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Original Article

# Long Term Patient Reported Urinary Function Following External Beam Radiotherapy for Prostate Cancer

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## Abstract

*Introduction:* This study reports long-term patient reported urinary function and urinary-related quality of life (uQoL) after external beam radiotherapy (EBRT) for localized prostate cancer.
*Methods:* 574 men underwent definitive prostate EBRT to 70–78 Gy ± androgen deprivation therapy between 2000 and 2009. The median follow-up from EBRT was 44 months. Patients were evaluated at baseline (pre-EBRT) and at intervals post-treatment using the International Prostate Symptom Score (IPSS) instrument.
*Results:* Patients with mild IPSS at baseline (total 0–7) reported median total scores of 3, 4 and 3 at baseline, 6 and 48 months respectively post-EBRT. For patients with moderate IPSS at baseline (total 8–19), median total IPSS was 12 at baseline and 9 at both 6 and 48 months. For the severe IPSS group at baseline (total 20–35), the median total IPSS was 24, 12 and 14 at baseline, 6 and 48 months post-EBRT. The cumulative risk of persistent IPSS increase (greater than 5 points above baseline) at 48 months was 16%, 10% and 6% for patients with mild, moderate and severe baseline IPSS respectively. 94%, 54% and 11% of patients with mild, moderate and severe baseline IPSS reported good uQoL at baseline respectively, with these proportions increasing to 95%, 83% and 69% at 48 months.
*Conclusion:* Urinary symptoms and uQoL as measured by the IPSS instrument remained stable or improved for the majority of men after definitive EBRT with or without ADT for prostate cancer. This was especially notable for the group of men with worse baseline symptoms or uQoL, with risk of persistent worsening of urinary symptoms decreasing with higher baseline IPSS category. Understanding the expected pattern of urinary symptoms and related uQoL in the months and years following EBRT taking into account baseline urinary function is highly valuable for counselling men as part of the therapeutic decision-making process.


*Key words:* External beam radiotherapy; lower urinary tract symptoms; prostate cancer; quality of life

## Introduction

External beam radiotherapy (EBRT) is an effective treatment for localized prostate cancer. Patients with prostate cancer often have several treatment options available and understanding the impact of each treatment modality on quality of life (QoL) is important in counselling patients. While EBRT causes short-term changes to urinary function, objective measurement of these suggests these effects appear to be transient [1,2].

Clinician reported toxicity grading systems such as the Radiation Therapy Oncology Group (RTOG) Common Toxicity Criteria (CTC) have recognized limitations in measuring urinary symptoms and toxicity post-EBRT. Many men with prostate cancer present with urinary symptoms prior to treatment. These are not accounted for in toxicity assessments [3]. Clinicians often underestimate symptoms [4,5], and 5-point scales such as the RTOG CTC may be insensitive to subtle changes in urinary function [6–8].

The International Prostate Symptom Score (IPSS) instrument was initially used as a patient reported measure of the symptoms of benign prostatic hyperplasia. It has good internal validity and was also found to be responsive to change [9]. It consists of 7 symptoms (frequency, nocturia, weak urinary stream, hesitancy, intermittency, incomplete emptying and urgency) and one urinary quality of life (uQoL) question. Each symptom is scored from 0 to 5, with total IPSS being a summation of all 7 symptom scores.

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Overall severity of symptoms is divided into three categories based on the total score. Total IPSS from 0–7 is defined as mild symptomatology, 8–19 moderate, and 20–35 as severe [10]. uQoL is scored from 0 (delighted with present function) to 6 (terrible uQoL). The IPSS thus has several advantages as a urinary symptom reporting tool including being patient self-reported and including a measure of uQoL. The IPSS also captures a wider range of symptoms compared to the mixed symptom/pathology-based RTOG-CTC system (frequency, dysuria, haematuria, degree of telangiectasia/necrosis). In addition, it can be administered pre- and post-treatment, thereby being a more accurate indicator of change in urinary function and uQoL. Along with the RTOG-CTC, Common Terminology Criteria for Adverse Events (CTCAE) and Late Effects in Normal Tissues Subjective, Objective, Management and Analytic (LENTSOMA) scales, the IPSS has been used previously to measure outcomes after EBRT.

While many studies report mean or median IPSS after EBRT [11–13], reporting of these scores does not provide information on the proportion of men experiencing an increase or decrease in IPSS. Particularly when changes occur in both directions, a proportion of patients may experience improved or worsening of symptoms with minimal change in the median scores. Categorization of patients by pre-treatment functional status and reporting of proportions of patients having changes in symptoms after treatment can help clinicians better inform patients regarding expected treatment impact, with one prior study reporting proportions of IPSS changes after IMRT to a dose of 86.4 Gy [14]. This study aims to report patterns of long-term patient reported urinary function and uQoL as measured by the IPSS in a large Australian cohort treated with EBRT to 70–78 Gy, taking into account their baseline function to assist clinicians in counselling men about their expected urinary function and uQoL.

## Methods

Men who underwent definitive EBRT with or without androgen deprivation therapy (ADT) for biopsy-proven T1c-T4 N0 M0 (TNM 6th edition, 2003) localized prostate cancer at Westmead and Nepean Cancer Centres between 2000 and 2009 were identified from a prospective electronic database. All consecutive patients with a minimum of 6 months follow up after EBRT were included, and patients who underwent previous prostatectomy or brachytherapy were excluded. Approval for the study was obtained from the institutional human research ethics committee (Westmead Scientific Advisory Committee).

Patients were classified into risk groups according to National Comprehensive Cancer Network (NCCN) criteria. Use of ADT related to cancer risk-grouping; generally, 6 months neoadjuvant ADT was prescribed for intermediate risk prostate cancers, while a total of 1.5–3 years ADT was prescribed for men with high risk disease.

Men were treated in the earlier cohort using a 6-field conformal radiotherapy (RT) technique using 2-phases and prescribed 70–74 Gy in 2 Gy fractions over 8 weeks to the ICRU reference point. From April 2009, men were treated with intensity modulated radiation therapy (IMRT) to 78 Gy in 2 Gy fractions with placement of fiducial markers and daily image-guidance. The CTV for the low-risk group encompassed the prostate only, with at least the proximal half of the seminal vesicles included for intermediate and high-risk patients, and the entire seminal vesicles if they were radiologically or pathologically involved with cancer. Organ at risk constraints, patient instructions and image verification have been described previously [15]. Patients were followed up in the clinic at 3 months after completion of EBRT, then 3 to 6 monthly out to 5 years, and annually thereafter. The follow-up period was divided into 6 monthly intervals up to 2 years after completion of EBRT, then 12 monthly.

Baseline IPSS was collected prior to commencement of ADT or EBRT (if no ADT given). At each follow up visit, clinical assessment, IPSS and RTOG toxicity was recorded prospectively. A retrospective review of patient records was performed for patients with baseline IPSS $>$ 20 to review the details of urinary interventions and/or use of alpha-blocker or antispasmodic therapies.

Mild, moderate and severe urinary symptoms based on the IPSS were classified according to the American Urological Association definition as total IPSS scores of 0–7, 8–19 and 20–35 respectively. IPSS uQoL was categorised into good (0 ‘Delighted’ to 2 ‘Mostly satisfied’) or poor (3 ‘Mixed’ to 6 ‘Terrible’). IPSS findings across all men for each time interval were grouped according to baseline severity status. The average IPSS was used in cases where there were multiple IPSS scores for the same patient within any given time period.

Actuarial risk of persistent IPSS increase according to baseline IPSS category were determined, along with proportions of patients experiencing change from one IPSS category (mild, moderate, severe) to another and changes in total IPSS from baseline to 6 and 48 months after EBRT.

A decrease in total IPSS of $\geq$5 points was defined as an improvement in urinary function, while an increase of $\geq$5 was defined as worsening in urinary function based on previous reports that IPSS changes of this degree have at least moderate patient impact [9]. Two total IPSS reports of $\geq$5 points above baseline made at least 3 months apart were considered to represent a persistent and hence more clinically meaningful worsening compared to one-off increases which subsequently resolve. IPSS changes of less than 5 compared to baseline between measurements were termed ‘stable’.

The level of statistical significance was set at $p < 0.05$, and estimates of persistent IPSS rise were determined using a Kaplan-Meier analysis and compared using the log-rank test. Patients with baseline IPSS $>$ 30 were excluded from the Kaplan Meier analysis as they were unable to report a 5 point increase. Proportional hazards regression was used to investigate the effect of baseline IPSS, use of ADT, age and T stage on the likelihood of having a persistent worsening of urinary function as measured by increased IPSS.

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