Preimplant Predictive Factors of Urinary Retention After Iodine 125 Prostate Brachytherapy

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OBJECTIVES To assess the rate and predictive factors of urinary retention after iodine 125 brachytherapy for localized prostate cancer.

METHODS Between 1998 and 2006, 655 patients with localized prostate cancer (T1-2, Gleason score 7 or less) were treated with brachytherapy at our institution. 42% received neoadjuvant hormone therapy for prostate downsizing or when brachytherapy was combined with external beam radiation (10%). They underwent real-time interactive implantation (79%) or a preplanned technique (21%). Clinical, treatment-related and dosimetric factors were evaluated for catheterization requirement because of urinary retention. All patients received α1-blockers before and throughout at least 30 days posttreatment.

RESULTS Twenty-one (3.2%) patients required catheterization because of urinary retention. Median time to retention onset was 1 day postimplantation. Univariate and multivariate analyses demonstrated that preimplant ultrasound (US)-based prostate volume and preimplant international prostate symptom scores (IPSS) were significant independent predictive factors for urinary retention (odds ratio [OR] = 6.8 and 3.1, 95% CI = 2.3–11.4 and 0.2–5.9, P = 0.02 and P = 0.03, respectively). Eight catheterized patients were successfully relieved from their catheter by nonsurgical means and 13 underwent minimal (channeling) transurethral resection of the prostate (TUR-P) not earlier than 6 months postimplant. Mean volume of resected prostate tissue was 9.9 mL (range 4.5–15). The perioperative and postoperative courses were uneventful. There was no TUR-P–related incontinence.

CONCLUSIONS Catheterization for acute urinary retention after brachytherapy is an uncommon event. Our data suggest that preimplant US-based prostate volume and IPSS are the strongest predictors for catheterization. Catheterized patients who are refractory to medical therapy can safely undergo a minimal TUR-P.


Over the past decade, transperineal permanent prostate brachytherapy has become an accepted treatment option for localized prostate cancer. Besides acute urinary irritative/obstructive symptoms that most patients have develop after brachytherapy, urinary retention requiring the use of a catheter was also reported in a substantial number of these patients. Several reports have assessed the predictive factors and treatment options for this complication. If retention is refractory, a postimplant transurethral resection of the prostate may ultimately be required to relieve obstruction, leading to an increased risk of urethral strictures and urinary incontinence.

We report our experience in acute urinary retention requiring catheterization among 655 consecutive patients and present an analysis to identify independent predictive factors associated with postimplant urinary retention. In addition, we describe the postoperative outcomes of surgically treated patients.

MATERIAL AND METHODS

Patients Between June 1998 and June 2006, we treated 655 consecutive patients with localized prostate cancer by using iodine 125 (125I) permanent seed implantation at the Tel Aviv Sourasky Medical Center as previously described. Patients with a gland larger than 50 cm³ were administered combined androgen blockade for median of 6 months (range, 3 to 18) to reduce the gland size to a desired volume of less than 50 cm³. Patients with a Gleason score of 7, independent of prostate-specific antigen (PSA) levels and clinical stage, were treated with a combination of 125I seed implantation at a reduced dose (107 Gy) and external beam radiation (EBRT) (45 Gy). A 6-month combined androgen blockade was prescribed to all patients treated with the combination. All participants completed the interna-
tional prostate symptom score (IPSS) questionnaire before treatment.

Seed Implantation
Brachytherapy was performed by using either the preplanning or the “real-time” intraoperative planning method as described previously. All patients underwent a computed tomography (CT)-based postimplant dosimetry evaluation at 1 month. The calculated dosimetry parameters were the percentage volume of the prostate receiving 90% and 100% of the prescribed dose (V90 and V100) and the values of the minimal dose (D90).

Follow-up
All patients were given α1-adrenoreceptor antagonists (α1-blockers) just before treatment for a minimum of 1 month and continued taking them for as long as deemed necessary by the physician. They were seen at 1, 3, 6, 9, and 12 months after implantation and once yearly thereafter. Information on the use of α1-blockers, incidence of acute urinary retention episodes, and any emergency department visits for urologic complications was gathered at each visit. Alpha-blockers were continued and trials for dispensing with the catheter among those in retention were performed at each catheter exchange for up to 6 months. Patients who failed conservative treatment were scheduled for surgery (TUR-P). All patients had surgery at our institution with one exception.

Statistical Analysis
Descriptive statistics, such as the mean, standard deviation (SD), range and proportion, were used to summarize the baseline characteristics of the patients. The clinical, treatment-related and dosimetric factors were assessed for univariate and multivariate correlations with the risk of urinary retention requiring catheterization. The clinical parameters included age, initial PSA values, preimplant IPSS, clinical T stage, Gleason score, and follow-up period. The treatment parameters included preimplant US-based prostate volume, the use of neoadjuvant hormonal manipulation, combination with EBRT, postimplant CT-based prostate volume, implant method, and the number of implanted radioactive seeds. Postimplant dosimetric quality indicators included V90, V100, and D90. A univariate analysis was performed by using an independent samples t test. The variables that showed univariate significance (P <0.10) were then included in a multivariate analysis that used a logistic regression test. Receiver operating characteristic (ROC) analysis and cutoff-point analysis were performed for US-based prostate volume and the IPSS. Potential associations between predictor variables were investigated with the use of the Pearson correlation coefficient. The analyses were carried out by using SPSS 13.0 (SPSS Inc., Chicago, Ill). Differences were regarded as statistically significant at a P-value less than 0.05.

RESULTS
Clinical characteristics of study participants are shown in Table 1. Baseline data, such as stage, Gleason grade, prostate volume, and IPSS, were available for 100% of cases. Treatment and implantation data as well as the postimplant dosimetric factors are shown in Table 2. During the follow-up, only 21 of the 655 patients (3.2%) had urinary retention develop requiring catheterization. Of the 21 patients, 20 were treated with brachytherapy only (19 with intraoperative planning and 1 with preplanning technique) and 1 was treated with brachytherapy (intraoperative planning) combined with EBRT.

On univariate analysis, urinary retention requiring catheterization had significant correlations with the preimplant US-based prostate volume (P = 0.003) and IPSS (P = 0.035) (Table 3). Univariate analysis also showed that urinary retention had nearly significant correlations with V100 (P = 0.077) and age (P = 0.096) (Table 3). On subsequent multivariate logistic regression analysis, the significant factors that remained were the preimplant US-based prostate volume and the preimplant IPSS (Table 3). The risk of catheterization was 6.8-fold higher for patients with larger US prostate volumes (95% CI = 2.3–11.4, P = 0.020) and 3.1-fold higher for patients with higher preimplant IPSS (95% CI = 0.2–5.9, P = 0.032). There was no significant association between US-based prostate volume and IPSS (Pearson’s correlation coefficient = 0.002, P >0.05).

ROC analysis for preimplant US-based prostate volume and IPSS revealed no cutoff points that had achieved both high sensitivity and specificity. The area under the ROC curve was 0.70 (95% CI = 0.59–0.81) (P = 0.002) for the US-based prostate volume (Fig. 1A) and 0.67 (95% CI = 0.55–0.78) (P = 0.012) for IPSS (Fig. 1B). The ROC analysis suggested that a cutoff point of 49.5 mL for the US-based prostate volume and a cutoff point of 9.5 for IPSS could be reasonable choices to balance sensitivity (0.57 and 0.75) and specificity (0.84 and 0.64), respectively, for predicting acute urinary retention after brachytherapy.

Median time to onset of urinary retention requiring catheterization was 1 day after implantation (range, 1–60

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**Table 1. Clinical characteristics of the patients**

<table>
<thead>
<tr>
<th>Total Number of Patients</th>
<th>655</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD (range)</td>
<td>67.3 ± 6.5 (48.6–83)</td>
</tr>
<tr>
<td>Initial PSA (ng/mL)</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD (range)</td>
<td>7.75 ± 3.45 (0.62–37.35)</td>
</tr>
<tr>
<td>Preimplant IPSS</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD (range)</td>
<td>8.7 ± 6.4 (0–32)</td>
</tr>
<tr>
<td>Clinical Stage (%)</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>68</td>
</tr>
<tr>
<td>T2x</td>
<td>5.1</td>
</tr>
<tr>
<td>T2a</td>
<td>20.6</td>
</tr>
<tr>
<td>T2b</td>
<td>5.2</td>
</tr>
<tr>
<td>T2c</td>
<td>1.1</td>
</tr>
<tr>
<td>Gleason score (%)</td>
<td></td>
</tr>
<tr>
<td>2–4</td>
<td>0.9</td>
</tr>
<tr>
<td>5–6</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>8</td>
<td>0.1 (1 patient)</td>
</tr>
<tr>
<td>Follow-up (months)</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD (range)</td>
<td>45.4 ± 27.7 (1–96)</td>
</tr>
</tbody>
</table>

PSA = prostate-specific antigen; IPSS = international prostate symptom scores.
days). Most of the patients were catheterized within 24 hours after brachytherapy (15 within 24 hours, 2 within 48 hours and 4 more than 48 hours). The median duration of catheterization was 6.25 months (range, 2 to 24 months). One patient was catheterized several times because of recurrent urinary retention and underwent a TUR-P for severe obstructive urinary tract symptoms 2 years after brachytherapy.

Of the 21 patients with urinary retention, 8 were weaned from catheterization by nonsurgical means, ie, continuation of $\alpha_1$-blockers (5 patients), continuation of $\alpha_1$-blockers with the addition of 5a-reductase inhibitor (2 patients) and Nissenkorn urethral stenting (1 patient), whereas 13 patients failed medical treatment ($\alpha_1$-blockers) and eventually needed surgery (TUR-P). The median time from brachytherapy to surgery was 7.9 months.
(range, 5.33 to 24 months). Prostate tissue resection in these procedures was "minimal" and performed exclusively to relieve obstruction. The mean ± SD resected prostate volume was 9.9 ± 3.5 mL (range, 4.5 to 15 mL). The operative and postoperative TUR-P course was unremarkable in all patients. Histopathologic analysis of the resected tissue showed no evidence of adenocarcinoma in any of the patients who had surgery; 2 of them had bladder neck stricture and needed transurethral resection of the bladder neck only. One patient had urethral stricture and was successfully treated by a single urethral dilation procedure. During postoperative follow-up (median, 13.4 months; range, 0.6 to 63.8 months), no incontinence was seen among patients who had surgery with the exception of 1 patient who had severe urge incontinence. This patient had surgery again for recurrent bladder neck stricture and subsequently had unstable low volume bladder diagnosed on urodynamic studies.

COMMENT
Prostate brachytherapy reportedly has a lower incidence of urinary incontinence and sexual dysfunction compared with other treatment options. Still, a number of patients may experience acute urinary retention and require indwelling catheterization.

Various studies have looked at the risk of catheterization after prostate brachytherapy and reported rates ranging between 1.5% and 43%. The rate of urinary retention requiring catheterization among our patients was low (3.2%), similar to other reported low rates by Gutman et al. (1.5%), Merrick et al. (2.1%), Flam et al. (3.1%) and Ohashi et al. (5.3%).

The preimplant factors that were reported as being significant for predicting acute urinary retention after brachytherapy varied among published studies. Larger prostate volume was the most uniformly described pre-implant risk factor for developing acute urinary retention postbrachytherapy, followed by baseline IPSS, the use of dexamethasone, age, diabetes, urodynamic status, peak urine flow and the effect of a learning curve. On the other hand, implant-related and postimplant factors that influenced the risk for urinary retention were the amount of radiation, percentage of urethra volume receiving radiation, number of needles, length of needles, postimplant prostate CT-based volume and the ratio between postimplant CT-based prostate volume and preimplant US-based prostate volume.

In our series, preimplant US-based prostate volume was also the most significant independent factor on univariate and multivariate analyses to predict urinary retention, in agreement with the vast majority of the reported studies. Interestingly, although neoadjuvant hormonotherapy was given to 42% of our patients (mostly for downsizing the prostate), it was not a significant predictive factor by itself (Table 3). Our results indicate that prostate volume at the time of treatment is an important factor in predicting subsequent urinary retention, regardless of the initial volume of the prostate before hormonal manipulation.

Despite our practice not to schedule brachytherapy for patients having moderate-to-severe urinary complaints (the mean IPSS ± SD of our cohort was 8.7 ± 6.4), IPSS was still a significant predictive factor for urinary retention on both univariate and multivariate analyses (Table 3). Most of the urinary retention episodes occurred shortly after the procedure (approximately 24 hours postbrachytherapy) when the dose deposited in the tissue was low, thus suggesting predisposing factors, such as the size of the prostate tissue edema and disturbances in urination rather than a dose-related factor. It is important to em-

Figure 1. Receiver operating characteristic (ROC) curves for ultrasonographic (US) prostate volume (A) and international prostate symptom score (IPSS) (B) to predict postbrachytherapy acute urinary retention. The area under the ROC curve was 0.7 for US prostate volume and 0.67 for IPSS. Dashed line = reference.
phasis that none of these predictive factors should represent a contraindication to brachytherapy but rather serve to identify patients at higher risk of urinary retention after brachytherapy and provide useful information in counseling patients before they undergo the procedure.

All of our patients received prophylactic α1-blockers to reduce urinary morbidity after brachytherapy. It is not clear whether the use of prophylactic α1-blockers was directly influential in reducing postbrachytherapy urinary retention in our series because their use was not shown by others to significantly decrease the rate of urinary retention. Other methods that had been successful include the use of corticosteroids and celecoxib, with the incidence of acute urinary retention after brachytherapy having been significantly reduced compared with the control groups in both studies.

Despite all the efforts to prevent acute urinary retention, it remains a clinical problem after brachytherapy and therapeutic management varies from the use of α1-blockers and intermittent self-catheterization to indwelling catheterization until surgical intervention (TUR-P). The major concern of performing TUR-P after brachytherapy is the risk of urinary incontinence. An acceptable rate of urinary incontinence after TUR-P for benign prostate hyperplasia ranges from 1% to 5%. The exact incidence of incontinence after TUR-P after brachytherapy has not yet been determined: it ranges widely, from none to 70%. Thirty-eight percent of our catheterized patients did not need surgery to be weaned from catheterization. Of the 13 patients who underwent TUR-P, none had true sphincteric incontinence, only one had severe urge incontinence: he was operated twice for recurrent bladder neck stricture and finally had severe overactive bladder diagnosed. It should be emphasized that the postoperative follow-up of 50% of patients is relatively short (median 13.4 months) and therefore some are still at risk for having long-term complications develop, including strictures.

If we exclude the patients who were nonsurgically relieved from catheterization before 6 months had elapsed since brachytherapy, the rate of urinary retention that necessitated surgical intervention would be only 2%. We believe that careful selection of patients to exclude those with moderate-to-severe urinary complaints and to include those with smaller (including downsized) prostate volumes who were routinely using perioperative α1-blockers all contributed to the achievement of very low rates of postbrachytherapy urinary retention.

CONCLUSIONS

Acute urinary retention after brachytherapy is an uncommon event. Our data show that the preimplant US-based prostate volume and the baseline IPSS are strong independent factors to predict catheterization after brachytherapy. A minimal (channeling) TUR-P can be performed safely in patients who fail medical therapy. The rate of postminimal TUR-P incontinence in these patients is generally negligible.

References

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