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Sexual potency preservation and quality of life after prostate brachytherapy and low-dose tadalafil

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ABSTRACT

PURPOSE: To prospectively determine sexual function, bother, and potency preservation in men treated with prostate brachytherapy and twice-weekly tadalafil.

METHODS AND MATERIALS: From 2005 to 2011, men treated with low-dose-rate prostate brachytherapy were treated on a prospective registration study. All patients were prescribed tadalafil 10 mg twice weekly. The expanded prostate cancer index composite questionnaire was administered before treatment and at each followup. A subgroup analysis of men with sexual potency at baseline was performed.

RESULTS: A total of 237 men were analyzed. Median age was 64 years (range, 44–86). Median followup was 24.8 months (range, 1–60). At baseline, 175 men (74%) reported erections firm enough for sexual activity and 148 (62%) were potent (erections firm enough for intercourse). Statistically significant changes in sexual function/bother were appreciated from baseline throughout the analysis period, although absolute changes were relatively small and did not meet criteria for clinical significance. At 24-months followup, 72% reported erections firm enough for sexual activity and 56% were potent. Of men with potency at baseline, 89% had erections firm enough for sexual activity and 76% remained potent 24 months after treatment.

CONCLUSIONS: Peri-procedural tadalafil and prostate brachytherapy resulted in high rates of sexual potency preservation and no clinically significant effect on sexual quality of life.

Keywords: Tadalafil; Brachytherapy; Prostate cancer; EPIC; Erectile dysfunction

Introduction

Low-dose-rate permanent prostate brachytherapy is a safe and highly effective treatment for men with organ-confined prostate cancer (1–3). Treatment involves the placement of small radioactive sources into the prostate gland to deliver radiation directly to the prostate. Because radiation dose delivery is inversely and exponentially related to the distance from the radiation source, radiation dose to the surrounding bladder, rectum, and connective tissue is minimized. Low-dose-rate prostate brachytherapy is more convenient than alternative treatments for prostate cancer as it can be delivered in a single outpatient visit. Erectile dysfunction (ED) is a common side effect of prostate cancer treatment, inclusive of prostate brachytherapy (4), with affected patients suffering significant health-related quality-of-life consequences (5–7). In men who are fully potent before prostate cancer treatment, sexual quality of life impairment is perhaps the strongest predictor of overall patient satisfaction (5). Partly because of the complexity of sexual function, varying definitions of ED, and the historical absence of a standardized sexual quality-of-life instrument, high-quality data on sexual function after prostate brachytherapy are limited (8).

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The term penile rehabilitation describes the use of medications or devices after definitive prostate cancer treatment delivered with the intent of preserving erectile tissue integrity and maximizing recovery of erectile function. The fundamental principle is to minimize post-treatment fibrosis of penile tissue through optimizing oxygenation and protecting endothelial cells.

Use of 5-phosphodiesterase inhibitors (PDE5i) with the intention of preserving sexual quality of life after prostate cancer treatment has been successfully implemented in men treated with radical prostatectomy (9–11). Although the primary mechanism of ED after prostatectomy is thought to be predominantly neurogenic (12), ED after radiation therapy is thought to be primarily vasogenic (13). After radiation therapy, sensitive endothelial cells lining the penile arteries and the sinusoids of the corpora cavernosa can be damaged, leading to luminal stenosis, arterial insufficiency, and induction of fibrosis in the corporal tissue months to years after radiation treatment (14, 15). Hypoxia in the erectile tissue microvasculature seems to mediate the process of postradiation fibrosis (16, 17). Achieving erections on a regular basis may prevent upregulation of transforming growth factor-beta, a cytokine believed to play a central role in postradiation fibrosis (18). The PDE5i use facilitates periodic oxygenation of erectile tissues, promotes endothelial cell/smooth muscle vitality, and allows many patients to achieve increased erection rigidity (19–23). Delayed initiation of PDE5i therapy in men with ED after prostate brachytherapy results in worse erectile function compared with early medical intervention (24). All the previously mentioned parameters suggest a role for peri-procedural PDE5i therapy in men treated with prostate brachytherapy. The present study reports the results of a prospective cohort of men treated with prostate brachytherapy and peri-procedural tadalafil for penile rehabilitation.

Methods and materials

Patient selection and treatment

The overseeing institutional review board approved patient data collection and analysis. All participants provided written informed consent for treatment. Patients treated with prostate brachytherapy monotherapy were eligible for analysis. Criteria for prostate brachytherapy monotherapy during the analysis period were generally restricted to the following parameters, namely American Joint Committee on Cancer seventh edition clinical stage T1c–T2c, presenting prostate-specific antigen level lower than 15 ng/mL, and Gleason score ≤7. Men with contraindications to PDE5i were excluded from participation. Men endorsing any of the following were also excluded from analysis: any prior PDE5i use, use of other sexual medications including intracavernosal injections, use of sexual devices for erection enhancement, receipt of androgen deprivation therapy with therapeutic or cytoreductive intent, or receipt of supplemental external beam radiation therapy. Men with penile prostheses were also specifically excluded.

All patients were prescribed oral administration of tadalafil 10 mg twice weekly starting 2 weeks before prostate brachytherapy. The dosing and schedule of tadalafil was based on the intention of encouraging spontaneous erections twice weekly. No specific duration of therapy was predetermined; however, continuation of tadalafil was encouraged for at least 6 months after the prescribed radiation dose was delivered (approximately six isotope half-lives). All patients were treated with ^{125}I, ^{103}Pd, or ^{131}Cs brachytherapy seeds to prescribed doses of 145, 125, and 115 Gy, respectively. A standard ultrasound-guided, transperineal technique using preloaded brachytherapy needles was used for all procedures. No patient received supplemental external beam radiation or androgen deprivation therapy.

Assessment of sexual function and bother

The expanded prostate cancer index composite (EPIC) and companion utilization of sexual medications and devices questionnaire are validated prostate cancer–specific instruments for assessment of patient-reported outcomes (25). All patients completed the EPIC questionnaires before initiation of the study treatment (baseline) and at regular followup intervals (1, 4, 8, and 12 months postbrachytherapy and every 6 months thereafter). Sexual function, bother, and summary scores were tabulated according to instrument guidelines scaled from 0 to 100; where lower scores represent worse sexual function and more bother. The companion utilization of sexual medications and devices questionnaire was co-administered at each assessment time point and is inclusive of patients-reported sexual potency in the absence of pharmaceutical or mechanical enhancement.

Definition of potency

Data regarding potency were derived from patient responses to EPIC-26 question #18 "How would you describe the quality of your erections during the last 4 weeks" with possible responses limited to the following, namely: (*1*) none at all, (*2*) not firm enough for any sexual activity, (*3*) firm enough for masturbation and foreplay only, (*4*) firm enough for intercourse. Potency was defined as erections firm enough for sexual intercourse. Men reporting erections firm enough for sexual intercourse, masturbation, or foreplay were defined as having erections firm enough for sexual activity. Preservation of sexual potency and sexual activity was determined through subgroup analysis at baseline and subsequent followup.

Statistical analysis

A paired *t* test was used for statistical comparisons to baseline with statistical significance defined as *p*-value