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Prospective trial comparing intraoperative flexible, rigid, and no cystoscopy after ultrasound-guided transperineal permanent seed prostate brachytherapy

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ABSTRACT

Objective: This is a prospective trial comparing the impact of intraoperative flexible, rigid, and no cystoscopy on dysuria immediately after permanent seed prostate brachytherapy (PB). It prospectively documents the time course and characteristics of dysuria, as well as the rates of urinary retention post-PB. Furthermore, this study attempts to establish the utility of routine, post-PB cystoscopy, by documenting the incidence of finding significant pathology on cystoscopy.

Materials and methods: Between January 2003 and January 2007, 225 patients deemed by their physician to be candidates for PB alone were recruited to the study. Patients who had external beam radiation therapy and/or androgen deprivation therapy were excluded. Preimplant International Prostate Symptom Score (IPSS), urinary quality of life score, urine leakage score, Sexual Health Inventory for Men score, and Radiation Therapy Oncology Group Bowel Health Inventory Scores were obtained. Patients were assigned to one of the following three groups: intraoperative rigid cystoscopy, flexible cystoscopy, or no cystoscopy following PB. Patient self-administered questionnaires were given to the patient in the recovery room after PB. These questionnaires evaluated the intensity, type, and duration of urinary symptoms associated with the first four urinations post-PB. All patients were seen on postoperative Day 1 when the surveys were retrieved. Patients were then followed up every 3 months. Acute urinary retention (AUR) was documented in the follow ups. Frequencies of significant pathology (defined as bladder tumor, urethral stricture, or large blood clots) were documented at the time of cystoscopy. AUR rates were also evaluated by the isotope used (I^{125}, Pd^{103}, or Cs^{131}).

Results: A total of 225 patients were enrolled into this study, but only 194 patients could be analyzed for dysuria. Thirty-one patients were excluded from analysis (6, 13, and 12 patients from the rigid, flexible, and no cystoscopy groups, respectively). These patients did not return the questionnaire, or were in retention, and thus did not have dysuria scores to report. Baseline characteristics for the 194 patients in terms of preimplant IPSS, quality of life, prostate volume, and isotope used were well balanced between all three groups. There were no significant differences in dysuria between the three cystoscopy groups at any time point following PB. The mean dysuria score across all time points was 5.5 of 10, with 0 representing “no pain” and 10 representing “the worst possible pain.” Pain was most often characterized as “burning” (78%), whereas dysuria most commonly was “only during urination” (56%). AUR rates (6.8–9.5%) and duration of catheter dependence (10.5–19 days) were not found to be significantly different between the assigned groups. When results were stratified by isotope, patients treated with I^{125}, Pd^{103}, and Cs^{131} seeds experienced a 6%, 14%, and 0% retention rate, respectively. The I^{125} and Pd^{103} patients had similar pretreatment IPSS and prostate volumes. Seven percent of patients undergoing cystoscopy had significant findings. The most common finding was “clots thought too large to void” (3%). Seeds in the bladder/urethra occurred in 1% of cases. Only 0.7% of patients were found to harbor unsuspected bladder tumors.

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Conclusion: There was no significant difference in dysuria in the first four urinations post-PB between patients in the rigid, flexible, and no cystoscopy groups. Larger blood clots that may have been difficult to void, seeds in the bladder and/or urethra, and other abnormalities were found in 7% of patients who had cystoscopy. This may suggest that cystoscopy may be worthwhile post-PB. The incidence of AUR was not significantly different between the three cohorts.

1. Introduction

Permanent prostate radioactive seed implantation has become a well-accepted primary treatment for clinically localized prostate cancer. Multiple reports demonstrate that well-performed brachytherapy at leading institutions could result in 5-, 10-, and 15-year biochemical relapse-free survival (BRFS) rates equal to those reported by top centers using radical prostatectomy or intensity modulated radiation therapy.[1–19] Although the risk of incontinence and impotence following brachytherapy is relatively low compared with radical prostatectomy, one of the major goals of brachytherapy currently is to further reduce any and all toxicities of treatment, including short-term side effects such as dysuria and acute urinary retention (AUR).[20–24]

Following permanent seed prostate brachytherapy (PB), patients often experience moderate to severe dysuria on initial urinations.[25] It has been a common, although not a universal, practice to use rigid cystoscopy at the end of an implant procedure to evaluate the overall condition of the urethra and bladder, and to evacuate any large blood clots and/or seeds.[26] One possible factor contributing to the dysuria and other postoperative urinary symptoms is the introduction of the rigid cystoscope. This may cause minor trauma to the urethra and prostate. In this regard, flexible cystoscopy can be utilized as it has the potential advantage of causing less trauma, and therefore, fewer or less intense postoperative urinary symptoms. Flexible cystoscopy with local anesthesia has previously been demonstrated to have significantly less postprocedure voiding discomfort than rigid cystoscopy under a general anesthetic.[27]

Cystoscopy is a well-accepted and widely used diagnostic and therapeutic tool in the field of urology, but currently little information is available about its potential risks and benefits for patients receiving PB.

The primary objectives of this study were to examine whether or not there are any significant differences between rigid, flexible cystoscopy, and no cystoscopy on postoperative dysuria and AUR. The secondary objectives were to document the need for cystoscopy in patients undergoing PB by documenting the incidence of significant pathology.

2. Materials and methods

The Swedish Medical Center Investigational Review Board and Western Investigational Review Board approved this prospective trial. A total of 225 patients undergoing PB as monotherapy were treated with I^{125}, Pd^{103}, or Cs^{131}. Isotope selection was determined by the treating physician. To reduce confounding factors, we did not include patients receiving supplemental external beam radiation therapy or androgen ablation therapy. In addition, patients with a history of prior transurethral resection of the prostate were excluded. At initial consultation, all patients filled out an International Prostate Symptom Score (IPSS) form. All patients were instructed to begin alpha blockers at least 4 days prior to the implant procedure. Preoperative and postoperative alpha blockers were used in 197 patients, preoperative alpha blocker use was not known in 20 patients, and postoperative alpha blockers were not needed in three patients. PB was performed using the standard Seattle transperineal, transrectal ultrasound, and template-guided preplan techniques, as described previously.[26,28] After informed consent was obtained, study participants were organized into the following cohorts: rigid cystoscopy, flexible cystoscopy, and no cystoscopy. If the urologist was unable to carry out a satisfactory flexible cystoscopy, a rigid cystoscopy using a 22-Fr cystoscope was performed. Patients were converted from no cystoscopy or flexible cystoscopy to rigid cystoscopy if pathological findings such as large blood clots, bladder tumors, or seeds embedded into the urethral mucosa were identified. Patients were ultimately grouped based on what technique they actually received and not based on what they were assigned to receive initially.

Prior to discharge from the ambulatory surgical center (ASC), patients had their Foley catheter removed and were given a survey form on which they noted the intensity and quality of the dysuria they experienced on the first four urinations after discharge. On postoperative Day 1, patients underwent a noncontrast prostate computer tomography scan for postoperative dosimetry purposes. Patients were then seen by their treating physician, turned in their dysuria scoring form, and filled out an IPSS form for comparison with their pretreatment IPSS form. Routine follow up continued every 3 months, alternating with the urologist and radiation oncologist for the 1st year and then every 6 months thereafter. At each visit, an IPSS form was filled out and the patient was interviewed to determine whether or not AUR had occurred in the interim. For out-of-town patients, follow up was arranged via telephone interviews and IPSS forms were faxed. The completed forms were then reviewed by their physicians. Follow-up documentation was obtained on all patients.

3. Results

Two hundred and twenty patients were included in the study; 74 patients were assigned to the rigid cystoscopy group, 88 to the flexible cystoscopy group, and 58 to the no cystoscopy group. Isotopes used were I^{125} (161 patients), Pd^{103} (56 patients), and Cs^{131} (3 patients). Several patients assigned to the no cystoscopy group or the rigid cystoscopy group demanded flexible cystoscopy on the day of the procedure. Three patients supposed to undergo rigid cystoscopy were converted to flexible cystoscopy because of their preference and/or a lack of available sterile rigid scope. Seven patients initially assigned to the no cystoscopy group were later converted to receive flexible cystoscopy due to their preference and/or difficulty in catheterization. No significant difference in dysuria intensity was noted between the three treatment arms on the first four urinations after discharge from the ASC (Table 1). The majority of patients experienced moderate to severe dysuria (Table 2). Typically, dysuria only occurred during urination; it rarely lasted more than 5 minutes after urination (Table 3). A vast majority of urinations were described as “burning” or “sharp” in quality (Table 1). Dysuria only lasted 1 day in 173/194 (89%) of the patients.

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Table 1
Different types of dysuria pain described by the patients in each randomized group during the first four urinations.

Description of pain	Rigid cystoscopy group (%)	Flexible cystoscopy group (%)	No cystoscopy group (%)
Sharp	23	22	28
Burning	78	80	70
Throbbing	3	2	2
Dull	4	5	12

Table 2
Pathology found at time of cystoscopy.

Major pathology	No.
Clot too large to void	5
Bladder cancer	1
Seeds in bladder/urethra	2
Urethral/meatal stricture	3
Total	11

It lasted from 2 days to 2 years and 7 months in the other 21 patients (11%).

When comparing dysuria scores between the three arms, there was no statistically significant difference among the three arms of the study ($p > 0.05$).

Patients who received rigid, flexible, or no cystoscopy all had the same rate of AUR (approximately 9%). Patients who received I^{125} monotherapy had less incidence of AUR (6%) than those who received Pd^{103} monotherapy (14%).

There was one bladder malignancy noted on cystoscopy, and two cases where patients were converted to rigid cystoscopy from planned flexible or no cystoscopy due to blood clots thought to be potentially too large to evacuate otherwise. On planned rigid cystoscopy, there were two patients with seeds embedded in the urethral mucosa, one patient with an early bladder cancer, five patients with large blood clots, and three patients with benign lesions biopsied at cystoscopy (Table 2).

4. Discussion

PB, radical prostatectomy, and external beam radiation therapy are the three most common definitive treatments for localized prostate cancer. Much debate exists as to which of these therapies is “superior” in terms of both BRFS and acute and long-term morbidity. The practitioners of these therapies continue to report BRFS outcomes and increasingly report quality of life outcomes. Quality of life outcomes are most reliable when validated patient self-administered questionnaires are utilized.[21,28,29] In an attempt to evaluate, characterize, and decrease the intensity of immediate post-PB dysuria, we analyzed patients’ responses between rigid, flexible, and no cystoscopy and had the study participants fill out questionnaires related to urinary functioning before and after postprostatectomy incontinence.

We expected that those who underwent a rigid cystoscopy at the time of PB would have more severe dysuria than those undergoing flexible cystoscopy or no cystoscopy. However, the patients reported no significant difference in severity, character, or duration of dysuria between the three arms of the trial.

One criticism of this prospective phase III study is the unequal number of patients in the three arms. Unequal distribution occurred due to several patients demanding (just prior to anesthesia) rigid cystoscopy rather than what they had been randomized to initially. We have reported on their outcomes based on how they were actually treated rather than on their intended treatment. In fact, the outcomes were no different whether reported by intention to treat or the actual treatment arm. Another weakness of this study is that some patients did not completely fill out their postoperative dysuria questionnaires. However, the questions that were answered were consistent between the three treatment arms. It seems unlikely that the study result would have differed significantly from that which is reported here even if 100% of the questionnaires had been filled out. All patients received a Foley catheter before the start of the implant procedure. This may in fact lead to some confounding of the levels of dysuria experienced by the participants. In addition, the three treatment arms of the study experienced approximately the same level of dysuria. Although the study was set up to detect the effect of various cystoscopy modalities on dysuria, it appears that most dysuria is due to the seed implantation brachytherapy itself.

This report prospectively documents a high incidence of moderate to severe dysuria in the first 24 hours following PB. The intensity, duration, and quality of the dysuria were not influenced by whether the patient received rigid or flexible or no cystoscopy during the PB procedure. Only 11% experienced dysuria for more than 24 hours and only 3% experienced it for more than 3 months. The dysuria typically occurred during the act of urination, but in 10% it lasted more than 5 minutes after the completion of urination. In most cases, dysuria responded to nonsteroidal anti-inflammatory medications.

AUR occurred in 9% of the patients in this study. The incidence of AUR was not influenced by which arm of the study the patient was in. Patients treated with Pd^{103} PB experienced a 14% incidence of AUR, whereas those treated with I^{125} PB experienced only a 6% incidence. The higher rate of AUR experienced by the Pd^{103} patients is likely due to the shorter half-life of Pd^{103} (17 days), compared with I^{125} (60 days), for radioactive seeds. As a result, we administered a higher effective dose to the prostate, which subsequently caused more interstitial edema after seed implantation. The typical predictors of AUR were well balanced between the isotopes (Table 3).

Table 3
Acute urinary retention rates stratified by isotope.

	I^{125} (161)	Pd^{103} (56)	Cs^{131} (3)
AUR (No. of patients needing catheter), *n* (%)	11 (6.8)	7 (12.5)	0
AUR median duration (postoperation), d	30	11	n/a
Median dysuria score (based on the first 4 urinations)	5	6	6
AUR mean pretreatment TRUS (cm^3)	36.7	29.8	n/a
AUR mean pretreatment IPSS	4.5	5.4	n/a
AUR mean pretreatment QOL	3.3	3.6	n/a

AUR = acute urinary retention; IPSS = International Prostate Symptom Score; QOL = quality of life; TRUS = transrectal ultrasound.

5. Conclusion

Cystoscopy at the time of PB does not influence the incidence, duration, or severity of immediate posttreatment dysuria or AUR. Dysuria is typically moderate to severe, occurs during the act of urination and rarely persists more than 1 day post-PB.

Conflicts of interest

All contributing authors declare no conflicts of interest.

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