Robotic versus Laparoscopic Retroperitoneal Lymph node Dissection for Clinical Stage I Non-seminomatous Germ Cell Tumor of Testis: A Comparative Analysis

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Purpose: To compare the treatment outcomes of robotic retroperitoneal lymph node dissection (R-RPLND) versus laparoscopic RPLND (L-RPLND) for clinical stage I non-seminomatous germ cell testicular tumors (NSGCTs).

Materials and Methods: We retrospectively reviewed the data of patients with stage I NSGCTs who underwent robotic or laparoscopic RPLND between 2008 and 2017. Perioperative data and oncologic outcomes were reviewed and compared between the two groups. Progression-free survival was analyzed using Kaplan-Meier survival curves and compared between two groups.

Results: A total of 31 and 28 patients underwent R-RPLND and L-RPLND respectively. The preoperative characteristics of the patients were comparable in the two groups. Patients in R-RPLND group had significantly shorter median operative time (140 vs. 175 minutes, $P < .001$), a shorter median duration to surgical drain removal (2 vs. 4 days, $P = .002$) and a shorter median postoperative hospital stay (5 vs. 6 days, $P = .001$). There were no statistical differences in intra- and post-operative complication rate between the groups and the oncologic outcomes were similar in the two groups.

Conclusion: In expert hands, R-RPLND and L-RPLND were comparable in oncological parameter and morbidity rate; R-RPLND showed superiority in operation duration, median days to surgical drain removal and postoperative hospital stay for stage I NSGCTs. Multicenter and randomized studies with good power of study and sufficient follow-up duration are required to validate our result.

Keywords: lapraroscopy; nonseminomatous germ cell tumor; retroperitoneal lymph node dissection; robotic surgical procedures; treatment outcomes

INTRODUCTION

According to the European Association of Urology (EAU) Guidelines, treatment options for stage I non-seminomatous germ cell tumors (NSGCTs) include active surveillance after orchiectomy, platinum-based chemotherapy, or primary retroperitoneal lymphnode dissection (RPLND)[(1)]. Risk of relapse is a major concern for active surveillance, with five year relapsing rate up to 30.6%[(2)]. Despite the good response of platinum-based chemotherapy in NSGCT, its usage is limited by complications, such as adverse cardiac events, deterioration of renal function, and the risk of secondary malignancies[(3)]. In spite of controversies, primary RPLND play a role in the management of patients with stage I NSGCTs in term of retroperitoneal local control, accurate clinical staging, removal of chemo-resistant tumor elements, and avoiding overtreatment of chemotherapy[(3)].

Traditionally, the RPLND was performed via open surgery through transperitoneal or retroperitoneal approach. Despite excellent oncologic outcomes, open-RPLND (O-RPLND) was associated with great operative trauma, significant morbidity, and prolonged hospitalization[(4,5)].

The first laparoscopic RPLND (L-RPLND) was described by Rukstalis et al. in 1992 for diagnostic purpose[(6)]. With the development and advancement of the technique, L-RPLND has been applied to testicular cancer for treatment purposes with less operative trauma and perioperative complications, more favorable cosmetic results, similar oncologic outcomes, and shorter hospitalization as compared with O-RPLND[(7-9)].

With the popularization of robotic technology in recent years, robotic surgery has replaced laparoscopy in many challenging urologic procedures. Robotic technology has demonstrated significant advantages in term of excellent 3-dimension vision, shorter learning curve, stability, and dexterity. R-RPLND was first described

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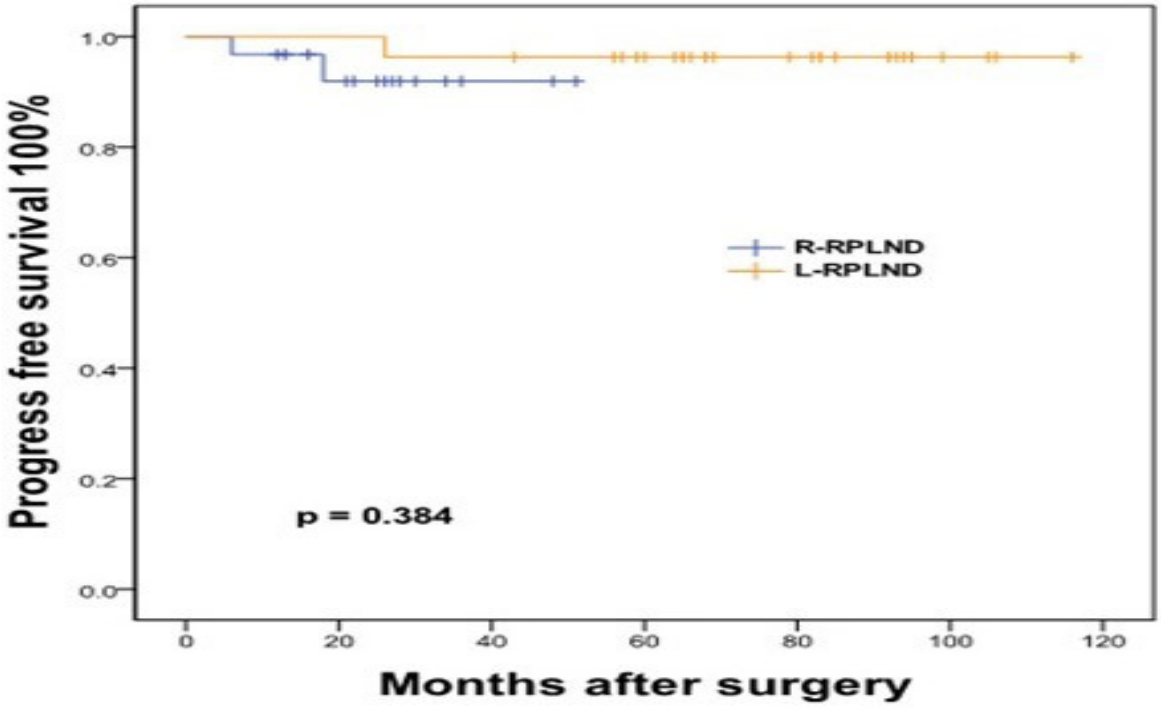

Figure 1. Progression-free survival

by Davol P et al in 2006[10,11]. Since then, the feasibility of R-RPLND has been fully demonstrated in several series reports[12-14]. Up to date, there is only one comparative analysis comparing R-RPLND with L-RPLND, and it remains to be demonstrated that R-RPLND offers a specific benefit over L-RPLND[15].

In this study, we compare the perioperative results and oncologic outcomes between R-RPLND and L-RPLND for clinical stage I NSGCTs.

MATERIALS AND METHODS

Study population

After the approval was obtained from the medical ethics committee of our institute, data of patients with clinical stage I NSGCT who had undergone L-RPLND or R-RPLND in our institute were retrospectively reviewed. Patients who had received chemotherapy prior to RPLND, patients with primary diagnosis other than NSGCT and patients with NSGCT higher than clinical stage I were excluded from this study. Clinical staging was performed according to the recommendation of EAU guideline on testicular cancer, including computed tomography of the chest or x-ray, computed tomography or magnetic resonance imaging of the abdomen and pelvis, and serum tumor markers consisting of α-fetoprotein (AFP), beta human chorionic gonadotropin (β-hCG), and lactate dehydrogenase (LDH). The patients were provided counseling on the advantages and disadvantages of treatment options including close surveillance, platinum-based chemotherapy and RPLND, and RPLND was their final choice.

Surgical Technique

All the procedures were performed transperitoneally by a single surgeon (Xu Zhang) with advanced laparoscopic and robotic experience. All the patients in both groups were positioned in 70° lateral and 15° Trendelenburg position. The time between the placement of the first trocar and removal of the last trocars was recorded as the duration of the operation.

For the patients with left testicular cancer, the template of lymph node dissection included left common iliac, preaortic above inferior mesenteric artery, paraaortic, retroaortic, interaortocaval and precaval lymph nodes. For the right-sided disease, the template included right common iliac, paracaval, precaval, retrocaval, interaortocaval, and preaortic above inferior mesenteric artery lymph nodes. The cranial border of dissection was the level of renal hilum and the lateral border was the ipsilateral ureter. Sympathetic nerves were meticulously recognized and spared during the operation.

Postoperative Surveillance

Patients with positive lymph node disease were recommended to adjuvant chemotherapy postoperatively. All the patients were regularly followed up postoperatively. Physical examination, ultrasound on scrotum and abdomen, serum tumor markers examination and thoracic x-ray were performed every 3 months for the first two years, every 6 months between year 3 and 5 and annually thereafter. Computerized tomography on abdomen and chest is done every 6 months for 5 years postoperatively and annually thereafter.

Statistical Analysis

The demographic and clinical data were collected and compared between L-RPLND and R-RPLND groups. IBM SPSS Statistics 19.0 for Windows (SPSS, IBM, Al monk, NY) was utilized for the data analysis, and the significance level was set at two-tailed $P < .05$. Continuous variables were presented as the median and IQR

Table 1. Patient Demographics and Tumor Characteristics

Variables	R-RPLND	L-RPLND	*P* value
Number of cases	31	28	
Median (IQR)			
Age (yrs)	27 (16-52)	29 (18-56)	0.429
BMI (kg/m2)	23.7 (18.7-29.4)	24.5 (17.3-29.3)	0.539
Primary laterality, n (%)			
Left	11(35.5)	12 (42.9)	0.602
Right	20(64.5)	16 (57.1)	
pT stage, n (%)			
pT1	21 (67.8)	22 (78.6)	0.478
pT2	9 (29.0)	6(21.4)	
pT3	1(3.2)	0	
Primary pathological type, n (%)			
Mixed	14 (45.2)	15 (53.6)	0.630
Embryona	14 (45.2)	11 (39.3)	
Teratoma	0	1(3.6)	
Yolk sac	1(3.2)	0	
Leydig cell tumor	2(6.4)	1(3.6)	
Elevation of tumor markers, n (%)			
AFP	2(6.54)	2(7.2)	1.000
β-hCG	0	1(3.6)	0.475
LDH	1(3.2)	1(3.6)	1.000

and compared with the Wilcoxon rank sum test. The χ^2 and Fisher's exact test were used for comparisons of categorical variables. The Kaplan-Meier method was used to estimate survival probabilities, which were compared by the log rank test.

RESULTS

From September 2009 to March 2018, 31 and 28 patients underwent R-RPLND and L-RPLND respectively for stage I NSCGT in our institute. The preoperative clinical characteristics of the patients were displayed in Table 1. Variables including age, BMI, primary laterality of the disease, pathological tumor-stage and histopathological result of orchidectomy were similar with P value > .05 between the groups.

The perioperative clinical data of the patients was displayed in Table 2. The estimated blood loss (EBL), LN yield, and median duration of Ryle's tube insertion were similar (P > .05) between the two groups. Intraoperative complications, including open conversion, major blood loss and major blood vessels injury, were not encountered in both groups. The robotic cohorts had significantly shorter operative duration (140 vs. 175 minutes $P < .05$), median duration to surgical drainage removal (removed when the drainage less than 100 mL 2 vs. 4 days $P = .002$) and median postoperative hospital stay (5 vs. 6 days $P = .001$). One patient from the R-RPLND cohort and 2 patients from the L-RPLND cohort were complicated with chylous ascites. They were treated conservatively. One patient in the L-RPLND cohort presented with hypertension as sequelae of right renal artery stenosis, and he was treated with percutaneous dilatation of stenotic renal artery. Two patients in the R-RPLND cohort and 1 patient in the L-RPLND cohort experienced retrograde ejaculation. The overall postoperative complication rate was similar between the two groups (9.7% vs. 14.3% $P = .609$). Eight patients in the R-RPLND cohort and 5 patients in the L-RPLND cohort had retroperitoneal metastasis. The distribution of

Table 2. Intra- and Post-Operative Information

Variables	R-RPLND	L-RPLND	*P* value
Number of cases	31	28	
Median (IQR) operative time, mins	140(100-210)	175(120-300)	0.000
Median (IQR) estimated blood loss, mL	50(20-200)	50(10-350)	0.847
Median (IQR) LN yield	23(14-33)	21(9-30)	0.150
Intraoperative complication, n (%)			
Open conversion	0	0	NS
Transfusion	0	0	
Major vessel injury	0	0	
Median (IQR) days			
To surgical drain removal	2(0-9)	4(1-25)	0.002
To ryle's tube removal	1(1-2)	1(1-3)	0.288
Median (IQR) hospital stay, days	5(3-9)	6(3-25)	0.001
Postoperative complication, n (%)	3(9.7)	4(14.3)	
chylous ascites	1	2	0.609
Renal artery stenosis	0	1	
Retrograde ejaculation	2	1	
pN stage, n (%)			
pN0	23(74.1)	23(82.1)	0.654
pN1	6(19.4)	3(10.7)	
pN2	2(6.5)	2(7.2)	
Median (IQR) follow-up, months	24(12-51)	68.5(42-116)	< 0.001

the pN stage was similar between the two groups (P = .654).

Median follow-up of the patients in the R-RPLND and L-RPLND group was 24 and 68.5 months respectively (P < .05). No patients with pN0 stage showed retroperitoneal recurrence in either groups but pulmonary replase was detected in 2 patients in the R-RPLND cohort and 1 patient in the L-RPLND cohort. All the patients with pN1 and pN2 disease in both groups selected chemotherapy, there was no retroperitoneal recurrence and systemic relapse detected in either group. There was no significant difference in PFS between the 2 groups (P = .384, **Figure 1**).

DISCUSSION

Testicular cancer is a common malignancy for males between 15 to 35 years old. It represents nearly 1% of male neoplasms and 5% of urological tumors[16,17]. The majority of the cases are germ cell tumors which can be further classified as seminoma or nonseminoma [1]. As compared to seminoma, nonseminoma is more aggressive in nature[1]. Up to 25-30% of patients with NSGCTs have retroperitoneal lymph nodal metastatic disease with negative imaging evidence[18]. According to EAU Guideline 2017, options for clinical stage I NSGCTs include close surveillance, chemotherapy, and RPLND. Despite controversies, RPLND remains its role in treatment options for some selected patients with stage I NSGCT[1].

Traditionally, the RPLND was performed via open surgery through a transperitoneal or retroperitoneal approach. While O-RPLND has shown excellent oncologic outcomes, these procedures were associated with great operative trauma, significant morbidity, and prolonged hospitalization[4,5]. With the advancement of minimally invasive techniques, L-RPLND and R-RPLND have become alternatives to open surgery and demonstrated the advantages of minimally invasive surgery such as less operative trauma and perioperative complications, favorable cosmetic results and shorter hospitalization time[7,8,12-14]. Robotic-assisted surgery has demonstrated advantages over laparoscopic surgery in many challenging urologic procedures[19-21]. In consideration of superior advantages of robotic technology, it is logical to suppose that R-RPLND offers a specific benefit over L-RPLND. However, the available published data are limited and there is only one direct comparative analysis of R-RPLND and L-RPLND for NSGCTs[15]. Unfortunately, according to the results of this study, it cannot be proved that R-RPLND offers any tangible benefits over conventional laparoscopy[15]. In our study, as compared to L-RPLND, R-RPLND demonstrated better results in a few parameters, which were, operative duration, median duration to the surgical drain removal, and hospitalization time. This finding is different from the study reported by Harris at el [15]. The mean operative duration was significantly shorter in R-RLPND group than that in L-RLPND group (140 vs. 175 minutes P < .05). This result could be attributed to the characteristics of robotic surgery, such as the enhanced three-dimensional magnification view, the stability and dexterity of the robotic equipment, and the assistance of third arm that allow a good operative field, a controlled and precise dissection as compared with laparoscopy surgery. According to our experience, robotic surgery offered significant advantages for dissection posterior to the great vessels or at the bifurcation of the major vessels. The flexibility of the wristed instruments offered good retraction of blood vessels to assess lymphatic tissue posterior to the great vessels [13]. Such retraction is difficult to achieve with straight and rigid laparoscopic instruments.

A shorter median time to the surgical drain removal was also noted in robotic group as compared to the laparoscopy group (2 vs. 4 days P = .002). This may also be attributed to the previously mentioned characteristics of robotic surgery. In our department, a surgical drain is routinely inserted for RPLND, which is removed when the drainage is less than 100 mL. Patients were discharged from the hospital after the removal of surgical drain. Thus postoperative hospitalization stay of the robotic group was shorter than the laparoscopic group. The postoperative hospitalization time in our study was significantly longer than studies from the western countries[8,9,12,14,22]. This finding might be due to differences in health-care system and culture background between China and western countries. Patients in China intend for longer hospital stay until full recovery even though they are fit to be discharged.

Regarding the overall complications, there was no statistically significant difference between the two groups (9.7% vs. 14.3%, P = .609). The overall complication rate of our cohort is similar to complication rates in other published studies[12,15,22]. In terms of safety, the result is comparable between the two groups.

At oncological aspect, no significant differences were observed in LN yield, frequency of LN positivity, and pN stage between the two groups. Kaplan-Meier curve showed no significant differences in PFS between the groups. Oncological control is comparable between the two study cohorts.

Since this surgery involves dissection of major vessel, it is a real challenge when major vessels injury failed to be repaired intracorporeally. Surgeon need to scrub and return to the operation table that may endanger patient life. In laparoscopic approach, the bleeding can be temporally controlled using a laparoscopy Satinsky clamp while converting to open surgery[15]. Even so, it cannot be denied that robotic approach really benefits the surgeons in term of shorter learning curve, more comfortability and less fatigue as compared with traditional laparoscopic approach[11,21].

There were some limitations of this study. First, it is a retrospective and nonrandomized controlled study with a small sample size, so that the power of study was not strong. Second, our targeted subjects were patients with NSGCT Stage I disease, where RPLND was expected to be simpler as compared with patients with higher clinical stage or residual masses post-chemotherapy. In addition, the surgeon for this study is a very skillful and has extensive experience in robotic and laparoscopic surgeries.

CONCLUSIONS

R-RPLND and L-RPLND were comparable in oncological parameter and morbidity rate; R-RPLND showed superiority in operation duration, median days to surgical drain removal, and postoperative hospital stay for stage I NSGCTs.

CONFLICT ON INTEREST

The authors have no conflicts of interest to declare.

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