Robot-Assisted Radical Prostatectomy in Patients with a Pathologic Prostate Specimen Weight ≥100 Grams versus ≤50 Grams: Surgical, Oncologic and Short-Term Functional Outcomes

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Introduction

Men diagnosed with localized prostate cancer (PCa) have various curative treatment options with the most popular of them being radical prostatectomy (RP), external beam radiotherapy and brachytherapy. For the ma-

Key Words
Prostate cancer • Robot-assisted laparoscopic radical prostatectomy • Large prostate glands • Oncologic outcomes • Functional outcomes

Abstract

Introduction: The objective of this study is to evaluate the surgical, oncological and short-term functional outcomes in patients with a pathologic prostate specimen weight ≥100 g versus patients with a pathologic prostate specimen weight ≤50 g undergoing robot-assisted radical prostatectomy (RARP). Patients and Methods: The records of 4,000 men who underwent RARP from February 2006 to April 2012 were reviewed retrospectively. A total of 185 men had a pathologic prostate specimen weight ≥100 g (group A). A matched pairs analysis was performed using our database to identify men with a pathologic prostate specimen weight ≤50 g but with equivalent clinicopathologic characteristics to serve as the control group (group B). Results: Our results indicated that although the intraoperative results were more than satisfying in patients with large glands, there is a significant increase in blood loss, operative time needed, increased need for bladder neck reconstruction as well as an increase in intraoperative complications. Nevertheless, patients with large glands exhibit less aggressive tumors, less positive surgical margins and a lower incidence of biochemical recurrence. Regarding functional outcomes, patients with larger glands had no difference regarding continence rates when compared to patients with smaller glands but exhibited significantly lower potency rates. Conclusions: Although RARP in patients with a pathologic prostate specimen weight ≥100 g is technically challenging, in experienced hands it can be considered a safe procedure with excellent surgical, oncological and functional outcomes. Nevertheless, this conclusion is limited, in that it is from a single institution with a large case volume and may not be reflective of outcomes at centers with smaller volumes and less experience.

Received: May 25, 2012
Accepted after revision: August 19, 2012
Published online: December 19, 2012

International Urologia

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jority of patients, the choice of treatment is based on personal preference of the patient or of the surgeon [1]. Nevertheless, some considerations such as age, preoperative urinary symptoms, stage and grade of PCA as well as size of the prostate may make one modality more suitable than another. Men with large glands are not ideal candidates for nonsurgical treatment modalities. External beam radiotherapy and brachytherapy are associated with urinary complications related to prostate size and thus are not recommended in this cohort of patients [2, 3]. However, prostate volume is an important consideration for surgery, particularly when patients have large glands. Surgery in such patients is challenging due to a reduced mobility in the pelvis, impaired visualization, limited working space as well as manipulation and rotation of the gland. Thus, these technical challenges result in greater blood loss, longer operative times, and inevitably, can translate into worse quality of life [4–7]. Although larger glands have been associated with lower grade and lower volume tumors, fewer positive surgical margins (PSM) and a lower likelihood of PSA relapse, in comparison with smaller glands [8, 9], whether prostate size has an impact on functional results is more controversial.

During the past years robot-assisted radical prostatectomy (RARP) has become profoundly popular among urologists for the treatment of localized PCA. Several studies suggest that the robotic approach may offer significant benefits in clinical outcomes, as well as a decrease in the number of major and minor complications [10–13]. The objective of this study is to evaluate the surgical, oncological and short-term functional outcomes in patients with a pathologic prostate specimen weight ≥100 g versus patients with a pathologic prostate specimen weight ≤50 g undergoing RARP and to evaluate if robotics may overcome the obstacles posed by larger prostates thereby broadening the treatment options for such patients.

Patients and Methods

The records of 4,000 men who underwent RARP from February 2006 to April 2012 were retrospectively reviewed. All perioperative and postoperative data were recorded prospectively in our database. A total of 185 men were identified as having a pathologic prostate specimen weight ≥100 g (group A). A matched pairs analysis was performed using our database to identify men with a pathologic prostate specimen weight ≤50 g but with equivalent clinicopathologic characteristics to serve as the control group (group B). None of the patients of both groups were diagnosed after transurethral prostate resection or prostatectomy and none had received neoadjuvant radiation or hormonal treatment. The matching criteria used to select patients were age, BMI, clinical stage, prostate-specific antigen (PSA) and biopsy Gleason score. RARP was performed by 5 experienced RARP surgeons using the Standard System, S System and Si System da Vinci® Robotic 4-Arm System (Intuitive Surgical, Sunnyvale, Calif., USA) via a transperitoneal approach reported previously by our group [14]. Pelvic lymph node dissection was avoided in patients with a low risk PCA. Bilateral intrafacial neurovascular bundle (NVB) preservation was attempted in patients with a PSA level <10 ng/ml and/or Gleason score <7 and/or in cases of only one positive core biopsy of Gleason 7 and/or in clinical T1c-T2a tumors.

Abnormal features that were intraoperatively encountered in the group A cohort of patients were a result of reduced mobility in the pelvis, impaired visualization, limited working space as well as manipulation and rotation of the gland. We noticed that RARP is challenging in large prostates firstly at the time of bladder neck division, since an enlarged prostate often has an associated median lobe. This feature often leads to an enlarged bladder neck opening, which then requires more time in the reconstructive phase with the vesicourethral anastomosis. Furthermore, a large prostate often has a broad base, a wide vascular pedicle and difficulty in the preparation of the dorsal prostatic fascia is also evident. During dissection of the vascular pedicle additional time must be taken to avoid a PSM in this area, adequately control bleeding and care should be taken not to injure the rectum. Additionally, due to difficult mobilization of the prostate in the pelvis, during cases of intrafacial NVB preservation, a large prostate does not provide adequate exposure for dissection, especially at the prostatic apex.

The parameters analyzed and compared between the two groups included patient preoperative clinicopathologic characteristics (age, BMI, prostate size in transrectal ultrasound (TRUS), PSA values, clinical stage, Gleason Score at biopsy, and preoperative functional status), intraoperative characteristics (bilateral intrafacial NVB preservation, estimated blood loss, bladder neck reconstruction, skin-to-skin operative time and intraoperative complications), postoperative oncologic characteristics (tumor volume, Gleason score, pathologic stage, PSA and lymph node status), postoperative characteristics (hospital stay, minor and major complications, length of catheterization and pathologic prostate specimen weight), functional characteristics (continence and potency), biochemical recurrence (BCR) and disease-specific mortality at the follow-up period. Postoperative complications and re-interventions encountered up to 30 days postoperatively stratified by the Clavien classification [15] and were characterized as minor (Clavien grade I–IIa) and major postoperative complications (Clavien grade IIb–IVa). Hemorrhage was defined as greater than 500 ml blood loss during the operation. PMS was defined as tumor at the inked surface of the specimen. All patients underwent cystography at postoperative day 4. The catheter was then removed if no extravasation was recorded. If extravasation was present, the catheter was left in place for 7 additional days. Functional results regarding urinary continence were evaluated prospectively prior to surgery, at day 1 after catheter removal, and 3, 6 and 12 months after surgery. Complete urinary continence was defined as no pad use and/or no urinary leakage. Requirement for 1–2 pads daily was considered as mild incontinence and >2 pads daily as incontinence. Functional results regarding potency were also evaluated prospectively prior to the procedure, 3, 6 and 12 months after surgery. Postoperative functional results
Regarding potency were only restricted in patients who had undergone a bilateral infracorporeal NVB preservation and who did not exhibit preoperatively any form of erectile dysfunction. Potency after RARP was defined as erections sufficient for penetration with or without phosphodiesterase inhibitors. Preoperative potency was evaluated with the five-item version of the International Index of Erectile Function (IIEF-5) [16]. The possible scores for the IIEF-5 ranged from 1 to 25, and a score above 21 was considered as normal erectile function and at or below this cut-off, erectile dysfunction. According to this scale, it was classified into four categories based on IIEF-5 scores: severe (1–7), moderate (8–11), mild to moderate (12–16), mild (17–21), and no dysfunction (22–25). Patients with a severe dysfunction were considered impotent.

BCR was defined as PSA \( \leq 0.2 \) ng/ml after nadir or never reached nadir. The median postoperative follow-up of the patients was 23.6 months (range 3–48 months) for group A patients and 21.6 months (range 3–60 months) for group B patients.

For comparison between 2 groups of continuous values Student’s t test was used. For comparison between 3 or more groups the one-way ANOVA with the Tukey correction for multiple comparisons was used. For comparison of binomial values, the \( \chi^2 \) test was used. Simple linear regression was used to test the effect of one continuous parameter against another. \( p < 0.05 \) was considered significant.

### Results

Regarding preoperative clinicopathologic characteristics when comparing group A to group B, the prostate size in TRUS was 65–170 ml (median 98.1 ml) versus 14–62 ml (median 31.1 ml) (\( p < 0.001 \)). The median age of the patients was 67.1 years old (46–77 years) versus 63.4 years old (43–79 years) and median BMI 27.5 (18–47) versus 27.1 (21–38). The preoperative PSA was 1.5–68 (median 12.7 ng/ml) versus 1.7–67 ng/ml (median 11.4 ng/ml). The Gleason biopsy score was Gleason \( \leq 7 \) in 122 (65.9%) versus 118 (63.7%) patients, Gleason 7 in 48 (25.9%) versus 48 (25.9%) patients and Gleason >7 in 15 (8.1%) versus 19 (10.2%) patients. The clinical stage was T1c for 127 (68.7%) versus 124 (67.2%) patients, T2a for 30 (16.2%) versus 28 (15.1%) patients, T2b for 4 (7.5%) versus 18 (9.7%) patients, T2c for 13 (7.1%) versus 14 (7.5%) patients and T3a for 1 (0.5%) versus 1 case (0.5%) (table 1).

Regarding preoperative functional status when comparing group A to group B, all patients from both groups were continent, 70 (37.9%) versus 54 patients (29.2%) (\( p < 0.05 \)) exhibited severe erectile dysfunction, 21 (11.3%) versus 18 patients (9.7%) had moderate erectile dysfunction, 11 (5.8%) versus 15 (8.1%) patients had mild-to-moderate erectile dysfunction, 25 (13.5%) versus 25 (13.5%) patients had mild erectile dysfunction and 58 (31.3%) versus 73 (39.5%) patients (\( p < 0.05 \)) did not exhibit erectile dysfunction (table 1).

Regarding intraoperative characteristics when comparing group A to group B, bilateral infravaginal NVB preservation was performed in 42 (22.7%) versus 48 (25.9%) patients, the median estimated blood loss was 192 (50–1,200 ml) versus 152 ml (50–1,100 ml) (\( p < 0.05 \)), a bladder neck reconstruction was performed in 52

| Table 1. Patient preoperative clinicopathologic and intraoperative characteristics |
|---------------------------------|-----------------|-----------------|-----------------|
| Age, years                      | 67.1 (46–77)    | 63.4 (43–79)    | \( p \)          |
| PSA, ng/ml                      | 12.7 (1.5–68)   | 11.4 (1.7–67)   | \( p \)          |
| Prostate size, ml               | 98.1 (65–170)   | 31.1 (14–62)    | \( <0.001 \)     |
| BMI, kg/m²                      | 27.5 (18–47)    | 27.1 (21–38)    | \( p \)          |
| Gleason score, %                |                 |                 |                 |
| \( <7 \)                        | 65.9            | 63.7            | \( p \)          |
| \( =7 \)                        | 25.9            | 25.9            | \( p \)          |
| \( >7 \)                        | 8.1             | 10.2            | \( p \)          |
| Clinical stage, %               |                 |                 |                 |
| Organ-confined disease          | 99.5            | 99.5            | \( p \)          |
| Extraprostatic extension        | 0.5             | 0.5             | \( p \)          |
| Continence, %                   | 100             | 100             | \( p \)          |
| No erectile dysfunction, %      | 31.3            | 39.5            | \( <0.05 \)      |
| Bilateral NVB preservation, %   | 22.7            | 25.5            | \( p \)          |
| Blood loss, ml                  | 192 (50–1,200)  | 152 (50–1,100)  | \( <0.05 \)      |
| Bladder neck reconstruction, %  | 28.1            | 5.9             | \( <0.001 \)     |
| Operative time, min             | 164 (90–320)    | 144 (80–300)    | \( <0.05 \)      |
| Intraoperative complications, % | 4.8             | 1.6             | \( <0.05 \)      |
(28.1%) versus 11 cases (5.9%) (p <0.001) and the median operative time was 164 (90–320 min) versus 144 min (80–300 min) (p <0.05). Intraoperative complications were encountered in 9 patients (4.8%), 7 hemorrhage and 2 large intestine injury versus 3 patients (1.6%) (p <0.05), and 2 hemorrhage and 1 small intestine injury (table 1).

Regarding postoperative oncologic characteristics when comparing group A to group B, the median tumor volume was 9.5% (0–66%) versus 17.1% (0.29–94%) (p <0.05). A Gleason <7 pattern was evident in 90 (48.7%) versus 76 cases (41.1%) (p <0.05), a Gleason 7 in was evident in 63 (34.1%) versus 80 (43.3%) cases (p <0.05) and a Gleason >7 in 28 (15.1%) versus 29 (15.6%) cases. The pathologic stage was T0 for 4 (2.1%) versus 0 patients (0%) (p <0.05), T2 for 136 (73.5%) versus 129 patients (69.7%), T3 for 45 (24.4%) versus 49 (26.5%) patients and T4 for 0 (0%) versus 7 (3.8%) patients (p <0.05). PSM were encountered in 9 (4.8%) versus 20 (10.8%) patients (p <0.05). Lymph nodes were removed in 137 (74.1%) versus 148 (80%) patients of whom 8 (4.3%) versus 9 patients (4.8%) exhibited lymph node metastatic disease (table 2).

Regarding postoperative characteristics when comparing group A to group B, hospital stay was 6–21 (median 7.1 days) versus 6–12 days (median 6.3), the median catheterization period was 5.9 (5–31 days) versus 5.4 days (5–28 days) and the pathologic prostate specimen weight was 100–204 g (median 125.7 g) versus 20–50 g (median 40.5 g) (p <0.001). Minor postoperative complications were encountered in 35 (18.9%) versus 26 (14.1%) cases and major in 6 (3.2%) versus 6 (3.2%) cases (table 2). Regarding minor postoperative complications in the group A cohort of patients, 12 exhibited a symptomatic urinary tract infection which was treated with antibiotics and 9 patients exhibited an extravasation at cystography which was treated by leaving the catheter in place for an additional day at which point point urine could be performed without further problems and the remaining 9 patients exhibited minor complications such as skin emphysema, scrotal edema, perivesical hematoma and constipation. Regarding major postoperative complications in the group A cohort of patients, all 6 patients had undergone a laparoscopic re-intervention due to hematoma.

Regarding minor postoperative complications in the group B cohort of patients, 7 exhibited a symptomatic urinary tract infection which was treated with antibiotics and 8 patients exhibited an extravasation at cystography which was treated by leaving the catheter in place for 1 additional day at which point urination could be performed without further problems and the remaining 8 exhibited minor complications such as skin emphysema, scrotal edema,
perivesical hematoma and constipation. Regarding major postoperative complications in the group B cohort of patients, 3 patients had undergone a laparoscopic re-intervention due to hematoma and 3 due to peritonitis secondary to small intestine injury.

Regarding continence status when comparing group A to group B, at day 1 after catheter removal, 37.2 versus 36.2% were continent, and 51.8 versus 57.2% and 10.8 versus 6.6% were incontinent. In 3 months, the pattern of continence changed; 50.9 versus 52.6% were continent, 37.9 versus 39.7% exhibited mild incontinence and 11.2 versus 7.7% were incontinent. In 6 months, there was further improvement with 63.3 versus 66.6% of patients being continent, 30.6 versus 32.1% exhibiting mild incontinence and 6.1 versus 1.3% (p < 0.05) remaining incontinent. In 12 months, 75.1 versus 76.8% of patients were continent, 23.3 versus 22.4% exhibited mild incontinence and 1.6 versus 0.8% remained incontinent (table 2).

As previously mentioned, postoperative functional results regarding potency were only restricted in patients who had undergone a bilateral intrafacial NVB preservation and who did not exhibit any form of erectile dysfunction preoperatively. According to these criteria, group A involved 34 patients and group B 38 patients. When comparing group A to group B, in 3 months 0 versus 10.5% of patients were no longer impotent (p < 0.001), 19.1 versus 33.3% were no longer impotent in 6 months (p < 0.05) and 61.9 versus 72.9% were no longer impotent in 12 months (p < 0.05) (table 2).

Regarding BCR, in group A and after a median follow-up of 23.6 months (range 3–48 months) 8% of the patients exhibited progression. In group B and after a median follow-up of 21.6 months (range 3–60 months) 13.1% of patients (p < 0.05) exhibited disease progression. No disease-specific mortality was evident during the follow-up period in both groups (table 2).

**Discussion**

During the past years, the average prostate size of PCa patients has increased and according to findings 25% of men who undergoing RP have a prostate size >60 g and more than 10% have a prostate size >80 g [17]. As more experience is gained with robotic techniques, surgeons have expanded its application to more technically challenging procedures such as in large prostates. Traditionally, with the conventional retropubic RP, larger prostate sizes have been associated with longer operative times and greater blood loss, suggesting a higher degree of technical difficulty [4–7]. Recent literature on this topic has demonstrated that stereoscopic visualization, magnification and the pressure exerted by the pneumoperitoneum during RARP are associated with less blood loss, better nerve sparing and better functional outcomes in comparison to open RP [18–21].

Link et al. [22] evaluated whether prostate weight has an impact on the pathological and operative outcomes of RARP. They reviewed the records of 1,847 patients and divided patients into four groups: group 1 <30 g, group 2 30–49.9 g, group 3 50–69.9 g and group 4 ≥70 g. Their results showed that patients with a larger prostate were older, had higher preoperative PSA values, lower Gleason score, longer operative times, higher blood loss and longer hospital stay. One-year continence rates and BCR rates were similar across all groups.

Boczko et al. [23] examined the effects of prostate size on treatment outcomes after extraperitoneal RARP. They evaluated 355 patients who underwent RARP and compared patients with prostate weight <75 g (n = 319) with those having glands ≥75 g (n = 36). A statistically significant difference was noted in age, PSA concentration and blood loss between patients with smaller versus larger prostates. No difference was seen in Gleason score, clinical T stage, operative time, or total PSM rates. The 6-month continence rate in patients with a prostate volume <75 g was 97 versus 84% in patients with larger prostate volumes.

Skolarus et al. [24] examined the relationships between large prostate size and RARP outcomes with respect to intraoperative and pathologic factors. The categorized prostate size into 3 groups (<50, 50–100 and >100 g) and compared surgical and quality of life outcomes among groups. Their results showed that patients with the largest prostates had longer operative times and more blood loss. Conversely, these patients had fewer positive surgical margins and lower Gleason sums. Despite worse baseline irritative symptoms and sexual function these differences resolved at 3 months. Recovery of continence was relatively sluggish compared with that in patients with the smallest prostates.

Chan et al. [25] evaluated the outcomes based on gland size between RARP and open RP. They reviewed 660 patients who had RARP and 340 who had open RP. The patients were divided into two groups with prostate weights of >75 and ≤75 g. Patients with large prostates were significantly older, but had a lower pathological stage than patients with small glands, regardless of technique. There was no difference in length of stay or transfusion rates between the groups. A large prostate increased the opera-
tive time of RARP but not of open RP. For both RARP and open RP, PSM rates were lower with larger glands. Overall, the PSM rates were lower with RARP than open RP among patients with larger or smaller glands, respectively.

Zorn et al. [26] examined the effect of prostate weight on RARP outcomes by evaluating 375 men. The patients were divided into four groups: group 1 >30 g, group 2 30–50 g, group 3 50–80 g and group 4 ≥80 g. Their results showed that a significant difference was found in age and PSA values among the four groups. No significant differences in operative time, estimated blood loss, transfusion rate, hospital stay, length of catheterization, and complication incidence were observed among the four groups. The overall rate of PSM was significantly different among the groups, demonstrating a trend of increasing PSM with a lower prostate weight. The objective return of baseline and subjective sexual and urinary function was not affected by the prostate weight.

Levinson et al. [27] assessed the effects of prostate size on long-term health-related quality of life and functional outcomes after laparoscopic RP by evaluating 729 patients. The patients were stratified by pathological prostate gland weight into three groups: group 1 >35 g, group 2 35–70 g and group 3 >70 g. Despite preoperative differences and possible confounders, all groups approached similar urinary health-related quality of life outcomes at all time points postoperatively. At 12 months, patients with the largest glands had improved Expanded Prostate Cancer Index Composite urinary irritative/obstructive and urinary bother subscale scores compared to their baseline scores. They concluded that in laparoscopic RP despite preoperative differences increasing prostatic size is not associated with delayed or worse postoperative urinary health-related quality of life.

Regarding preoperative clinicopathologic characteristics, we could not draw any conclusions regarding BMI, clinical stage, PSA values and biopsy Gleason score as this was a matched pairs analysis and the values were used as matching criteria. An interesting finding that our group noticed is that patients with a pathologic prostate specimen weight ≥100 g exhibited higher preoperative rates of erectile dysfunction when compared to patients with smaller prostates. Unfortunately, this finding is not supported by the literature and cannot be explained from our group.

Regarding intraoperative characteristics, there are indeed technical difficulties when performing RARP in this cohort of patients. These are a result of reduced mobility in the pelvis, impaired visualization, limited working space as well as manipulation and rotation of the gland, which makes RARP in this patients challenging even for experienced RARP surgeons. Our results indicated that although the intraoperative results were more than satisfying in patients with large glands, there is a significant increase in blood loss, operative time needed, increased need for bladder neck reconstruction as well as an increase of intraoperative complications.

Regarding postoperative oncologic characteristics, patients with large glands, indeed exhibit less aggressive tumors, less PSMs and a lower incidence of BCR.

Regarding functional outcomes, patients with larger glands had no difference regarding continence rates when compared to patients with smaller glands but exhibited significantly lower potency rates.

Although this study represents the largest series of patients with a pathologic prostate specimen weight ≥100 g who underwent RARP, there are some severe limitations to be addressed. The first limitation is that these results come from a single institution with a large case volume and experienced surgeons and may not be reflective of outcomes at centers with smaller volumes and less experience. The second limitation is that median postoperative follow-up of the patients was low so the long-term functional and oncological results cannot be evaluated. And finally, the third limitation is that as stated, patients with a pathologic prostate specimen weight ≥100 g exhibited higher preoperative rates of erectile dysfunction when compared to patients with smaller prostates so this could have influenced the functional outcomes regarding potency rates in this study.

Conclusions

Although RARP in patients with a pathologic prostate specimen weight of ≥100 g is a technically challenging procedure due to reduced mobility in the pelvis, impaired visualization, limited working space as well as manipulation and rotation of the gland, in experienced hands it can be considered a safe procedure with excellent surgical, oncological and functional outcomes. Nevertheless, this conclusion is limited, in that it is from a single institution with a large case volume and may not be reflective of outcomes at centers with smaller volumes and less experience. We propose that these patients should be operated only by experienced RARP surgeons.
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