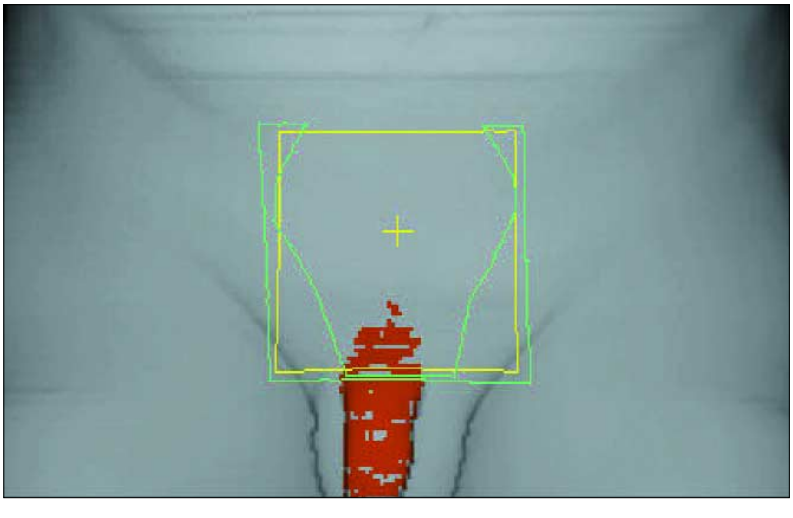
external beam radiotherapy (Incrocci et al, 2002). In the 1980s, external beam radiotherapy was delivered using more modern machines. Post-radiation erectile dysfunction was mentioned in most studies affecting 11–73% of the patients treated (Incrocci et al, 2002). The 1990s were characterized by the three-dimensional conformal techniques that use more fields, shaped blocks, a computer planning system and three-dimensional treatment plans resulting in smaller treatment volumes and therefore reduced toxicity. Only a few prospective studies from the 1990s dealt specifically with sexual functioning after external beam radiotherapy; in these studies erectile dysfunction varied from 7% to 72% (Incrocci et al, 2002).

Brachytherapy was originally introduced not only to limit the detrimental effects of external beam radiotherapy on bowel and urinary function, but also to help preserve sexual function. Rates of erectile dysfunction after brachytherapy monotherapy were usually lower than after external beam radiotherapy alone. Rates of erectile dysfunction ranged from 0 to 61%, being highest when brachytherapy was used in combination with external beam radiotherapy (25–89%) (Incrocci et al, 2002).

INCIDENCE OF OTHER SEXUAL DYSFUNCTIONS AFTER RADIOTHERAPY FOR PROSTATE CANCER

A deterioration of sexual activity has been associated with the severity of ejaculatory dysfunction, particularly a decrease in volume or an absence of semen. Ejaculatory disturbances in brachytherapy studies vary from a reduction or absence of ejaculate volume (7–45%) to discomfort during ejaculation (3–11%) and haemospermia (5%). After external beam radiotherapy, a lack of ejaculation was reported in up to 56% of patients, dissatisfaction with sex life in 25–60%, decreased libido in 8–53% and decreased sexual desire in 12–58% (Incrocci et al, 2002).

Figure 1. Example of an anterior-posterior radiation field (yellow) with shaped blocks (green) and its relation to the penis (red).



AETIOLOGY OF ERECTILE DYSFUNCTION AFTER RADIOTHERAPY FOR PROSTATE CANCER

Goldstein et al (1984) performed a detailed study on 23 patients treated with radiotherapy for prostate cancer in order to understand the aetiology of post-radiation erectile dysfunction. Subjects were considered potent if they could develop an erection sufficiently rigid for vaginal penetration and sustain it until ejaculation. Fifteen patients met the criteria for potency; 14 months after radiotherapy, they all complained of a worsening in erectile function. Neurological examinations were normal, while penile Doppler evaluation was abnormal in all 15 patients. The authors concluded that the aetiology of post-radiation therapy was vascular (Goldstein et al, 1984).

Mittal (1985) published a study on penile circulation, before and after external beam radiotherapy; he concluded that penile circulation was not abnormal after radiation and that the aetiology of erectile dysfunction was a more complex mechanism not directly attributable to vascular damage as previously suggested. Zelefsky and Eid (1998) evaluated 98 patients who became impotent after external beam radiotherapy. The penis was scanned with Duplex ultrasound before and after an intracavernosal injection of prostaglandin. Of these patients, 32% had cavernosal dysfunction and 63% arteriogenic dysfunction, while neurogenic dysfunction was found in only 3%. The authors concluded that the predominant aetiology of post-radiation erectile dysfunction was arteriogenic (Zelefsky and Eid, 1998).

Fisch et al (2001) evaluated the effect of the external beam radiotherapy dose to the bulb of the penis on erectile function; a strong dose–volume relationship with the likelihood of remaining potent after external beam radiotherapy was observed. Similar results were reported after brachytherapy (Merrick et al, 2001). *Figure 1* shows the relation between radiation fields and the penis. DiBiase et al (2000) postulated that brachytherapy-related impotence might be caused by excessive radiation to the neurovascular bundles but Merrick et al (2000) found no significant difference in the mean dose to the neurovascular bundles between potent and impotent men after brachytherapy. One animal study

suggested that a decrease in nitric oxide synthase-containing nerve fibres in the corpora cavernosa may contribute to post-radiation erectile dysfunction (Carrier et al, 1995), but no clinical studies have been performed to confirm these findings.

It is vital to determine the patient's pre-treatment sexual functioning; up to 60% of patients may report erectile difficulties before radiation therapy and these patients are more likely to become fully impotent after treatment. Furthermore, it is not possible to draw final conclusions on post-radiation erectile dysfunction when its assessment is done too early because it takes at least 18–24 months before erectile dysfunction occurs and reaches a maximum (Turner et al, 1999).

THERAPY OF ERECTILE DYSFUNCTION AFTER RADIOTHERAPY FOR PROSTATE CANCER

Before sildenafil citrate (Viagra) was introduced in 1998, only two studies had reported on the efficacy of intracavernosal injection of phentolamine-papaverine (Pierce et al, 1991) and of penile implants (Dubocq et al, 1997) in the treatment of post-radiation erectile dysfunction. The efficacy of sildenafil after radiotherapy in open-label studies was reported in up to 90% of patients (Kedia et al, 1999; Zelefsky et al, 1999; Weber et al, 1999; Valicenti et al, 2001) and it was confirmed in the only double-blind study performed so far (Incrocci et al, 2001).

Sildenafil improved erections significantly as compared to placebo; 55% of patients had successful intercourse with sildenafil compared with 18% of patients taking the placebo ($P<0.001$) (Incrocci et al, 2001). These numbers were confirmed in a continuation of the open-label phase of the trial. Ninety per cent of patients needed the 100 mg dose, and side effects were mild or moderate (Incrocci et al, 2001). Sildenafil has been found to be highly effective also in patients complaining of erectile dysfunction after brachytherapy (Merrick et al, 1999; Potters et al, 2001).

COUNSELLING PATIENTS ABOUT SEXUAL FUNCTION

Most radiotherapy studies do not include sexual responses of partners to the patients' illnesses, although in a study by Schover et al (1987) in 308 men and 76 women with pelvic, genital and other cancers, partners reported no sexual dysfunction. For different reasons sexual counselling has not become a routine part of oncology care in most hospitals. There is a time constraint: in busy oncology clinics, where the outpatient visit is focussed on addressing prognosis and treatment, physicians do not have time to assess quality of life.

Another barrier is the discomfort physicians have when discussing sexuality. Sexual counselling should be routinely provided in an oncology clinic, for example having a health-care professional (physician or oncology nurse specialist) to assess quality of life issues, including sexuality (Schover, 1999). The interview should assess the patient's social support network, reaction to cancer, current mood, relationship, and any sexual problems or concerns. In most cases patients do not require extensive medical or psychological treatments, but need information about the impact of cancer treatment on sexuality. Patients and their partners are often unaware of the anatomy of sexual organs so they have to be counselled, for example, on the effects that radiotherapy for prostate cancer has on ejaculation.

Counselling on the safety of sexual activity during radiation therapy is also important. Men irradiated for prostate cancer often think that cancer can be spread by sexual contact and that ejaculation may be harmful to their partner. Open sexual communication between partners should be encouraged; often a couple does not even discuss sex after many years of routine lovemaking. Changes after cancer treatment can disturb the sexual relationship, requiring adaptations to the new situation, for example in case of painful orgasm after brachytherapy.

CONCLUSIONS

Before final conclusions can be drawn on the incidence of post-radiation erectile dysfunction, an accurate method of evaluating it is mandatory. The definition of (im)potence advocated by the National Institutes of Health should always be used, and erectile dysfunction evaluation should be standardized by using prospectively validated questionnaires on sexual functioning. Final assessment should be done at 18–24 months post-treatment when erectile dysfunction occurrence reaches a maximum. Although arterial damage seems to be the main cause of erectile dysfunction after radiotherapy, a multifactorial aetiology has to be considered, taking into account comorbidity, drugs, and more importantly pre-treatment erectile function. Patients need to be correctly informed about the anatomy of the prostate, the possible sequelae of radiation on their sexual functioning, and the currently available effective treatments for erectile dysfunction such as sildenafil, intracavernosal injections and erection prostheses. HM

Conflict of interest: none.

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KEY POINTS

- The number of patients diagnosed with prostate cancer has greatly increased.
- Radiation therapy, together with surgery, is the most effective treatment for localized disease.
- The incidence of post-radiation erectile dysfunction is high.
- Most of the studies on post-radiation sexual functioning are retrospective, and use different definitions of erectile (dys)function.
- A multifactorial aetiology has to be considered.
- Patients need to be informed about the availability of effective treatments.