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ORIGINAL ARTICLE

Does size matter? The significance of prostate size on pathologic and functional outcomes in patients undergoing robotic prostatectomy

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Potency;
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Margins

ABBREVIATIONS

RALP, robotic-assisted

Abstract *Background:* We examined the effect of prostate weight on perioperative data, and the pathological and functional outcomes of robotic-assisted laparoscopic prostatectomy (RALP).

Patients and methods: Data were available from 716 consecutive patients before, during and after undergoing RALP at one institution. Prostate size was arbitrarily stratified by recorded prostate weight into <50, 50–80 and >80 g, corresponding to small, moderate and large glands, respectively. Perioperative data and the histopathological and functional outcomes were compared across these groups by both univariable and multivariable-adjusted analyses.

Results: Increased prostate size was associated with increased age, preoperative prostate-specific antigen levels, body mass index, operative duration, blood loss, lower biopsy and pathological Gleason scores, and lower pathological staging ($P < 0.05$). The incidence of extensive positive surgical margins was 14.8%, 9.7%, and 5.3% in small, moderate and large prostates, respectively

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laparoscopic prostatectomy; PSM, positive surgical margin; OR, operating-room; EBL, estimated blood loss; LOS, length of hospital stay; BMI, body mass index; SHIM, sexual health inventory for men

($P < 0.001$). However, after multivariable adjustment, only Gleason score and pathological stage were significantly associated with the incidence of positive margins ($P < 0.05$); prostate weight was not significantly associated. Overall, 78% and 92% of patients were potent and continent at 12 months, respectively, which was not affected by prostate size.

Conclusion: Patients with larger prostates had favourable pathological outcomes after RALP. When controlling for pathological stage, prostate size was not associated with margin positivity. Functionally, neither continence nor potency at 12 months was affected by prostate size.

Introduction

The effect of prostate size on outcomes after robotic-assisted prostatectomy remains unclear. Previous studies concluded that higher-volume prostates are associated with more favourable pathological outcomes, lower rates of positive surgical margins (PSMs) and improved long-term biochemical disease-free survival [1,2]. In open radical retropubic prostatectomy series, larger glands are associated with longer operating-room (OR) time, higher estimated blood loss (EBL) and blood transfusions, but with no difference in functional outcomes [3,4]. However, there are conflicting results in previous reports of robotic prostatectomy. Zorn et al. [5] found no difference in EBL, transfusion rate, OR time, or length of hospital stay (LOS) in patients with larger (>80 g) prostates. However, others have reported that in patients with large prostates (>70 g), EBL, OR time, and LOS significantly increased [6].

In an effort to elucidate the association of prostate size on perioperative data, as well as pathological and functional outcomes, we evaluated the effect of prostate weight on these variables among patients undergoing robotic-assisted laparoscopic prostatectomy (RALP).

Patients and methods

An institutional review board-approved database comprising all patients undergoing RALP by one surgeon (D.B.S.) is maintained by research staff at the Mount Sinai Medical Center. Consecutive patients undergoing RALP from May 2007 until February 2009 formed the base population for the current analyses (784 men). Patients were excluded for the following missing data: body mass index (BMI, 3), preoperative PSA level (23), preoperative Gleason score (8), operative duration (5), EBL (10), prostate weight (15), and margin status (4). After these exclusions, perioperative and histopathological data were available on 716 patients. Patients were divided arbitrarily into three categories according to their prostate weight, i.e. <50, 50–80 and >80 g, corresponding to small, moderate and large glands, respectively.

Functional outcomes and PSA data were collected at baseline, 6 weeks, and then every 3 months for the first year after surgery, using the IPSS and sexual health inventory for men (SHIM) scores. Continence was defined as the use of either no pads or one security pad daily. Potency was defined as a SHIM score of >16, with or without the use of phosphodiesterase-5 inhibitors, in patients who were preoperatively potent (SHIM > 16). A single postoperative PSA level of >0.2 ng/mL was considered to indicate a biochemical recurrence.

Excised prostate specimens were sectioned in four quadrants and mounted in a standard fashion. The volume of cancer was estimated based on the percentage of slides containing tumour (the positive-block ratio). Tumour at the inked resection margin was considered a PSM, which was dichotomized into 'focal' or 'extensive' if the length of the PSM was < or >3 mm, respectively [7].

Demographic, pre and peri-operative, and pathological characteristics of patients undergoing RALP were calculated using means for continuous variables and proportions for categorical variables. These characteristics were calculated for each prostate weight category of patients separately. The statistical significance of differences, comparing the three prostate weight groups, was calculated using *t*-tests for continuous variables and chi-square tests for categorical variables. Additionally, the prevalence of extensive surgical margins (>3 mm) was calculated by prostate weight category, overall and by pathological staging. The statistical significance of linear trends across prostate weight categories was tested by linear and logistic regression models for continuous and dichotomous variables, respectively. The multivariable-adjusted odds ratios of patient characteristics associated with prostate weight were determined using a multinomial logistic regression model with the small prostate weight group as the reference category. The odds ratios of extensive PSMs associated with patient characteristics and prostate weight were calculated using logistic regression models adjusted for all patient characteristics simultaneously. Significance was defined as $P < 0.05$, and all tests were two-sided.

Results

Among the 716 patients undergoing RALP, 400 (56%) had a prostate weight of <50 g, 259 (36%) of 50–80 g, and 57

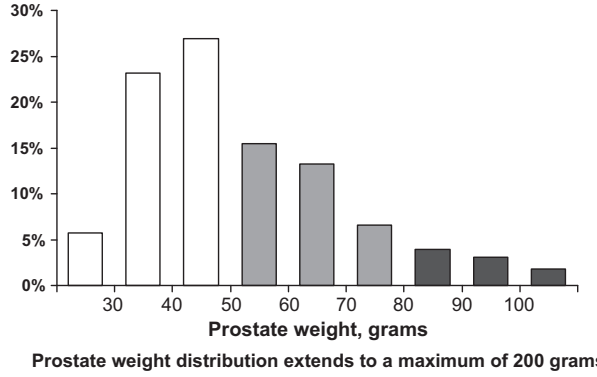

Figure 1 Distribution of prostate weight among 716 patients undergoing RALP (prostate weight distribution extends to a maximum of 200 g).

Table 1 Characteristics of 716 patients undergoing robotic prostatectomy overall and by prostate weight categories.

		Prostate weight, grams			*p*-trend
	Overall (n = 716)	⩽50 (n = 400)	50–80 (n = 259)	>80 (n = 57)	
Age, years	59.1 (6.9)	57.4 (7.1)	60.7 (5.9)	63.4 (5.8)	<0.001
Body mass index (kg/m^2)	27.5 (3.6)	27.4 (3.5)	27.5 (3.5)	28.6 (3.8)	0.051
Estimated blood loss (mL)	51.4 (10.3–256.5)	45.6 (9.5–218.8)	58.9 (12.0–286.5)	75.2 (14.8–382.5)	<0.001
Time in operating room (min)	124.7 (28.4)	121.4 (28.6)	126.0 (26.0)	140.1 (32.7)	<0.001
Hospital stay of 1 day (%)	74.2	75	74.5	66.7	0.258
Pathologic stage					
T2 (%)	83.8	79.5	86.9	94.7	<0.001
T3 (%)	16.2	20	12.7	5.3	<0.001
PSA (ng/mL)	6.0 (4.4)	5.5 (3.2)	6.4 (5.4)	7.8 (5.2)	<0.001
Gleason score, biopsy					
6 (%)	61.3	56	66.8	73.7	0.001
7 (%)	31.6	37	25.9	19.3	
8–10 (%)	7	7	7.3	5.3	
Gleason score, pathologic					
6 (%)	32.3	22.5	43.6	49.1	<0.001
7 (%)	61.5	72	48.7	45.6	
8–10 (%)	6.2	5.3	7.7	5.3	
Extensive positive margins (%)	12.2	14.8	9.7	5.3	<0.001

Numbers in table are mean (standard deviation) or percentage except for estimated blood loss which is presented as geometric mean (95% confidence interval).

(8%) had glands of >80 g (Fig. 1). The mean (range) prostate weight was 50.1 (22–200) g. All clinical and pathological variables examined except LOS were associated with prostate weight (Table 1). Specifically, greater age, longer OR time and a higher EBL were significantly associated with larger prostates. Pathological stage was lower in patients with larger prostates, and there were significantly higher proportions of patients with lower biopsy and histopathological Gleason sums in those with larger prostates.

Prostate weight was inversely associated with higher-stage disease and extensive PSMs (Fig. 2). Overall, extensive PSMs decreased at higher prostate weights, i.e. 14.8%, 9.7% and 5.3% extensive PSMs in small, moderate, and large prostates, respectively (P < 0.05).

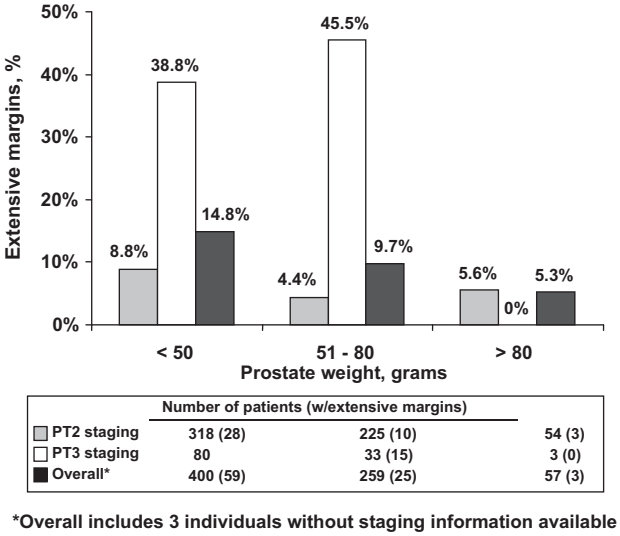

Figure 2 The proportion of extensive PSMs stratified by prostate weight and pathological stage. *Overall includes three men without staging information available.

Prostate size had no effect on functional outcomes. At 12 months of follow-up, 92% of patients were continent (Fig. 3); continence was not associated with prostate size (P = 0.77). The overall rate of potency at 12 months was 78% (Fig. 4); this rate was also not associated with prostate size (P = 0.069).

On multivariable analysis of moderate (50–80 g) and large (>80 g) vs small (<50 g) prostates, age, EBL, pT2 staging, and PSA level were all independently associated with larger prostates (Table 2). Patients with moderate or large prostates were less likely to have Gleason scores of ⩾7 than those with smaller glands. BMI and OR time were also associated with size, but only in prostates of >80 g. Neither LOS nor extensive PSMs were associated with prostate size when controlling for other variables.

Multivariable analysis of characteristics possibly associated with PSMs only identified pathological stage and Gleason score as independent predictors of extensive PSMs (Table 3).

Discussion

The relationship between prostate size and perioperative data, as well as functional and histopathological variables, is a subject of debate. Previous studies have examined this relationship, specifically evaluating the effect of prostate size on surgical margin status, histopathological findings, and functional outcomes. Most studies have shown improved histopathological cancer features in larger prostates, including decreased rates of PSMs [1,2]. For example, Link et al. [6] and Msezane et al. [8] both found larger prostate weights to be associated with more favourable pathological staging, similar to the present findings. However, unlike the present study, both reported improved PSM rates with increasing prostate size in multivariable-adjusted analysis.

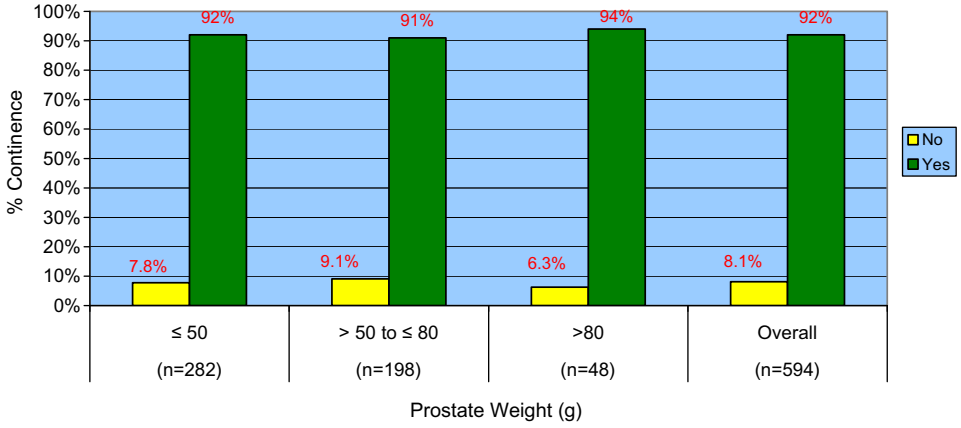

Figure 3 Continence rates at 12 months (one or fewer pads per day) stratified by prostate weight ($P = 0.77$).

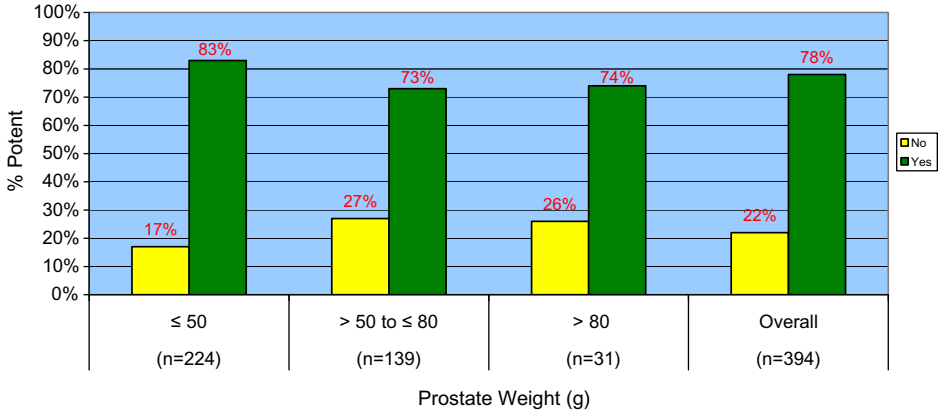

Figure 4 Potency rates at 12 months (SHIM > 16), at 12 months, stratified by prostate weight ($P = 0.069$).

Table 2 Multivariable analysis comparing prostate weight and various patient characteristics. Results are adjusted odds ratios (95% confidence interval).

	Prostate weight, grams		
	⩽50 ($n = 400$)	> 50 to ⩽80 ($n = 259$)	> 80 ($n = 57$)
Age, 5 years	1 (reference)	1.70 (1.47–1.96)*	2.90 (2.15–3.92)*
Body mass index, 5 kg/m^2	1 (reference)	1.13 (0.88–1.46)	1.84 (1.20–2.82)*
Estimated blood loss, 20 ml	1 (reference)	1.10 (1.03–1.16)*	1.15 (1.04–1.26)*
Time in operating room, 30 min	1 (reference)	1.19 (0.97–1.45)	1.91 (1.38–2.65)*
Hospital stay of 1 day	1 (reference)	0.96 (0.64–1.45)	0.79 (0.39–1.63)
Pathologic stage pT2	1 (reference)	1.78 (1.02–3.11)*	4.94 (1.16–21.0)*
PSA, 5 units	1 (reference)	1.70 (1.30–2.24)*	2.23 (1.57–3.16)*
Gleason score, post-operative			
7 versus 6	1 (reference)	0.26 (0.17–0.39)*	0.15 (0.08–0.31)*
8 or 9 versus 6	1 (reference)	0.59 (0.25–1.42)	0.19 (0.03–1.12)
Extensive margins	1 (reference)	0.58 (0.32–1.06)	0.35 (0.09–1.33)

All variables were included in the model simultaneously.
* $p < 0.05$.

The evidence for less aggressive pathological outcomes and even decreased PSM rates in large prostates has also been reported in open and laparoscopic prostatectomy cohorts [1,4,9–12], although a study by Levinson et al. [13] found no such association. Another negative study by Singh et al. [14] failed to detect a difference in the rate of PSM, but that study pooled all prostates >50 g together, whereas most other reports set the threshold for large prostates at 70–80 g.

Histopathologically, men with larger prostates were found to have significantly lower pathological stage and Gleason

Table 3 Multivariable analysis of an extensive positive margin associated with patient characteristics.

	Odds ratios (95% CI) of extensive margins
Age, 5 years	1.10 (0.91–1.32)
Body mass index, 5 kg/m^2	0.84 (0.58–1.19)
Estimated blood loss, 20 ml	1.02 (0.93–1.11)
Time in operating room, 30 min	0.99 (0.76–1.29)
Hospital stay of 1 day	1.12 (0.63–2.00)
PT2 pathology stage	0.19 (0.11–0.33)*
PSA, 5 units	1.22 (0.98–1.52)
Gleason score, post-operative	
7 versus 6	2.43 (1.09–5.46)*
8 or 9 versus 6	3.94 (1.35–11.5)*
Pathology weight, grams	
50–80	0.67 (0.37–1.20)
>80	0.47 (0.12–1.74)

Multivariable adjusted model includes all variables simultaneously.
* $p < 0.05$.

scores. Patients with smaller prostates had higher rates of PSMs, although this association was lost in a multivariable analysis, probably reflecting the effect of the higher pathological stage seen in patients with smaller prostates.

Thus, recent reports are somewhat divided on the relationship between prostate size and pathological stage, Gleason score and margin status. Differences in statistical methods, surgical technique, definitions of PSMs, stratification of prostate size, and baseline patient characteristics are probably responsible for the discrepancies. Differences among these studies and ours might also be secondary to surgeon-specific approaches towards large prostates. The high volume of RALP procedures performed at our institution, coupled with the use of a non-traditional approach to robotic extirpation of large prostates described elsewhere [15], might have positively affected our results. Our study is one of only a few examining this issue using multivariable analysis, which is important given the discrepancy noted between our univariable and multivariable results for PSMs.

The data suggest that surgical difficulty might be higher but functional outcomes are unaffected in RALP performed in men with large prostates [3,5]. To better evaluate this problem, we analysed prostate weight among patients who underwent RALP by one surgeon. The postoperative continence rate of 92% and potency rate of 78% among all study participants, regardless of prostate size, are similar to those from other large published robotic prostatectomy series [16–20]. When patients were stratified by prostate weight we found no significant differences in postoperative potency or continence between the groups, a finding consistent with that reported by Zorn et al. [5]. As expected, patients with larger prostates were older and had higher preoperative PSA levels. We also noted that patients with larger prostates had a higher BMI, perhaps due to a different hormonal milieu or PSA haemodilution in the obese. Larger prostates were associated with longer OR times and higher EBL, although the 30 mL difference in EBL is of minimal clinical significance.

Although we found no difference in postoperative continence or potency among patients with larger prostates, several reasons can explain why the removal of a sizeable gland could affect functional outcomes. Assuming the patient regains continence, the removal of a large obstructive gland will likely improve urinary flow and increase a patient's subjective assessment of urinary functional improvement. Conversely, the increased bladder outlet resistance associated with a large prostate over time might result in an overactive bladder, potentially leading to increased rates of incontinence. Continence might also be adversely affected by a shorter urethral stump after removing a large prostate.

A large prostate makes exposing and dissecting the neurovascular bundles more difficult, potentially leading to either direct injury from poor visualization or traction injuries that can cause neuropraxia. Postoperative potency could therefore be compromised. That the present patients with larger prostates had no decreased urinary or sexual function after RALP, compared to their smaller-prostate counterparts, is an interesting finding that could reflect surgeon-specific variables.

Improved histopathological outcomes among men with larger prostates are understandable. Larger prostates have been shown to be associated with higher preoperative PSA levels due to PSA production from BPH tissue [21]. This increased PSA might lead to earlier biopsy and detection in the natural history of the disease, leading to the diagnosis of comparatively lower-risk cancers [6].

Prostate size might be a therapeutic issue to be considered by the patient with prostate cancer. Men with the most severe preoperative LUTS have been shown to experience the greatest improvement in their symptoms after radical prostatectomy. This finding is presumably due to the association between prostate size and severity of LUTS, and the beneficial effects of removing a large, obstructive gland. When combined with the increased likelihood of having lower grade cancer on pathological examination, the choice to undergo radical prostatectomy could become a more appealing treatment option for men with large prostates. This is especially relevant given the need for neoadjuvant androgen deprivation, higher radiation dose treatment, and higher subsequent risk for acute urinary toxicity among men with large prostates who choose to undergo brachytherapy or intensity-modulated radiotherapy [22].

Our study has several limitations, including problems of generalisation and selection bias arising from a single-surgeon cohort. There were relatively few patients with prostates of >80 g (57). The overall number of patients in our study, while greater than those analysed in some other studies, is also relatively small. To attain consensus on the nature of prostate weight and RALP outcomes, our results should be confirmed in larger cohorts with more men having larger prostates.

Last, we did not analyse each patient's LUTS before and after RALP. This might have provided additional useful information given the postoperative improvement seen among men with large prostates. Further studies are needed to show this benefit.

In conclusion, Larger prostates are associated with increased BMI, greater age, higher preoperative PSA levels, longer OR time, higher EBL, and lower Gleason scores and pathological staging in patients undergoing RALP. While the incidence of extensive PSMs was higher in patients with smaller prostates, we found this to be an artefact of the differences in pathological stage. Neither continence nor potency at 12 months was associated with prostate size. RALP remains a good option for patients with large prostates.

Conflict of interest

This article contains no references to any commercial organization, pharmaceutical firm or medical device manufacturer. As such, none of the authors have any conflict of interest.

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