LAPAROSCOPIC RADICAL PROSTATECTOMY: A SINGLE CENTER EXPERIENCE

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Minimally invasive techniques including robotic-assisted and laparoscopic radical prostatectomy have become the preferred approach for operative treatment of prostate cancer. The aim of this study was to evaluate and compare results of laparoscopic radical prostatectomy (LRP) and open retropubic radical prostatectomy (ORRP) for localised prostate cancer, in terms of safety, eficacy and oncological outcome.

A total of 123 radical prostatectomies (RPs) for low-risk localised prostate cancer were performed between January 2016 and June 2019 at the University Clinic of Urology Skopje. Of these, 61 (49.6%) were LRP and 62 (50.4%) ORRP, mean patients age was 54 years (33 to 67) Indications for operative procedure included: pathohistological finding of prostate cancer, age ≤ 70 years, PSA<10ng/ml, Gleson score ≤ 7 (3+3 or 3+4), negative bone scintigraphy, stage ≤T2a, N0, M0. All patients were assessed regarding the demographic data, PSA level, Gleason score, operative time, conversion to open surgery for LRP, blood loss, intra and post operative complications, catheter removal, number blood transfusion, hospital stay and oncological outcomes. LRP proved superior to ORRP, resulting in shorter operating time, less blood loss (p < 0.5), shorter time to resumption of oral intake, shorter postoperative hospital stay (p < 0.5), and less analgesic requirements. In terms of oncological outcomes, we observed less positive margins in the LRP group (p < 0.5). Our results indicate that although both operative techniques represent safe procedures, offering good qualiy of operation, in our series, LRP was superior in terms of safety, eficacy and oncological outcomes.

Acta Medica Medianae 2020;59(3):xx-xx.

Key words: *prostate cancer, laparoscopic radical prostatectomy, open retropubic radical prostatectomy*

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Introduction

Recent epidemiological data show that at the end of 2018, prostate cancer was second in respect to all cancers in the male population, with an incidence that varies by region, from the age-standardized rate of 11.5/100 000 in Asia to 62.1/100 000 in Europe (1, 2). There are several treatment modalities for patients diagnosed with localized prostate cancer. According to EAU Guidelines 2019, it includes deffered treatment (active surveillance/

watchful waiting) and active (curative) treatment. Active treatment encompass a wide range of options, including radical prostatectomy, external beam radiation therapy, brachytherapy (both high and low dose), hormonal therapy, cryotherapy, high-intensity focused ultrasound, focal therapy (3). With respect to all of these therapeutic options, radical prostatectomy is the therapeutic option of choice for patients with localized prostate cancer whose survival is expected to be longer than 10 years (4). According to a 2014 study by Bill Axelson et al, radical prostatectomy with respect to it significantly reduces CSS, with a relative risk of 0.56 (5). The same authors said in a 2018 study that the survival benefit for patients with localized prostate cancer who underwent radical prostatectomy was at least 2.9 years (6). In regard of lymph node dissection following RP, it has been stated that low-risk disease is rarely associated with nodal involvement (7).

Open radical prostatectomy has long been the only operative technique for the treatment of prostate cancer. It has undergone many modifications and among them is the anatomical retropubic radical

prostatectomy, which he introduced into the clinical practice of Walsh in 1982, and which is characterized by a better knowledge of hemostasis and cavernous nerve preservation (8). Further progress was directed towards reducing the invasiveness of the procedure, and at the end of the 20th century the technique of laparoscopic radical prostatectomy was promoted, with a positive growth trend over the coming years (9, 10). Drawbacks of the laparoscopic technique, which are primarily related to limitations in performing certain manual operations and movements, the absence of a third dimension, as well as a long learning curve, led to the emergence of a new operative technique - robotic assisted radical laparoscopic prostatectomy (RALP), which had been introduced in 2000 by Binder et co-workers (11). According to the results of recently published studies, as well as the EAU Guidelines, it cannot be stated with certainty that any of the above techniques has clinically significant advantages over the other two in terms of oncological and functional results (12).

The aim of this study was to evaluate and compare results of open retropubic radical prostatectomy (ORRP) and laparoscopic radical prostatectomy (LRP) for localised prostate cancer, in terms of safety, eficacy and oncological outcome.

Patinents and methods

A total of 123 radical prostatectomies (RPs) for low-risk localised prostate cancer were performed between January 2016 and June 2019 at the University Clinic of Urology Skopje. Of these, 61 (49.6%) were LRP and 62 (50.4%) ORRP, mean patients age was 54 years (33 to 67). Indications for operative procedure included: pathohistological finding of prostate cancer, age ≤ 70 years, PSA < 10 ng/ml, Gleson score ≤ 7 (3 + 3 or 3 + 4), negative bone scintigraphy, stage ≤ T2a, N0, M0. All patients were assessed regarding the demographic data, PSA level, Gleason score, operative time, conversion to open surgery for LRP, blood loss, intra and post operative complications, catheter removal, number blood transfusion, hospital stay and oncological outcomes. Mean follow-up was 6 months (5 to 36). All patients had undergone standardized preoperative procedure of our clinic, including:. complete blood count, biochemical analysis, urine, urine culture, PSA, multislice computerized abdomino-pelvic tomography, histopathological result of transrectal ultrasound guided prostate biopsy, cardiac and anesthesiologic evaluation, urological evaluation. Statistical analysis is estimated by using of Fisher's test and Hi-squared test.

Surgical technique of ORRP was as described by Walsh (8). Surgical technique of laparoscopic prostatectomy was performed by the same surgical team, as follow:

An infraumbilical incision is made with approximatelly 1 cm of lenght in the midline. Incision of rectus fascia is performed on the linea alba. Creation of preperitonenal space is performed using a the fingers and the camera and then insufflation with CO_2 tension of 12 mmHg. We introduce a 0 ° grade optics through the infraumbilical port and additional four ports are placed under visual control. Two 11 mm trocars are inserted on the pararectal lateral border while two 5 mm are placed halfway between the anterior – superior iliac crest and pararectal trocars. During the procedure we used only bipolar tools (clamps and grasps) including the forceps for the operator's left hand. We found this tool comfortable for both dissection and coagulation. After entering into the retropubic space, dissection of the praevesical space of Retzius is performed in a deliberate manner. The superficial dorsal vei, is coagulated with bipolar electrocautery. Subsequently, the endopelvic fascia is cleaned billateraly. The endopelvic fascia is incised on both sides by bipolar scissors. The fascial incision is carried distally up to the most lateral puboprostatic ligament. The fibers should not be divided close to the prostate to avoid injury of large veins that cross on the lateroposterior side of the prostate. Visualization of the prostate apex is the endpoint of this dissection. The apex of the prostate is defined bilaterally. The deep venous complex of Santorini (DVC) is ligated with a 2-0 vicryl suture. In order to locate the bladder neck, an Foley catheter is pulled and inflated with 10-15 ml. The bladder is incised at its junction with the prostate with bipolar forceps. The urethra is dissected at its anterior and lateral aspect and then transversally transected with scissors. The Foley catheter is removed and replaced by an ureteric stent (ch 16), which provides a good visualization of the bladder. This is an important step in order to ensure good preservation of the bladder neck. Next by pulling the prostate upward, in the direction of the pubic symphysis, we are able to uncover vertical fibers of the anterior layer of the Denonvilliers' fascia. Its incision shows the retrovesical space in which the vas deferens and seminal vesicals are located. During preparation of the seminal vesicles we perform a good hemostasis of the medially situated vessels. The posterior lip of the bladder neck is grasped with forceps and lowered to provide access to the interprostatorectal plane. The vertical fibers of the anterior plane of Denonvillier's fascia covering the seminal vesicles are incised. The ampoule of the right vas deferens is sectioned after coagulation with cold scissors or clipped with a Hem-o-lock clip . A large grip is used to simultaneously coagulate the anterior deferential artery. The seminal vesicle is dissected circumferentially from the base to the apex, taking care to control the vessels. The lateral pedicle of the seminal vesicle is dissected and coagulated following the inferior pedicle dissection and coagulation. We proceede with the dissection of the lateral surface of the prostate. After sectioning of neurovascular bundle (NVB) and local hemostasis with both bipolar forceps and Hem-o-lok clips we continue with prostate apex section. Dissection of the apex starts with retraction of the preprostatic tissues using unipolar scissors. The urethra is reached gradually by incising the tissues covering the anterior surface of the urethra. The stent is advanced to make the urethra more prominent. The posterior surface of the urethra is sectioned at the end. Fibers of the rectourethral muscle are sectioned, revealing the plane of the rectum. After freed-

ing prostate we perform the urethrovesical V anastomosis. Prostate gland is placed in endobag catch and extracted trough right pararectus trocar port. Afterward trocar is taken out and inserted again in the same port beside the endobag. The urethrovesical anastomosis is performed using a running continuous unidirectional barbed (V-Loc® 180) running sutures. The right tail of the suture starts from 5 h to 12 h position. The left tail of the suture starts from 7 h to 12 h position. Assurance of watertight closure with an intraoperative 150-200 cc saline is performed in all cases. Finally a Foley catheter ch 16 is placed. Once the vesicourethral anastomosis is completed, a 16 F drain is introduced and fixed. The drain is placed in the Retzius space. The endobag is extracted by applying traction and rotation movements throughout the right port followed with incision of rectus fascia and distraction of rectus muscle fibers that ease extraction.

Results

Basic demographic data and perioperative parameters are listed in Table 1. There were no statistical difference between LRP and ORRP in terms of number of patients, mean age (65.46 ± 3.3 and 65.3 ± 2.5, respectively), clinical stage, preoperative PSA values (6.6 ± 1.8 and 7.7 ± 1.6, respectively), as well as GS values on biopsy and on final operative specimen. However, positive surgical margins were statistically different in favor of ORRP group ($p < 0.05$).

Table 1. Perioperative parameters

	LRP	ORRP	p
Number of patients	61	62	
Age	65.46 ± 3.3	65.3 ± 2.5	NS
Prostate volume	68 ± 22	72 ± 41	NS
Clinical stage	≤ T2a	≤ T2a	
Preoperative PSA (ng/ml)	6.6 ± 1.8	7.7 ± 1.6	NS
Gleason score (GS) (biopsy)			
≤ 6	37	42	NS
7 (3+4)	24	20	NS
GS (postoperative)			
≤ 6	29	39	NS
7 (3+4)	32	23	NS

Data on intraopereative and postoperative parameters show that mean surgical time was similar in both groups, with no statistical difference (126.18 ± 19.5 and 126.66 ± 12.3, respectively). Patients who underwent ORRP had higher blood loss and that difference is statistically significant (355.17 ± 57.75 vs. 275.4 ± 39.79, separately, $p < 0.5$). It was observed that both period of postoperative hospitalization as well as postoperative catheter removal were shorter in LRP group (6.2 ± 0.4 vs. 7.43 ± 0.49, $p < 0.05$; and 6.2 ± 0.4 vs. 7.43 ± 0.49, $p < 0.05$) (Table 2).

Table 2. Intra- and postoperative parameters

	LRP	ORRP	p
Mean surgical time (minutes)	126.18 ± 19.5	126.66 ± 12.3	NS
Blood loss (ml)	275.4 ± 39.79	355.17 ±5 7.75	p < 0.5
Postoperative hospitalization (days)	6.2 ± 0.4	7.43 ± 0.49	p < 0.5
Catheter removal (days)	6.2 ± 0.4	7.43 ± 0.49	p < 0.5

When perioperative complications according to Clavien-Dindo classification have been analyzed, there were 11 grade I events (18%) in LRP group and 8 (12.9%) in ORRP group ($p > 0.05$). Grade II

that reffers to intraoperative blood loss was more frequent in ORRP (12% vs. 27%, p < 0.05). There was 1 (1.6%) LRP event of grade IIIa and 2 (3.2%) ORRP (p > 0.5). In all cases, urethral catheter was dropped out, so recatheterization was performed endoscopically. In one case (1.6%) we observed rectal injury during LRP (grade IIIb), so the laparo-scopic intervention had been converted into the open. Rectal injury was completely repaired, with no additional complications, and the patient was discharged from the hospital at day 12th. Complications of higher grade (IV and V) were not observed. Data on perioperative complications according to Clavien-Dindo classification are summarized in Table 3.

Table 3. Perioperative complications (Clavien-Dindo classification)

Procedure	LRP (n = 61)		ORRP (n = 62)		p
Patients	No	%	No	%	
Grade I	11	18	8	12.9	p > 0.05
Grade II	7	12	17	27	p < 0.05
Grade IIIa	1	1.6	2	3.2	p > 0.05
Grade IIIb	1	1.6	-	-	p > 0.05
Grade IVa	-	-	-	-	
Grade IVb	-	-	-	-	
Grade V	-	-	-	-	

Our results indicate that the histopathological finding of the positive surgical margin was significantly more common in the ORRP group (19.6 % vs. 35.5 %) and this difference is statistically significant (p <0 .5). Data on postoperative PSA values indicate that it was statistically significantly higher in the ORRP group, after 3 months and after 6 months, respectively (0.0455 ± 0.0524 vs. 0.1708 ± 0.23 and 0.0781 ± 0.0995 vs. 0.115 ± 0.0931) (Table 4).

Table 4. Postoperative PSA and surgical margins

	LRP (n = 61)	ORRP (n = 62)	p
Positive surgical margins (PSM)	12 (19.6%)	22 (35.5%)	p < 0.5
After 3 months	0.0455 ± 0.0524	0.1708 ± 0.23	p < 0.5
After 6 months	0.0781 ± 0.0995	0.115 ± 0.0931	p < 0.5

Discussion

In this study, we presented our initial experience with LRP, with particular focus on results regarding perioperative complications and oncological outcomes, comparing these data with the data from literature. To the best of our knowledge this is one of the first reports of this procedure in the Balkan region. Radical prostatectomy is a common curative treatment for localized prostate cancer. In this procedure, both oncological and functional outcomes based on health-related quality of life are taken into account. Radical prostatectomy has been developed from an open surgery to a laparoscopic procedure, with improved surgery made possible by magnification of the view of the anatomy around the prostate. Many authors have studied the effects of each of the radical prostatectomy surgery techniques (open, laparoscopic and robotic assisted).

Laparoscopic surgery gained great popularity in the early 21st century. The basic motives and reasons for developing this technique are contained in its minimal invasiveness. The effects of laparoscopic technique on tissue have been the subject of study in many studies. Thus, Fornara and co-workers (13) determined its benefits over open kidney tumor surgery, followed by a decreased inflammatory mediator response. Frakalanca and colleagues (14) studied the extent of tissue damage using open and laparoscopic radical prostatectomy techniques and found that there were very small differences in favor of laparoscopic technique. Similar conclusions were reached by Jurczok and colleagues in their prospective nonrandomized stuidy (15). Open radical retropubic prostatectomy has its qualities, among which stand out especially: availability of performing in smaller centers, short duration of procedure, favorable cost of bone, relatively small invasiveness,

possibility of working exclusively in extraperitoneal space, possibility of performing quality lymphadenectomy and relatively fast recovery (16, 17).

There were a total of 123 patients in our study series, 61 LRPs and 62 OORPs. There was no statistically significant difference in the number of subjects, their age and disease stage.

Preoperative PSA levels in both groups were below 10 ng/ml (low risk) and according to the recommendations by the EAU Guidelines, no lymphadenectomy was required. With regard to GS, no statistically significant differences were observed either in the preoperative biopsy appliance or in the definitive histopathological findings (18). Mean surgical time was similar in our two groups, with the period of time consistent with published data which had shown range from 100 to 151 minutes, as reported by Curto and co-workers, and Stolzenburg and co-workers (19, 20).

In regard to blood loss, in our series it was higher in ORRP group and it had been statistically significant. The range of blood loss was 235.61 ml to 315.19 ml in LRP and 297.42 ml to 412.92 ml in ORRP group. Average blood loss following LRP is reported to be from 200 ml to 390 ml (Curto, Goeman), and for ORRP 750 ml to 1284 ml (21, 22). Transfusion rates in our series were in 27% of patients after ORRP and in 12% after LRP. The difference is statistically significant and in favor of LRP group. It has been reported by several authors that transfusion rates ranges between 0.9% and 5.3% for LRP (19, 23) and 9.7% and 29% for ORRP (22, 24). We believe that slightly higher transfusion rates as compare to the literature data, with real blood loss consistent with the results of published studies, are primarily the result of a learning curve and increased caution during postoperative recovery in the intensive care unit.

Regarding the duration of hospitalization and removal of the urethral catheter, in both cases the period was shorter in the LRP group and the difference is statistically significant. Several authors, including Bhayani and co-workers and Reissweiler

and co-workers, stated that the benefits of minimally invasive radical prostatectomy techniques over open include lower blood loss, lower blood transfusion rates, less need for analgesia, and shorter hospitalization, catheterization and recovery (25, 26). In regard to perioperative complicatio rates, according to Clavien Dindo classification, in our series there were higher rate of grade I, grade II, grade IIIa and grade IIIb complications in ORRP group. However, statistical difference is observed only for grade II (transfusion rates). Other complications were presented at a low rate and with no statistical differences between the observed groups, and are consonant with other series.

The oncologic outcome of surgery as seen through positive surgical margins in the definitive histopathologic specimen, has been better after LRP because the PSM rate was 19.6%, while in the ORRP group it was 35.5%, and this difference had been statistically significant. The range of PSM varies from 4.7% to 18.3% after LRP, and from 51% to 76.6% after ORRP (24-29). It is evident that the incidence of PSM following ORRP is much higher over LRP, which is in accordance to our results. Finally, PSA values measured at postoperative 3 and 6 months, although in both groups within the low risk range, were statistically significanly higher after ORRP. This can be explained by a more accurate resection line at LRP as well as a higher rate of PSM at ORRP.

Conclusion

Our results concur with other retrospective reviews comparing laparoscopic and open radical prostatectomy, demonstrating unequivocal advantages of LRP in terms of blood loss, blood transfusions, average rates of Clavien Dindo complications of grade I to IIIb,duration of hospitalization, catheter removal, positive surgical margins and postoperative values of PSA at 3. and 6. month.

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LAPAROSKOPSKA RADIKALNA PROSTATEKTOMIJA- ISKUSTVO JEDNOG CENTRA

Baškim Šabani[1], Ognen Ivanovski[1], Slobodan Gurmeševski[1], Gordana Petruševska[2], Sašo Dohčev[1], Sotir Stavridis[1], Oliver Stankov[1]

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Minimalno invazivne tehnike, uključujući robotski-potpomognutu i laparoskopsku radikalnu prostatektomiju postale su operativne tehnike izbora za operativno lečenje karcinoma prostate. Cilj studije bio je proceniti i uporediti rezultate laparoskopske radikalne prostatektomije (LRP) i otvorene retropubične radikalne prostatektomije (ORRP) u pogledu bezbednosti, efikasnosti i onkološkog ishoda.

Ukupno 123 radikalne prostatektomije (RP) za nisko-rizični lokalizovani karcinom prostate obavljene su u periodu od januara 2016. do juna 2019. na Univerzitetskoj klinici za urologiju Skoplje. Od toga je 61 (49,6%) bila LRP, a 62 (50,4%) ORRP, uz prosečnu starost pacijenata 54 godine (33 do 67). Indikacije za operativni postupak bile su: patohistološki nalaz adenokarcinoma prostate, starost ≤ 70 godina, PSA <10ng/ml, Gleson-skor ≤ 7 (3 + 3 ili 3 + 4), negativna scintigrafija kostiju, stadijum ≤T2a, N0, M0. Svi pacijenti su sagledani kroz demografske podatke, nivoe PSA, Gleason-skora, trajanja operactivnog zahvata, konverzije iz LRP u ORRP, gubitaka krvi, perioperativnih komplikacija, uklanjanja operativnog katetera, transfuzija krvi, boravka u bolnici i onkološkog ishoda.

LRP se pokazao superiornijim u odnosu na ORRP, što je rezultovalo kraćim operativnim vremenom, manjim gubicima krvi (p < 0.5), kraćim vremenom za nastavak oralnog unosa hrane i tečnosti, kraćim postoperativnim boravkom u bolnici (p < 0.5) i manjim potrebama za analgetskom terapijom. Što se tiče onkološkog ishoda, primetili smo manje pozitivnih resekcionih ivica u grupi LRP (p < 0.5). Naši rezultati pokazuju da iako obe operativne tehnike predstavljaju bezbedne procedure i pružaju dobar kvalitet operativnog zahvata, u našoj seriji LRP je pokazala bolje rezultate u pogledu bezbednosti, efikasnosti i onkološkog ishoda.

Acta Medica Medianae 2020;59(3):xx-xx.

Ključne reči: karcinom prostate, laparoskopska radikalna prostatektomija, otvorena retropubična radikalna prostatektomija