

Prostate Volume and Its Correlation with Histopathological Outcomes in Prostate Cancer

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Key Words

Prostate volume · Histopathology · Positive surgical margins · Extraprostatic extension

Abstract

Introduction: There is a paucity of data investigating the relationship between histopathological variables of oncologic importance and prostate volume, and we aimed to investigate this. **Patients and Methods:** 2,207 consecutive patients who underwent robotic-assisted radical prostatectomy were studied. Preoperative demographic and both pre- and postoperative histopathological parameters were compared among the small (<40 cm³), intermediate (40–70 cm³), and large (>70 cm³) prostate groups. **Results:** Patients with smaller prostates were younger, had slightly lower BMIs, and lower prostate-specific antigen (PSA) levels than those with larger prostates ($p < 0.001$). They also had worse histopathological criteria (Gleason, core positivity, and maximum percent cancer) on preoperative biopsy and had worse radical specimen Gleason sums ($p < 0.001$), percent cancer ($p < 0.001$), and pathological stage ($p = 0.016$). 11.5% of the men in the small prostate group suffered a positive surgical mar-

gin (PSM) compared to 8.3 and 5.6% in the intermediate and large prostate groups, respectively ($p = 0.008$). Basilar, posterolateral, and multifocal PSMs were commoner in the small prostate group. **Conclusions:** Younger men have smaller prostates and worse preoperative histopathological parameters despite lower PSA values. Men with small prostates undergoing robotic-assisted radical prostatectomy have worse final Gleason sums, tumour volume, extraprostatic extension, and PSM rates than those with larger prostates.

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Introduction

Prostate cancer is the commonest non-dermatological cancer affecting men in the Western world [1]. Radical prostatectomy (RP) remains the gold standard management for localized prostate cancer, but roughly 20% of all

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Table 1. Demographic details and preoperative characteristics of patient groups

	<40 cm ³ (n = 667)	40–70 cm ³ (n = 1,256)	>70 cm ³ (n = 284)	p
Age, years	58 (52–63)	60 (55–65)	64 (60–69)	<0.001*
BMI	26 (24–28)	27 (25–29)	27 (25–30)	<0.001*
PSA	4.5 (3.3–5.8)	4.8 (3.7–6.5)	6.3 (4.7–9.2)	<0.001*
Biopsy Gleason, %				<0.001*
≤6	54.7	61.1	69.4	
7	39.3	31.6	23.9	
≥8	6.0	7.3	6.7	
% of cores that are positive	25 (13.3–41.7)	20 (10.6–36.3)	12.5 (8.3–23)	<0.001*
Max % cancer on single core	20 (10–50)	20 (6–50)	10 (5–25)	<0.001*
Clinical stage, %				0.027*
T1	82.6	83.2	89.4	
T2	17.4	16.4	10.6	
T3	0	0.4	0	

Figures are percentages or medians with interquartile ranges in parentheses. * = Statistically significant.

men suffer biochemical recurrence (BCR) following it [2]. There are a number of pre- and postoperative predictors of BCR and progression of disease, of which Gleason sum, prostate-specific antigen (PSA) level, and stage of tumour are the most important [2]. Extraprostatic extension (EPE) and positive surgical margin (PSM) rates postoperatively are also associated with a higher rate of BCR [3–10]. Multifocality of PSMs is predictive of higher BCR rates, but the location of PSMs is less established as a predictor [11]. Godoy et al. [7] found in 128 men with PSMs after RP that 5-year actuarial BCR rates varied based on the following rank order of sites of PSMs: base > posterolateral > apex (100, 49.7, 41.5%, respectively). Tumour volume, lymph node positivity, and the number of positive lymph nodes can also predict BCR [12–14]. What remains unclear is the relationship of prostate volume to the above predictors. We have previously reported on 700 consecutive patients who underwent robotic-assisted radical prostatectomy at a single institution by a single surgeon, and found that prostate volume was inversely associated with EPE. However, although a trend for higher PSMs was noted in men with smaller prostates, this did not reach statistical significance [15]. Herein, we report on our current patient cohort of 2,207 men in which we investigated relationships of prostate volume with the above oncological prognosticators and demographic parameters.

Patients and Methods

Between January 2005 and April 2010, 2,207 men with clinically localized prostate cancer who opted for surgery underwent robotic-assisted radical prostatectomy at a single institution by a single surgeon (A.T.). All preoperative biopsy slides were reviewed by the uropathologists at our institute who reported on relevant histopathological data including Gleason sum, number of positive cores, and maximum percent cancer in any positive core. All RP specimens were subjected to weighing to determine prostate volume, and relevant histopathological data (Gleason sum, percent cancer, margin status, EPE, and lymph node positivity) were extracted from the specimen reports. All data were entered into our Institutional Review Board-approved customized secure database.

Patients were divided into small (<40 cm³), intermediate (40–70 cm³), and large (>70 cm³) prostate volume groups. All statistical analyses were performed using SPSS 15.0 (SPSS Inc., Chicago, Ill., USA). χ^2 analysis was performed for comparisons of groups with categorical variables, and Kruskal-Wallis analysis of variance was used for comparisons of groups with continuous variables. A double-sided p value <0.05 was considered statistically significant, and in such cases, further pairwise comparisons were done between the small and large prostate volume groups to confirm these differences.

Results

Patient demographic data and preoperative characteristics are shown in table 1: prostate volume correlated with age, BMI, and preoperative PSA level; small prostates were associated with younger men, lower BMI, and lower PSA

Table 2. Postoperative histopathological characteristics of patient groups

	<40 cm ³ (n = 667)	40–70 cm ³ (n = 1,256)	>70 cm ³ (n = 284)	p
RARP Gleason, %				<0.001*
≤6	26.6	32.0	44.7	
7	68.5	61.3	49.3	
≥8	4.8	6.7	6.0	
PSM	11.5	8.3	5.6	0.008*
N+	0.5	1.1	0.4	0.206
Pathological stage, %				0.016*
T2	83.1	83.0	89.8	
T3	16.9	17.0	10.2	
% cancer ^a	5 (3–10)	5 (2–10)	5 (1–5)	<0.001*

* = Statistically significant; RARP = robotic-assisted radical prostatectomy; N+ = node-positive.

^a Figures are medians with interquartile ranges in parentheses.

Table 3. Location of PSMs in each of the patient groups

	<40 cm ³ (n = 667)	40–70 cm ³ (n = 1,256)	>70 cm ³ (n = 284)	p
Total PSM rate, %	11.5	8.3	5.6	0.008*
PSM rates stratified by location, %				0.271
Apex	42.7	35.1	71.4	
Base	4.9	2.1	0	
Posterolateral	19.5	26.6	14.3	
Multifocal	17.1	13.8	7.1	
Other location	15.9	22.3	7.1	

levels (all $p < 0.001$). Small prostates were also associated with worse oncological prognosticators on preoperative biopsy, with worse Gleason sums, increased tumour volume (surrogated by percent positive cores and maximum percent cancer), and higher clinical stage. Table 2 shows that prostate volume correlated with worse Gleason sums ($p < 0.001$) and more cancer on the RP specimens ($p < 0.001$). Men with small prostates had the highest risk of positive margins (11.5 vs. 8.3% for intermediate and 5.6% for large prostates). A subgroup analysis found that men >70 years old had similar PSM rates to the small volume group as a whole (11.8 vs. 11.5%; $p > 0.05$). Table 2 also shows that men with small and intermediate-sized prostates had more pT3 disease (16.9 and 17%, respectively) compared to men with large prostates (10.2%). However,

there was no difference in risk of nodal disease based on prostate volume. Table 3 demonstrates that basilar, posterolateral, and multifocal PSMs are more common in men with smaller prostates, though comparison of basilar versus non-basilar ($p = 0.455$), posterolateral versus non-posterolateral ($p = 0.395$), and multifocal versus non-multifocal ($p = 0.412$) showed no significant differences.

Discussion

We found that men with small prostates were younger and had lower BMIs and PSA levels than those with larger prostates. However, these men had worse cancer characteristics on both their preoperative biopsy and their RP specimens, suggesting that small prostates are associated with worse tumour behaviour than large prostates. This may be because of increased intrinsic aggressiveness and/or greater tumour bulk making EPE more likely. Other investigators have found similar results of worse tumour biology and volume in men with smaller prostates [16–18]. We have previously shown a trend towards higher PSM rates in men with smaller prostates, but this was not statistically significant [15]. However, in this study of our entire patient cohort, we found that PSM rates were significantly different between the groups ($p = 0.008$). This finding is likely to be related to worse tumour biology as discussed above, as well as a more technically difficult operative dissection in small prostates because of a larger contact area with the vascular pedicle as well as less well-defined prostatovesical and prostates-urethral junctions [15].

There is evidence, albeit controversial, that basilar, posterolateral, and multifocal PSMs represent the highest risk of BCR [7, 11]. Our data show that these PSMs occurred more frequently in men with smaller prostates, though these trends did not reach statistical significance, possibly due to a low power effect with small numbers in the groups once they are subdivided by PSM site. We also did not find that older men with small prostates had increased positive margin rates compared to that group as a whole, and thus cannot surmise that they have a different prognosis for a given volume. We also did not find any difference in lymph node positivity between the prostate volume groups. However, taken together, our findings suggest that men with smaller prostates have an increased risk of predictors for worse oncological outcome.

Our study has certain limitations. Prostate volume was determined on the RP specimen rather than by transrectal ultrasound or MRI preoperatively. Other investiga-

tors, however, have confirmed a strong positive association between pre- and postoperative volume measurements [19], suggesting that RP prostate weight can be used as a surrogate to prostate volume obtained by transrectal ultrasound or MRI. Another consideration in our study is that representative sections rather than whole-mount slides were used to estimate percent cancer and to evaluate margin status, Gleason grade, and pathological stage. However, this was a consistent method utilized for all RP specimens, and thus any underestimation of these prognostic variables should be consistent throughout all study groups.

Conclusions

Prostate volume is associated with a number of histopathological parameters of oncological importance. Small prostates have a constellation of worse prognostic indicators despite being associated with more favourable demographic criteria on which to operate (younger age and lower BMI). Thus, we would recommend that men with clinically localized prostate cancer should have their prostate volume determined as part of initial clinical risk assessment.

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