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Prostate Volume and the Incidence of Extraprostatic Extension: Is There a Relation?

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Abstract

Background and Purpose: Extraprostatic extension (EPE) of tumor is an important prognostic indicator that has an impact on long-term survival after radical prostatectomy. We investigated whether the prostate size has any association with the tumor volume and the incidence of EPE.

Patients and Methods: Seven hundred consecutive robot-assisted radical prostatectomy procedures performed by a single surgeon at a single center were studied. Preoperative parameters (demographic details, prostate-specific antigen (PSA) level, biopsy characteristics, and tumor volume) and the postoperative histopathologic details of the specimen (prostate volume, Gleason sum, EPE, and surgical margin status) were compared among the small prostate (< 40 cc), intermediate size (40–70 cc), and large prostate (>70 cc) groups. Chi-square analysis was performed for comparison of groups with nominal variables while continuous variables were compared using analysis of variance. A double-sided P value of less than 0.05 was considered statistically significant.

Results: A greater proportion of patients in the large prostate group had T_{1c} tumor compared with those in the small prostate group (90.2% *v* 78.3%). Younger men and smaller prostates had lower preoperative PSA levels ($P < 0.001$). A significantly higher PSA density (0.16 *v* 0.07) and cancer density (0.0102 *v* 0.0025), however, was observed in patients with small prostates compared with those with large prostates. A total of 102 (14.6%) patients had EPE on the final pathologic analysis while 8.6% of the patients had positive surgical margins. Greater incidence of EPE was observed in the group with smaller prostates compared to those in the large prostate group (16.7% *v* 7.3%).

Conclusion: Small prostates have a higher cancer density and a greater incidence of EPE of tumor.

Introduction

Biopsy Gleason score and extraprostatic extension (EPE) are well-established prognosticators for biochemical recurrence and long-term survival after radical prostatectomy in patients with localized prostate cancer.[1,2] Incidence and oncologic impact of various biopsy Gleason sum and EPE varies significantly with increasing serum prostate specific antigen (PSA) level, tumor volume, and sometimes volume of the gland harboring the tumor. While the relationship between Gleason sum, EPE, PSA level, and tumor volume are well studied,[3–6] there is paucity of data regarding relationship between prostate volume and known oncologic variables, such as Gleason sum, percentage cancer, clinical stage, and EPE.

This is the exact question we have studied in our current analysis of 700 systemic biopsy data with matching oncologic and volumetric information. We noted an interesting and clinically significant relationship between a small prostate and Gleason sum and the incidence of EPE. We present the details of our study.

Patients and Methods

Patient population

Between January 2005 and June 2007, 700 patients with clinically localized adenocarcinoma of the prostate who opted for surgery underwent robot-assisted laparoscopic prostatectomy by a single surgeon (AT). Surgery was performed using a robotic daVinci Surgical System (Intuitive Surgical, Sunnyvale, CA) by the athermal robotic technique of prostatectomy via a transperitoneal approach.[7,8]

Patients underwent a standardized preoperative workup, including determination of serum PSA level, digital rectal

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Table 1. Demographic Details and Characteristics of Patients

Patients (*n*)	700
Age (yr), mean ± SD (range)	62.5 ± 7.1 (36.1–80.2)
Body mass index (kg/m^2), mean ± SD	27.51 ± 7.1
Serum PSA level (ng/mL) (range)	5.9 ± 4.3 (1.0–66.4)
Prostate weight (g), mean ± SD (range)	50.61 ± 19.2 (15.8–346)
Clinical stage (% no. of patients)	
T_1	80%
T_2	19.1%
T_3	0.9%
Biopsy Gleason score (% no. of patients)	
≤6	61.9%
7 (3 + 4)	20%
7 (4 + 3)	5.9%
8–10	5.1%
Preoperative risk group	
Group 1	28.9%
Group 2	29.9%
Group 3	18.2%
Group 4	23.1%
Pathologic stage (% no. of patients)	
T_0	0.4%
T_2	85.2%
T_3	13.4%
T_4	1%
Pathologic Gleason score (% no. of patients)	
≤6	40.1%
7 (3 + 4)	44.9%
7 (4 + 3)	9.1%
8–10	5.8%

SD = standard deviation.

examination, and systematic prostate biopsy. In selected cases (those with a PSA level >10 ng/mL and/or Gleason sum of ≥7, or clinical T_3 prostate cancer), bone scans and CT scans of the abdomen and pelvis were obtained.

Preoperative information about patient age, previous abdominal surgery, comorbidity, body mass index, serum PSA level, and clinical stage and prostate weight was noted. Prostate biopsy was performed under transrectal ultrasonographic guidance by the referring urologist. All patients had a minimum of 6 and most had 12 to 14 core extended biopsy of the prostate. A few patients had saturation biopsy involving up to a 40-core sampling.

All biopsy slides were reviewed by the uropathologist at our institute. Data were abstracted from the biopsy reports and entered into the customized database. In a situation of change in the Gleason grade or other information, we used data from our uropathologist for the purpose of analysis. Prostate biopsy data that we collected included the number and location of positive cores, Gleason score, percent of cancer involvement in positive biopsy cores, and percent of positive biopsy cores (biopsy density). "Cancer density" was calculated as a ratio of percentage of number of positive cores and the prostate weight. Pathologic data, including prostate weight, Gleason grades, EPE of tumor (if any), and margin status, were recorded.

Pathologic analysis

All specimens were weighed and analyzed by the uropathology service at our institute. The surgical specimen was inked and processed for histopathologic analysis. Margins were considered positive if there was a tumor present at the ink. Patients with extension of tumor through the prostatic capsule were considered to have EPE.

Statistical analysis

For the purpose of analysis, the patients were divided into groups depending on their prostate volume (<40 cc, 40–70 cc, and >70 cc). For further discussion, group 1 will be referred to as having a small prostate (<40 cc), group 2 as having a prostate of intermediate size (40–70 cc), and group 3 as having a large prostate (>70 cc).

Statistical analysis was performed using SPSS 15.0 (SPSS Inc, Chicago, IL). Chi-square analysis was performed for comparison of groups with nominal variables, while continuous variables were compared using analysis of variance. Comparative analysis was made between the large prostate volume (≥70 g) group 3 and small prostate volume (<40 g) group 1. A double-sided *P* value of less than 0.05 was considered statistically significant.

Results

Patient demographic data for 700 patients are detailed in Table 1. The overall mean age at the time of operation was 62.5 years (range 36.1–80.2 years, standard deviation 7.1). The mean preoperative serum PSA level was 5.9 ± 4.3 ng/mL. The majority of the patients (80%) had nonpalpable disease on clinical evaluation. A relatively greater proportion of patients in the large prostate group had T_{1c} tumor compared with those in the small prostate group (90.2% *v* 78.3%).

Table 2. Comparative Preoperative Data of Patient Groups

	Group 1 (PW <40 g)	*Group 2 (PW 40–70 g)*	*Group 3 (PW ≥70 g)*	P *value*
Patients (*n*)	217	375	108	
Age in years (SD)	60.2 (7.2)	62.7 (6.7)	66.4 (6.1)	0.001
BMI kg/m^2 (SD)	26.6 (5)	27.7 (5)	28.5 (4.8)	0.002
PSA ng/mL	5.2 (2.7)	6.1 (5.2)	6.9 (3.4)	0.001
PSA density	0.16 (0.09)	0.12 (0.10)	0.07 (0.03)	0.001

PW = prostate weight; SD = standard deviation; BMI = body mass index; PSA = prostate-specific antigen.

Table 3. Preoperative Prostate Biopsy Parameters Among Groups

	Group 1 (PW <40 g)	*Group 2 (PW 40–70 g)*	*Group 3 (PW ≥70 g)*	P *value*
Total no. of cores taken	10.6 (4.6)	11.2 (4.6)	12.3 (7.7)	0.05
Biopsy density	0.3395 (0.25811)	0.2785 (0.20970)	0.2286 (0.24213)	0.001
Cancer density	0.010277 (0.0078268)	0.00561 (0.0043043)	0.002588 (0.0028616)	0.001
Maximum % in a core	28.7% (24.1)	28.7% (26.6)	16.45% (19.5)	0.001
Gleason score				
≤6	62.3%	65.9%	77.8%	0.007
7 (3 + 4)	25.1%	20.6%	17.2%	NS
7 (4 + 3)	8%	6.6%	2%	0.04
8–10	4.5%	6.9%	3%	NS

PW = prostate weight; NS = not significant.

Patient age, preoperative PSA level, and the prostate weight were observed to be correlated. The average age in the large prostate group was significantly higher than that in the small prostate group (66.4 *v* 60.2 years, $P < 0.001$). Similarly, younger men and those with smaller prostates had lower preoperative PSA levels ($P < 0.001$) (Table 2).

The PSA density, however, which denotes the PSA per unit volume of prostate, is significantly higher in small prostates compared with large prostates (Table 2). A greater proportion of patients had Gleason sum 6 or less on both the biopsy as well as on final histopathology findings in the larger prostate group ($P < 0.01$). Indicators of the tumor volume status in the prostate—ie, maximum percentage cancer and the cancer density—were higher in those with small prostates ($P < 0.001$) (Table 3).

Of the total patient population, 14.6% (102 subjects) had EPE of tumor on the final pathologic analysis, while 8.6% of patients had positive surgical margins. While the incidence of EPE was less in those in the large prostate group compared with those in the small prostate group (7.3% *v* 16.7%), no significant difference in the rate of positive surgical margins was noted between the groups (Table 4).

Discussion

We found a significantly higher overall incidence of EPE in patients with smaller prostates compared with those with larger prostates. Another interesting observation was that in smaller prostates, the chance of EPE is significantly more, even in the presence of a low Gleason grade tumor. Approximately 12% (n = 22) of the smaller prostates had EPE *v* only 6.5% ($n = 6$) of larger prostates, even in the presence of low Gleason grade disease ($P < 0.05$).

These observations pose two interesting questions regarding tumor behavior in small prostates: 1) Whether small prostates have the tumor with an intrinsically different biologic behavior in terms of aggression or 2) a relatively larger tumor bulk, lesser resistance to the tumor spread, thereby allowing direct extension outside the prostate. The first possibility seems to be less plausible, because the incidence of high-grade tumor is not significantly different between the groups. In the presence of high Gleason sum disease, although the tendency for EPE is relatively higher in both the groups, the percentage possibility of EPE in smaller prostates is twice that observed in large prostates.

Several previous studies have attributed favorable outcomes after surgery of larger prostates to the "lead time bias" and the greater incidence of low grade and low volume cancer in larger prostates.[9,10] The observation of a significantly higher cancer density in smaller prostates ($P < 0.001$) in our patients endorses the fact that the tumor volume is indeed higher in small prostates compared with that in the large prostate group. In addition, a high level of PSA density observed in small prostates further indicates higher volume of tumor in small prostates responsible for a greater amount of PSA per unit volume of tissue.

As observed in our patients, Freedland and associates,[11] in a study that involved 1602 open radical prostatectomies, also reported a significant inverse association of smaller prostate weight with EPE and the more advanced stage.

Although the rate of positive surgical margins was also more in patients with small prostates (12.6% *v* 9.3%), there was no significant difference between the groups. Similar observation of higher positive surgical margins in patients with small prostates has been reported by several other investigators.[9,11–13] The higher incidence of positive surgical margins noted in patients with small prostates is primarily related to two issues: Technical and tumor characteristics (tumor volume, grade, and EPE) related. Contrary to the belief that small prostates are easier to remove, the dissection in small prostates is technically more demanding, because of a wider contact area with the vascular pedicle and

Table 4. Pathologic Results Stratified According to Prostate Volume

	Group 1 (PW <40 g)	*Group 2 (PW 40–70 g)*	*Group 3 (PW ≥70 g)*	P *value*
Gleason score				
≤6	33.3%	39.8%	55.1%	0.001
7 (3 + 4)	51.9%	44.7%	31.8%	0.001
7 (4 + 3)	11.1%	8.7%	6.5%	NS
8–10	3.7%	6.8%	6.5%	NS
Extraprostatic extension	16.7%	15.2%	7.3%	0.05
Positive surgical margins	12.6%	6.8%	9.3%	NS

PW = prostate weight; NS = not significant.

less well-defined prostate-vesicle and prostate-urethral junction. As revealed in our study, a higher tumor volume and associated EPE in small prostates may also contribute to a higher surgical margin rate.

Conclusion

The prostate size could serve as a useful predictor for cancer aggressiveness. Small prostates may not only be technically more difficult on which to operate but also have a constellation of adverse prognostic markers that may have an adverse impact on outcome.

Disclosure Statement

No competing financial interests exist.

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Abbreviations Used

CT = computed tomography
EPE = extraprostatic extension
PSA = prostate-specific antigen

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