Overactive Bladder and Storage Lower Urinary Tract Symptoms Following Radical Prostatectomy

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OBJECTIVE To describe the rate of overactive bladder (OAB) and storage lower urinary tract symptoms following radical prostatectomy (RP) and determine if subsequent radiation increases the risk of OAB.

METHODS We reviewed all patients who underwent open RP at our tertiary care institution from January 2006 to June 2011. Primary outcomes were the proportion of patients with new OAB and time to development of OAB in those treated with RP alone vs RP plus radiation. Secondary outcomes included the proportion of patients treated for OAB. A Cox survival analysis was used to assess the impact of radiation on development of OAB.

RESULTS Of the 875 patients who met study criteria, 19% of patients developed de novo OAB defined as urgency with or without frequency and nocturia. A total of 256 patients (29%) developed 1 or more urinary symptoms including nocturia (22%), frequency (21%), urgency (19%), and urge incontinence (6%) following RP. After adjusting for age, body mass index, smoking status, cancer stage, and nerve-sparing status, radiation therapy was associated with an increased relative hazard of OAB (5.59; 95% CI 3.63-8.61, $P < .001$). Among men classified with de novo OAB, only 41% received treatment.

CONCLUSION OAB and storage lower urinary tract symptoms are prevalent in men post-RP. Adjuvant or salvage radiation therapy increases the risk of developing OAB after RP. OAB may be undertreated in men following prostate cancer treatment. UROLOGY 94: 193–197, 2016.

Radical prostatectomy (RP) is the most common definitive treatment for clinically localized prostate cancer.[1] Following RP, a proportion of men will receive additional radiation therapy based on poor pathological features, or biochemical recurrence of disease. Although 10-year survivorship after RP is excellent at 95%-100%,[1] RP is associated with a number of adverse effects including urinary leakage and/or erectile dysfunction.[2,3] Recent survey and urodynamic studies suggest that men may also develop overactive bladder (OAB) following treatment for localized prostate cancer.[4-7]

OAB is a subset of storage lower urinary tract symptoms (LUTS) that is defined as urinary urgency, with or without urgency incontinence, usually with frequency and nocturia.[8] OAB negatively impacts quality of life and often requires medications with bothersome side effects.[9] Blaivas et al found that 20% of men with OAB symptoms had a history of prostate cancer treatment.[5] A review by Porena et al reported that the rate of de novo detrusor overactivity on urodynamic studies after RP ranged from 2% to 77%.[4] One recent survey study found that 13% and 30% of patients treated with RP and radiation therapy, respectively, had OAB 3 years after treatment.[6] Consequently, there is some evidence to suggest that men are at an increased risk of developing OAB after RP for localized prostate cancer. However, the rate of OAB has yet to be investigated in a large cohort of individuals who have undergone RP.

The goal of our study was to investigate the rate of OAB and storage LUTS in men following RP for localized prostate cancer and to determine whether the risk of OAB was higher in men who underwent additional radiation therapy (adjuvant or salvage) vs RP alone. We also assessed the rate of treatment of OAB in our cohort.

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METHODS

Study Design and Subject Selection

We performed a retrospective cohort study of men who underwent open RP at our institution between January 1, 2006 and June 1, 2011. Patients were identified through billing records for RP. We followed the health records of all identified patients at our institution for as long as follow-up records were available. A total of 9 academic urologists performed open RP at our institution during this time period. Exclusion criteria included: (1) the presence of preoperative urgency, frequency, or nocturia; (2) the presence of a neurological disorder such as stroke, Parkinson's disease, multiple sclerosis, or spinal cord injury (which may be independently associated with the development of OAB irrespective of RP); and (3) patients treated with laparoscopic RP, which was represented by only a few patients. We did not include patients who underwent salvage RP postradiation therapy.

The treating urologist assessed for the presence of OAB and storage LUTS at each postoperative visit based on clinical history. The first visit was typically 6 weeks postoperatively. As per the International Continence Society definition, OAB was defined as the documentation of urinary urgency, with or without urgency incontinence.[7] Storage LUTS included nocturia defined as waking 1 or more times to void; frequency defined as the patients feeling they void too often during the day; urgency defined as sudden compelling desire to pass urine; urge incontinence defined as involuntary leakage of urine associated with urgency; and stress incontinence defined as involuntary leakage of urine with exertion. Presence of preoperative LUTS was determined by reviewing patient charts 1 year prior to the date of surgery. This included a standardized preoperative anesthesia report that documented presence of urgency, frequency, nocturia, urge incontinence, and stress incontinence according to the previously mentioned definitions. Patients undergoing adjuvant or salvage radiation therapy were treated as one group.

Outcomes

The primary outcomes were the proportion of patients who developed OAB, time to development of OAB (as determined from the time of surgery), and the relative hazard of developing OAB in patients who received RP alone vs RP plus radiation therapy. Secondary outcomes included the proportion of patients treated for OAB following RP. Treatment of OAB was defined as: conservative measures (eg, fluid/caffeine restriction), anticholinergic agents, beta 3-agonists, intravesical onabotulinumtoxinA injection, sacral neuromodulation, or augmentation cystoplasty.

Statistical Analysis

Baseline characteristics were reported as medians (with 25th to 75th percentiles) for continuous variables and number with percentages for categorical variables. Comparisons between the RP and RP plus radiation groups were made using the Wilcoxon rank-sum test and Fisher's exact test for continuous and categorical variables, respectively. OAB free survival was graphically displayed using the Kaplan-Meier product limit method. Multivariable Cox proportional hazard models were used to calculate relative hazard and 95% confidence intervals (CIs) for those who received RP plus radiation vs RP alone. For the Cox model, exposure to radiation after RP was treated as a time-varying covariable; OAB outcome events and OAB free survival time that occurred prior to radiation treatment were attributed to the RP alone group. A two-sided *P* value of <.05 was the threshold for statistical significance in all comparisons. Approval to conduct this study was provided by the research ethics board at our institution. All analyses were performed using Stata version 12.0 (College Station, TX).

RESULTS

After excluding patients with preoperative urgency, frequency, or nocturia, our cohort consisted of 712 patients who underwent RP alone and 163 patients who received radiation therapy (109 adjuvant, 54 salvage radiation) following RP. Median follow-up time was 2.7 years (0.6-4.8 years). The median age at time of surgery was 68 years (interquartile range 63-72). Baseline characteristics are shown in Table 1.

Development of OAB and Storage LUTS

Of the 875 patients who met study criteria, 165 (19%) developed de novo OAB (urgency ± frequency, nocturia, urge incontinence) following RP (Table 2). A total of 256 patients (29%) developed 1 or more urinary symptom including nocturia (22%), frequency (21%), urgency (19%), and urgency incontinence (6%) following RP. In our cohort, 297 (33%) reported new symptoms of stress incontinence. There was a progressive increase in the proportion of men with new OAB symptoms over time (Fig. 1).

Effect of Radiation Therapy

Overall, 86/712 (12%) in the RP and 79/163 (48%) in the RP plus radiation groups developed de novo OAB ($P < .001$). However, 30 patients in the RP plus radiation group developed these symptoms prior to receiving radiation therapy and were therefore considered in the RP alone group. Still, this did not change the statistically significant difference of de novo OAB between the two groups (15% vs 36%, $P < .001$). Those who received RP plus radiation had significantly higher rates of urgency, frequency, nocturia, and urgency incontinence compared to those who received RP alone (Table 2). The presence of stress incontinence was also increased with subsequent radiation therapy (32% vs 45%, $P < .002$).

Multivariable analysis revealed an increased hazard of 5.44 (95% CI 3.53-8.39, $P < .001$) for the development of de novo OAB in men treated with both RP and radiation vs RP alone after adjusting for age, body mass index, smoking status, cancer stage, nerve-sparing status, and the presence of postoperative stress incontinence. As postoperative stress incontinence is technically an outcome in