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Sexual function after external-beam radiotherapy for prostate cancer: What do we know?

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Contents

Abstract

Quality of life in general and sexual functioning in particular have become very important in cancer patients. Due to modern surgical techniques, improved quality of drugs for chemotherapy and very modern radiation techniques, more patients can be successfully treated without largely compromising sexual functioning. One can assume that because of the life-threatening nature of cancer, sexual activity is not important to patients and their partners, but this is not true. Prostate cancer has become the most common non-skin malignant neoplasm in older men in Western countries.

In this paper, we discuss the various methods used to evaluate erectile and sexual dysfunction and the definition of potency. Data on the etiology of erectile dysfunction after external-beam radiotherapy for prostate cancer is reviewed, and the literature is been summarized. Patients should be offered sexual counseling and informed about the availability of effective treatments for erectile dysfunction, such as sildenafil,

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intracavernosal injection, and vacuum devices. Cancer affects quality of life and sexual function. The challenge for oncologists is to address this with compassion.

Keywords: Prostate cancer; Radiotherapy; Radiation; Erectile (dys)function; Sexual (dys)function

1. Introduction

Despite the decrease in overall cancer incidence and mortality rates in developed countries since the early 1990s, cancer remains a major public health problem. Among men, the most common cancer affects the prostate and occurs more often in the older population [1]. In recent years, the number of patients diagnosed with prostate cancer (PC) has increased dramatically because of the widespread use of prostate specific antigen testing and the possibility for cure of early disease. Standard treatments for PC are radical prostatectomy, external-beam radiotherapy (EBRT), brachytherapy, or observation. The choice of treatment is usually determined by tumor staging, patient's age and comorbidity, urologist's and patient's preferences. Sexual dysfunction is one of the more common consequences of cancer treatment [2]. Patient's quality of life, including sexual functioning, should play a more significant role in decision making about treatment type. Men may remain interested in sex and eroticism well into old age [3]. Men are less likely than women to seek professional help for mental and physical health problems. Addis and Mahalik hypothesized that cultural norms of masculinity conflict with help-seeking behavior [4]. Erectile dysfunction (ED) is a medical problem often crucial to men's self-esteem. In the 1980s and 1990s, penile prostheses and penile injections created a market for male sexual dysfunction. With the introduction of sildenafil (Viagra®) in 1998, media attention to ED has made sexual problems more normative and has increased acceptance of help-seeking [4].

The purpose of this paper is to present an overview of the peer-reviewed articles dealing with ED after EBRT. Articles dealing with PC-patients with metastatic disease, or on hormone therapy, are not included in this review. Firstly, the various methods used to evaluate and define ED will be discussed. Then, the etiology of ED after EBRT will be reviewed. The literature on the incidence of erectile and other sexual dysfunctions after EBRT will be summarized. Finally, the therapy of post-radiation ED and prevention possibilities will be discussed.

2. Methods of evaluating erectile dysfunction

The most practical and quickest way to evaluate ED is by using a questionnaire. Different questionnaires have been used in the published literature. Questions on sexual functioning were quite often limited to two to six items, and were incorporated into a more general questionnaire on toxicity of radiation treatment, or quality of life in general [2,5–14]. With a few exceptions [2,6,7,15,16], the entire questionnaire used was not included in the paper, and only selected questions were listed [5,8,12,17–21]. In many of the older papers, mainly from the 1970s and the 1980s, only rates of potency or impotence were mentioned [22–35], without reference to the methodology used. Seldom was a complete questionnaire on various aspects of sexuality used [17–19,36,37]. Validation of the instrument used was seldomly reported [5,7,10,13,38]. More recently an international questionnaire, the International Index of Erectile Function (IIEF) has been introduced [39]. The IIEF has been translated and validated in many countries and offers the possibility to make comparisons between different studies. Though, it has not been specifically developed for cancer patients.

2.1. Summary

Internationally validated questionnaires are available to evaluate sexual functioning. These should always be used, to ensure comparisons between different studies.

3. Definition of potency

Another significant feature of literature on ED after radiation for PC is the definitions of potency and impotence used. A clear definition is mandatory in order to make meaningful comparisons of the different studies. The National Institutes of Health (NIH) Consensus on ED defined impotence as: the consistent inability to attain and maintain a penile erection sufficient to permit satisfactory sexual intercourse [40]. One could argue that such a definition is strictly relevant in the presence of a willing partner. As such, use of the general term sexual activity, i.e. intercourse or masturbation, would be more appropriate. Rigidity of erections, presence of spontaneous daytime erections or morning/night erections (quite relevant in the differentiation between organic and psychological etiology) are also important issues. It is also necessary to differentiate between ED and not being sexually active, often due to reasons not correlated to erectile insufficiency, such as absence of a willing partner or the lack of interest in sex. Psychological factors in irradiated patients may play a role in post-radiation ED and have to be kept in mind.

In most published studies, authors referred to the general terms potency or impotence without giving a proper operational definition [5,7,8,10,15,20,33]. In some articles, a detailed definition of potency was provided [2,7,12,13,16,19,24,35,37,41], though this was often not comparable: Is a good erection one that is assessed by the patient, or by his physician? Is it necessary to use a compli-

cated definition, or is the NIH definition sufficient? Is only the presence of an erection important, or do we need to know the duration and the rigidity of these erections which allows sexual activity? Such questions remain unanswered in the radiotherapy literature.

3.1. Summary

In most of the published studies, a definition of potency is lacking. The definition advocated by the NIH should be used, also to allow comparisons of data among different studies.

4. Etiology of post-radiation erectile dysfunction

See Fig. 1 for a schematic of the male genitalia.

Goldstein et al. [42] performed a detailed study on 23 patients treated with radiotherapy for PC in order to understand the etiology of radiation-induced impotence. Nocturnal penile tumescence testing, bulbo-cavernous reflex latency, perineal electromiography, penile Doppler ultrasonography, and endocrine screening of the hypothalamic-pituitary-gonadal axis were performed. Subjects were considered potent if they could develop an erection sufficiently rigid for vaginal penetration and sustain it until ejaculation. All the 15 patients who met the criteria for potency before radiation complained of a worsening in erectile function 14 months after radiotherapy. Neurological examinations were normal, while penile Doppler evaluation was abnormal in all the patients. A selective pudendal arteriography performed in two subjects revealed occlusive vascular disease within the pelvic radiation field. The authors concluded that post-radiation ED was due to vascular damage [42]. One year later, a study by Mittal [43] on penile circulation measured with Penile Brachial Index and Penile Flow Index in six patients did not show any statistically significant differences between pre- and post-radiation values. Mittal [43] concluded that penile circulation was not abnormal after radiation and that the etiology of ED was a more complex mechanism not directly attributable to vascular damage as previously suggested by Goldstein et al. [42]. More recently, Zelefsky and Eid [44] evaluated 98 patients who became impotent after EBRT or prostatectomy, and confirmed the findings by Goldstein et al. [42]. Median time from surgery and radiation to evaluation was 11 and 14 months, respectively. The penis was scanned with Duplex ultrasound before, and after, an intracavernosal injection of prostaglandin. Among EBRT patients, 32% had cavernosal dysfunction (abnormal cavernosal distensibility with a normal penile peak blood flow) and 63% arteriogenic dysfunction (peak penile blood flow rates less than 25 cm/s). Neurogenic dysfunction was found in 3% of the EBRT patients. Comorbidity, hormonal manipulation, smoking and age did not influence the type of dysfunction observed. The authors concluded, as Goldstein et al. [42], that the predominant etiology of radiation-induced impotence was arteriogenic. The Mittal's study [43] was not consistent with these two other studies [42,44]. Different reasons can explain this: the evaluation of erectile function at 6–9 months after radiation is too early to detect radiation damage to vessels; the tests used are obsolete, and not reliable; the number of patients evaluated is too small (only six).

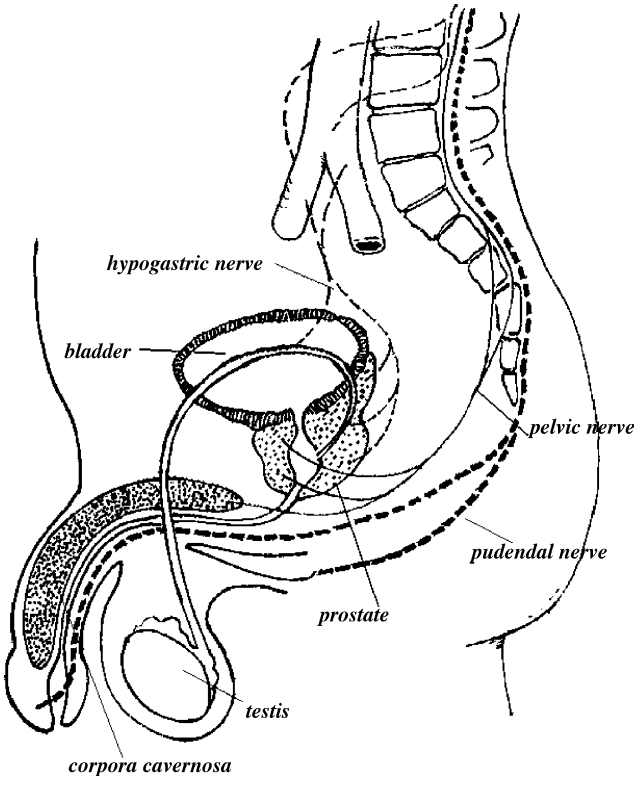

Fig. 1. Schematic of the male genitalia and innervation.

Very recently Fisch et al. [45] evaluated the effect of the EBRT dose to the bulb of the penis on erectile function in 21 patients, at 2 years after treatment. A strong dose–volume relationship with the likelihood of remaining potent after EBRT was observed. Patients who received 70 Gray or more to 70% of the bulb of the penis appeared to be at very high risk of developing radiation-induced ED. See Fig. 2 for the relation of the penile bodies with the radiation fields. Selek et al. [46] could not find any correlation between the dose and volume of radiation to proximal penile structures and the development of ED after EBRT. The authors reported on 28 patients treated with 78 Gy and potent prior to radiation. At 2 years follow-up 10 patients reported ED. There was no statistically significant difference in the radiation dose to the corpus spongiosum, corpora cavernosa, and crura and total penile structure between potent and non-potent patients [46]. A fused computer tomography (CT)/magnetic resonance imaging (MRI) simulation study before treatment in 29 intensity-modulated radiation therapy (IMRT) patients showed that the dose to the penile bulb and corporal bodies is low with IMRT. MRI appeared to be superior to CT for the imaging of erectile tissues [47]. Although these data have to be confirmed by larger studies, it seems warranted to limit the dose to the bulb of the penis to prevent post-radiation ED

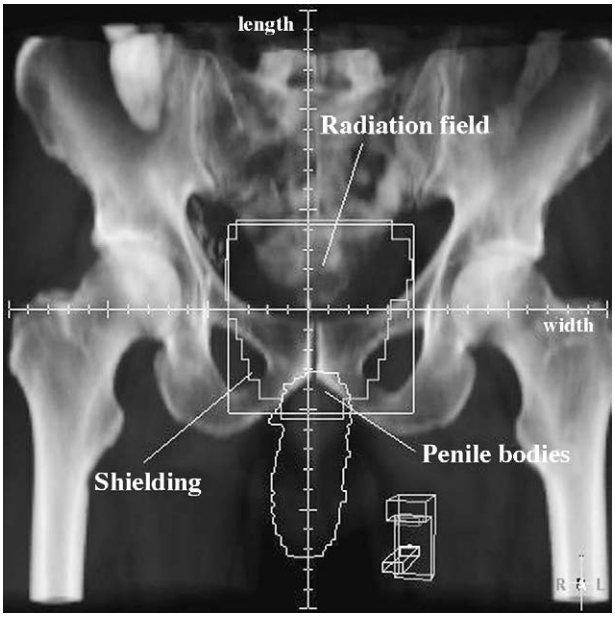

Fig. 2. Example of an anterior–posterior conformal radiation field for prostate cancer. Relation of the penile bodies and radiation field.

[45]. However, there is no data on PC control, when the dose to the bulb of the penis is limited.

4.1. Summary

Although very few studies have been performed on the etiology of post-radiation ED, the most likely mechanism seems to be radiation damage to the pelvic vasculature and penile bodies.

5. Incidence of ED after external-beam radiotherapy

5.1. Studies published in the 1970s

Papers from the 1970s dealt with the introduction of EBRT for PC in the pre-PSA era. Until then, surgery was the main stay of treatment as most urologists considered PC to be a relatively radio-resistant tumor, an idea derived from the poor results obtained using conventional orthovoltage therapy. Although studies in the 1970s reported on treatment outcome, and urinary and bowel sequelae, mention of sexual potency or impotence was also frequently made (see Table 1). ED incidence was reported in up to 41% [22,23,25–27]. In most cases methods of evaluation, definition of potency, indication of a trans-urethral resection of the prostate (TURP) prior to EBRT, comorbidity and the time of assessment of ED were not reported. The percentage of patients who were potent before EBRT was often not provided. Consequently, the percentage of patients who became impotent after treatment may have been overestimated.

5.2. Studies published in the 1980s

In the 1980s, EBRT was delivered using megavolt energies. Papers from the 1980s did not differ much from the 1970s (see Table 1). Radiation-induced sexual dysfunction was mentioned in most studies with percentages from 11 to 73% [24,28,29,31]. Only two papers [30,35] reported more extensively on post-radiation sexual dysfunction, including libido, frequency of coitus, and ejaculation. Men who were sexually active before treatment had a good chance of retaining potency 8–12 months after EBRT [30], and, for the first time, the need for adequate information on sexual functioning before treatment was emphasized [36].

5.3. Retrospective studies published in the 1990s

This period was characterized by PSA testing, and the widespread use of EBRT. More specifically, three-dimensional conformal techniques (3DCRT), with the use of more fields, and shaped/customized blocks, a computer planning system and three-dimensional treatment plans resulted in smaller treatment volumes. A common aspect of the reported papers was the use of retrospective assessments (recall bias) or the use of medical chart records (no stan-

Table 1
Erectile dysfunction after external-beam radiotherapy (EBRT) for prostate cancer: studies from the 1970s and the 1980s

Authors	Patients, *n*	Mean age[a] years (range)	Patients potent prior to EBRT, *n* (%)	Mean follow-up months (range)	ED, *n* (%)
Ray et al. [22]	310	63 (39–89)	96 (31)	n.a	30 (29/96) at 15 months
Bagshaw et al. [23]	430	59 (n.a.)	110 (26)	n.a.	41 (65/110) at 15 months
McGowan [25]	107	64 (50–79)	n.a.	n.a. (24–65)	6 (7/107)
Perez et al. [26]	112	n.a. (40–81)	n.a.	n.a. (12–60)	13 (15/112)
Taylor [27]	278	n.a.	108 (39)	n.a.	22 (24/108)
Forman et al. [28]	240	68 (52–86)	105 (44)	40[b] (12–108)	43 (45/105)
Asbell et al. [29]	445	68 (n.a.)	n.a.	84[b] (n.a.)	11–53 (n.a.)
Bagshaw et al. [24]	914	63 (35–86)	434 (47)	up to 180	14 (n.a.) at 15 months
Banker [30]	85	n.a.	26 (30)	n.a. (8–12)	73 (19/26)
Van Heeringen et al. [36]	18	71 (60–82)	11 (61)	20 (4–45)	27 (3/11)
Shipley et al. [31]	121	68 (n.a.)	54 (45)	n.a. (60–114)	37 (20/54) at >36 months

n.a., data not available.
[a] Mean age for entire group.
[b] Median.

Table 2
Erectile dysfunction after external-beam radiotherapy (EBRT) for prostate cancer: retrospective studies from the 1990s

Authors	Patients, *n*	Mean age[a] years (range)	Patients potent prior to EBRT, *n* (%)	Mean follow-up months (range)	ED, *n* (%)
Mameghan et al. [32]	218	67[b] (45–87)	42 (19)	55 (n.a.)	45 (19/42) at 24 months
Helgason et al. [18]	53	70 (53–80)	33 (66)	n.a. (18–24)	50 (26/53)
Roach et al. [19]	124	72[b] (48–87)	60 (48)	21[b] (7–40)	38 (23/60)
Crook et al. [15]	192	70 (49–87)	158 (82)	33 (12–72)	35 (55/158)
Fransson and Widmark [7]	199	71[b] (51–86)	n.a.	48 (24–56)	56 (n.a.)
Mantz et al. [34]	114	68 (52–85)	n.a.	18 (n.a.)	2 (n.a.) at 1 month 8 (n.a.) at 12 months 25 (n.a.) at 24 months 34 (n.a.) at 36 months
Fosså et al. [20]	114	69 (n.a.)	22 (19)	n.a.	61 (13/22)
Nguyen et al. [11]	101	n.a.	81 (80)	>24	49 (40/81)
Zelefsky et al. [35]	743	69[b] (51–84)	544 (73)	42[b] (18–109)	39 (211/544)
Wilder et al. [41]	51	68[b] (n.a.)	35 (69)	15[b] (n.a.)	0 at 12 months 17 (9/51) at 24 months 37 (19/51) at 36 months
Hamilton et al. [13]	457	n.a.	251 (55)	n.a.	58 (n.a.) at 12 months 68 (n.a.) at 24 months

n.a., data not available.
[a] Mean age for entire group.
[b] Median.

dardized methods). The time at which sexual function was evaluated was often not indicated. As time since radiotherapy is important [7,13,34,35,41], it is mandatory to mention it before proper comparisons of percentages of ED between different studies can be made. Furthermore, comorbidity, age, and pre-EBRT TURP were seldom mentioned. Cardiovascular disease, diabetes or impaired potency prior to EBRT were often correlated with a higher incidence of ED post-treatment in one study [34], but the contrary view was reported by other authors [19,35,37,41]. Percentages of ED varied from 0 to 61% [7,11,13,15,18–20,32,34,41]. See Table 2 for an overview. Lack of erections was reported in 56% of the EBRT patients and in 12% in age-matched controls, more obviously in men younger than 70 years [7]. Volume of tissue irradiated did not influence sexual complications [7,11]. Patients who were potent before EBRT, and who received a dose of 76 Gray or greater, had an impotence percentage of 68% at 5 years versus 52% for those treated to 70 Gray or less ($p < 0.001$) [35]. This is the first report to document a higher incidence of ED with dose escalation after 3DCRT. Furthermore, neo-adjuvant androgen deprivation, TURP, diabetes, age, and tumor stage were not significantly correlated to ED rates [35].

5.4. Prospective studies published in the 1990s

A few studies from the 1990s (see Table 3) dealt specifically with sexual functioning after EBRT and evaluated patients prospectively. Such methodology is the only correct way to avoid recall bias of pre-treatment potency and incomplete medical charts. Percentages of ED varied from 7 to 72% [8,9,16,17,33,37]. Radiation field size and technique seemed to influence sexual function at 3 and 12 months after EBRT, though this was not statistically significant [8].

Table 3
Erectile dysfunction after external-beam radiotherapy (EBRT) for prostate cancer: prospective studies from the 1990s

Authors	Patients, *n*	Mean age[a] years (range)	Patients potent prior to EBRT *n* (%)	Mean follow-up months (range)	ED, *n* (%)
Zinreich et al. [17]	27	68 (52–80)	10 (37)	n.a.	20 (2/10) at 12 months
Pilepich et al. [33]	230	71[b] (49–84)	102 (44)	54[b] (n.a.)	72 (74/102)
Beckendorf et al. [37]	67	68 (54–84)	40 (60)	n.a. (8–12)	33 (13/40)
Beard et al. [8]	121	n.a.	69 (57)	n.a.	57 (39/69) at 3 months 64 (44/69) at 12 months
Borghede and Hedelin [9]	184	67 (46–83)	134 (73)	46 (24–96)	7 (9/134)
Turner et al. [16]	290	69 (44–82)	182 (63)	23[b] (n.a.)	38 (56/146) at 12 months 59 (40/68) at 36 months

n.a., data not available.
[a] Mean age for entire group.
[b] Median.

5.5. Summary

In the 1970s, studies reported on treatment outcome and only incidentally on ED. The 1980s were characterized by more focus on ED, although only two papers extensively reported on post-radiation sexual dysfunction. Only in the 1990s a particular interest in post-radiation ED was shown. Only studies that prospectively evaluated erectile functioning, using validated questionnaires and using a proper definition of potency are useful to draw conclusions on the incidence of post-radiation ED. In general, this reaches about 60–70% in prospective studies. Time elapsed since radiation is important: prospective studies show an increase of ED between 1 and 2 years after radiotherapy, but it does not seem to change after 3 years.

6. Ejaculatory and other sexual dysfunctions

A deterioration of sexual activity has been associated with the severity of ejaculatory dysfunction, particularly a decrease in volume or an absence of semen [48]. After EBRT, a lack of ejaculation was reported in 2–56% of patients [6,18,25]. Dissatisfaction with sex life was reported in 25–60% [49,50], decreased libido in 8–53% [36,37,50], and decreased sexual desire in 12–58% [18,51]. One study reported a decreased intensity of orgasm, decreased frequency and rigidity of erections, and decreased importance of sex [18].

6.1. Summary

After radiotherapy, other sexual dysfunction than ED have been reported, such as a decreased libido, ejaculation disturbances, and dissatisfaction with sex.

7. Therapy of post-radiation erectile dysfunction

If there is still uncertainty about the etiology of post-radiation ED, what sort of therapy is to be recommended? Prior to the introduction of sildenafil citrate), there were only three treatment options: intracavernosal injection (ICI), vacuum devices, and penile implants, all three with or without concomitant sexual counseling. To our knowledge, only two papers were published on therapy of post-radiation ED, before sildenafil was introduced.

Pierce et al. reported on eight patients who used an ICI of phentolamine and papaverine [52]. All patients had erections sufficient for vaginal penetration with an ICI. One patient had a penile haematoma, two reported penile discomfort, no priapism was encountered. Seven patients continued ICI for 6–32 months. This study comprised a small sample of patients, but is the only one reporting on ICI after radiation, and demonstrating its efficacy. Dubocq et al. reported on 34 patients who were interviewed about sexual function, satisfaction and frequency of intercourse after receiving a penile implant [53]. A hydraulic one to two or three pieces or a semirigid prosthesis was implanted. None of the patients had infections or erosions. Thirty-two patients stated they would undergo surgery again, if necessary or recommend the prosthesis; two were dissatisfied, three underwent re-implantation because of fluid leakage and two complained of penile discomfort. The authors concluded that penile implants had low morbidity and a high satisfaction rate; complications were intrinsic to the device and not related to previous radiation [53]. With the availability of sildenafil, these methods of therapy are loosing popularity. Sildenafil citrate is a selective inhibitor of cyclic guanosine monophosphate (cGMP) specific phosphodiesterase type 5, and hence inhibits the degradation of cGMP in the cavernosal smooth-muscle cells, restoring erectile response to sexual stimulation in patients with ED of different etiologies. The efficacy of sildenafil after EBRT in open-label studies was reported in up to 90% of patients [54–57]. However, sildenafil was less effective in the only double-blind study recently performed [58,59]. Zelefsky et al. [54] reported on 50 patients who presented with progressive deterioration of sexual functioning, following 3DCRT for PC. At a median time of 19 months after EBRT, treatment with sildenafil resulted in an improvement in the firmness of erections in 74% of the patients [54]. Kedia et al. [55] and Weber et al. [56], using the IIEF questionnaire, reported an improvement of erectile function with sildenafil in 71 and 77% of the patients, respectively. A prospective study by Valicenti et al. [57] reported on 23 patients, with pre-EBRT data on sexual functioning. The use of a 100 mg dose of sildenafil citrate, at a median time 12 months post-EBRT, restored sexual functioning to pre-RT levels in 21 out of 23 patients. Incrocci et al. performed a randomized, double-blind, placebo-controlled, cross-over trial in 60 patients, who complained of ED at a mean time of 39 months post-3DCRT [58]. Sildenafil improved erections significantly as compared to placebo; 55% of the patients had successful intercourse with sildenafil. Ninety percent of the patients needed the 100 mg dose, and side effects were mild or moderate. We should not forget about patient's compliance; in a follow-up study of patients who had previously participated in a sildenafil study, 2 years after only 24% were till using the drug [59]. The reasons for attrition were lack of efficacy (60%), costs (24%), and side effects (16%). Almost one half of the patients were dissatisfied with their sexual life. This indicates that patients with a history of cancer treatment and subsequent ED should be informed on treatment modalities but also followed-up, and adequately counseled to improve their sexual life.

7.1. Summary

Few data are available on the efficacy of ICI in the treatment of post-radiation ED. Most of the data regard the efficacy of sildenafil, which has been reported to be effective in about 60% of the patients treated by EBRT in a randomized, placebo-controlled trial.

8. Prevention of post-radiation ED

Prevention is a difficult matter. If one accepts the hypothesis that radiation induces vascular damage, then decreasing the dose to pelvic vascular structures could decrease ED rate. Both conventional and conformal radiation techniques seem to result in the same rates of ED [11]. But, a relationship between radiation field size and sexual function (i.e. the smaller the field size, the better sexual functioning) has also been reported [8]. However, prospective studies with large series of patients, and the use of standardized validated questionnaires, have to confirm these findings. Conformal techniques using shaped blocks do not appear to spare the neuro-vascular bundles as these are always entirely in the high-dose prostate field. Nevertheless, no reliable data are available to correlate doses in this region with the occurrence of ED after EBRT [60,61]. Furthermore, special radiation beams (such as proton, pion, and neutron) have been reported to have detrimental effects on potency similar to those reported for the more commonly used photon beams [60].

Recently, the IMRT techniques have been introduced. IMRT is an advanced 3DCRT that uses a computerized treatment plan optimization with an inverse technique, and intensity-modulated radiation beams with dynamic multileaf collimator. IMRT was introduced in the treatment of PC already in 1996 resulting in a significantly lower incidence of rectal toxicity [62]. A comparison of 3DCRT and IMRT plans of 10 patients with PC showed a significantly lower radiation dose to the corporal bodies in favor of the IMRT techniques [63]. Because of a strong relationship between radiation dose in the penile bulb and ED [45], it seems warranted to limit this dose to prevent post-radiation ED.

8.1. Summary

Assuming that the etiology of post-radiation ED is vascular, a decrease of the radiation dose to the pelvic vasculature and penile bodies might result in a decrease of ED. This needs to be further investigated.

9. Conclusion

There are still no conclusive data on EBRT techniques, field sizes, energy used, and their specific influence on erectile dysfunction. Both conventional EBRT and conformal techniques seem to result in the same rates of ED. However, prospective studies with large series, and the use of standardized validated questionnaires, have to confirm these findings. Conformal techniques using shaped blocks do not appear to spare the neuro-vascular bundles as these are always entirely in the high-dose prostate field. No reliable data are available to correlate doses in this region with the occurrence of ED after EBRT. Although arterial damage seems to be the main cause of ED after EBRT, the radiation dose received by the corpora cavernosa at the crurae of the penis might be important in the etiology of ED. Furthermore, nerve injury cannot be excluded. A multi-factorial etiology has to be considered, taking into account comorbidity, previous prostate surgery, drugs, and pre-treatment erectile function. Prevention is a difficult matter. If one accepts the hypothesis that radiation induces vascular damage, then decreasing the dose to pelvic vascular structures could decrease ED rate. The time elapsed between EBRT and ED evaluation is important as one should wait at least 18–24 months when ED occurrence reaches a maximum, and remains stable further on. Too many studies do not indicate properly when sexual function is assessed. The definition of (im)potence advocated by the NIH should always be used, and ED evaluation should be standardized by using, prospectively, validated questionnaires on quality of life, and sexual functioning. A better understanding of the etiology would allow more specific therapeutic modalities. Finally, sexual counseling is an important aspect. Patients need to be correctly informed on the anatomy of the prostate, on the possible sequelae of radiation on their sexual life and functioning. Being treated for cancer is clearly detrimental to patient's frequency of sexual activity, also in other than prostate cancer. Sexual activity dropped from two times weekly to once a month in one study [64]. The stability of sexual function in husbands and wives of cancer patients suggest that the problem developing after cancer treatment in patients are caused by the emotional and medical impact of illness rather than by stress in the couple's relationship [64]. Evaluating sexual functioning in an oncology population is different from evaluating it in a healthy population because of its specific medical, psychological, and social factors. In busy oncology clinics where outpatient visits must include educating patients about their disease, prognosis, and treatment, physicians and nurses often do not have the time of assessing quality of life issues [65]. Not only a functional penis but a functional man, including his partner, has to be the goal. Thus, sexual desire, satisfaction with sexual life, libido, and frequency of intercourse have to be assessed as well. Patients should also be informed about the various effective treatments for ED which include sildenafil and autoinjection therapy.

9.1. Recommendations

- Always define impotence using the definition advocated by the NIH.
- Use internationally validated questionnaires and collect data on sexual functioning prospectively, because time since radiotherapy is an important factor.
- The incidence of post-radiation ED and of other sexual dysfunctions is high, thus inform correctly your patients.
- There are good treatment options, sildenafil is effective in about 60% of the patients.
- Take the time to discuss sexual matters after radiotherapy, not only with the patient but with his partner as well.
- Cancer patients have the right to enjoy sexual life.

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References

[1] Jemal A, Murray T, Ward E, et al. Cancer Statistics. CA Cancer J Clin 2005;55:10–30.
[2] McCammon KA, Kolm P, Main B, Schellhammer PF. Comparative quality-of-life analysis after radical prostatectomy or external beam radiation for localized prostate cancer. Urology 1999;54:509–16.
[3] Mulligan T, Moss CR. Sexuality and aging in male veterans: a cross-sectional study of interest, ability, and activity. Arch Sex Behav 1991;20:17–25.
[4] Addis ME, Mahalik JR. Men, masculinity, and the context of help-seeking. Am Psychol 2003;58:5–14.
[5] Litwin MS. Health-related quality-of-life after treatment for localized prostate cancer. Cancer 1995;75:2000–3.
[6] Lim AJ, Brandon AH, Fiedler J, et al. Quality of life: radical prostatectomy versus radiation therapy for prostate cancer. J Urol 1995;154:1420–5.
[7] Fransson P, Widmark A. Self-assessed sexual function after pelvic irradiation for prostate carcinoma. Cancer 1996;78:1066–78.
[8] Beard CJ, Propert KJ, Rieker PP, et al. Complications after treatment with external-beam irradiation in early-stage prostate cancer patients: a prospective multiinstitutional outcomes study. J Clin Oncol 1997;15:223–9.
[9] Borghede G, Hedelin H. Radiotherapy of localised prostate cancer. Analysis of late treatment complications. A prospective study. Radiother Oncol 1997;43:139–46.
[10] Shrader-Bogen CL, Kjellberg JL, McPherson CP, Murray CL. Quality of life and treatment outcomes. Prostate carcinoma patients' perspectives after prostatectomy or radiation therapy. Cancer 1997;79:1977–86.
[11] Nguyen LN, Pollack A, Zagars GK. Late effects after radiotherapy for prostate cancer in a randomized dose–response study: results of a self-assessment questionnaire. Urology 1998;51:991–7.
[12] Lilleby W, Fosså SD, Waehre HR, Olsen DR. Long-term morbidity and quality of life in patients with localized prostate cancer undergoing definitive radiotherapy or radical prostatectomy. Int J Radiat Oncol Biol Phys 1999;43:735–43.
[13] Hamilton AS, Stanford JL, Gilliland FD, et al. Health outcomes after external-beam radiation therapy for clinically localized prostate cancer: results from the Prostate Cancer Outcomes Study. J Clin Oncol 2001;19:2517–26.
[14] Potosky AL, Legler J, Albertsen PC, et al. Health outcomes after prostatectomy or radiotherapy for prostate cancer: results from the Prostate Cancer Outcomes Study. J Natl Cancer Inst 2000;92:1582–92.
[15] Crook J, Esche B, Futter N. Effect of pelvic radiotherapy for prostate cancer on bowel, bladder, and sexual function: the patient's perspective. Urology 1996;47:387–94.
[16] Turner SL, Adams K, Bull CA, Berry MP. Sexual dysfunction after radical radiation therapy for prostate cancer: a prospective evaluation. Urology 1999;54:124–9.
[17] Zinreich ES, Derogatis LR, Herpst J, Auvil G, Piantadosi S, Order SE. Pre and posttreatment evaluation of sexual function in patients with adenocarcinoma of the prostate. Int J Radiat Oncol Biol Phys 1990;19:729–32.
[18] Helgason AR, Fredrikson M, Adolfsson J, Steineck G. Decreased sexual capacity after external radiation therapy for prostate cancer impairs quality of life. Int J Radiat Oncol Biol Phys 1995;32:33–9.
[19] Roach III M, Chinn DM, Holland J, Clarke M. A pilot survey of sexual function and quality of life following 3D conformal radiotherapy for clinically localized prostate cancer. Int J Radiat Oncol Biol Phys 1996;35:869–74.
[20] Fosså SD, Wæhre H, Kurth KH, et al. Influence of urological morbidity on quality of life in patients with prostate cancer. Eur Urol 1997;31:3–8.
[21] Talcott JA, Rieker P, Clark JA, et al. Patient-reported symptoms after primary therapy for early prostate cancer: results of a prospective cohort study. J Clin Oncol 1998;16:275–83.
[22] Ray GR, Cassady JR, Bagshaw MA. Definitive radiation therapy of carcinoma of the prostate. Radiology 1973;106:407–18.
[23] Bagshaw MA, Ray GR, Pistenma DA, Castellino RA, Meares EM. External beam radiation therapy of primary carcinoma of the prostate. Cancer 1975;36:723–8.
[24] Bagshaw MA, Cox RS, Ray GR. Status of radiation treatment of prostate cancer at Stanford University. NCI Monogr 1988;7:47–60.
[25] McGowan DG. Radiation therapy in the management of localized carcinoma of the prostate. Cancer 1977;39:98–103.
[26] Perez CA, Bauer W, Garza R, Royce RK. Radiation therapy in the definitive treatment of localized carcinoma of the prostate. Cancer 1977;40:1425–33.
[27] Taylor WJ. Radiation oncology. Cancer 1977;39:856–61.
[28] Forman JD, Zinreich E, Lee DJ, Wharam MD, Baumgardner RA, Order SE. Improving the therapeutic ratio of external beam irradiation for carcinoma of the prostate. Int J Radiat Oncol Biol Phys 1985;11:2073–80.
[29] Asbell SO, Krall JM, Pilepich MV, et al. Elective pelvic irradiation in stage A2, B carcinoma of the prostate: analysis of RTOG 77-06. Int J Radiat Oncol Biol Phys 1988;15:1307–16.
[30] Banker FL. The preservation of potency after external beam irradiation for prostate cancer. Int J Radiat Oncol Biol Phys 1988;15:219–20.
[31] Shipley WU, Prout Jr GR, Coachman NM, et al. Radiation therapy for localized prostate carcinoma: experience at the Massachusetts General Hospital (1973–1981). NCI Monogr 1988;7:67–73.
[32] Mameghan H, Fisher R, Watt WH, et al. Results of radiotherapy for localised prostatic carcinoma treated at the Prince of Wales Hospital, Sydney. Med J Aust 1991;154:317–26.
[33] Pilepich MV, Krall JM, Al-Sarraf M, et al. Androgen deprivation with radiation therapy compared with radiation therapy alone for locally advanced prostatic carcinoma: a randomized comparative trial of the Radiation Therapy Oncology Group. Urology 1995;45:616–23.
[34] Mantz CA, Song P, Farhangi E, et al. Potency probability following conformal megavoltage radiotherapy using conventional doses for localized prostate cancer. Int J Radiat Oncol Biol Phys 1997;37:551–7.
[35] Zelefsky MJ, Cowen D, Fuks Z, et al. Long term tolerance of high dose three-dimensional conformal radiotherapy in patients with localized prostate carcinoma. Cancer 1999;85:2460–8.
[36] Van Heeringen C, De Schryver A, Verbeek E. Sexual function disorders after local radiotherapy for carcinoma of the prostate. Radiother Oncol 1988;13:47–52.
[37] Beckendorf V, Hay M, Rozan R, Lagrange JL, N'Guyen T, Giraud B. Changes in sexual function after radiotherapy treatment of prostate cancer. Br J Urol 1996;77:118–23.
[38] Smith DS, Carvalhal GF, Schneider K, Krygiel J, Yan Y, Catalona WJ. Quality-of-life outcomes for men with prostate carcinoma detected by screening. Cancer 2000;88:1454–63.

[39] Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The International Index of Erectile Function (IIEF). A multidimensional scale for assessment of erectile dysfunction. Urology 1997;49:822–30.
[40] NIH consensus development panel on impotence. JAMA 1993;270:83–90.
[41] Wilder RB, Chou RH, Ryu JK, et al. Potency preservation after three-dimensional conformal radiotherapy for prostate cancer. Am J Clin Oncol 2000;23:330–3.
[42] Goldstein I, Feldman MI, Deckers PJ, Babayan RK, Krane RJ. Radiation-associated impotence. JAMA 1984;251:903–10.
[43] Mittal B. A study of penile circulation before and after radiation in patients with prostate cancer and its effect on impotence. Int J Radiat Oncol Biol Phys 1985;11:1121–5.
[44] Zelefsky MJ, Eid JF. Elucidating the etiology of erectile dysfunction after definitive therapy for prostatic cancer. Int J Radiat Oncol Biol Phys 1998;40:129–33.
[45] Fisch BM, Pickett B, Weinberg V, Roach M. Dose of radiation received by the bulb of the penis correlates with risk of impotence after three-dimensional conformal radiotherapy for prostate cancer. Urology 2001;57:955–9.
[46] Selek U, Cheung R, Lii M, et al. Erectile dysfunction and radiation dose to penile base structures: a lack of correlation. In J Radiat Oncol Biol Phys 2004;59:1039–46.
[47] Buyyounouski MK, Horwitz EM, Uzzo RG, et al. The radiation doses to erectile tissues defined with magnetic resonance imaging after intensity-modulated radiation therapy or iodine-125 brachytherapy. In J Radiat Oncol Biol Phys 2004;59:1383–91.
[48] Arai Y, Aoki Y, Okubo K, et al. Impact of interventional therapy for benign prostatic hyperplasia on quality of life and sexual function: a prospective study. J Urol 2000;164:1206–11.
[49] Tomic R. Some effects of orchiectomy, oestrogen treatment and radiation therapy in patients with prostatic carcinoma. Scand J Urol Nephrol 1983;(Suppl. 7):1–37.
[50] Joly F, Brune D, Couette JE, et al. Health-related quality of life and sequelae in patients treated with brachytherapy and external beam irradiation for localized prostate cancer. Ann Oncol 1998;9:751–7.
[51] Caffo O, Fellin G, Graffer U, Luciani L. Assessment of quality of life after radical radiotherapy for prostate cancer. Br J Urol 1996;78:557–63.
[52] Pierce LJ, Whittington R, Hanno PM, English W, Wein AJ, Goodman RL. Pharmacologic erection with intracavernosal injection for men with sexual dysfunction following irradiation: a preliminary report. Int J Radiat Oncol Biol Phys 1991;21:1311–4.
[53] Dubocq FM, Bianco Jr FJ, Maralani SJ, Forman JD, Dhabuwala CB. Outcome analysis of penile implant surgery after external beam radiation for prostate cancer. J Urol 1997;158:1787–90.
[54] Zelefsky MJ, McKee AB, Lee H, Leibel SA. Efficacy of oral sildenafil in patients with erectile dysfunction after radiotherapy for carcinoma of the prostate. Urology 1999;53:775–8.
[55] Kedia S, Zippe CD, Agarwal A, Nelson DR, Lakin MM. Treatment of erectile dysfunction with sildenafil citrate (Viagra) after radiation therapy for prostate cancer. Urology 1999;54:308–12.
[56] Weber DC, Bieri S, Kurtz JM, Miralbell R. Prospective pilot study of sildenafil for treatment of postradiotherapy erectile dysfunction in patients with prostate cancer. J Clin Oncol 1999;17:3444–9.
[57] Valicenti RK, Choi E, Chen C, et al. Sildenafil citrate effectively reverses sexual dysfunction induced by three-dimensional conformal radiation therapy. Urology 2001;57:769–73.
[58] Incrocci L, Koper PCM, Hop WCJ, Slob AK. Sildenafil citrate (Viagra) and erectile dysfunction following external-beam radiotherapy for prostate cancer. A randomized, double-blind, placebo-controlled, cross-over study. Int J Radiat Oncol Biol Phys 2001;51:1190–5.
[59] Incrocci L, Hop WCJ, Slob AK. Efficacy of sildenafil in an open-label study as a continuation of a double-blind study in the treatment of erectile dysfunction after radiotherapy of prostate cancer. Urology 2003;62:116–20.
[60] Incrocci L, Slob AK, Levendag PC. Sexual (dys)function after radiotherapy for prostate cancer: a review. Int J Radiat Oncol Biol Phys 2002;52:681–93.
[61] Incrocci L, Slob AK. Incidence, etiology, and therapy for erectile dysfunction after external beam radiotherapy for prostate cancer. Urology 2002;60:1–7.
[62] Zelefsky MJ, Fuks Z, Happersett L, et al. Clinical experience with intensity modulated radiation therapy (IMRT) in prostate cancer. Radiother Oncol 2000;55:241–9.
[63] Sethi A, Mohideen N, Leybovich L, Mulhall J. Role of IMRT in reducing penile doses in dose escalation for prostate cancer. Int J Radiat Oncol Biol Phys 2003;55:970–8.
[64] Schover LR, Evans RB, von Eschenbach AC. Sexual rehabilitation in a cancer center: diagnosis and outcome in 384 consultations. Arch Sex Behav 1987;16:445–61.
[65] Schover LR. Counseling cancer patients about changes in sexual function. Oncology 1999;11:1585–90.

Biography

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