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Open, laparoscopic and robot-assisted laparoscopic radical prostatectomy: comparative analysis of operative and pathologic outcomes for three techniques with a single surgeon's experience

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Abstract. – OBJECTIVE: To compare outcomes of open (O-), laparoscopic (L-) and robot-assisted laparoscopic (RAL-) radical prostatectomy (RP) performed by the same surgeon.

PATIENTS AND METHODS: From May 1999 to April 2012, 484 RPs were performed by a single surgeon. Patients' data including age, body-mass index, serum prostate specific antigen (PSA) level, Gleason score of prostate biopsy and prostatectomy specimen, preoperative prostate and specimen volumes, clinical and pathologic stages, operation time, estimated blood loss (EBL), catheterization time, blood transfusion rate were recorded. Prospectively collected data was evaluated retrospectively by statistical analyses.

RESULTS: Of 484 radical prostatectomies, ORP (50), LRP (308) and RALRP (79) done by the same surgeon were included into study. Mean ages were 63.8, 62.7 and 60.3 years for ORP, LRP and RALRP respectively. Operation times for ORP, LRP and RALRP were 255, 208 and 242 minutes. EBL and hospitalization time were 602, 526, 234 mL, and 9.1, 3.2, 3.2 days for ORP, LRP and RALRP, respectively. While a significant advantage was found for EBL and complication rates in RALRP and for operation time in LRP, significant disadvantages were found in terms of catheterization time, hospitalization time, decrease in hemoglobin and blood transfusion in ORP. However, preoperative prostate volume and serum PSA level, oncologic outcomes and positive surgical margins were nearly similar in all operative techniques.

CONCLUSIONS: Minimally invasive techniques such as LRP and RALRP are promising techniques with comparable outcomes with ORP. Shorter catheterization time, less blood loss and fewer complication rates can be provided by RALRP.

Key Words:
Laparoscopy, Open surgery, Prostate cancer, Radical prostatectomy, Robot-assisted laparoscopic surgery.

Abbreviations

PCa: Prostate cancer; RP = Radical prostatectomy; ORP = Open radical prostatectomy; LRP = Laparoscopic radical prostatectomy; RALRP = Robot-assisted laparoscopic radical prostatectomy; BMI = Body-mass index; PSA = Prostate specific antigen; TRUS = Transrectal ultrasound; P-Bx = Prostate biopsy; EBL = Estimated blood loss; TNM = Tumor-Node-Metastasis; AJCC = American Joint Committee on Cancer; PSM = Positive surgical margin; LC = Learning curve.

Introduction

Prostate cancer (PCa) is the most common cancer among men when skin cancer is excluded, and is the second leading cancer-related cause of death[1]. Although there are some different ways to treat PCa, surgery still remains very important for organ confined PCa and radical prostatectomy (RP) is the gold standard in the treatment. Walsh and Donker introduced nerve-sparing open radical prostatectomy (ORP) in 1982[2]. By developing technology, surgical techniques have been evolved and minimally invasive laparoscopic approach came into question. Although it had been concluded that laparoscopic radical prostatectomy (LRP) seemed not to have promising results when it was first performed, a new era has begun

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with the publication of their LRP technique by Guillonneau et al in 1998[3]. Since then, many clinical series were reported with acceptable oncologic and functional results with LRP[4-6].

By the first introduction of robot-assisted laparoscopic radical prostatectomy (RALRP) by Binder, this reconstructive operation had moved to a new dimension[7]. In a short time period, high-volume centers reported outcomes with RALRP[8,9]. Both LRP and RALRP had better outcomes for continence and potency as well as oncologic safety when compared with ORP[4-6,8,9]. Although there are high-volume centers' data reported about ORP, LRP and RALRP, according to our knowledge there is no reported data of changing operative techniques for RP by single surgeon's experiences. The aim of our study was to evaluate the operative and pathologic outcomes of ORP, LRP and RALRP performed by the same surgeon (TE). This is a unique study about comparison of ORP, LRP and RALRP by single surgeon.

Patients and Methods

Study Group

From May 1999 to April 2012, 484 RPs were performed by a single surgeon (TE). Of the 484, 437 RPs were included in our study, with 50 ORPs, 308 LRPs and 79 RALRPs respectively. Patients with a history of neoadjuvant hormonotherapy and/or adjuvant therapy before PSA relapse were excluded. A history of previous abdominal surgery, transurethral prostate surgery or hernia repair was not a contraindication. The prospectively collected medical recordings of the patients were reviewed retrospectively. All patients had given written informed consent before the surgery for giving permission for the use of the collected data at any time. The principles of the Helsinki Declaration were followed during the study, and the confidentiality of the patients' data was guaranteed. Institutional Ethics Committee has approved the study.

Preoperative Evaluation

Preoperative clinical parameters of patients including age, body-mass index (BMI), level of serum prostate specific antigen (PSA), clinical stage, Gleason score sum of transrectal ultrasound (TRUS) guided prostate biopsy (P-Bx), prostate volume measured by TRUS were recorded from the patients' files retrospectively.

Operative Data

Operation and anastomosis time, duration of hospitalization and catheterization, quality of anastomosis and estimated blood loss (EBL) were recorded. Quality of anastomosis was evaluated by giving 200 mL saline into bladder through a urethral catheter after vesicourethral anastomosis was completed, and was classified into four groups: water-tight, mild leak, moderate leak and severe leak.

Surgical Techniques

Between May 1999 and June 2003, our surgeon (TE) performed ORP for all organ confined PCa patients after beginning his academic career. He had a fellowship training program for urologic laparoscopic surgery during 2003-2004. After this, he performed LRP to all organ confined PCa patients between 2004 and 2010. With a switch to robotic surgery after a short training program, RALRP was performed to all organ confined diseases during 2010-2012.

Pathologic Evaluation, Tumor Grading And Staging

Firstly, the 1997 Tumor-Node-Metastasis (TNM) staging system was used for both clinical and pathologic staging. After the revision was made by the American Joint Committee on Cancer (AJCC), the 2002 TNM staging system has been used. All RP specimens were evaluated according to the Gleason grading system before 2005 and the modified Gleason grading system after 2005. A positive surgical margin (PSM) was defined as the presence of tumor tissue on the inked surface of the specimen.

Postoperative Data

Postoperative parameters including pathologic stage and Gleason score, specimen volume, tumor volume and PSM were recorded. Postoperative complications were collected and were classified according to modified Clavien-Dindo classification system.

Statistical Analysis

A p value < 0.05 was considered statistically significant. All statistical analysis tests were performed with the GraphPad Prism Version 6 (GraphPad Software Inc., CA, USA). Numeric values were compared by using one-way ANOVA and independent t-test where applicable, and chi-square test is used for the comparison of the non-numeric values.

Results

The mean ages were 63.8, 62.7 and 60.3 years for ORP, LRP and RALRP respectively. The patients' demographic and operative results are presented in Table I. No statistically significant difference was determined for age, BMI, preoperative PSA value and TRUS prostate weight between the three groups.

However, operation time in LRP was statistically significantly lower than ORP and RALRP (208.5, 255, 242.6 min respectively, $p < 0.001$); but there was no difference between ORP and RALRP ($p > 0.05$). Regarding hospitalization time, although no difference was found between minimally invasive techniques (LRP and RALRP, $p > 0.05$), it was significantly longer in ORP (3.2, 3.2, 9.1 days respectively, $p < 0.001$). When catheterization time was evaluated, a statistically significantly difference was calculated among three groups with the lowest value in RALRP (16.3, 8.2 and 6.8 days for ORP, LRP and RALRP respectively; $p < 0.001$ for open vs. minimally invasive surgery, and $p < 0.01$ for LRP vs. RALRP). It has been observed that EBL was the lowest in RALRP group (602, 526, 234 mL for ORP, LRP and RALRP respectively; $p < 0.001$ for RALRP vs. the others, and $p > 0.05$ for ORP vs. LRP) with a lowest transfusion rate again in RALRP among three groups ($p < 0.001$).

The pathologic findings are listed in Table II. Preoperative P-Bx and postoperative specimen Gleason scores, specimen weights and tumor volumes were not statistically different among three groups. Regarding PSMs, no significant difference was observed among the groups, which is consistent with the literature (30.0%, 28.6% and 27.8% for ORP, LRP, RALRP respectively; $p = 0.966$). Perioperative complications according to Clavien-Dindo classification are shown in Table III. The majority of the complications were classified in Grade 2 in each group, as these complications were due to hemorrhage and subsequent blood transfusion. When compared to ORP and LRP, RALRP had a statistically significant advantage for overall, minor and major complication rates ($p < 0.001$). The same advantage is also valid if the rates of the cases without any complication have been compared ($p < 0.001$).

Discussion

RP is the treatment of choice with curative intent in PCa, and ORP is accepted as the gold standard. Since the introduction of the anatomical concept of nerve sparing ORP by Walsh and Donker[2] and with addition of several modifications to the original technique, good results have

Table I. Demographic and operative results of open (ORP), laparoscopic (LRP) and robot-assisted laparoscopic (RALRP) radical prostatectomies.

Operation period	1999-2003 ORP (n: 50)	2004-2010 LRP (n: 308)	2010-2012 RALRP (n: 79)	*p* value
Age (years)	63.8	62.7	60.3	> 0.05
BMI (kg/m^2)	25.4	26.1	26.9	> 0.05
PSA (ng/mL)	7.33	10.47	8.32	> 0.05
TRUS prostate weight (g)	38.4	37.1	39.8	> 0.05
Operation time (min)	255*	208.5	242.6*	< 0.001
Catheterization time (day)	16.3	8.2**	6.8**	< 0.001
Hospitalization time (day)	9.1	3.2†	3.2†	< 0.001
EBL (mL)	602§	526§	234	< 0.001
Delta Hb (g/dL)	3.06	2.35††	2.0††	< 0.05
Blood transfusion	27 (54%)	54 (17.5%)	7 (8.9%)	< 0.001
Anastomosis time (min)$^{\#}$	N/A	28.8	19.7	< 0.001
Anastomosis quality$^{¥}$				
• Water-tight	N/A	258 (83.7%)	69 (87.3%)	> 0.05
• Mild leak	N/A	39 (12.6%)	9 (11.3%)	
• Moderate leak	N/A	8 (2.5%)	1 (1.2%)	
• Severe leak	N/A	3 (0.9%)	0 (0%)	

BMI: Body mass index; PSA: Prostate specific antigen; TRUS: Transrectal ultrasonography; EBL: Estimated blood loss; Delta Hb: Decrease in hemoglobin. $^{\#}$Independent *t*-test, $^{¥}$Chi-square test. Data are shown as mean or n (%). N/A: Not applicable. *> 0.05, **< 0.01, †> 0.05, §> 0.05, ††> 0.05.

Table II. Pathologic results of open (ORP), laparoscopic (LRP) and robot-assisted laparoscopic (RALRP) radical prostatectomies.

	ORP (n: 50)	LRP (n: 308)	RALRP (n: 79)	*p* value
Clinical stage				N/A
T1a	–	4 (1.3%)	–	
T1b	–	6 (1.9%)	3 (3.8%)	
T1c	38 (76%)	175 (56.8%)	63 (79.9%)	
T2a	7 (14%)	63 (20.5%)	9 (11.4%)	
T2b	4 (8%)	52 (16.9%)	3 (3.7%)	
T2c	1 (2%)	6 (1.9 %)	1 (1.2%)	
T3a	–	2 (0.6%)	–	
Biopsy GS	5.88	6.25	6.23	> 0.05
Specimen weight (g)	45	50.4	44	> 0.05
Pathologic stage				N/A
T2a	6 (12%)	59 (19.2%)	10 (12.7%)	
T2b	15 (30%)	45 (14.6%)	15 (19.0%)	
T2c	11 (22%)	63 (20.5%)	32 (40.5%)	
T3a	12 (24%)	88 (28.6%)	16 (20.3%)	
T3b	6 (12%)	51 (16.6%)	6 (7.6%)	
T3c	–	1 (0.3%)	–	
T4	–	1 (0.3%)	–	
Pathologic GS	6.60	6.57	6.68	> 0.05
Tumor volume (%cc)	3.35	5.12	3.40	> 0.05
PSM				> 0.05
Overall	15/50 (30.0%)	88/308 (28.6%)	22/79 (27.8%)	
pT2	5/32 (15.6%)	15/167 (8.9%)	4/57 (7.0%)	
pT3	10/18 (55.5%)	71/140 (50.7%)	18/22 (81.8%)	

GS: Gleason score; PSM: Positive surgical margin. Data are shown as mean or n (%). N/A: Not applicable.

been obtained both for oncologic[10,11] and functional[12,13] results in high-volume series.

After Guillonneau et al[3] standardized the LRP technique, the use of this minimally invasive procedure has gradually risen. Because of its steep learning curve (LC) and necessity of high numbers of operation to gain enough experience, few centers succeeded to improve a structured program with high caseloads. Experienced surgeons have reported promising good results for oncologic and functional outcomes that are comparable with open surgery[5,6,14].

For evaluating the efficacy of any treatment with a curative intent for PCa, it is important to

Table III. Postoperative complications grouped according to Clavien-Dindo classification

	ORP (n: 50)	LRP (n: 308)	RALRP (n: 79)	*p* value
No complication	5 (10%)	223 (72.4%)	68 (86.1%)	< 0.001
Minor (Grade 1-2)	31 (62%)	73 (23.7%)	8 (10.1%)	< 0.001
Grade 1	3	11	0	
Grade 2 (only Tx)	27	54	7	
Grade 2 (total)	28	62	8	
Major (Grade 3-5)	14 (28%)	12 (3.9%)	3 (3.8%)	< 0.001
Grade 3a	9	4	2	
Grade 3b	1	3	1	
Grade 4a	4	4	0	
Grade 4b	0	0	0	
Grade 5	0	1	0	
Overall	45 (90%)	85 (27.6%)	11 (13.9%)	< 0.001

Data are shown as n (%). Tx: Blood transfusion.

look at the oncologic control. Oncologic outcomes after RP can be measured by PSM, biochemical recurrence rate and disease-specific survival rate postoperatively. Although PSM is an independent predictive factor for biochemical recurrence, local recurrence and distant metastasis, it is important to keep in mind that a positive PSM does not always indicate the presence of residual disease where a negative PSM may not mean total eradication of cancer[12]. Overall PSM rates are reported as ranging from 11 to 46% for ORP[15,16], from 11 to 39.4% for LRP[15,17] and from 6 to 29.3% for RALRP[18,19]. The PSM rates for LRP and RALRP are generally higher in the LC period as expected.

Guazzoni et al[20] showed in their study that PSM rates for LRP are comparable with that of ORP. Other papers also confirmed that PSM rates in LRP are at most equal to or lower than ORP[15,17,21]. When comparing ORP with RALRP, some authors found lower incidence for overall PSM favoring RALRP[18,22,23], while the others did not find a statistically significant difference in PSM rates[19,24-26]. In some series, no statistical difference was found for PSM rates when LRP and RALRP are compared[27-29]. In the cumulative analysis of all the comparative studies reporting data on PSM status, Ficarra et al[30] found a statistically significant difference in PSM rates only between ORP and RALRP; but similar PSM rates between both ORP and LRP, and LRP and RALRP. In our series, we did not find any difference in overall PSM rates among the three groups, which are consistent with the data in the literature.

In our study, duration of urethral catheterization and hospitalization, and decrease in hemoglobin were found to be statistically significantly more in ORP group when compared to LRP and RALRP as estimated (p values < 0.001, < 0.001 and < 0.05, respectively). RALRP has an advantage in terms of EBL and transfusion rate among three groups via the properties of high capability of movement of the robotic arms, high magnification rate and 3-dimensional vision supplied by the da Vinci® robotic system (Intuitive Surgical, Inc., Sunnyvale, CA, USA). And this advantage has led a significant decrease in minor and overall complication rates in RALRP group. When LRP was compared to RALRP, although no difference was recorded for hospitalization time and decrease in hemoglobin ($p > 0.05$ for both), catheterization time and anastomosis time were found to be significantly less in RALRP ($p < 0.01$ and $p < 0.001$, respectively). Moreover, LRP and RALRP31 has very well-known advantages that less analgesics have been used after these procedures[32].

As this study is a retrospective study, no data regarding anastomosis time and quality was collected at the time of open surgeries; so, we could not make a comparison for these two parameters between open and minimally invasive modalities. When anastomosis time is compared among minimally invasive techniques, RALRP has a significant advantage over LRP (19.7 min vs. 28.8 min respectively, $p < 0.001$). For the quality of anastomosis, although the percentages of mild, moderate and severe leakage were very slightly higher in LRP group, no statistical difference was noted ($p = 0.699$). This shows us that a good vesicourethral anastomosis can be done in both techniques, but in a shorter time in RALRP with the ease of the robotic surgical system.

To our knowledge, this study is the first one in the literature evaluating the operative and pathologic outcomes of open, laparoscopic and robot-assisted laparoscopic surgery performed by the same surgeon. Additionally, experienced uropathologist has been important for successful outcomes[31]. In a previous series we presented impact of frozen sections[31] and consistency in Gleason scores[33] during surgical process of RALRP. There are some data for comparison of these three techniques that are performed by different surgeons. Different techniques done by different surgeons may probably form a bias when evaluating the complexity or oncologic and functional outcomes of the procedures.

We would like to underline some considerations. Understanding the anatomy of RP surgery in the time of LC of open surgery may have had an impact on performing LRP. Also, learning surgical anatomy and steps of the procedure, and gaining experience for minimally invasive techniques by performing LRP have certainly affected the transition from LRP to RALRP, and accelerated the LC of robot-assisted surgery. It is almost impossible to assess which has affected the other at what extend. Moreover, a retrospective study instead of a prospective randomized one provides lower level evidence. Organizing a prospective randomized study with high case volume (preferably a matched-pair analysis) would prevent selection bias and provide much more accurate results. The number in open and robotic groups in our study is relatively small; this can make the statistical significance questionable. Minor complications (especially blood loss and subsequent transfusion) may have been lower if the surgeon had continued to do open surgeries. Additionally, comparing oncological and functional results would put on additional value to this paper when follow-up periods of robotic cases increase.

A restriction of the study is the stage-specific PSM rates. Although overall PSM rates are similar among three groups, the PSM rate in patients with pT3 disease in RALRP group was found to be higher when compared to experienced groups. Evaluating all patients, including the ones in LC period, in all groups may have had an effect on this result. When the patients in RALRP group were evaluated in detail, it was found that most of the pT3 disease patients with PSM had been operated in LC period (data not shown). Also relatively small number of patients in ORP and RALRP may have affected the result.

From now on, it may be difficult to randomize the candidates of RP either into ORP, LRP or RALRP, as this procedure is affected by various factors. By being in today's world with a fast communication all over the world via internet and with the commercial effects, patients want to have and/or are more directed to robot-assisted surgery. For this reason, the vast majority of RPs is performed robotically (especially in the United States) and performing a head-to-head comparison with open and/or laparoscopic surgery in the future seems nearly impossible.

Conclusions

Although ORP currently remains the gold standard treatment of organ-confined PCa, minimally invasive techniques, LRP and RALRP, seem to be promising modalities for the treatment of organ-confined PCa with comparable operative and oncologic outcomes up to now. RALRP allows for faster anastomosis, less blood loss and fewer complications compared to ORP and LRP for an experienced fellowship-trained surgeon. To assess whether these techniques have a superiority over open surgery or not, further prospective, randomized, controlled studies with high caseloads are needed.

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Conflict of Interest

The Authors declare that there are no conflicts of interest.

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