

Robot-Assisted Radical Prostatectomy in Patients with Enlarged Median Lobe: Matched Analysis

Büyük Median Loblu Prostatı Olan Prostat Kanseri Hastalarında Robot Yardımlı Laparoskopik Radikal Prostatektomi: Eşleştirilmiş Analiz

Taner Kargi¹, Kamil Gokhan Seker², Abdullah Hızır Yavuzsan³, Bugra Dogukan Torer⁴, Muhammed Yusuf Demir¹, Deniz Noyan Ozlu¹, Serdar Karadag¹, Selcuk Sahin¹, Volkan Tugcu², Ali Ihsan Tasci¹

¹Department of Urology, University of Health Sciences, Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey

²Department of Urology, Liv Hospital Vadiistanbul, Istanbul, Turkey

³Department of Urology, University of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey

⁴Department of Urology, Reyhanlı State Hospital, Hatay, Turkey

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Corresponding Author: Muhammed Yusuf Demir / University of Health Sciences, Dr. Sadi Konuk Training and Research Hospital, Department of Urology, Istanbul, Turkey / myusuf95@hotmail.com / ORCID ID: 0000-0003-0927-3593

Abstract

Objective: Evaluation of surgical, oncological and functional results in patients with prostate cancer and enlarged median lobe who underwent robot-assisted radical prostatectomy (RARP).

Materials and Methods: Medical records of 489 patients who underwent RARP between August 2009 and December 2013 were retrospectively evaluated. Among them, 40 patients who had enlarged median lobe were included in Group 1. Forty patients without median lobe hyperplasia were included with matched analysis (Group 2). Patients who were followed up for 12 months were assessed.

Results: No significant differences were found between the two groups in terms of demographic values, preoperative erectile function, prostate-specific antigen (PSA) levels, prostate dimensions, distribution of clinical stages, Gleason scores and D'Amico risk classification ($p>0.05$). Perioperative data revealed that mean operative times were 219.9 ± 64.5 (130-360) min and 185.6 ± 57.1 (120-355) min in Groups 1 and 2, respectively which was significantly prolonged in Group 1 ($p<0.05$). Bladder neck reconstruction was performed in Groups 1 ($n=14$: 35%) and 2 ($n=1$: 3%). Rates of full continence after removal of urethral catheter on day 7 and at the end of months 1, 3, 6 and 12 were similar in Groups 1 and 2 ($p>0.05$). Rates of potency and biochemical recurrence were similar at the end of the postoperative 6 months and one year in Groups 1 and 2 ($p>0.05$).

Conclusion: RARP in patients with prostate cancer with an enlarged median lobe is a challenging operation with significantly longer operative times. RARP is a good treatment option in patients with prostate cancer and an enlarged median lobe with its successful surgical dissection and anastomosis possibilities.

Keywords: median lobe, prostate cancer, robot-assisted radical prostatectomy

Öz

Amaç: Robot yardımlı radikal prostatektomi (RYRP) operasyonu geçiren median loblu prostatı olan prostat kanseri hastalarında cerrahi, onkolojik ve fonksiyonel sonuçların değerlendirilmesi.

Gereçler ve Yöntemler: Ağustos 2009 ile Aralık 2013 tarihleri arasında RYRP operasyonu geçiren 489 hastanın tıbbi kayıtları geriye dönük olarak incelendi. Bu hastalardan orta loblu prostatı olan 40 hasta Grup 1 olarak alındı. Orta lob prostatı olmayan diğer kırk hasta eşleştirilmiş analize dahil edildi (Grup 2). 12 ay takip edilen hastalar değerlendirildi.

Bulgular: Hastaların demografik verileri, preoperatif erektil fonksiyon, prostat spesifik antijen (PSA) seviyesi, prostat boyutları, klinik evre dağılımı, Gleason skoru ve D'Amico risk sınıflaması açısından iki grup arasında anlamlı fark bulunmadı ($p>0.05$). Perioperatif veriler, operasyon süresinin Grup 1 ve 2'de sırasıyla $219,9 \pm 64,5$ (130-360) dakika ve $185,6 \pm 57,1$ (120-355) dakika olduğunu ve Grup 1'de anlamlı olarak daha yüksek olduğunu gösterdi ($p<0,05$). Grup 1 ve 2'de sırasıyla 14 (%35) ve 1 (%3) hastaya mesane boynu rekonstrüksiyonu yapıldı. Grup 1 ve Grup 2'de 7. gün ve 1, 3, 6 ve 12. ay sonunda üretral kateter çıkarıldıktan sonra tam kontinans oranları benzerdi ($p>0,05$). Grup 1 ve Grup 2'de 6. ay ve 1. yılın sonunda potens ve biyokimyasal nüks oranları benzerdi ($p>0,05$).

Sonuç: Orta lob prostatı olan prostat kanserli hastalarda RYRP prosedürü, önemli uzun ameliyat süreleri olan zorlu bir ameliyattır. RYRP, başarılı cerrahi diseksiyon ve anastomoz imkanları ile orta loblu prostatı olan prostat kanserli hastalarda iyi bir tedavi seçeneğidir.

Anahtar kelimeler: median lob, prostat kanseri, robot yardımlı radikal prostatektomi

ORCID ID: T. Kargi 0000-0001-5874-3489
K.G. Seker 0000-0003-4449-9037
A.H. Yavuzsan 0000-0002-1561-895X

B.D. Torer 0000-0003-1847-6798
D.N. Ozlu 0000-0003-2435-5482
S. Karadag 0000-0002-1420-4536

S. Sahin 0000-0002-0903-320X
V. Tugcu 0000-0002-4136-7584
A.I. Tasci 0000-0002-6943-6676

Introduction

Radical prostatectomy (RP) is the gold standard treatment option in cases with organ limited prostate cancer (PCa) with a life expectancy of more than 10 years. Primary goal of the operation is complete removal of the tumor. However, it is very important that the patient maintains its postoperative erectile function and urinary continence [1]. Although the oncological results are positive, there is an increasing interest in minimally invasive methods due to the higher perioperative complication rates of open surgery and the negative consequences of postoperative functional outcomes such as erectile dysfunction and incontinence [2]. However, there are randomized controlled studies showing that the functional results are similar [3].

Laparoscopic radical prostatectomy has not been widely used due to its technical difficulties and long learning curve [4]. It was possible to overcome the challenges of the complex laparoscopic method when Da Vinci robotic system was introduced in that it enhanced movement ability of the operator's wrist, eliminated hand tremors of the surgeon, enabled more sensitive work in a three-dimensional medium with greater possibility of successful surgical dissection and anastomosis [5,6].

Large prostates cause difficulties in treatment. Large prostates restrict mobilization in the pelvis and may distort the visual appearance [7]. However, the stereoscopic visualization, magnification, and improved ergonomics of robot-assisted radical prostatectomy (RARP) can reduce the challenges posed by enlarged prostates with hyperplastic median lobes. However, RARP was found to be associated with more bleeding and longer operative times in some studies performed in patients with a large prostate and especially a voluminous median lobe, although functional and oncological results were not significantly different [7-10].

The aim of this cross-sectional study is to evaluate the effect of the enlarged median lobe on the surgical, oncological and functional outcomes of RARP in patients with enlarged median lobe and PCa in our patient series.

Materials and Methods

Patients

Local ethics committee approval was obtained prior to study (Dr. Sadi Konuk Training and Research Hospital Ethics Committee approval number: 2015/247). Medical records of 489 patients who underwent RARP between August 2009 and December 2013 were retrospectively evaluated. Among 489 patients aged between 47 and 78 years who had not undergone prior prostate surgery (transurethral resection of the prostate [TUR-P], transvesical prostatectomy [TVP]) and abdominal surgery were included in the study. Patients included in the study in both groups were operated through an intraperitoneal posterior approach by the same surgeon (A.I.T.). Since achievement of 150 cases of RARP was accepted as the criterion for the completion of the learning curve in the literature [11], we also excluded the first 150 patients to eliminate the effect of the learning curve. After inclusion and exclusion criteria were applied, the first 40 patients with, large median lobes were chronologically classified as Group 1, and the first 40 patients

without as Group 2, according to the time of operation.

Preoperative parameters of the patients (age, body mass index [BMI], preoperative prostate-specific antigen [PSA] level, clinical stage, biopsy Gleason score, International Prostate Symptom Score [IPSS], prostate dimensions, risk groups according to D'Amico risk classification and American Society of Anesthesiologists [ASA] scores were recorded. Since our patient series started in 2009, multiparametric magnetic resonance imaging (mpMRI) of the prostate could not be used in many patients. Therefore, preoperative transrectal ultrasonography (TRUS) measurements were used as a reference to ensure homogeneity in prostate volume measurements. Since the dimensions of the median lobe are important during the operation, size of the median lobe was measured separately during the measurement of the prostate dimensions. Prostate cancer patients with an enlarged median lobe of the prostate with its largest diameter greater than 1 cm were accepted as having prostate cancer with a large median lobe.

Amount of perioperative blood loss, total duration of operation, robotic docking, and operative console times, duration of the anastomosis procedures, whether or not a nerve sparing technique was used, requirement for bladder neck reconstruction, postoperative hospital stay, dwell time of urethral catheter, pathological stage, Gleason score and surgical margin positivity were recorded for all RARP cases. Perioperative and postoperative complications were evaluated using modified Clavien classification [12].

Preoperative evaluation demonstrated that all patients included in the study were fully continent. Functional results associated with urinary incontinence were evaluated after postoperative removal of urethral catheters on day 7 and at the end of the 1., 3., 6., and 12. months for the first postoperative year. Complete urinary continence was defined as no need to use pads or lack of urinary leakage. Daily requirement for one pad (safety pad) was considered as mild incontinence (stress incontinence) and use of more than one pad as incontinence.

Prior to RARP, each patient responded to five items of The International Index of Erectile Function (IIEF-5) questionnaire to evaluate their potency. Evaluation of erectile function was performed in postoperative 6 and 12 months. Potency was defined as rigid erection required for penetration. Individuals with a score of greater than 17 were accepted as having a normal potency [13].

Surgical Technique

All RARP operations were performed using the Frankfurt technique defined by Wolfram et al. [14]. Some technical modifications were applied during the stages of RARP operation in patients with an enlarged median lobe. For example, the margin of bladder neck and prostate was dissected transversely by the aid of a monopolar cautery. When an indented median lobe was encountered at this stage upon entrance into the bladder, the indented part was hung using a 2/0 vicryl suture or by the help of a grasper that was the fourth arm of the robot and dissection was started with its aid. During the anastomosis, bladder reconstruction was performed in the shape of an inverse racquet in patients with an enlarged median lobe. In patients in

whom bladder neck reconstruction was required, the large base of the racquet was completed with bilateral continuous sutures applied on the bladder neck up to the 12 o'clock level, starting the anastomosis from 6 o'clock level using side- to- side and outside-in suturing techniques. Subsequently, the sutures were crossed reciprocally, and continuous sutures were applied until the defect on the bladder was closed and thus the handle of the racquet was created (**Figure 1**). None of the patients required ureteral stent placement to protect the ureteral orifices.

Statistical analysis

Mean, standard deviation, median, lowest, highest, frequency and percent values were used in the descriptive statistics of the data. Distribution of the variables was measured using Kolmogorov-Smirnov test. Mann-Whitney U test

and independent samples t-test were used in the analysis of quantitative data. Chi-square test and Fisher's exact test were used in the analysis of the qualitative data where appropriate. The $p < 0.05$ was accepted as statistically significant. SPSS 22.0 program was used in the analysis.

Results

Preoperative clinicopathological specifications of the two groups such as age of the patients, BMI, preoperative PSA level, prostate dimensions, clinical stage, Gleason scores, ASA scores, D'Amico classification and preoperative potency and continence status were comparable. Percent of patients with higher preoperative IPSS scores was significantly greater in Group 1 compared to Group 2 ($p < 0.05$) (**Table 1**).

Mean duration of operation, operative console times and

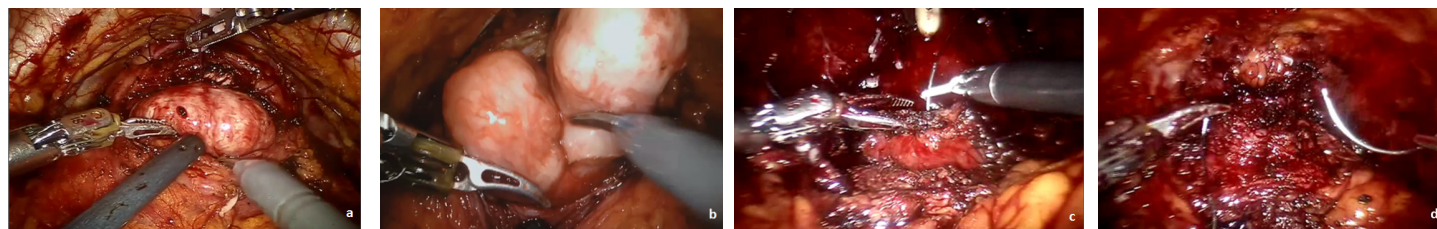


Figure 1. Bladder neck and median lobe (a). Bilobar median lobe (b). Wide open bladder neck (c). Bladder neck reconstruction reverse racket movement (d).

Table 1. Patient demographic characteristics

		Prostate median lobe (+)						Prostate median lob (-)						p		
		Mean±s.s./n-%			Med (Min-Max)			Mean±s.s./n-%			Med (Min-Max)					
Age (year)		61,4	±	4,8	61	51	-	71	61,4	±	5,9	62	45	-	71	0,855
BMI (kg/m2)		27,4	±	1,8	27	24	-	32	27,5	±	1,6	28	25	-	30	0,628
ASA score	I	12		30%					12		30%					1,000
	II	28		70%					25		63%					
	III	0		0%					3		8%					
Preop PSA (ng/ml)		9,0	±	5,5	7	3	-	27	8,4	±	4,3	7	1	-	20	0,889
Prostate volume (ml)		67,6	±	26,5	65	30	-	130	55,8	±	25,4	50	20	-	120	0,046
Clinical stage	T1c	32		80%					32		80%					1,000
	T2a	8		20%					8		20%					
Preop IPSS	Mild	1		3%					24		60%					0,000
	Modarate	13		33%					2		5%					
	Severe	26		65%					14		35%					
Preop IIEF-5	≥17	24		60%					24		60%					1,000
	<17	16		40%					16		40%					
D'Amico risk classification	0	18		45%					20		50%					0,654
	I	20		50%					20		50%					
	II	2		5%					0		0%					
Preop Gleason	6	28		70%					28		70%					1,000
	7	12		30%					12		30%					

PSA: prostate-specific antigen; ASA: American Society of Anesthesiologists; BMI: body mass index; IPSS: International Prostate Symptom Score; IIEFF: International Index of Erectile Function; Mann-whitney u test / Chi-square test

duration of urethrovesical anastomosis (UV) anastomosis was found to be significantly longer in Group 1 compared to Group 2 ($p < 0.05$). Amount of mean perioperative bleeding, duration of catheterization and hospital stay were similar in both groups ($p > 0.05$). Data of perioperative findings are demonstrated in **Table 2**.

No significant differences were found in the rates of using nerve preserving technique, positive surgical margin, Gleason score distribution of the specimen and biochemical recurrence rates between Groups 1 and 2 ($p > 0,05$). Bladder neck reconstruction was performed in 14 (35%) patients in Group 1 and 1 patient (3%) in Group 2. Rate of bladder neck reconstruction was significantly higher in Group 1 compared to Group 2 ($p < 0.05$) (**Table 3**).

Anastomotic leak was detected in 3, urinary system infection in 1, bleeding requiring blood transfusion in 1, pulmonary embolus necessitating intensive care stay in 1 and urethral stenosis during follow-up in 3 patients in Group 1. On the other hand, anastomotic leak was found in 1, ileus resolving by conservative treatment in 2, and bleeding requiring blood transfusion in 1 patient in Group 2. Complications are demonstrated in **Table 4**.

Results of postoperative functional evaluation are demonstrated in **Table 5**. Rates of complete urinary continence was similar in both groups following removal of urethral catheters on postoperative day 7, months 1, 3, 6 and 12 ($p > 0.05$). No significant differences were found in the rates of potency in the postoperative 6th month and 1st year between Groups 1 and 2 ($p > 0,05$).

Table 2. Perioperative and postoperative data

	Prostate median lobe (+)						Prostate median lobe (-)						p		
	Mean.±s.s			Med (Min-Max)			Mean±s.s.			Med (Min-Max)					
Operation time (min)	219,9	±	64,5	210	130	-	360	185,6	±	57,1	180	120	-	355	0,010
Consol time (min)	175,3	±	63,3	160	100	-	320	146,0	±	53,6	130	90	-	300	0,022
Urethrovesical anastomosis time (min)	34,3	±	8,7	33	20	-	50	29,1	±	7,1	30	20	-	45	0,008
Perop hemorrhage (ml)	124,1	±	44,1	105	75	-	300	110,5	±	33,5	100	50	-	200	0,163
Catheterization time (day)	10,0	±	0,7	10	8	-	12	10,1	±	1,4	10	7	-	14	0,571
Lenght of hospitalization (day)	4,5	±	1,7	4	4	-	14	4,5	±	1,8	4	4	-	14	0,472

Mann-whitney U test; min:minute

Table 3. Perioperative technique and postoperative oncological data

		Prostate median lobe (+)		Prostate median lobe (-)		p
		%	n	%	n	
NVB sparing	Unilaterally	1	3%	-	0%	0,396
	Bilaterally	35	88%	38	95%	
	None	4	10%	2	5%	
Positive surgical margin	Negative	36	90%	36	90%	1,000
	Positive	4	10%	4	10%	
Postoperative gleason score	6	29	73%	28	70%	0,805
	7	9	23%	11	28%	
	8	2	5%	1	3%	
Bladder neck reconstruction	No	26	65%	39	98%	0,000
	Yes	14	35%	1	3%	
Pathological stage	T2a	2	5%	3	5%	1,000
	T2b	0	0%	1	2,5%	
	T2c	36	90%	33	82,5%	
	T3a	1	2,5%	0	0%	
	T3b	1	2,5%	3	7,5%	
Biochemical recurrence	Yes	36	90%	36	90%	1,000
	None	4	10%	4	10%	

NVB: neurovascular bundle; Chi-square test/ Mann-whitney u test

Table 4. Complication rates

	Prostate median lobe (+) N (%)	Prostate median lobe (-) N (%)
Minor (Clavien 1-2)		
Anastomosis leakage	3 (7.5%)	1 (2.5%)
Urinary tract infection	1 (2.5%)	0 (0%)
Ileus	0 (0%)	2 (5%)
Bleeding, hemorrhage	1 (2.5%)	1 (2.5%)
Major (Clavien 3-4)		
Pulmonary embolism	1 (2.5%)	0 (0%)
Urethral stricture	3 (7.5%)	0 (0%)
Totals	9 (22.5%)	4 (10%)

Table 5. Functional outcomes

		Prostat Median Lob (+)		Prostat Median Lob (-)		p
		%	n	%	n	
Urinary continence status 7. days	Complete	13	33%	7	18%	0,121
	Mild	18	45%	25	63%	
	Incontinent	9	23%	8	20%	
Urinary continence status 1. months	Complete	13	33%	11	28%	0,626
	Mild	23	58%	25	63%	
	Incontinent	4	10%	4	10%	
Urinary continence status 3. months	Complete	23	58%	24	60%	0,820
	Mild	16	40%	15	38%	
	Incontinent	1	3%	1	3%	
Urinary continence status 6. months	Complete	28	70%	29	73%	0,805
	Mild	11	28%	11	28%	
	Incontinent	1	3%	0	0%	
Urinary continence status 1. year	Complete	35	88%	34	85%	0,745
	Mild	4	10%	6	15%	
	Incontinent	1	3%	0	0%	
Potency 6. months	Yes	10	43%	8	30%	0,309
	None	13	57%	19	70%	
Potency 1. year	Yes	16	70%	19	70%	0,951
	None	7	30%	8	30%	

Chi-square test

Discussion

Widespread use of medical treatment in benign prostatic hyperplasia (BPH) results in postponed surgical treatment and encountering patients diagnosed with clinically localized prostate cancer detected during PSA screening tests and enlarged prostates [15]. Due to the increasing popularity of active observation, the dimensions of the prostate may increase during the follow-up period, and the necessity of performing curative treatment of the prostate with larger dimensions arises.

Radical prostatectomy has become the emerging curative treatment in patients with a large prostate due to the limitations of radiotherapy and brachytherapy in patients with greatly enlarged prostates [16,17]. Challenges of RARP operation in patients with a large prostate and especially with an enlarged median lobe have been scrutinized in many studies and the results of the studies have been published [7-10].

Operative time is a significant perioperative parameter. Considering the Trendelenburg position of the patients during the operation, prolonged surgeries may carry life-threatening

risks. The mean duration of operation was significantly longer in patients with an enlarged median lobe compared to those without (219.9 ± 64.5 minutes vs 185.6 ± 57.1 minutes). In their study, Huang et al., emphasized that the greatly enlarged median lobe significantly lengthened the duration of operation when compared to those without (185.8 ± 65.8 minutes vs 155.0 ± 40.8 minutes) [18]. Similarly, Meeks et al. found that the mean duration of operation was significantly longer in BPH patients with an enlarged median lobe compared to those without (349 and 287 minutes, respectively) [19]. The authors stated that the causes longer operative times were difficulty encountered in the posterior dissection of the prostate and dissection of vesicula seminalis in patients with an enlarged median lobe. Freeing the vesicula seminalis using intraperitoneal posterior approach through the Douglas space resolved this problem in the present study. The authors reported that another and the most significant cause was that the defect was larger than normal during the bladder neck opening in patients with an enlarged median lobe and stated that 40% of those patients required bladder neck reconstruction. In another study Link et al., stated that patients with larger prostates frequently had an enlarged median lobe, and this condition caused a larger opening in the bladder neck during the dissection of the prostate from inside the bladder. They emphasized that the requirement of bladder neck reconstruction was thus increased, and the operation was lengthened during the stage of vesicourethral anastomosis [10]. In the present study, we also found that 35% of the patients with an enlarged median lobe required bladder neck reconstruction which lengthened the duration of vesicourethral anastomosis and operation.

Another important parameter of the RARP operation is perioperative bleeding. Huang et al. reported the mean perioperative amount of bleeding as 236.4 ± 99.9 ml and 193.3 ± 93.1 ml in patients with and without enlarged median lobe, respectively [18]. Similarly, Meeks et al. found a significantly increased amount of bleeding in patients with an enlarged median lobe (464 ml and 380 ml) [19]. In this present study, on the other hand, no statistically significant difference was found in the mean perioperative amount of bleeding between the two groups. Similar to our study, Hamidi et al., reported no significant effect of the presence of the enlarged median lobe on the amount of bleeding compared to those without (285 ml vs 280 ml) [20].

Meeks et al. evaluated postoperative bladder neck stenosis in patients with an enlarged median lobe who underwent RARP, and found that the incidence of bladder neck stenosis (7% vs 4%) and urinary incontinence (22% vs 15%) was higher compared to patients with normal prostate anatomy, though without any statistically significant difference between them [19]. Similarly, in this study any statistically significant differences were not found between the two groups in terms of the incidence of postoperative bladder neck stenosis and urinary incontinence.

Positive surgical margin (PSM) following RARP is one of the independent factors affecting biochemical recurrence and development of local recurrence and metastasis [21]. In the present study, the rate of positive surgical margin was 10%, in both groups, similar to the literature data [22,23]. Similar to our study, many authors reported that the presence of an enlarged median lobe had no effect on the surgical margin positivity

following RARP [18,19].

Although the primary aim of radical prostatectomy is complete excision of the tumor, the maintenance of postoperative erectile function and urinary continence are of utmost importance. Preservation of neurovascular bundle (NVB) during radical prostatectomy is not only effective in the maintenance of erectile function, but also in the recovery of the urinary functions. Comparative studies demonstrated a complete continence rate of 70-81% in patients who did not undergo NVB sparing RP, while higher continence rates such as 90-94% were seen following nerve preserving surgery with a statistically significant difference between the two techniques [24,25]. The rates of complete continence in the present study are similar to the those reported in the literature. Among the authors evaluating the effect of prostate volume on continence, Huang et al. reported that dimensions of the prostate had no effect on the recovery of urinary functions following RARP [18]. Meek et al. found no significant difference in general continence rates between BPH patients with and without an enlarged median lobe [19]. Contrarily, some authors emphasized that prostate volume affected continence rates and large prostate volume negatively affected the continence rate [26]. In our study, no significant difference was found in incontinence rates at 6th and 12th months after RARP when patients with and without enlarged median lobes were compared.

Preservation of potency is important and possible after radical prostatectomy. Age, using a NVB sparing surgical technique, preoperative state of potency, and some chronic diseases are conditions affecting postoperative erectile function. Age is especially one of the most important factors affecting the severity of erectile dysfunction (ED) that develops following RP [27]. Young patients report a low rate of ED postoperatively and the rate of recovery of erection has been reported to be 92% following RP in patients between the ages of 40 and 49 years [28]. Catalona et al. reported that potency was preserved at rates of 68% and 47% during postoperative follow-up after RP in cases with bilateral and unilateral preservation of NVB, respectively [29]. On the other hand, some authors evaluated the effects of prostate dimensions on post-RP potency and found no significant difference [30]. Huang et al. also reported that the size of the prostate did not effect the post-RARP erectile function [18]. In this study, we evaluated the effect of an enlarged median lobe on potency after RARP and found no significant difference between the groups with and without enlarged median lobes in terms of potency rates at postoperative 12th-month.

One of the limitations of this present study is its retrospective nature. The second limitation is the low number of patients. In addition, as another limiting factor the surgeries were performed by a surgeon who had completed his learning curve, thus the results of RARPs conducted by a surgeon who hasn't completed the learning curve are not known.

Conclusion

RARP in prostate cancer patients with an enlarged median lobe is a difficult procedure with significantly longer operative times. For this reason, preoperative USG should be planned for patients who are scheduled for RARP and the median lobe

should be evaluated. Considering our study results, no significant difference was found between the groups with and without enlarged median lobes in terms of clinical and functional results, except for the duration of the operation. This finding reveals us that although RARP is a challenging procedure, it is a good treatment option in prostate cancer patients with an enlarged median lobe.

Ethics Committee Approval: The study was approved by the Ethics Committee of University of Health Sciences, Dr. Sadi Konuk Training and Research Hospital (Approval date, and registration number: 07.12.2015/247).

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