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Reporting Erectile Function Outcomes After Radiation Therapy for Prostate Cancer: Challenges in Data Interpretation

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ABSTRACT

Background: Choice of prostate cancer treatment is frequently influenced by the expected chance of treatment-induced side effects such as erectile dysfunction (ED). However, great discrepancy in cited ED rates exists in the contemporary radiation therapy literature.

Aim: To analyze the reported ED rates and cause of discrepancies and explore the strengths and limitations in the literature on radiation-induced ED.

Methods: We performed a PubMed literature search and reviewed the literature on ED rates associated with external-beam radiotherapy and brachytherapy from the past 10 years. Eighteen studies were eligible for inclusion and subsequently reviewed.

Outcomes: Variables required for interpretation of erectile function outcomes, including patient demographics, treatment characteristics, and sexual function outcomes.

Results: A large variety in the reported incidence of ED was found among studies. In part, these differences resulted from large variations in (i) study populations, (ii) patient characteristics, (iii) treatment characteristics, (iv) prescription of androgen deprivation therapy, (v) means of data acquisition, (vi) definitions of ED, (vii) temporal considerations, and (viii) erectile aid use. Relevant data required for adequate appraisal of sexual function outcomes were not always reported.

Clinical Implications: Based on the present findings, we present general recommendations for reporting of erectile function outcomes after radiotherapy for prostate cancer. These should improve future reports.

Strengths and Limitations: This is the first report that presents general requirements on reporting erectile function outcomes in the setting of radiotherapy for prostate cancer. We did not conduct a formal meta-analysis because we focused on concepts of research design; this might be considered a limitation.

Conclusion: In this review, we have highlighted the strengths and deficiencies of the current literature on ED after external-beam radiotherapy and brachytherapy for prostate cancer. We have made general recommendations to achieve some degree of standardization among reports and improve clinical interpretability. **Wortel RC, Incrocci L, Muhall JP. Reporting Erectile Function Outcomes After Radiation Therapy for Prostate Cancer: Challenges in Data Interpretation. J Sex Med 2017;14:1260−1269.**

Key Words: Erectile Dysfunction; External Beam Radiotherapy; Brachytherapy; Research Design; Patient Questionnaires

INTRODUCTION

Patients with early-stage localized prostate cancer have favorable relapse-free survival outcomes regardless of treatment.[1] Therefore, the choice of treatment is frequently based on the expected treatment-induced side effects including sexual side effects. Over the years, large prospective studies have focused on analyzing side effects of various treatments. Sanda et al[2] analyzed quality-of-life outcomes after radical prostatectomy (RP; n = 602), external-beam radiotherapy (EBRT; n = 292), and brachytherapy (BT; n = 306). They reported that at 2-year follow-up erections not firm enough for intercourse were present in 64%, 66%, and 56% after RP, EBRT, and BT, respectively. Cautious interpretations of these results are warranted because of the lack of randomization and differences among

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patient populations.[2] Resnick et al[3] also analyzed outcomes after RP (n = 1164) vs EBRT (n = 491) and found that patients who underwent RP were more likely to have erectile dysfunction (ED) at 2- and 5-year follow-ups. The radiotherapy populations in these two studies were on average substantially older than the RP population (range = 5−10 years).[2,3] Such differences impede comparisons between prostate cancer treatments and adequate patient counseling before treatment selection.

However, large discrepancies also exist when comparing sexual function outcomes of treatments separately. In a review by Incrocci et al,[4] the reported incidences of ED varied from 6% to 84% after conventionally fractionated EBRT and from 0% to 51% after BT. Although differences in applied techniques, treatment planning, and expertise between treatment centers can contribute to apparent discrepancies in ED rates, we believe that the differences in populations studied, means of data collection, and data presentation are more important contributors to the rate of discrepancies.

The main objective of this review was to explore the cause of such discrepancies in reported ED rates. To do so, we conducted a review of the contemporary literature on radiation-induced ED after conventionally fractionated EBRT and BT. This is not an effort to conduct a meta-analysis; rather, we attempted to address the strengths and limitations of the literature and provide general recommendations for the reporting of erectile function outcomes after radiotherapy for prostate cancer. This might lead to some degree of standardization among future reports and thus improve clinical data interpretability. By including literature on EBRT and BT, we aimed to demonstrate that our findings are applicable to all aspects of modern pelvic radiotherapy.

METHODS

On February 25, 2017, we conducted a literature search using title search terms (radiotherapy OR brachytherapy OR radiation therapy) AND (erectile OR potency OR sexual OR patient-reported outcomes) AND prostate. Eligible for inclusion were studies written in English that reported on original clinical data with a study population of at least 100 men. In addition, we included only reports from the past 10 years, because older studies generally report on previous two-dimensional radiation techniques that cannot be compared with modern and generally applied techniques such as three-dimensional conformal radiotherapy (3D-CRT), intensity-modulated radiotherapy (IMRT), and volumetric modulated arc therapy (VMAT). We excluded all studies that presented data on techniques or treatments other than BT or conventionally fractionated EBRT and all studies that focused mainly on erectile devices or medication.

RESULTS

We retrieved 81 studies that were screened for title and abstract. After careful review, 63 studies did not meet the inclusion criteria. Eighteen studies met all inclusion criteria and therefore were included in this review (Table 1). The complete flowchart is presented in Figure 1. Investigated radiation techniques included EBRT (3D-CRT, IMRT, VMAT), low-dose rate (LDR) and high-dose rate (HDR) BT, or a combination of these techniques (Table 2).

Erectile Function After Radiotherapy for Prostate Cancer

The National Institutes of Health (NIH) define ED as "the consistent inability to obtain and/or maintain an erection sufficient for satisfactory sexual performance."[23] A modified variation of this definition was frequently used (Table 3). The reported preservation rates of erectile function after treatment varied from 22% to 70% for reports on EBRT and from 20% to 81% for studies concerning BT with or without additional EBRT (Table 3). Large variation in study populations, data acquisition, data reporting, and definitions of erectile function and dysfunction contributed to reported differences in sexual function outcomes.

In the following sections, we discuss the key elements that, in our opinion, should be considered when reporting on erectile function outcomes after radiotherapy for prostate cancer. These include (i) study populations, (ii) patient characteristics, (iii) treatment characteristics, (iv) prescription of androgen deprivation therapy (ADT), (v) means of data acquisition, (vi) definitions of ED, (vii) temporal considerations, and (viii) erectile aid use.

Study Population

All reviewed studies included more than 100 patients, and two major centers reported on at least 1,000 patients.[15,17] However, the validity of studies should be defined not only by the included study sample but also by the proportion of patients who actually completed follow-up. As presented in Table 1, substantial differences can be found in the reported number of patients who were included for analysis at baseline and those who actually completed follow-up. In addition, some investigators included only patients with functional erections at baseline,[13,15,18] whereas others reported only erectile function outcomes of a proportion of the patient population and not the entire study cohort.[10,24] This patient selection bias of choosing the youngest, healthiest patients with the best baseline erectile function can lead to erectile function outcomes that are unrealistic for the general population. In our series, the highest erectile preservation rates were reported by single-center series for EBRT[8] and BT[15,21] (Table 3). Although these centers might offer higher-quality treatment, patient selection also is likely a relevant factor contributing to such high erectile preservation rates. In general, when reviewing data on erectile function outcomes, it should be clear how many centers were involved in the study, what inclusion criteria were applied, and how many patients completed follow-up.