Impact of Prostate Weight on Radical Prostatectomy Outcomes

Raanan Tal MD[1], Myriam Konichezky MD[2] and Jack Baniel MD[1]

Departments of [1]Urology and [2]Pathology, Assuta Medical Center, Tel Aviv, Israel

ABSTRACT: **Background:** The management of localized prostate cancer in patients with large prostates is controversial.

Objectives: To investigate the impact of prostate weight on radical prostatectomy outcomes.

Methods: The files of 244 patients who underwent radical prostatectomy were reviewed. Data were collected on patient and tumor characteristics and on oncological, urinary and erectile function outcomes. Results were compared between patients with prostates weighing ≤ 60 g or > 60 g.

Results: A prostate weight of › 60 g was documented in 25% of the patients. There was no difference in clinical stage distribution between patients with smaller and patients with larger prostates. Patients with a larger prostate were characterized preoperatively by higher levels of prostate-specific antigen (9.8 vs. 7.3 ng/ml, $P = 0.009$), lower tumor grade (biopsy Gleason score ≤ 6: 77.6% vs. 90.2% $P = 0.04$), and a higher incidence of moderate-severe urinary symptoms (69.8 vs. 38.8%, $P = 0.0003$). Analysis of pathological stage distribution yielded a higher proportion of lower stage disease and a lower incidence of positive margins in the large-prostate group (11.7 vs. 25.8%, $P = 0.024$). There were no statistically significant between-group differences in the rate of persistent postoperative detectable PSA, biochemical recurrence, urinary incontinence and erectile function.

Conclusions: The outcomes of radical prostatectomy in patients with large prostate are favorable in terms of cancer characteristics despite their higher preoperative PSA levels, and comparable to that in patients with small prostate in terms of urinary continence and erectile function. Surgery may be particularly beneficial in patients with preoperative urinary symptoms. Hence, radical prostatectomy should not be discouraged as a treatment for localized prostate cancer in patients with sizeable prostates.

IMAJ 2009;11:354–358

KEY WORDS: prostate cancer, treatment, radical prostatectomy, prostate weight, outcomes

Men diagnosed with localized prostate cancer have various curative treatment options. The selection of a specific treatment modality depends on patient and tumor characteristics as well as on patient and surgeon preferences [1]. In addition to other parameters, prostate gland size has been suggested as a factor that needs to be considered when making treatment decisions; however, evidence in the literature on the role of prostate size in treatment selection is scarce and even contradictory. Open radical prostatectomy in patients with a large prostate has been shown to be associated with increasing intraoperative blood loss, a higher risk of perioperative complications, and surgical complexity [2-4]. Moreover, identification of the neurovascular bundles, displaced by a large prostate, and excessive bleeding from paraprostatic vascular plexus may make preservation of erectile function particularly challenging [5]. Despite these anatomical considerations, radical prostatectomy can be performed in men with large prostates by open, laparoscopic or robot-assisted approaches with favorable results [6-8]. Men with sizeable prostates are not ideal candidates for non-surgical treatment modalities either. External beam radiotherapy carries genitourinary toxicity and may impose an additional insult on urinary function in men with large prostates and coexisting lower urinary tract symptoms. Brachytherapy for prostate cancer is also associated with urinary complications related to prostate size and currently is not recommended for men with large prostates [9,10]. Unfortunately, the proportion of men with larger prostates seeking treatment for prostate cancer has increased in the era of prostate-specific antigen as these men have higher PSA levels and are more likely to undergo prostate biopsies and to be diagnosed with early-stage localized prostate cancer [11]. Some patients with large prostates may even present with urinary retention and an indwelling urinary catheter, needing a dual solution to both cure their cancer and treat their obstructed lower urinary tract.

This study presents a detailed and comprehensive analysis of the impact of prostate size on various radical prostatectomy outcomes, including cancer control, urinary continence and erectile function, adding to the body of evidence already existing in the literature and aiding in treatment decision making in men with prostate cancer and large prostate glands.

PSA = prostate-specific antigen

PATIENTS AND METHODS

We reviewed a contemporary series of consecutive patients who underwent open radical prostatectomy for localized prostate cancer in the period 2004–2005. Preoperatively, patients were asked whether they have LUTS and to rank the impact of these symptoms on their everyday life as mild, moderate, or severe. Intact preoperative sexual function was defined as being sexually active without the use of erectile function-related therapies. PSA values, detailed prostate biopsies data and clinical stage were recorded. All patients underwent radical prostatectomy by a single surgeon (J.B.) and bilateral nerve sparing was attempted in all preoperatively fully potent sexually active men with biopsy Gleason score of ≤ 7, as described by Walsh et al. [12]. All surgical specimens were examined by a single pathologist (M.K.) for tumor grade and extension. Outcomes, including oncology results, urinary continence and erectile function were collected. A PSA value of 0.2 ng/ml and rising in patients with a postoperative undetectable PSA was defined as a biochemical failure. The number of elapsed days from catheter removal to achievement of urinary continence (no pad or need of one slim pad daily) served as an endpoint of urinary function quality. Postoperative erectile function was assessed by questioning patients whether they have no erection, some erection not sufficient for penetration, erection not fully rigid but sufficient for penetration without or without phosphodiesterase 5 inhibitors, or a fully rigid erection. Though the Erection Hardness Score was not used, the definitions of "some erection not sufficient for penetration," "erection not fully rigid but sufficient for penetration," and "a fully rigid erection" correspond to EHS of 1-2, 3 and 4, respectively [13].

The study population was subclassified by prostate weight (surgical specimen weight) into two groups, ≤ 60 g and > 60 g (prostate weight was used as a proxy for prostate volume), and outcomes were compared to detect unique considerations that pertain to radical prostatectomy in patients with large prostates. A weight cutoff point of 60 g was selected, since prostate weight of 60 g is the upper weight limit for brachytherapy and radical prostatectomy for prostate > 60 g is surgically more challenging, as judged by the surgeon (J.B.). To confirm that the results were not biased by the selection of a weight of 60 g as a cutoff point, we repeated the analysis with a cutoff point of 80 g.

STATISTICAL ANALYSIS

Statistical analysis was performed with commercially available statistical software (SPSS 15.0 for Windows). Patient and tumor characteristics were analyzed with descriptive statistical methods. Group comparison was performed with Student's *t*-test for continuous variables and with chi-square test for categorical variables. A *P* value of < 0.05 was considered statistically significant.

RESULTS

The study group comprised 244 patients who had undergone radical prostatectomy for clinically localized prostate cancer and had preoperative and follow-up data. The study population was subdivided into two groups according to prostate weight: group 1 consisting of men with prostate weight ≤ 60 g and group 2 with prostate weight > 6 0g. Patients' characteristics and treatment outcomes, with comparison by prostate weight, are depicted in Table 1. Men with large prostates weighing > 60 g were not uncommon, and their relative share was 25% (61/244) of the study group. The median age in group 2 was slightly higher; however, mean age did not differ significantly (61.1 vs. 62.8 years, $P > 0.05$). Patients in group 2 reported statistically significant greater urinary bother with 70% of subjects ranking the impact on their everyday lives as moderate to severe. One subject in each group had an indwelling catheter prior to the operation, due to urinary retention. Regarding preoperative prostate cancer characteristics, the two groups did not differ in clinical stage distribution; however, patients in group 2 had significantly higher preoperative PSA values (9.8 vs. 7.3 ng/ml, $P = 0.009$), they were more likely to have low grade cancer (90.2 vs. 77.6% had Gleason score ≤ 6, $P = 0.04$) and had fewer cores involved (24.3 vs. 37.6% involved cores/cores taken, $P = 0.0003$) compared with patients in group 1. Subjects in group 2 tended to undergo more biopsy sessions to establish cancer diagnosis, but this difference did not reach statistical significance.

Postoperative pathological analysis of the surgical specimen revealed that men in group 2 were more likely to have lower stage disease (36% T2a-b vs. 19.8% in group 1, $P = 0.031$) and negative surgical margins (88.3 vs. 74.2%, $P = 0.024$); however, the difference in incidence of extra-capsular tumor extension and in Gleason score distribution did not reach statistical significance. Despite the relatively favorable pathological features of tumors in group 2, there was no statistically significant difference in percentage of patients with detectable PSA postoperatively (11.1 vs. 11.4%, $P > 0.05$) or in the incidence of biochemical failure after a median follow-up of 21 months (range 9–33, interquartile range: 14–27). Urinary continence, represented by the mean required time interval to achieve continence, was 15.6 days (standard deviation 19.0, confidence interval 13.1–18.1) for the whole study group. Of the preoperatively fully potent patients, erection hardness sufficient for penetration without PDE5-I use (EHS 3-4) was

LUTS = lower urinary tract symptoms
EHS = Erection Hardness Score

PDE5-I = phosphodiesterase 5 inhibitors

Table 1. Patients' characteristics and outcomes: comparison by prostate weight

	Prostate weight ≤ 60 g	Prostate weight > 60 g	*P* value
N	183 (75%)	61 (25%)	
Median age (yrs, range, IQ range)	61 (47–73, 56–67)	63 (51–72, 58–67)	
Bothersome LUTS (preoperative)			0.0003
No	60 (37.5%)	6 (11.3%)	
Mild	37 (23.1%)	9 (17.0%)	
Moderate	35 (21.9%)	15 (28.3%)	
Severe	27 (16.9%)	22 (41.5%)	
Indwelling catheter	1 (0.6%)	1 (1.9%)	
Mean preoperative PSA, ng/ml (SD, CI)	7.3 (5.0, 6.6–8.1)	9.8 (6.5, 8.1–11.5)	0.009
Clinical stage			> 0.05
T1c	169 (97.7%)	57 (96.6%)	
T2a-b-c	4 (2.3%)	2 (3.4%)	
No. of prostate biopsy sessions required for cancer diagnosis			> 0.05
1	160 (90.9%)	51 (83.6%)	
2	12 (6.8%)	5 (8.2%)	
3	3 (1.7%)	2 (3.3%)	
4	1 (0.6%)	2 (3.3%)	
7	0	1 (1.6%)	
Biopsy Gleason score			0.04
4	0	1 (1.6%)	
5	1 (0.6%)	2 (3.3%)	
6	137 (77%)	52 (85.2%)	
7	38 (21.3%)	6 (9.8%)	
8	2 (1.1%)	0	
% cores involved (CI) (Cores involved/cores taken)	37.6 (33.8–41.3)	24.3 (18.8–29.7)	0.0003
Neurovascular bundle preservation			> 0.05
No	26 (14.7%)	14 (23.3%)	
Unilateral	38 (21.5%)	10 (16.7%)	
Bilateral	113 (63.8%)	36 (60.0%)	
Pathological stage			0.031
No tumor/PIN	1 (0.6%)	2 (3.3%)	
T2a	28 (17.3%)	21 (34.4%)	
T2b	4 (2.5%)	1 (1.6%)	
T2c	121 (74.7%)	36 (59.0%)	
T3a	2 (1.2%)	1 (1.6%)	
T3c	6 (3.7%)	0	
Margins status			0.024
Negative	121 (74.2%)	53 (88.3%)	
Positive	42 (25.8%)	7 (11.7%)	
Specimen Gleason score			> 0.05
6	132 (78.6%)	47 (82.5%)	
7	28 (16.7%)	9 (15.8%)	
8	8 (4.8%)	1 (1.8%)	
Postoperative detectable PSA	20 (11.4%)	6 (11.1%)	> 0.05
Biochemical failure	0 (0%)	0 (0%)	N/A
Mean interval to achieve continence (days, SD, CI)	14.4 (18.6, 11.6–17.2)	19.2 (20.2, 13.7–24.7)	> 0.05
Erectile hardness			> 0.05
No erection	3 (4.1%)	1 (6.3%)	
Not sufficient for penetration (EHS 1-2)	12 (16.2%)	0 (0.0%)	
Not fully rigid, but sufficient for penetration (EHS 3)	28 (37.8%)	8 (50.0%)	
Full rigidity (EHS 4)	16 (21.6%)	2 (12.5%)	
Sufficient for penetration (EHS 3-4) with PDE5-I	15 (20.3%)	5 (31.3%)	

CI = confidence interval, PIN = prostatic intraepithelial neoplasia.

achieved in approximately 60.0%; 13.3% had some erectile response not sufficient for penetration (EHS 1-2), 22.2% had functional erection with PDE5-I, and 4.4% had no erectile activity. We did not find statistically significant differences in urinary continence quality or in erectile function between the two groups [Table 1].

We repeated the analysis for a weight cutoff point of 80 g (≤ 80 in group 1, > 80 in group 2) and found similar trends, even more pronounced: 11.5% of the men (28/244) had prostates weighing over 80 g. Mean age in both groups did not differ significantly (61.4 vs. 62.9 years, $P > 0.05$). Patients in group 2 had a statistically significant greater incidence of moderate to severe LUTS (82.8 vs. 42.1%, $P < 0.001$). The groups did not differ in clinical stage distribution; however, patients in group 2 had significantly higher preoperative PSA values (11.6 vs. 7.5 ng/ml, $P = 0.008$) and were more likely to have low grade cancer on biopsy (92.9 vs. 79.2% had Gleason score ≤ 6, $P = 0.021$). More subjects in group 2 had at least one biopsy to establish cancer diagnosis (21.4% vs. 9.6%), and unlike the case for a cutoff weight of 60 g, here the difference was statistically significant ($P < 0.001$).

Postoperatively, pathological stage in group 2 was lower (46.4% T2a-b vs. 21.1% in group 1, $P = 0.017$) and negative surgical margins rate was higher (96.4 vs. 75.4%, $P = 0.012$). As for a cutoff point of 60 g, the difference in incidence of extra-capsular tumor extension, pathological Gleason score distribution, postoperative PSA > 0, and biochemical recurrence did not reach statistical significance. Urinary continence, represented by the mean required time interval to achieve continence, was not statistically different for the two groups (14.8 vs. 22.4 days for groups 1 and 2, respectively, $P > 0.05$), nor were the potency results.

DISCUSSION

The characteristics of prostate cancer have changed over the last decades with the introduction of PSA testing. Patients with localized disease are diagnosed at a younger age and are good candidates for curative treatments. Prostate size, though determined mainly by the benign hyperplastic component, may have an impact on prostate cancer detection: patients with larger glands have higher PSA levels, and they are more likely to undergo prostate biopsies and to be diagnosed with prostate cancer. Thus, the average prostate size of prostate cancer patients has increased in the PSA era, and according to our findings 25% of men undergoing radical prostatectomy have a prostate > 60 g and more than 10% have prostate > 80 g [11]. Prostate size impacts not only detection, but also treatment decisions. A sizeable gland is not consid-

ered an advantage for any of the available local treatment modalities. External beam radiotherapy is not desirable since irradiation-related urinary toxicity may worsen preexisting LUTS associated with a large obstructing prostate gland and adversely affect quality of life. Brachytherapy is currently recommended for patients with prostates not larger than 50–60 cm^3 because larger prostates are associated with technical difficulties in seed implantation, increased urinary morbidity and higher incidence of urinary retention [10,14]. Open radical prostatectomy may be technically more challenging in men with large prostates and the neurovascular bundle may be displaced and difficult to dissect. This surgical complexity may be translated to increased blood loss and/or intra- or perioperative complications [2-5]. Laparoscopic and robot-assisted radical prostatectomy have also been shown to be feasible in men with large prostates, with encouraging results, despite the technical issues associated with prostate size [7,8,15,16]. To answer the question whether prostate size should hinder us from prostate cancer surgery we must consider the long-term outcomes of surgery in terms of cancer control, urinary function and erectile function. With regard to cancer control, D'Amico and collaborators [17] found that patients with larger prostates have significantly more favorable pathological features at radical prostatectomy (pathological stage T2, 85%; Gleason score ≤ 6, 78%; negative margins, 95%) and improved PSA failure-free survival (100% at 4 years), despite higher preoperative PSA values. Foley et al. [6] reported that tumors within larger prostates were of a lower stage, lower Gleason grade, of smaller volume and more often "clinically insignificant"; however, they found no difference in the incidence of positive surgical margins. Our results confirm previous findings of favorable oncological characteristics in patients with larger prostates. Despite higher PSA levels, larger prostates have significantly lower biopsy Gleason scores, fewer positive biopsy tissue cores, lower stage and lower incidence of positive margins. There were no cases of biochemical recurrence in either of our groups, probably due to a relatively short follow-up, and we found no difference in the incidence of cases in which PSA remained detectable after radical prostatectomy, implying extra-prostatic disease at the time of diagnosis. To account for differences in tumor features we assume that PSA, secreted by the cancer cells as well as by the benign hyperplastic component, probably indicates biopsy at an earlier stage of tumor growth, which is translated into a better oncological long-term outcome of radical prostatectomy. Preoperative high PSA in patients with large prostates may represent the benign component rather than be associated with high grade or advanced prostate cancer. Besides the oncological outcome, patients with large prostates, especially with coexisting LUTS, benefit from radical prostatectomy in terms of bothersome urinary symptoms. Kumar et al. [18] studied the impact of radical prostatectomy on LUTS and symptom-associated quality of life and found that men with moderate to severe LUTS before surgery had significant improvement in total International Prostatic Symptom Score, symptom-associated quality of life, mean peak flow rate and post-void residual volume. In the present series, about 70% of men with large prostates had moderate-to-severe LUTS, most of them managed by alpha-blockers, a significantly greater incidence compared to only about 40% of men with small prostates, and one patient in each group had an indwelling catheter preoperatively. Hence, in patients with large prostates the existence of moderate-to-severe LUTS and adverse impact on quality of life should argue for surgical treatment of their prostate cancer. After radical prostatectomy, LUTS secondary to urinary incontinence may still occur and be bothersome. The present study used the time interval to achieve continence as an endpoint of continence quality. Patients with larger prostates needed slightly longer time to achieve continence, but as found by Foley et al. [6], the difference in urinary continence was not statistically significant between the two groups. Erectile function quality after radical prostatectomy, a significant treatment outcome for sexually active men, was also not associated with prostate size, according to the findings of both the present study and that of Foley et al. [6].

Our study is not without drawbacks. Although we presented detailed pathological results and a favorable pathological outcome in men with large prostates and although our results were consistent for two different prostate weight cutoff points, a true disease-specific survival benefit of radical prostatectomy for men with large prostates may be demonstrated only after a longer follow-up. Another disadvantage of the present study was the lack of data on the duration of surgery, estimated blood loss, transfusion rate and early complications, as the focus of the present study was on long-term outcomes. In a review published in this journal in 2005 by Stav et al. [19], prostate size > 50 g was considered a risk factor for intraoperative bleeding, and bleeding was suggested to be associated with adverse long-term outcome. However, in light of the excellent long-term outcomes in our study, we believe that intraoperative bleeding and other short-term manageable disadvantages of surgery for large prostates should not hinder surgeons from operating on large prostates. Lastly, another drawback of the present study was the lack of questionnaires to assess bothersome urinary symptoms and sexual function pre- and postoperatively. An accurate assessment of these outcomes mandates a prospective study design, validated tools and a larger patient population. Until results of a large-scale, randomized prospective trial accurately comparing different local treatment modalities in patients with large prostates become available, the present study adds to the existing data favoring surgical treatment for these patients.

CONCLUSIONS

In the PSA era patients with larger prostates are more likely to be diagnosed early with localized prostate cancer. Thus, a significant number of patients with large prostates will present for treatment. Prostate size sub-selects patients for treatment since patients with larger prostates are not ideal candidates for any form of radiotherapy and they are likely to be bothered by LUTS which may be aggravated by irradiation. Considering brachytherapy, technical difficulties in seed implantation is another argument against treatment of patients with larger prostates. Surgical treatment – namely, open, laparoscopic or robot-assisted radical prostatectomy – has been successfully performed in patients with large prostates. The present study adds to the body of evidence already existing in the literature presenting favorable outcomes of open radical prostatectomy in patients with large prostates. Thus surgical treatment is preferred in these patients.

Correspondence:
Dr. J. Baniel
Dept. of Urology, Assuta Medical Center, 63 Jabotinsky Street, Tel Aviv 62487, Israel
Phone: (972-52) 377-7772
Fax: (972-3) 579-4747
email: baniel@netvision.net.il

References

1. Fowler FJ Jr, McNaughton CM, Albertsen PC, Zietman A, Elliott DB, Barry MJ. Comparison of recommendations by urologists and radiation oncologists for treatment of clinically localized prostate cancer. *JAMA* 2000; 283: 3217-22.
2. Hsu EI, Hong EK, Lepor H. Influence of body weight and prostate volume on intraoperative, perioperative, and postoperative outcomes after radical retropubic prostatectomy. *Urology* 2003; 61: 601-6.
3. Hong SK, Chang IH, Han BK, et al. Impact of variations in bony pelvic dimensions on performing radical retropubic prostatectomy. *Urology* 2007; 69: 907-11.
4. Meraj S, Nagler HM, Homel P, Shasha D, Wagner JR. Radical prostatectomy: size of the prostate gland and its relationship with acute perioperative complications. *Can J Urol* 2003; 10: 1743-8.
5. Myers RP. Practical surgical anatomy for radical prostatectomy. *Urol Clin North Am* 2001; 28: 473-90.
6. Foley CL, Bott SR, Thomas K, Parkinson MC, Kirby RS. A large prostate at radical retropubic prostatectomy does not adversely affect cancer control, continence or potency rates. *BJU Int* 2003; 92: 370-4.
7. Boczko J, Erturk E, Golijanin D, Madeb R, Patel H, Joseph JV. Impact of prostate size in robot-assisted radical prostatectomy. *J Endourol* 2007; 21: 184-8.
8. Chang CM, Moon D, Gianduzzo TR, Eden CG. The impact of prostate size in laparoscopic radical prostatectomy. *Eur Urol* 2005; 48: 285-90.
9. Salem N, Simonian-Sauve M, Rosello R, et al. Predictive factors of acute urinary morbidity after iodine-125 brachytherapy for localised prostate cancer: a phase 2 study. *Radiother Oncol* 2003; 66: 159-65.
10. Ash D, Flynn A, Battermann J, de RT, Lavagnini P, Blank L ESTRO/EAU/EORTC recommendations on permanent seed implantation for localized prostate cancer. *Radiother Oncol* 2000; 57: 315-21.
11. Feneley MR, Landis P, Simon I, et al. Today men with prostate cancer have larger prostates. *Urology* 2000; 56: 839-42.
12. Walsh PC, Lepor H, Eggleston JC. Radical prostatectomy with preservation of sexual function: anatomical and pathological considerations. *Prostate* 1983; 4: 473-85.
13. Mulhall J, Althof SE, Brock GB, Goldstein I, Junemann KP, Kirby M. Erectile dysfunction: monitoring response to treatment in clinical practice – recommendations of an international study panel. *J Sex Med* 2007; 4: 448-64.
14. Kelly K, Swindell R, Routledge J, Burns M, Logue JP, Wylie JP. Prediction of urinary symptoms after 125iodine prostate brachytherapy. *Clin Oncol* 2006; 18: 326-32.
15. Zorn KC, Orvieto MA, Mikhail AA, et al. Effect of prostate weight on operative and postoperative outcomes of robotic-assisted laparoscopic prostatectomy. *Urology* 2007; 69: 300-5.
16. Singh A, Fagin R, Shah G, Shekarriz B. Impact of prostate size and body mass index on perioperative morbidity after laparoscopic radical prostatectomy. *J Urol* 2005; 173: 552-4.
17. D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Tomaszewski JE, Wein A. A prostate gland volume of more than 75 cm^3 predicts for a favorable outcome after radical prostatectomy for localized prostate cancer. *Urology* 1998; 52: 631-6.
18. Kumar V, Toussi H, Marr C, Hough C, Javle P. The benefits of radical prostatectomy beyond cancer control in symptomatic men with prostate cancer. *BJU Int* 2004; 93: 507-9.
19. Stav K, Rahimi-Levene N, Lindner A, Siegel Y, Zisman A. Retropubic radical prostatectomy: associated blood loss and transfusion requirements – a two-decade perspective review. *Isr Med Assoc J* 2005; 7: 103-6.