

Significance of prostate weight on peri and postoperative outcomes of robot assisted laparoscopic extraperitoneal radical prostatectomy

Satya B. Allaparthi, MD, Thomas Hoang, MD, Nadeem N. Dhanani, MD, Ingolf A. Tuerk, MD

Caritas St. Elizabeth's Medical Center, Tufts University School of Medicine. Brighton, Massachusetts, USA

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Introduction: To determine the significance of prostate weight (PW) on clinical and pathological outcomes in patients undergoing da Vinci robot assisted laparoscopic extraperitoneal radical prostatectomy (EP-RARP).

Methods: From November 2008 to January 2010, 295 men underwent EP-RARP at our institution. We retrospectively reviewed our database and stratified patients into four groups based on pathologic PW: Group 1, less than 30 g; Group 2, 30 g to less than 50 g; Group 3, 50 g to less than 80 g; and Group 4, 80 g or larger. We prospectively compared these groups with respect to patient age, body mass index, prostate-specific antigen, Gleason score, pathological stage, margin status, operative time, blood loss, transfusion rate and length of stay. Statistical analysis was performed using SYSTAT 13 software. An analysis of variance (ANOVA) model was used to compare the continuous variables among the groups. Chi-square and Fisher's exact tests were used to compare categorical variables.

Results: Of the 295 patients, 10, 182, 91, and 12 had a PW of

less than 30 g; 30 g to less than 50 g; 50 g to less than 80 g; and 80 g or larger, respectively. A significant difference was found in age, prostate weight and prostate-specific antigen values among the four groups ($p < 0.05$). Patients in Group 4 had larger prostates, were older (mean age 65 years), had higher pretreatment prostate-specific antigen (median 5.85 ng/mL) and lower Gleason score (mean 6.2). Based on the D'Amico risk stratification, our study showed a trend toward higher risk disease, presence of extra capsular extension, seminal vesicle invasion and positive margin status in Groups 1, 2 and 3 rather than in Group 4. No significant differences in operative time, estimated blood loss, transfusion rate, hospital stay, and postoperative complication rate were observed among the four groups.

Conclusions: Da Vinci robot assisted laparoscopic extraperitoneal radical prostatectomy (EP-RARP) is feasible in patients with larger prostates, offering acceptable operative times, blood loss, hospital stay and complication rates. In our cohort of patients, we found pathologically smaller prostates are generally associated with higher Gleason score, higher risk group stratification and positive surgical margin status. Although technically challenging, increased prostate weight should not be considered a contraindication for EP-RARP if performed by experienced surgeons.

Key Words: prostatectomy, prostate weight, robotic

Introduction

In the year 2000, Binder and colleagues performed the first robot assisted laparoscopic prostatectomy (RALP)

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Address correspondence to Dr. Satya Allaparthi, Caritas St. Elizabeth's Medical Center, Tufts University School of Medicine, 11 Nevins Street, Suite 303, Boston, MA 02135 USA

in Frankfurt, Germany.¹ Since its introduction in the United States in 2001, RALP has increasingly become the surgical treatment of choice by both patients and physicians. In recent years there has been an exponential increase in the number of procedures performed, and has become the dominant approach here in the United States and worldwide. However, a large sized prostate can distort the anatomy by displacing the neurovascular bundles posteriorly, obscuring the correct plane for the bladder neck

dissection and interfering with the apical dissection, thereby complicating the robotic approach. Numerous studies have sought to characterize the impact of prostate size on open, laparoscopic and robotic approaches to prostate excision, however the findings have lacked consensus.²⁻⁷

Joseph et al reported their experience from 355 extraperitoneal RARPs performed by a single surgeon. However, their data used 75 g as a cut off point based on a study by D'Amico and coworkers.⁴ In our study of 295 EP-RARP, we made an effort to stratify our patients into four groups based on the pathological weight of prostate as Group 1, less than 30 g; Group 2, 30 g to less than 50 g; Group 3, 50 g to less than 80 g; and Group 4, 80 g or larger. Zorn et al assessed this topic in four groups of patients undergoing trans peritoneal (TP) RARP based on pathological weight.⁵ We report our experience in this cohort of patients and evaluate the effects of prostate size on peri and postoperative clinical and functional outcomes after EP-RARP.

Materials and methods

At our institution from November 2008 to January 2010, 295 extraperitoneal RARPs were performed for clinically localized prostate cancer (clinical stage T1b-T2 disease) by a single surgeon. We collected the data from an IRB approved prospective database. Patients were stratified into four groups, 1 to 4 based on the pathological weight as Group 1, less than 30 g; Group 2, 30 g to less than 50 g; Group 3, 50 g to less than 80 g; and Group 4, 80 g or larger respectively.

Pre, peri and postoperative data were collected for these cases, including patient demographics, preoperative and postoperative staging, perioperative complications, operative parameters and quality of life outcomes. We used the validated modified EPIC-26⁸ questionnaire to evaluate postoperative quality of life and functional outcomes. In our cohort, continence is commonly assessed by pad use, and we also compared the EPIC item querying pad use by dichotomizing at no pads versus one pad or more per day. Patients were deemed continent if they used 1 pad per day or less for security reasons only. Men were assessed for frequency and quality of erections and were deemed potent when the quality of erections were firm enough for intercourse.

Study design

Institutional review board at our institution granted the study exempt status because the patient identifiers were deleted after retrieval of the necessary data. All patients underwent extraperitoneal robotic radical prostatectomy (EP RARP) performed by a single

surgeon at our institution between November 2008 and January 2010. All patients provided fully informed consent before surgery after discussing all the risks, benefits and alternatives to robotic assisted laparoscopic radical prostatectomy.

Surgical team and technique

A single dedicated surgical team led by a well experienced robotic and laparoscopic urologic oncologist, fellows, nurses, surgical assistants and anesthesia teams trained in the da Vinci surgical robotic system were set up to plan for the study.

A 1 cm infraumbilical incision was made and carried down to anterior rectus fascia. The extraperitoneal space was developed bluntly followed by the balloon dissector under direct vision with a conventional laparoscopic 0-degree lens. The extraperitoneal space was further extended laterally and superiorly using blunt dissection below the epigastric vessels under direct vision. Trocars were then placed in the standard fan shaped distribution. Bilateral 8 mm trocars were placed 9 cm from the camera port inferior to the umbilicus. A left sided 12 mm assistant port was placed as well as an 8 mm right sided fourth robotic arm medial to the anterior superior iliac spine. The robot was docked after the five ports were placed. Pelvic lymphadenectomy was performed in patients with Gleason score greater than 7 or a serum prostate-specific antigen (PSA) concentration greater than 10 ng/dL. The endopelvic fascia was incised bilaterally and the dorsal vein complex (DVC) was suture-ligated. The bladder neck was preserved, as it was dissected free from the base of the prostate. The vas deferens and seminal vesicles were then isolated and dissected free from Denonvilliers' fascia. The vascular pedicles were secured using titanium and Weck clips (Weck Surgical Instruments, Teleflex Medical, Durham, NC, USA) as needed. The apical urethra and DVC were transected, with subsequent completion of the vesicourethral anastomosis.

Histopathological analysis

At our institution, all specimens were reviewed and weighed by the genitourinary pathology service. The prostate was entirely sectioned at 1 mm intervals in a stepwise fashion from the apex to the base. In brief, the exterior of the specimen was marked appropriately and inked in its entirety. Positive surgical margins are defined as extension of tumor to the inked surface. Patients with tumor extension through the prostate capsule were considered to have extracapsular extension. Lymph nodes from patients who underwent lymphadenectomy were sent for pathologic study and carefully examined for metastatic disease.

Statistical analysis

Statistical analysis was performed using SYSTAT 13 software. We summarized the data using descriptive statistics, including the mean, median and proportions for normally distributed continuous data, non-normally distributed continuous data and for categorical data respectively. Comparative analysis was performed using the Student t-test, with $p < 0.05$ considered statistically significant for normally distributed continuous data. The Kruskal-Wallis test for non-normally distributed continuous data and Chi-square and Fisher's exact tests were used to compare categorical outcome variables.

Results

Patient demographics

Table 1 details patient demographics and clinical

characteristics stratified by prostate weight. As expected, an increased proportion of clinical T1c tumors were found in those with a prostate weight of 50 g or larger ($p < 0.01$), older men were found to have larger prostates ($p < 0.05$), higher PSA ($p < 0.05$) and lower preoperative Gleason scores ($p < 0.05$). There were no statistically significant differences in body mass index among these groups.

Operative outcomes grouped by prostate weight are shown in Table 2. The mean operative time, estimated blood loss (EBL) and length of hospital stay were similar in the four groups. In our cohort of patients, there were no open conversions or conversion to a pure laparoscopic approach. Table 3 shows the overall postoperative complication rates and functional outcomes among the groups using the Clavien classification and validated questionnaires. Lymphocele accumulation, urinary tract infection,

TABLE 1. Preoperative characteristics

Variable	< 30 g	> 30, < 50	> 50, < 80	> 80	p value
Patients (n)	10	182	91	12	
Race (%)					0.758
White	10 (100)	173 (95)	91 (100)	12 (100)	
Asian		1 (0.6)			
Hispanic		4 (2.2)			
African American		4 (2.2)			
Mean \pm SD (yr)	55.3 \pm 9.7	58.5 \pm 6.4	61 \pm 7.3	65 \pm 6	< 0.001
age at surgery					
Mean \pm SD prostate weight (g)	27.7 \pm 1.016	40.3 \pm 4.8	60.3 \pm 7.3	102 \pm 14.8	< 0.01
Median serum PSA (ng/dL) (IQR)	3.7 (0.6-30.4)	4.7 (0.5-18.7)	5.2 (0.6-22)	5.85 (4.2-13.9)	0.004
Mean \pm SD BMI (kg/m ²)	26.6 \pm 3.975	27.4 \pm 3.4	27.2 \pm 3.3	28.9 \pm 3.5	0.350
Preoperative Gleason score (%)					< 0.01
5-6	6 (60)	88 (48.9)	56 (61.5)	9 (75)	
7 (3 + 4)	2 (20)	5 (29.5)	22 (24.1)	3 (25)	
7 (4 + 3)	1 (10)	25 (13.8)	8 (8.8)		
8	1 (10)	12 (6.6)	2 (2.2)		
9 (4 + 5)	0	2 (1.1)	2 (2.2)		
9 (5 + 4)	0	0			
10 (5 + 5)	0	0	1 (1.2)		
Clinical stage (%)					< 0.01
T1c	4 (40)	124 (68.2)	51 (56)	10 (83.3)	
T2a	3 (30)	36 (19.8)	28 (30.7)	1 (8.3)	
T2b	2 (20)	14 (7.7)	10 (11.1)	1 (8.3)	
T3	1(10)	8 (4.3)	2 (2.2)		

TABLE 2. Intraoperative characteristics

Variable	< 30 g	> 30, < 50	> 50, < 80	> 80	p value
Patients (n)	10	182	91	12	
Mean \pm SD operative time (mins)	129.1 \pm 28.2	127.2 \pm 19.7	127.6 \pm 3.3	127 \pm 20.5	0.988
Median EBL (ml) IQR	200 (100-550)	150 (25-1200)	200 (50-1200)	162.5 (50-550)	0.231
Postoperative Gleason score (%)					< 0.001
5-6	3 (30)	47 (26.1)	35 (38.5)	7 (63.6)	
7 (3 + 4)	6 (60)	97 (53.8)	37 (40.7)	5 (36.4)	
7 (4 + 3)	0	28 (15.5)	10 (11)		
8	1 (10)	4 (2.2)	3 (3.2)		
9 (4 + 5)		4 (2.2)	4 (4.3)		
9 (5 + 4)			1 (1)		
10 (5 + 5)			1(1)		
No. seminal vesicle invasion (%)					0.013
Negative	7 (70)	172 (94.5)	87 (95.6)	12 (100)	
Positive	3 (30)	10 (5.5)	4 (4.3)		
No. extracapsular extension (%)					0.049
Negative	7 (70)	122 (67)	71 (78)	12 (100)	
Positive	3 (30)	60 (33)	20 (22)		
Nerve sparing (%)					0.173
None	1 (10)	19 (10)	16 (17.5)	4 (33.3)	
Unilateral	2 (20)	29 (16)	17 (18.9)	2 (16.6)	
Bilateral	7 (70)	134 (74)	58 (63.7)	5 (50)	
Lymph node dissection(%)					0.352
None	5 (50)	82 (45)	53 (58.2)	9 (75)	
Unilateral	2 (20)	46 (25)	20 (22)	2 (16.6)	
Bilateral	3 (30)	54 (30)	18 (19.8)	1 (8.3)	
Pathological stage(%)					0.076
pT2a		13 (7.2)	9 (9.8)	3 (25)	
pT2c	7 (70)	108 (58.3)	61 (67)	9 (75)	
pT3a		51 (29)	16 (17)		
pT3b	3 (30)	10 (5.5)	5(6.2)		
Positive margin(%)					< 0.001
Negative	6 (60)	141 (77.5)	81 (89.1)	11 (91.6)	
Positive	4 (40)	41 (22.5)	10 (10.9)	1 (8.3)	
pT2	2 (20)	18 (9.8)	5 (50)	1 (8.3)	
pT3	2 (30)	23 (12.8)	5 (50)		

urinary retention, postoperative ileus, urinary leak and bladder neck contracture were the primary complications thought to be potentially related to the PW and thus were compared among the four groups. No significant differences were noted.

Histopathological outcomes

The pathologic stage was similar among all four groups. We noted a significantly greater incidence of PSMs in the smaller PW groups (< 80 g) compared to larger groups (> 80 g). Furthermore, smaller

TABLE 3. Postoperative and clinical outcomes

Variable	< 30 g	> 30, < 50	> 50, < 80	> 80	p value
Patients (n)	10	182	91	12	
Mean length of hospital stay (days)	1	1.2 (1-12)	1.02 (1-2)	1.4 (1-5)	0.4
Mean length of catheterization (days)	0	2 (2.66)	1 (0.7)	0	
Postoperative complications (Clavien classification)					0.159
I	0	3	0	0	
IIa	1 (lymphocele)	6 (lymphocele)	2 (lymphocele), 1 leak	0	
IIb	0	1 postop MI	0	0	
III	0	0	0	0	
Mean % return of baseline urinary function (patients evaluated)					
6 months	85.72 (8)	90.7 (108)	86.7 (61)	71.6 (7)	0.24
12 months	90.3 (7)	93.81 (88)	91.8 (49)	83.3 (6)	0.16
Mean percent return of baseline sexual function (patients evaluated)					
6 months	62.5 (8)	72.4 (108)	70.5 (61)	77.7 (9)	0.69
12 months	71.4 (7)	82.8 (64)	79.6(49)	75 (6)	0.87

glands had significantly higher rates of extracapsular extension and seminal vesical invasion.

Discussion

In this study, we evaluated our experience with respect to the impact of prostate weight in patients undergoing EP-RALP. Unlike the transperitoneal approach, an extraperitoneal approach limits the amount of working space potentially making it technically challenging for the surgeon to manipulate the gland effectively.⁴ However, in our cohort of patients we have demonstrated no significant difference in mean operative time, EBL, length of hospital stay, Foley catheterization or complications.

Several published series have reported significantly longer operative times for patients with larger PW when undergoing LRP.⁹⁻¹¹ Zorn et al postulated that this difference between the LRP series and RLRP series can be attributed to the steep learning curve associated with LRP, which becomes increasingly obvious when performing more complicated cases such as patients with large glands.⁵ Additionally, the attributes of robotic surgery compared with LRP, such as the instruments' endo-wrists capabilities, three-dimensional vision and compensation for hand

tremors become especially valuable in the more challenging cases.

In comparison with published open series, our results offer several important differences. In open radical prostatectomy (ORP) blood loss requiring transfusion is considered the most common intraoperative complication. A study by Hsu et al¹² in 1024 men reported that PW was significantly and directly related to the EBL and transfusion rate. RLRP series have consistently reported significantly decreased EBL rates compared with ORP series.¹³⁻¹⁵ Our results confirm this benefit of RLRP to hold true regardless of PW.

In our study the pathological outcomes were consistent with findings of previously published open, laparoscopic and RALP series in that disease extent inversely related to gland size. As stated by Link et al,¹⁶ this may be explained as a lead time bias due to increased PSA or possibly as an indication that cancers in larger prostates are biologically different than those in smaller glands. As has been shown in previous studies, prostate size and BPH are directly related to PSA values.¹⁷ Therefore, it would follow that men with enlarged prostates due to BPH would have higher PSA, leading to more frequent biopsies and the identification of prostate cancers that would have otherwise gone undetected. Several studies found that prostate volumes larger than 75 cc were associated

with more favorable outcomes after RP; the studies all concluded that lead time bias accounted for most or all of the results.¹⁸⁻²⁰ In the Shared Equal Access Regional Cancer Hospital SEARCH based study, Freedland et al²¹ demonstrated a significant association between smaller prostates, higher grade and more advanced disease even after controlling for preoperative PSA. It was stated that smaller prostate weight (PW) was an independent predictor of biochemical progression. Our study shows a lower rate of positive surgical margins in men with prostates larger than 75 g and were consistent with findings of previously published series by Msezane et al²² where in PW is an independent predictor of both extracapsular extension and PSM, with an inverse relationship having been demonstrated between both variables. Our outcomes were similar to that of the largest transperitoneal series reported by Zorn et al⁵ however, the approach differed in between the two series.

Our data indicates that an enlarged prostate has several effects on EP-RALP. Technically, with a limited working space, the extraperitoneal approach demands meticulous care when dealing with a prominent median lobe, which is commonly seen with enlarged prostates. This mandates a wider resection at the bladder neck and a larger defect to reconstruct. In our series we incorporated the bladder neck reconstruction with the running urethrovesical anastomosis using a modified van Velthoven technique.²³ We have only encountered two cases of anastomotic leakage with this technique. Moreover, an enlarged gland often has a broad base and wide vascular pedicle that requires additional time for vascular control. Although, our data does not demonstrate a statistically significant difference in operative time, we have noticed that large glands obscure and distort the neurological anatomy, making it technically challenging to manipulate the gland during neurovascular bundle preservation and prostatic apical dissection.

In our study, we evaluated our clinical outcomes with validated modified EPIC-26 questionnaires and found that there were no significant differences between the groups. Previous studies, reported that both continence and potency were depend on factors such as age, surgical technique used, and surgeon experience.^{24,25} As, discussed above in EP-RALP though large glands obscured and distorted the neurological anatomy, in our study we found that prostate size did not have a significant effect on return of baseline sexual and urinary function.

There are several limitations to our study. First, it is a single institutional study in a community hospital setting and may not be representative of outcomes at larger academic centers. Second, the number of

patients at the extreme PWs (less than 30 g and 80 g or larger) was small compared with the numbers in the other groups, limiting the power of the data analysis. Third, follow up time is relatively short, with a mean of 10.4 months, thus preventing meaningful assessment of biochemical failure and functional outcomes. Finally, our follow up method using validated questionnaires could have been subject to recall bias.

Conclusion

In conclusion, we report our experience with EP-RALP with respect to the impact of prostate weight on perioperative and pathological outcomes. EP-RALP in patients with an enlarged prostate appears feasible with comparable results in operative time, EBL, intraoperative, postoperative complications and hospital stay as compared with men with smaller glands. However, PSM rate and extracapsular extension were indirectly related to prostate volume, with higher rates of each seen in smaller prostates. Even though the surgery may pose technical challenges in patients with large prostate weights, experienced surgeons should not consider gland size this to be a contraindication for EP-RARP. □

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EDITORIAL COMMENT

The impact of prostate weight (PW) have been a topic of analysis for radical prostatectomy (open, laparoscopic and robotic approaches) for quite some time. Recently, Yong et al from Duke University, observed in a population of 523 RARPs, that larger prostates were associated with longer operative times (OT) and this effect was maintained independently of cumulative robotic experience (another independent factor in determining OT).¹ Moreover, other large robotic series, including the current series, have not observed such time-related outcomes.^{2,3} Possible explanations of the discordance

include the lack of overcoming the learning curve and other patient-related factors (degree of nerve sparing, performance of a pelvic lymph node dissection and pelvic anatomy).

Prostate weight however does appear to impact pathological outcomes in RARP series. Zorn et al previously published on a transperitoneal series of 375 RARP cases which were stratified by PW similar to the current study (<30, 30-50, 50-80 and >80 g). While age and PSA were significantly higher in larger prostates, no significant differences in OT, blood loss, transfusion rate, hospital stay, length of catheterization, anastomotic leakage or complications were observed.³ The objective return of baseline and subjective sexual and urinary function, as determined by validated questionnaire scores, was not affected by the PW. Pathologically, the overall rate of positive surgical margins (PSM) was significantly different among the groups ($p = 0.002$), demonstrating a trend of increasing PSM with a lower PW. Within the patients with stage pT2, a significant increase in PSM was found with lower PWs ($p = 0.026$).

In a follow up paper from the same institution, Msezane et al reported on the relationship of PW with PSM and extracapsular extension (ECE). In a series of 709 consecutive RARP cases (stratified by PW of <50, 50-70, >70 g), PW was observed to be an independent predictor in multivariate-logistic regression analysis, of both ECE (20%, 15% and 9%, $p = 0.01$) and PSM (25%, 14% and 7%, $p > 0.01$), respectively. The authors conclude that PW should be considered when counseling patients for RARP, especially when bilateral interfascial nerve preservation is desired.

The current authors further support this inverse relationship by demonstrating increased ECE ($p = 0.04$) and PSM ($p < 0.01$) rates in men with smaller PW. Similar perioperative outcomes (blood loss, hospital stay, complications) were also observed in this large extraperitoneal RARP series. This paper is meaningful insofar that it helps reaffirm the protective oncological impact of large prostate size. Being one of the largest extraperitoneal RARP series, the authors should be commended on their excellent oncological outcomes supporting that the extraperitoneal approach (often considered more difficult with a more restricted working space) can produce comparable outcomes to other large transperitoneal RARP series.

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Kevin C. Zorn, MD, FRCSC, FACS
Assistant Professor
Director of Robotic Surgery
University of Montreal
Montreal, Quebec Canada