

Prostate Capsule Sparing versus Nerve Sparing Radical Cystectomy for Bladder Cancer: Results of a Randomized, Controlled Trial

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Abbreviations and Acronyms

BCI = Bladder Cancer Index
PSA = prostate specific antigen
SHIM = Sexual Health Inventory for Men

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Purpose: Prostate capsule sparing and nerve sparing cystectomies are alternative procedures for bladder cancer that may decrease morbidity while achieving cancer control. However, to our knowledge the comparative effectiveness of these approaches has not been established. We evaluated functional and oncologic outcomes in patients undergoing these procedures.

Materials and Methods: We performed a single institution trial in patients with bladder cancer in whom transurethral prostatic urethral biopsy and transrectal prostate biopsy were negative. Men were randomized to prostate capsule sparing or nerve sparing cystectomy with neobladder creation and stratified by Sexual Health Inventory for Men score (greater than 21 vs 21 or less). Our primary end point was 12-month overall urinary function as measured by Bladder Cancer Index. Secondary end points included sexual function, cancer control and complications.

Results: A total of 40 patients were enrolled in the study with 20 patients in each arm. Urinary function at 12 months decreased by 13 and 28 points in the prostate capsule and nerve sparing groups, respectively ($p = 0.10$). Sexual function followed a similar pattern ($p = 0.06$). There was no difference in recurrence-free, metastasis-free or overall survival (each $p > 0.05$). The rate of incidentally detected prostate cancer was similar ($p = 0.15$).

Conclusions: Our study provides a randomized comparison of prostate capsule sparing and nerve sparing cystectomy techniques. We found no difference in functional or oncologic outcomes between the 2 approaches, although our study was underpowered due to a lack of patient accrual.

Key Words: urinary bladder neoplasms, prostate, cystectomy, urinary diversion, mortality

RADICAL cystectomy is the standard treatment in patients with localized muscle invasive cancer or non-muscle invasive urothelial cancer refractory to intravesical therapy¹ and yet it is associated with

significant morbidity.² To decrease morbidity prostate capsule sparing and nerve sparing cystectomies have been described in case series as potential ways to decrease side effects and improve quality of life outcomes

without jeopardizing oncologic control. The 2 approaches attempt to preserve the neurovascular bundles lateral to the prostate. In addition, the prostate capsule sparing technique avoids extensive dissection of the pelvic floor musculature and the external urethral sphincter. These approaches may result in improved erectile and urinary function.³⁻⁹

However, compared to the more traditional radical cystectomy technique the benefits of these 2 approaches are largely demonstrated in retrospective studies. Limited evidence from randomized trials is available on the relative effectiveness of the prostate capsule sparing and nerve sparing approaches in terms of functional outcomes. Further, and perhaps more importantly, the relative cancer control of these 2 approaches is unknown. Despite the appeal of prostate capsule sparing radical cystectomy there is concern that leaving behind part of the prostate may lead to a higher rate of positive surgical margins and residual or future prostate cancer.¹⁰ Even if voiding and sexual function are improved in these patients, the prostate capsule sparing approach would ultimately be detrimental.

For these reasons we performed a phase II, randomized clinical trial to evaluate functional and oncologic outcomes in patients treated with prostate capsule sparing or nerve sparing radical cystectomy with neobladder creation. We sought to understand potential differences in voiding function, sexual function and cancer control between these 2 patient populations to determine the potential of the approaches as alternative extirpative techniques for bladder cancer.

METHODS

Study Design

We performed a single institution clinical trial in which patients with urothelial cancer were randomized to prostate capsule sparing or nerve sparing cystectomy (ClinicalTrials.gov NCT01824329). The study protocol was approved by our institutional review board and patients provided written informed consent. Five surgeons participated in this study. Enrollment began in August 2007 and was completed in October 2011. Followup was completed in January 2013.

Patient Population

Patients eligible for study included men 18 years old or older with clinical stage T2 or less urothelial cancer diagnosed within 3 months of enrollment.¹¹ Cases down staged after neoadjuvant chemotherapy, eg from stage cT3 to cT2 or less, were eligible. Concern for nodal or metastatic disease on preoperative imaging was a finding that excluded patients from participation. The Appendix (<http://jurology.com/>) shows the specific imaging, laboratory and followup requirements.

All men underwent transurethral biopsy of the prostatic urethra and 12-core transrectal ultrasound guided prostate biopsy.¹² Transurethral biopsy was performed with a resectoscope and tissue was sampled from the 5 and 7 o'clock positions. Transrectal prostate biopsy targeted all areas of the prostate as much as was feasible via the transrectal approach, including the anterior apex. Additional study exclusion criteria were creatinine greater than 2.2 mg/dl, prior pelvic radiation to the bladder or prostate, or a history of a radical prostatectomy. Of men who consented to randomization 5 were excluded from analysis due to prostate cancer on biopsy, 2 withdrew consent and 1 was excluded due to surgeon judgment.

Intervention

Patients were randomly assigned to prostate capsule sparing or nerve sparing radical cystectomy with neobladder urinary diversion. Randomization was done the morning of surgery and patients were informed of the assignment as part of informed consent. These procedures share many common steps and the main difference is how the prostate is managed.¹³ With the prostate capsule sparing approach supra-ampullar dissection was performed to develop a plane anterior to the seminal vesicles. The endopelvic fascia was preserved on each side of the prostate. The prostate capsule was incised with a transverse incision on the distal anterior surface of the prostate and the adenoma was dissected from the capsule. For the nerve sparing approach the entire prostate and seminal vesicles were removed along with the bladder. The neurovascular bundles were spared by performing intrafascial dissection in retrograde fashion.

These different cystectomy techniques necessitated different approaches to the urethral anastomosis. With the prostate capsule sparing approach the neobladder was anastomosed to the prostate capsule while with the nerve sparing approach the neobladder was anastomosed to the urethral stump.¹³ Extended pelvic lymph node dissection was performed with each approach, including dissection around the common iliac arteries.

Measures

Men were stratified based on SHIM, a 5-question validated questionnaire used to evaluate sexual function. SHIM provides a score of 5 to 25 with 98% sensitivity and 88% specificity.¹⁴ Because a score of 21 or less indicates erectile dysfunction, stratification was based on a SHIM score of greater than 21 vs 21 or less.

Baseline assessments included patient demographics and tumor characteristics. Urinary and sexual function was measured by BCI, a validated bladder cancer specific, health related quality of life instrument that measures urinary, sexual and bowel function, and bother domains.¹⁵ The index consists of 34 items in a total of 3 primary domains (urinary, bowel and sexual) and 2 subdomains (function and bother). Item responses are based on Likert scales with scores standardized to a scale of 0 to 100 points on which higher scores correspond to better health states. Each domain has been independently validated.

The perioperative characteristics examined included estimated blood loss and operative time. Measured clinical outcomes included hospital length of stay, and 30-day

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