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Candidacy for active surveillance may be associated with improved functional outcomes after prostatectomy

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Abstract

Objective: In an effort to curb overtreatment, active surveillance (AS) has grown in popularity as an option for men with low-risk prostate cancer. We evaluated the histopathologic and functional outcomes of patients who qualified for AS, but opted for robotic-assisted laparoscopic prostatectomy (RALP), and compared them to non-AS candidates.

Methods: An institutional database of 1,477 RALP performed by a single surgeon was queried for AS candidates, defined as PSA <10 ng/mL, biopsy Gleason score ≤6 with a minimum of 10 biopsy cores, <3 positive cores with <50% tumor volume in a single core and clinical stage ≤T2a.

Results: Of the 352 patients who would have qualified for AS, 159 (45%) were upgraded: 143 (41%) to Gl 3 + 4, 16 (4.5%) to 4 + 3, zero to Gleason 8 or higher. Seventeen (4.8%) patients were upstaged to pT3. AS candidates were younger and had more favorable tumor characteristics, but similar preoperative functional status. Bilateral nerve sparing was performed on 96% of AS candidates vs. 86% of non-AS candidates ($P < 0.001$). After 12 months of follow-up in patients who received bilateral nerve sparing, continence was higher in the AS cohort (98% vs. 92%, $P < 0.001$) but potency was equivalent (87% in each, $P = 0.89$). On multivariable analysis, candidacy for AS was independently associated with improved continence, but not potency.

Conclusions: In addition to having the expected favorable histopathologic features, AS candidates who desire definitive therapy have a high likelihood of achieving excellent functional outcomes, perhaps superior to non-AS candidates, following RALP.

Keywords: Neoplasm; Prostate; Prostatectomy; Robotics; Outcomes; Active surveillance

1. Introduction

With conflicting data regarding the significance of prostate cancers detected by PSA screening, concern for overtreatment has grown [1,2]. Recent studies have questioned the use of radical therapy for all patients with prostate cancer, especially those with very low risk disease, in favor of active surveillance (AS) [3]. Contemporaneously, improvements in surgical techniques and perioperative management have decreased the morbidity of radical prostatectomy [4]. Despite these improvements, a significant percentage of patients continue to experience incontinence and erectile dysfunction after prostatectomy.

The benefit of AS is the avoidance of perioperative morbidity at the risk of missing the opportunity to treat a significant cancer at a curable stage. To accurately counsel men who qualify for AS on their treatment options, it is important for urologists to have knowledge of the expected oncologic and functional outcomes of these patients following prostatectomy. While it may be assumed that their favorable oncologic risk factors and low volume of disease would lead to favorable pathologic and oncologic outcomes, we hypothesized that these same favorable oncologic risk factors might also lead to favorable functional outcomes [5,6]. We thus the report the histopathologic and functional outcomes of a large series of patients who qualified for AS, but opted for robotic-assisted laparoscopic prostatectomy (RALP), and com-

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pare them to the outcomes of those patients who did not qualify for AS.

2. Materials and methods

We retrospectively reviewed our prospectively maintained, institutional-review board approved oncologic database for all patients undergoing RALP by a single surgeon between January 2005 and March 2010 (n = 1,477). Patients were classified as AS candidates according to the following criteria as described by Klotz et al. [7]: PSA <10 ng/mL, clinical stage ≤T2a, biopsy Gleason score ≤6, <3 positive cores, and <50% tumor volume in a single core. Additionally, to ensure adequate sampling, we limited our series to patients who had a minimum of 10 biopsy cores taken. A total of 352 patients met these criteria and formed our primary study population.

As a tertiary referral center, approximately 95% of the prostate biopsies were performed by referring urologists, 73% of which were re-reviewed by a dedicated genitourinary pathologist. The database does not include if referral prostate biopsies were initial or repeat biopsies, as only actionable biopsies were sent for review. Biopsy reports were considered sufficient for inclusion if they reported Gleason score, total number of positive cores, percentage of positive cores, and greatest percentage of tumor volume in a single core. Biopsy data on 41 patients were incomplete, leaving complete data available for 1,436 patients (97% of the overall series). Our technique for robotic prostatectomy has been previously described [8], and all patients underwent a limited bilateral pelvic lymphadenectomy.

All pathologic prostatectomy specimens were examined by our dedicated genitourinary pathologists. The prostate specimen was sectioned in four quadrants and mounted in standard fashion. PSA density was calculated by dividing the preoperative PSA by the pathologic prostatic specimen weight. Tumor at the inked resection margin was considered a positive surgical margin (PSM), which was dichotomized into "focal" or "extensive" if the length of the PSM was less than or greater than 2 mm, respectively.

Functional outcomes and PSA were collected at baseline, 6 wk, and then every 3 mo for the first year after surgery using International Prostate Symptom Scores (IPSS) and Sexual Health Inventory for Men (SHIM) scores. Continence was defined as the use of either no pads or one security pad daily [9]. Overall functional outcomes are reported for patients who had at least 12 mo of follow-up. Potency was defined as a SHIM ≥16, with or without the use of phosphodiesterase-5 inhibitors, in patients who were preoperatively potent (SHIM ≥ 16) [10]. A single postoperative PSA >0.2 ng/ml beyond 6 weeks following surgery was considered a biochemical recurrence. Histopathologic and biochemical data of men with and without 12 mo of follow-up were compared to assess if a time-related phenomenon may be responsible for our oncologic findings.

2.1. Statistical analysis

Preoperative and pathologic characteristics were reported using means for continuous variables and proportions for categorical variables. Differences between study groups were calculated using t-tests for continuous variables and χ^2 tests for categorical variables, as appropriate. We created multivariable logistical regression models using pre- and perioperative characteristics to assess for independent predictors of improved functional outcomes, as well as predictors of tumor upgrading at the time of pathologic examination. Significance was defined as a two-sided P value <0.05. Analyses were conducted using SPSS ver. 17.1 (SPSS Inc., Chicago, IL).

3. Results

Preoperative tumor characteristics of the 352 patients meeting criteria for AS were significantly favorable compared with the 1,084 patients ineligible for AS (Table 1). Specifically, AS candidates were younger, had lower PSAs and rates of palpable nodules, and less cancer in their biopsies (all $P < 0.05$). Functionally, they had similar preoperative continence and potency rates. We did not have records of any patients in the AS cohort receiving a restaging biopsy following a positive initial biopsy.

Histopathologic characteristics of the prostate specimen in patients qualifying for AS were also more favorable (Table 2). AS candidates had lower rates of locally ad-

Table 1
Preoperative characteristics

	All patients	Candidates for active surveillance*		
		No	Yes	P value
Number of patients	1436	1084	352	
Age, mean	59.4	59.7	58.5	0.007
PSA, mean	6.15	6.65	4.74	<0.001
Preoperative continence, %	83%	85%	80%	0.06
Preoperative potency, %	77%	76%	79%	0.28
Clinical T1c, %	85%	81%	95%	<0.001
Clinical T2, %	15%	19%	4.6%	
Greatest percent cancer in a single core, mean %	30.8%	37.9%	11.6%	<0.001
Percent of positive cores,** mean %	25.8%	31.4%	10.5%	<0.001
Perineural invasion on Bx, %	18%	23%	3.4%	<0.001

* Active surveillance candidates: PSA <10, GL ≤6, clinical stage ≤T2a, <3 positive cores, <50% cancer in any core.

** Percent positive cores = number of positive cores/total number of cores sampled.