

ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Perioperative outcomes of laparoscopic and open retropubic radical prostatectomy

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SUMMARY

Introduction/Objective Radical prostatectomy (RP) is a treatment option with high curative potential in patients with prostate cancer of moderate-risk.

The aim of the study is to assess perioperative results of laparoscopic RP (LRP) and open retropubic RP (ORRP).

Methods From 2016 to 2020, a total of 244 patients undergone RP, as follow: 145 patients LRP and 99 patients ORRP. Demographic data, preoperative parameters, perioperative and pathological outcomes were analyzed and compared among LRP and ORRP groups.

Results In regard to demographic data and preoperative parameters (BMI, mean age, median pretreatment prostate-specific antigen, clinical stage and Gleason score from biopsy), there are no differences between the observed groups. Patients from ORRP group had significantly shorter operative time ($p < 0.05$). Patients from LRP group had major advantages in regard to estimated blood loss (EBL) (550 ml for LRP vs. 1450 ml for ORRP), hospitalization time (six days for LRP vs. nine days for ORRP), catheter removal (6.5 days for LRP vs. 12 days for ORRP), overall complication rates (29% for LRP vs. 48.4% for ORRP) and blood transfusion rates (22.7% for LRP and 37.4% for ORRP).

Conclusion Both LRP and ORRP provide favorable operative results in terms of efficacy, safety and oncologic outcome. However, patients undergoing LRP were more likely to have less EBL, shorter length of hospital stay, earlier catheter removal and lower rates of overall perioperative complications.

Keywords: prostate cancer; laparoscopic radical prostatectomy; open retropubic radical prostatectomy

INTRODUCTION

Current epidemiological data show that prostate cancer is the second most common cancer affecting the male population, with the increasing incidence in recent years [1, 2]. Radical prostatectomy is a treatment option with high curative potential in patients with prostate cancer of moderate-risk [3, 4]. Nowadays, operative techniques include open, laparoscopic and robotic-assisted RP. Open RP (ORRP) has been in use for the longest time, but is associated with certain disadvantages, including intraoperative hemorrhage and length of hospital stay [5]. Minimally invasive RPs including laparoscopic (LRP) and robot-assisted (RARP), are designed as technically innovative operative techniques and had been introduced into clinical practice in the late 20th and early 21st centuries [6, 7]. Regardless of the type of operative technique, the basic goal of RP remains the same – removal of cancer while achieving good functional results in terms of continence and sexual function [6]. Published results of numerous studies on the effects of the aforementioned operative techniques on the oncological and functional outcomes are still not

completely consistent [5, 7]. Herein, we present the results of our prospective study regarding the perioperative surgical outcomes and complications of LRP and open retropubic radical prostatectomy (ORRP).

METHODS

From January 2016 to June 2020, a total of 244 study patients, mean age 67.2 years (61–74; SD = 10.72) had undergone radical prostatectomy at the University Clinic of Urology in Skopje. Depending on the applied operative technique, the patients were divided into two groups, as follows:

- 1) Group LRP – 145 patients who had undergone laparoscopic radical prostatectomy;
- 2) Group ORRP – 99 patients who had undergone radical retropubic radical prostatectomy.

All applied procedures on the examined groups of patients were carried out in accordance with the ethical principles of the Declaration of Helsinki, with guaranteed discretion in regard to personal data.

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Ethical Committee of the Mother Teresa University Clinical Center in Skopje approved the study (Number of Approval 03-116/4).

We applied for ORRP the operative technique described by Walsh [8]. Surgical technique of laparoscopic prostatectomy was performed by the same surgical team, according to Heilbronn technique [9]. Both techniques were performed without pelvic lymph node dissection, since only patients with pretreatment prostate-specific antigen (PSA) levels ≤ 10 ng/mL were included in the study. All patients underwent standardized preoperative procedure of our clinic, including: complete blood count, biochemical analysis, urine, urine culture, serum PSA, multislice computerized abdomino-pelvic tomography, histopathological result of transrectal ultrasound guided prostate biopsy, cardiac and anesthesia evaluation, urological evaluation, decision for the operative treatment by the Council for uro-oncology and patient informed consent form. Demographic data and preoperative parameters included the following: mean age, body mass index (BMI), median pretreatment prostatic specific antigen (PSA) values (ng/ml), clinical stage and Gleason score (GS) from biopsy. Perioperative and pathological outcomes included the following: operation time, estimated blood loss (ml), pathological stage, pathologic GS, prostate volume and positive surgical margins (PSM). Operative complications have been classified and recorded according to Clavien–Dindo classification [10].

Statistical analysis was performed using R Studio. Two-proportions z-test was used to conduct a hypothesis test about the difference between the proportions of the observed two groups of patients. A p-value of < 0.05 was deemed statistically significant.

RESULTS

Basic demographic and preoperative data are listed in Table 1.

Table 1. Demographic data and preoperative parameters

Parameters	LRP	ORRP	p-value
No. of patients	145	99	
Mean age	67 (61–74)	67.5 (63–73)	0.3685
BMI (kg/m ²)	23.2 (21.7–26.8)	23.6 (22.1–27)	0.3043
Median pretreatment PSA (ng/ml)	10.6 (6.3–18.6)	10.9 (7.1–17.5)	0.3870
Clinical stage, No. (%)			
T1	128 (88.3)	90 (90.9)	0.5157
T2	2 (1.4)	1 (1.02)	0.7949
T3	14 (9.6)	8 (8.08)	0.6745
T4	1 (0.7)	0 (0)	0.4065
GS from biopsy	6.77 \pm 1.1	6.85 \pm 1.33	0.6091
GS ≤ 6 , n (%)	65 (44.8)	42 (42.4)	0.7114
GS = 3+4, n (%)	30 (20.7)	20 (20.2)	0.9283
GS = 4+3, n (%)	26 (18)	14 (14.2)	0.4295
GS = 8, n (%)	15 (10.3)	12 (12.1)	0.6672
GS = 9, 10, n (%)	9 (6.2)	11 (11.1)	0.1707

LRP – laparoscopic radical prostatectomy; ORRP – open retropubic radical prostatectomy; BMI – body mass index; PSA – prostate-specific antigen; GS – Gleason score

In regard to mean age, BMI and median PSA before treatment, no statistically significant differences were found among the analyzed groups ($p = 0.3685$ vs. 0.3043 vs. 0.3870 , respectively). In relation to each of the clinical stages, there are no statistically significant differences between the observed groups ($p = 0.5157$ for T1, $p = 0.7949$ for T2, $p = 0.6745$ for T3, $p = 0.4065$ for T4, respectively). There is no statistical difference between the groups in the prevalence of GS from biopsy ($p = 0.6091$).

Regarding the representation of each of the mentioned values of GS biopsy samples (GS ≤ 6 , GS = 3 + 4, GS = 4 + 3 GS = 8), there are no statistically significant differences between the examined groups.

The most common pathological stage was T2c with 40% (in the LRP group), while the least represented stage was T4 with 0%, but in relation to the representation of all the stages shown, no statistically significant differences were found between the observed groups.

GS of biopsy samples did not differ significantly, both between the two groups (6.77 ± 1.1 for LRP vs. 6.85 ± 1.33 for ORRP; $p = 0.6091$), and between each of the analyzed intervals, respectively (Table 2).

Table 2. Perioperative and pathological outcomes

Parameters	LRP	ORRP	p-value
Operation time (min), median (IQR)	207 (173–250)	151 (127–220)	0.0021
EBL (ml), median (IQR)	550 (250–850)	1450 (500–2400)	0.0000
Hospitalization time (day)	6 (5–8)	9 (6–12)	0.0000
Catheter removal (day)	6.5 (5–8)	12 (10–14)	0.0000
Nerve-sparing, No. (%)	84 (58)	64 (65)	0.2937
Unilateral nerve-sparing, No. (%)	33 (23)	27 (27)	0.4237
Bilateral nerve-sparing, No. (%)	68 (47)	58 (57)	0.0735
Pathological stage, No. (%)			
T2a	22 (15.2)	8 (8.1)	0.0969
T2b	7 (4.8)	8 (8.1)	0.2983
T2c	58 (40)	38 (38.3)	0.8026
T3a	32 (22)	19 (19.2)	0.5892
T3b	26 (18)	26 (26.3)	0.1188
T4	0 (0)	0 (0)	-
Pathologic GS			
2–6	34 (23.4)	27 (27.3)	0.4965
7	76 (52.4)	48 (48.5)	0.5485
8–10	35 (24.2)	24 (24.2)	0.9840
Prostate volume (g), median (IQR)	38.2 (29.1–49)	39.1 (28.8–50)	0.3675
PSM, n (%)	58 (40)	35 (35.3)	0.4654

LRP – laparoscopic radical prostatectomy; ORRP – open retropubic radical prostatectomy; IQR – interquartile range; GS – Gleason score; PSM – positive surgical margins

The average operative time was shorter in the ORRP group and this difference was statistically significant in favor of the ORRP group (207 for LRP vs. 151 for ORRP; $p = 0.0021$). However, the average estimated blood loss (EBL) was lower in the LRP group (550 ml) compared to the ORRP (1450 ml) and this difference was statistically significant in favor of the LRP group ($p = 0.0000$). Hospitalization time was longer in the ORRP group compared to LRP (nine days vs. six days, $p = 0.0000$) and this

difference is statistically significant in favor of the LRP group. Patients from the ORRP group had a urinary catheter longer than patients from the LRP group (12 days vs. 6.5 days; $p = 0.0000$) and this difference is statistically significant in favor of the LRP group. When analyzing the overall frequency of the nerve-sparing procedure, it was more frequent in the ORRP group compared to the LRP group (65% vs. 58%, $p = 0.2937$), but this difference between the observed groups was not statistically significant. Both unilateral and bilateral nerve-sparing procedures were applied more often in the ORRP group compared to the LRP group (27% vs. 23%, $p = 0.4237$; 57% vs. 47%, $p = 0.0735$, individually), but neither in the first nor in the second case is this difference between the observed groups statistically significant.

Regarding the pathological stage, stages T2a, T2c and T3a were more often represented in the LRP group compared to the ORRP group, respectively (15.2% vs. 8.1%, $p = 0.0969$; 40% vs. 38.3%, $p = 0.8026$; 32 vs. 19%, $p = 0.5892$, respectively) and that difference between the observed groups is not statistically significant. Stages T2b and T3b, respectively, were more prevalent in the ORRP group than in the LRP group (8.1% vs. 4.8%, $p = 0.2983$; 26.3% vs. 18%, $p = 0.1188$, respectively) but the difference in favor of the ORRP group is not statistically significant. Stage T4 was not detected in both observed groups. Among the observed groups, there are no statistically significant differences in relation to the representation of each of the categories of pathological GS, respectively. GS 2–6 was more prevalent in the ORRP group compared to the LRP group (27.3% vs. 23.4%, $p = 0.4965$); GS7 was more prevalent in the LRP group compared to the ORRP group (52.4% vs. 48.5%, $p = 0.5485$), while GS 8–10 was equally represented in both observed groups (24.2% vs. 24.2%, $p = 0.9840$). The average prostate volume was higher in the ORRP group compared to the LRP group (38.2g vs. 39.1 g; $p = 0.3675$) and this difference between the observed groups is not statistically significant. Among the observed groups, no statistically significant difference was found in terms of PSM representation either (40% for LRP vs. 35.3% for ORRP, respectively, $p = 0.4654$).

Table 3. Operative complications

Perioperative and early postoperative complications, < 30 days, n (%)	LRP No. (%)	ORRP No. (%)	p-value
Overall	42 (29)	48 (48.4)	0.0083
Grade I	6 (4.1)	5 (5.055)	0.7279
Grade II	28 (19.3)	40 (40.4)	0.0030
Grade IIIa	2 (1.4)	4 (4.055)	0.1868
Grade IIIb	5 (3.4)	8 (8.08)	0.1141
Grade IVa	1 (0.8)	1 (1.01)	0.7872
Grade IVb	0 (0)	0 (0)	-
Grade V	0 (0)	0 (0)	-
Blood transfusion, n (%)	33 (22.7)	37 (37.4)	0.01314

LRP – laparoscopic radical prostatectomy; ORRP – open retropubic

The total share of perioperative and early postoperative complications was higher in the ORRP group (80.8% for ORRP vs. 29% for LRP, $p = 0.0000$) and this difference is

statistically significant in favor of the ORRP group (Table 3). The share of these complications in all analyzed categories (according to the Clavien–Dindo classification) respectively was higher in the ORRP group, but this difference compared to the LRP group is statistically significant only for the Grade 2 category (62.6% for ORRP vs. 19, 3% for LRP, $p = 0.0000$). No Grade IVb and Grade V complications were recorded. Transfusion rates were higher in the ORRP group (69.6% for ORRP vs. 22.7% for LRP, $p = 0.0000$), and that difference is statistically significant.

DISCUSSION

Radical prostatectomy is the usual curative treatment for localized prostate cancer. The operative technique of radical prostatectomy developed from open surgery to laparoscopic procedure, and the latest robot-assisted technique (RARP), which is today the most common technique in developed countries, with a growing trend of popularity [11]. Laparoscopic surgery gained great popularity at the beginning of the 21st century. The basic motives and reasons for the development of this technique are contained in its minimal invasiveness, which creates the conditions for improving operative results in terms of complications, bleeding and length of hospitalization [12]. Open radical retropubic prostatectomy has its own qualities, including availability of performing in smaller centers, short duration of the procedure, financial profitability, relatively low invasiveness, possibility of performing quality lymphadenectomy and relatively quick recovery. The presented results of randomized controlled studies on the oncological results of operative treatment of patients with localized prostate cancer show high rates of cancer-specific survival, namely: 80.4% after 23 years, 91.5–95.9% after 19.5 years, and 99% after 10 years of follow-up [13]. When it comes to the results achieved by applying each of the aforementioned operative techniques respectively, several systematic analyzes have been presented to date comparing the results of open versus laparoscopic robot-assisted radical prostatectomy, and the results were inconsistent [14].

The results of our study show that there are no statistically significant differences among the observed groups in terms of demographic and preoperative parameters, which makes the examined sample consistent for objective comparison.

Analyzing the perioperative results of robotic-assisted laparoscopic radical prostatectomy, laparoscopic radical prostatectomy and open radical prostatectomy, Sirisopana et al. [14] stated an average operative time of 160, 210 and 200 minutes, respectively, and that the difference was statistically significant in favor of the ORRP group. Similarly, the results of our study show that the average operative time in the ORRP group was statistically significantly shorter compared to the LRP group (151 minutes for ORRP vs. 207 minutes for LRP, $p < 0.05$). The results of several large studies, including a systematic review and meta-analysis by Cao et al. [15], as well as by Forsmark et al. [16], whose study was included in the LAPRO trial,

are consonant with our results regarding operative time, favoring the ORRP group. On the other hand, our results show that EBL is statistically significantly higher in the ORRP group compared to the LRP group, which is in line with the experiences of other authors [12, 14, 15, 16]. The literature also states that the reduction of EBL is directly correlated with the quality of visualization, which is one of the advantages of the laparoscopic technique compared to the open [14]. In our series, the average hospitalization time was nine days in the ORRP group and it was statistically significantly longer than in the LRP group with six days. The average duration of catheterization in the ORRP group was 12 days, statistically significantly longer than in the LRP group (6.5 days). The results of many studies confirm our findings regarding the duration of hospitalization and catheterization, favoring the laparoscopic operative technique [14, 15, 17].

In our series, the nerve sparing technique was applied more often in the ORRP group, but without a statistically significant difference compared to the LRP group. This technique certainly contributes to the quality of the preservation of the bladder neck and to the preservation of potency and continence, which primarily depends on the operator's skills [15, 18]. However, in our study we did not study the effects of this technique on the rate of potency and continence, but this will certainly be the subject of future consideration. Differences between pathological GS categories among the observed groups are not statistically significant, which confirms clear inclusion criteria and good selection of our study patients.

PSM is an indicator of the oncological outcome of surgery, but also a predictor of biochemical relapse [19]. In our study, the PSM rate was higher in the LRP group (40%) compared to the ORRP group (35.3%), but without statistical significance. In a recent meta-analysis by Cao et al. [15], the overall PSM rate for LRP/RARP was 22.3% and for ORRP 28.6%, with no statistical differences. Analyzing RARP, Wang et al. [20] reported variations in PSM rates from 12.1% to 41.3%. Our results are in the range of values shown by other authors, but we are convinced that this result can be improved by using a unique operative technique for all operators participating in the study [21]. Prostate volume was slightly higher in the ORRP group, but this difference compared to the ORRP group is not statistically significant. Prostate volume along with GS has been reported to be the most reliable predictor of PSM [15].

Perioperative and early postoperative complications (< 30 days), classified according to the Clavien–Dindo system were detected in a total of 122 patients, namely: 42 in the LRP group and 48 in the ORRP group. The relative share of 48.4% of complications in the ORRP group is higher than the relative share of 29% in the LRP group, and the difference is statistically significant ($p = 0.0083$). Among the analyzed complications, Grade 2 complications dominated

in both examined groups, in a total of 68 patients. Relative share of these complications is higher in the ORRP group (40.4% for ORRP vs. 19.3% for LRP, $p = 0.0030$) and this difference is statistically significant in favor of the ORRP group. Relative share of complications of the other categories (Grade I, Grade IIIa, Grade IIIb and Grade IVa) was higher in the ORRP group compared to the LRP group, but this difference is not statistically significant for any individual category. Complications of Grade IVb and Grade V were not determined. There are few head-to-head studies in the literature comparing the operative complications of LRP versus ORRP. Pompe et al. [22] reported that in their series of 13924 RPs, the average operative complication rate was 20.6%, with Grade I and Grade II predominating. Analyzing the operative complications of ORRP and LRP in a series of 4592 patients, Rabbani et al. [23] reported an average rate of 30.3%, which did not include the relative share of blood transfusion in the ORRP group, which was 55% and was higher than the share in the LRP group. Sirisopana et al. [14] reported an overall complication rate of 81.25% for ORRP and 29.05% for LRP, among which Grade 1 and 2 complications predominate, with blood transfusions of 69.35% for ORRP and 23.4% for LRP [14]. The presented rates of perioperative and early postoperative complications in our series are in compliance with the results presented in the literature. Blood transfusions were significantly more frequent in the ORRP group (22.7% for LRP vs. 37.4% for ORRP, $p = 0.01314$). We want to emphasize that blood transfusions are included into Grade II complications, and they are also separately compared in relation to the studied groups. There is no doubt that the outcome of operative treatment is influenced by the experience of the operative team, as well as the number of operations performed annually. A recently published study by Ploussard et al. [24] states that 10 cases per year represents the lower limit of the number of operative interventions, which is associated with an unfavorable operative outcome. The results of our research show that in the mentioned period we performed an average of 61 radical prostatectomies per year, which ranks our hospital among high-volume institutions, and this certainly contributes to the improvement of perioperative results.

CONCLUSION

For patients with moderate-risk prostate cancer, both LRP and ORRP provide favorable operative results in terms of efficacy, safety and oncologic outcome. However, patients undergoing LRP were more likely to have less EBL, shorter length of hospital stay, earlier catheter removal and lower rates of overall perioperative complications.

Conflict of interest: None declared.

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Периоперативни исходи лапароскопске и отворене ретропубичне радикалне простатектомије

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САЖЕТАК

Увод/Циљ Радикална простатектомија је опција лечења са високим куративним потенцијалом код болесника са карциномом простате умереног ризика.

Циљ рада је процена периоперативних резултата лапароскопске (ЛРП) и отворене ретропубичне радикалне простатектомије (ОРРП).

Метод Од 2016. до 2020. године укупно 244 болесника подвргнута су радикалној простатектомији, и то: 145 болесника ЛРП и 99 болесника ОРРП. Демографски подаци, преоперативни параметри, периоперативни и патолошки исходи анализирани су и упоређени између група ЛРП и ОРРП.

Резултати У погледу демографских података и преоперативних параметара (индекс телесне масе, средња старост, средња вредност простатичног специфичног антигена пре третмана, клинички стадијум и биопсијски Глисонов скор) није било статистички значајних разлика између анализираних група. Болесници из групе ОРРП имали су значајно кра-

ће време операције ($p < 0,05$). Међутим, болесници из групе ЛРП имали су велике предности у поређењу са болесницима из групе ОРРП у погледу процењеног губитка крви (550 ml за ЛРП наспрам 1450 ml за ОРРП), времена хоспитализације (шест дана за ЛРП наспрам девет дана за ОРРП), уклањања катетера (6,5 дана за ЛРП наспрам 12 дана за ОРРП), укупне стопе компликација (29% за ЛРП наспрам 48,4% за ОРРП) и трансфузије крви (22,7% за ЛРП и 37,4% за ОРРП).

Закључак И ЛРП и ОРРП обезбеђују повољне оперативне резултате у погледу ефикасности, безбедности и онколошког исхода. Међутим, вероватније је да ће болесници који су били подвргнути ЛРП-у имати мањи процењени губитак крви, да ће краће боравити у болници, да ће им се раније уклонити катетер и да ће имати ниже стопе укупних периоперативних компликација.

Кључне речи: карцином простате; лапароскопска радикална простатектомија; отворена ретропубична радикална простатектомија