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Retrospective Descriptive Study on Patients with Low-Intermediate Risk Prostate Cancer Treated with HDR Interstitial Brachytherapy

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Abstract

Introduction: Primary objective is PSA relapse-free survival. Secondary objectives are description of chronic toxicity and rate of local/regional recurrences/metastases.

Material and Methods: Between 14/06/2016 and 13/02/2023 we included 60 patients diagnosed with low or intermediate risk prostate cancer according to D'Amico criteria. They received interstitial HDR brachytherapy treatment exclusively.

Measured chronic toxicity of urinary function, sexual dysfunction, and gastrointestinal function according to CTCAE 5.0 criteria 6 months after starting treatment and annually thereafter. We also monitored PSA values every 6 months and considered biochemical recurrence, according to the Phoenix criteria (PSA NADIR + 2 ng/ml). Statistical analysis was developed by SPSS 29.0.

Results: Median follow-up was 38 months (range: 5 and 80 months). At 38 months and 80 months, PSA relapse-free survival was 98% and 84%, respectively (confidence interval 95%). Chronic gastrointestinal toxicity rates were G0 100%, genitourinary G0 55%, G1 43.3% and G2 1.7% and sexual dysfunction G0 58.3%, G1 8.3% and G2 33.3%. Local relapse rate was 5% and no regional recurrence or distant metastasis appeared.

Discussion: HDR interstitial brachytherapy is a highly effective treatment. A lot of scientific publications have demonstrated high rates of local control and PSA recurrence free survival (97%-85%) for low and intermediate risk prostate cancer. Our results are similar in terms of PSA relapse-free survival and toxicity with respect to studies in the scientific literature.

Keywords: Low-intermediate risk; Prostate cancer; High dose rate; Brachytherapy; Toxicity and PSA relapse-free survival

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Introduction

Standard options for the initial treatment of men with clinically localized prostate cancer include radiation therapy (brachytherapy and/or external beam), radical prostatectomy, or in carefully selected patients, active surveillance.

High Dose Rate (HDR) brachytherapy involves the temporary placement of radioactive sources that are implanted directly into the prostate gland to administer a high dose of radiation directly to the prostate while minimizing radiation to normal tissues. Observational data indicate that as monotherapy, brachytherapy has similar efficacy compared with other forms of radiation and is comparable with other modalities (e.g., surgery) in the treatment of low/intermediate-risk prostate cancer.

The most frequent complications associated with brachytherapy are toxicity to the urinary tract and rectum, as well as sexual dysfunction. The severity of complications is significantly influenced by pretreatment functional level [1].

We started a retrospective descriptive study on patients with low-intermediate risk prostate cancer treated with HDR interstitial brachytherapy. Our primary objective was PSA-relapse free survival and secondary objectives were description of chronic toxicity and rate of local/regional recurrences/metastases.

Material and Methods

Median follow-up was 38 months (range: 5 and 80 months).

Between 14/06/2016 and 13/02/2023 we included 60 patients diagnosed with low or intermediate risk prostate cancer according to D´Amico criteria [2]. All patients received interstitial brachytherapy treatment exclusively and we added Androgen Deprivation Therapy (ADT) during 3 to 6 months for patients with intermediate risk prostate cancer and prostate volume >50 cc.

Brachytherapy total dose was 27 Gy (13.5 Gy/fraction 1 fraction/week) in 55 patients or 20.5 Gy (single fraction) in 5 patients who were older than 80 years old with Performance Status 2.

Brachytherapy was performed under spinal anesthesia. We place the patient in the forced lithotomy position and, guided by transrectal ultrasound, the needles are placed inside the prostate volume (Gross Tumor Volume). Planning is carried out in real time in the operating room and the scheduled brachytherapy treatment is administered using Co-60 as a radioactive source.

Measured chronic and acute toxicity of urinary function, sexual dysfunction, and gastrointestinal function according to CTCAE 5.0 criteria 6 months after starting treatment and annually thereafter to evaluate chronic toxicity and 2 weeks after brachytherapy for acute toxicity. We also monitored PSA values every 6 months and considered biochemical recurrence, according to the Phoenix criteria (PSA NADIR + 2 ng/ml). When biochemical recurrence was detected, pelvic MRI, PET-CT and prostate biopsy were performed to confirm local recurrence in all patients.

SPSS 29.0 was used to carry out statistical analysis and survival curves. We used a Kaplan-Meier test to calculate probability PSA free survival recurrence.

Results

We include 60 patients and describe the baseline characteristics of the patients.

At 38 and 80 months, PSA relapse-free survival was 98% and 84%, respectively (confidence interval 95%).

Only 3 patients showed local relapse into prostate volume (local relapse rate of 5%) and no regional recurrence or distant metastasis appeared.

Chronic gastrointestinal toxicity rates (rectal bleeding or fistula) were G0 100%, genitourinary (hematuria or urinary tract obstruction) G0 55%, G1 43.3%, G2 1.7% and G3 0% and sexual dysfunction (erectile dysfunction) G0 58.3%, G1 8.3%, G2 33.3% and G3 0%. Acute gastrointestinal toxicity rates (diarrhea or proctitis) were G0 100% and genitourinary (bladder spasm, dysuria or urinary emergency) G0 30%, G1 60%, G2 10% and G3 0%.

Discussion

There are no randomized trials that provide adequate data to compare brachytherapy with other treatment modalities as initial therapy in men with low-risk or intermediate-risk, localized prostate cancer. The choice of brachytherapy over External Beam Radiation Therapy (EBRT), radical prostatectomy, or active surveillance is generally based on a combination of factors, including treatment-related complications as well as clinician and patient preferences.

The Surgical Prostatectomy versus Interstitial Radiation Intervention Trial (SPIRIT) was designed to compare brachytherapy with radical prostatectomy, but it was discontinued because of poor accrual [3]. Health-related quality of life was analyzed after five years in patients who either had been randomized or had undergone screening for the trial. In the 168 men who completed a follow-up survey five years later, brachytherapy was significantly better in terms of urinary and sexual functioning.

In addition, several retrospective analyses have compared outcomes following brachytherapy versus high-dose EBRT, and these results suggest that brachytherapy is at least equivalent for biochemical control and may be more effective at achieving lower Prostate-Specific Antigen (PSA) nadirs [4-7].

In an analysis of data performed by the Prostate Cancer Results Study Group (PCRSG), treatment outcomes for both LDR and HDR brachytherapy, both alone and in combination with EBRT, appeared similar to those with other treatment modalities when patients were stratified according to risk [8]. A similar conclusion was reached in a retrospective review of the 10-year outcomes of 1,503 men with intermediate-risk prostate cancer who were treated with EBRT, radical prostatectomy, or LDR brachytherapy [7].

When brachytherapy is used as monotherapy, clinically significant long-term urinary toxicity following brachytherapy is uncommon. In a series of 1,989 men treated with LDR brachytherapy, the rates of severe, late, genitourinary and gastrointestinal toxicities were 7.6 and 0.8 percent, respectively [9], and similar results have been seen in other series [10].

Late urethral strictures are an uncommon complication following brachytherapy [11,12]. In a series of 1,030 patients treated with brachytherapy, 94 and 92 percent of patients were free of stricture one year after treatment with brachytherapy alone and brachytherapy plus EBRT, respectively [11]. At four years, 89 and 84 percent remained stricture free.

Although some rectal bleeding is relatively common, more serious complications are rare [13-16]. As an example, in a retrospective series of 2,752 patients treated with LDR brachytherapy over a 17-year period, the actuarial risk of grade 2 or higher rectal bleeding was 6.4 percent. However, only 27 patients (1%) required medical intervention (formalin treatment or cauterization), and fistula or ulceration occurred in only nine cases (0.3%). Radiation-related rectal fistulas are a serious but rare complication, occurring in fewer than 1 percent of cases [17].

The reported incidence of erectile dysfunction varies widely among men who were potent prior to brachytherapy, depending in part on whether data are clinician or patient reported. Rates of erectile dysfunction are similar to that seen with EBRT. The impact of LDR brachytherapy on erectile function is illustrated by results from a prospective multicenter analysis of prostate cancer survivors that included 306 patients who were treated with LDR brachytherapy [18]. In this study, poor sexual function was reported in 43 to 48 percent of patients from 2 to 24 months after therapy. Approximately one-third of patients considered sexual dysfunction a moderate or big problem. Similar rates of dysfunction have been reported in other studies [19,20].

HDR interstitial brachytherapy is a highly effective treatment. Scientific publications have demonstrated high rates of local control and PSA recurrence free survival (97% to 85%) for low and intermediate risk prostate cancer. Our results are similar in terms of

PSA relapse-free survival and toxicity with respect to studies in the scientific literature.

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