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Original Article

Laparoscopic retroperitoneal lymph node dissection versus open retroperitoneal lymph node dissection for testicular cancer: A comparison of clinical and perioperative outcomes

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Abstract Objective: This study was performed to evaluate the clinical and perioperative outcomes of laparoscopic retroperitoneal lymph node dissection (L-RPLND) and open retroperitoneal lymph node dissection (O-RPLND) performed by one surgeon at a single center.

Methods: We evaluated 30 patients with stage IIA germ cell tumors who underwent retroperitoneal lymph node dissection (15 underwent L-RPLND and 15 underwent O-RPLND) at our institution between April 1, 2010 and March 31, 2018. The clinical parameters were compared between patients who underwent L-RPLND using the retroperitoneal approach and those who underwent O-RPLND using the transperitoneal approach. There were no significant differences in the background characteristics of the two groups except for the median follow-up duration (46 months for L-RPLND and 71 months for O-RPLND, $p=0.02$).

Results: L-RPLND was associated with a shorter mean operative time (mean 222 min for L-RPLND vs. 453 min for O-RPLND, $p<0.001$). There was significantly less blood loss during surgery in the L-RPLND group compared to the O-RPLND group (mean 165 mL for L-RPLND vs. 403 mL for O-RPLND, $p<0.001$). Parameters related to postoperative recovery were significantly better for the L-RPLND group than for the O-RPLND group. There were no differences

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in the histopathological characteristics between the two groups. No patients in either group exhibited disease recurrence.

Conclusion: Patients who underwent L-RPLND had more rapid recovery, and shorter hospital stay compared to those who underwent O-RPLND; complications were comparable between the two groups. L-RPLND is an efficient procedure with the benefits of minimally invasive surgery.

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1. Introduction

Multidisciplinary management in testicular cancer has resulted in survival rates exceeding 90%. However, surgery remains a critical form of treatment. Retroperitoneal lymph node dissection (RPLND) is useful for patients undergoing active chemotherapy and those undergoing surveillance. RPLND can be curative in patients with low-volume metastatic disease; a subset of patients can avoid the need for chemotherapy and the potential risk of secondary malignancies associated with chemotherapy and repeated computed tomography scans. RPLND is also effective for patients with teratomas that are resistant to chemotherapy. The long-term cancer-specific survival rate after RPLND in patients with testicular cancer is approximately 100% [1].

Traditional open RPLND (O-RPLND) is a classical form of open surgery that involves a large midline incision from the xiphoid process to the pubic connection. Laparoscopic RPLND (L-RPLND) was first reported by Rukstalis and Chodak [2], in 1992. The benefits of the laparoscopic approach include pain relief, shorter postoperative hospital stay, improved esthetic outcomes, and an enlarged view of the delicate retroperitoneal structure [3]. However, most reports have shown the feasibility of L-RPLND without a direct comparison with O-RPLND.

The aim of the present study is to compare the clinical and perioperative outcomes of L-RPLND and O-RPLND procedures performed by one surgeon at a single center.

2. Patients and methods

2.1. Patient population

The study subjects comprised patients who underwent L-RPLND or O-RPLND for stage IIA germ cell tumors between April 1, 2010, and March 31, 2018, at the Kyorin University Hospital, Tokyo, Japan. Before performing L-RPLND for stage IIA/B germ cell tumors, O-RPLND was the standard treatment in our hospital. After starting L-RPLND, L-RPLND or O-RPLND was selected according to patient preference. This study was approved by the ethics committee of the hospital (Kyorin-337), and all patients provided written informed consents to participate prior to surgery. All patients underwent induction or salvage chemotherapy and exhibited serum tumor marker normalization. The background patient characteristics are summarized in Table 1. A

significant difference was observed only in the median follow-up duration (46 months for L-RPLND vs. 71 months for O-RPLND, $p=0.02$). The follow-up included visits at three-month intervals for 5 years and annually thereafter.

2.2. Chemotherapy

All patients received cisplatin-based chemotherapy either as induction (30 patients) or adjuvant therapy (three patients). Twenty-seven (90.0%) patients received three cycles of bleomycin, etoposide, and cisplatin (BEP), and three (10.0%) patients received four cycles of BEP as induction therapy. Adjuvant therapy was given to three patients, and all received two cycles of BEP.

2.3. Surgical technique

2.3.1. O-RPLND using the transperitoneal approach

All patients underwent a complete bilateral RPLND through a midline peritoneal incision. A posterior peritoneal incision was made through the mesenteric root from the Treitz ligament to the cecum. Lymph tissue was dissected on the front of the aorta and inferior vena cava. The anterior cavity incision was extended from the origin of the renal vein to the confluence of the internal iliac vein, and the periaortic incision was made from the renal artery to the internal iliac artery. Upper and lower abdominal plexuses were identified and stored around the aortic bifurcation. For lymph node dissection, we followed exactly the template described by Weissbach and Boedefeld [4].

2.3.2. L-RPLND using the retroperitoneal approach

All patients were placed in the supine position. Placement of the ports are shown in Fig. 1A. An initial 11 mm port was made approximately 3 cm medial to the anterior iliac spine. The retroperitoneal space was developed by inflating a preperitoneal distension balloon. Two additional 11 mm ports were positioned in the midaxillary line at navel height and below the subcostal margin at the external clavicular line under direct vision, respectively. A fourth 5 mm port was used if necessary. A retroperitoneal cavity was developed between the psoas muscle and ureter until the ipsilateral large blood vessel was visible (Fig. 1B). Lymph node dissection was performed using the template described by Weissbach and Boedefeld [4] as mentioned above (Figs. 1C and 1D). Ten of the 15 patients with L-RPLND were performed with a full bilateral. The modified unilateral

Table 1 Patient characteristics.

Characteristic	L-RPLND, <i>n</i> = 15	O-RPLND, <i>n</i> = 15	<i>p</i> -Value
Age, mean (range), year	26 (18–52)	27 (19–48)	0.156
BMI, mean (range), kg/m ²	24.2 (19.2–30.5)	25.3 (18.9–31.1)	0.207
Tumor side, left/right	13/2	14/1	0.425
Pathology diagnosis, <i>n</i> (%)			0.161
Seminoma	6 (40.0)	5 (33.3)	
NSGCT	9 (60.0)	10 (66.7)	
Embryonal carcinoma	2 (13.3)	1 (6.7)	
Mixed	6 (40.0)	8 (53.3)	
Teratoma	1 (6.7)	1 (6.7)	
IGCCC, <i>n</i> (%)			0.253
Good	12 (80.0)	11 (73.3)	
Intermediate	3 (20.0)	4 (26.7)	
Poor	0	0	
Pre-chemotherapy tumor size, mean (range), mm	25.6 (5–49)	28.5 (8–48)	0.318
Post-chemotherapy tumor size, mean (range), mm	12.3 (4–23)	13.1 (7–21)	0.285
Blood loss, mean (range), mL	165 (68–371)	403 (220–1355)	<0.001
Operation time, mean (range), min	222 (186–324)	453 (280–780)	<0.001
Oral intake (postoperative), mean (range), day	2 (2–5)	3 (2–6)	0.002
Permission of discharge (postoperative), mean (range), day	8 (6–20)	11 (10–18)	0.014
Histology of RPLND, <i>n</i> (%)			0.028
Necrosis	13 (86.7)	10 (66.7)	
Teratoma	1 (6.7)	3 (20.0)	
Viable cancer	1 (6.7)	2 (13.3)	
Antegrade ejaculation, <i>n</i> (%)	15 (100)	14 (93.3)	0.371
Follow-up, median (range), month	46 (13–61)	71 (22–96)	0.023

BMI, body mass index; IGCCC, International Germ Cell Consensus Classification; NSGCT, non-seminomatous germ cell tumors; RPLND, retroperitoneal lymph node dissection; L-RPLND, laparoscopic RPLND; O-RPLND, open RPLND.

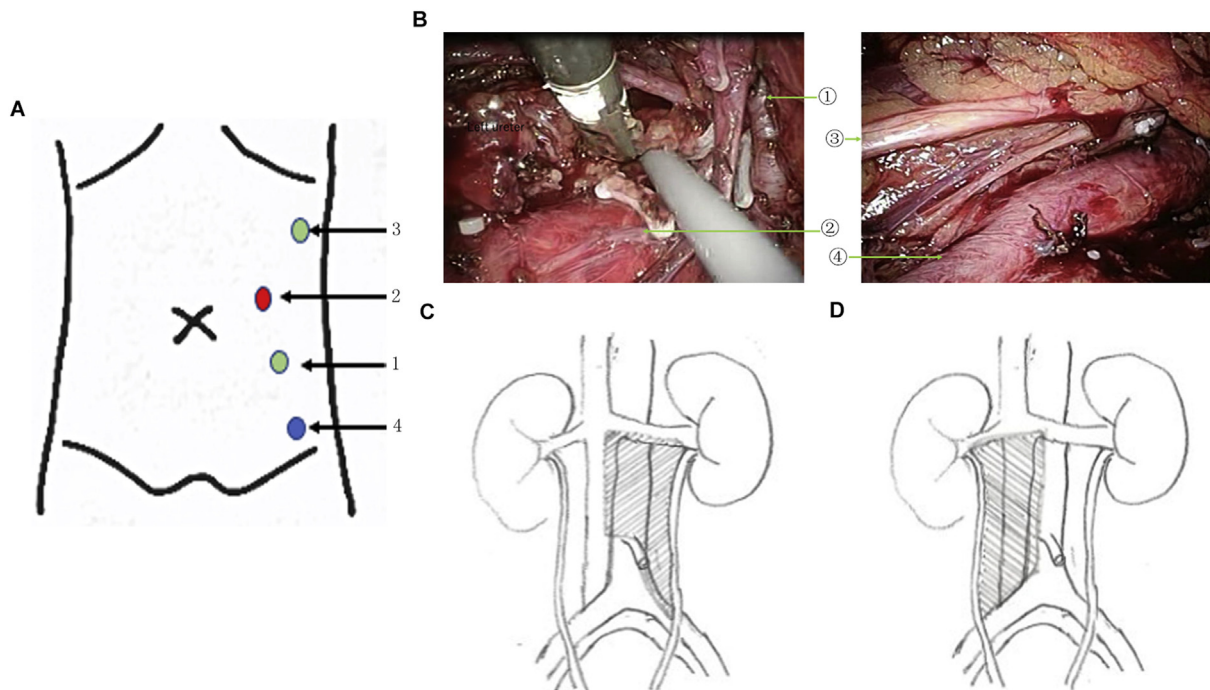


Figure 1 Placement of the ports for left-sided retroperitoneal lymph node dissection and intraoperative view. (A) Schematic diagram of placement of left retroperitoneal lymph node dissection port. 1. First port for the left hand (11 mm); 2. Second port for the laparoscope; 3. Third port for the right port (5 mm); 4. Fourth port (5 mm). (B) Para-aortal area after dissection shown (① Left renal artery; ② abdominal aorta; ③ Left ureter; ④ Left common iliac artery). (C) Template dissection limits for left-sided tumors consist of ureter (lateral), midpoint of vena cava (medial), bifurcation of iliac vessels (distal), and renal hilum (superior). (D) Template dissection limits for right-sided tumors consist of ureter (lateral), midpoint of aorta (medial), bifurcation of iliac vessels (inferior), and renal hilum (superior).

template dissection was performed in five patients who were localized to the lymph nodes on the same side of the primary lesion and had a reduction rate of 90% or more after chemotherapy. The patients' positive sympathetic nerves were identified and reserved.

2.4. Assessment of complications

Intra- and postoperative complications were categorized using the Clavien-Dindo classification [5].

2.5. Statistical analysis

The results are expressed as means (or median) and range values. Continuous variables were compared between the two groups using Student's *t*-test and the Mann-Whitney *U* test. All statistical analyses were performed using JMP software, version 12.0 (SAS Institute, Cary, NC, USA).

3. Results

The perioperative variables are summarized in Table 1. Blood loss during surgery was significantly less in the L-RPLND group compared with the O-RPLND group (mean 165 mL vs. 403 mL; $p < 0.001$). Operative time was significantly shorter in the L-RPLND group than in the O-RPLND group (mean 222 min vs. 453 min; $p < 0.001$). Ten of the 15 patients with L-RPLND were performed with a full bilateral. In comparison between these 10 patients and O-RPLND group, L-RPLND group showed a shorter operative time (mean 187 min vs. 412 min; $p < 0.001$) and lower blood loss (mean 285 mL vs. 485 mL; $p < 0.001$). The patients in the L-RPLND group did not require conversion to open surgery. Furthermore, the time to start oral ingestion and discharge in the L-RPLND group (mean 2 and 3 days, respectively) was significantly shorter than those in the O-RPLND group (mean 8 and 11 days, respectively; $p = 0.002$ and $p = 0.014$, respectively).

On histopathological examination, both groups showed similar proportions of necrosis, teratoma, and viable cancer. Two cases with viable cancer (embryonal carcinoma and seminoma) were detected in the O-RPLND group, whereas only one case with viable cancer (fetal cancer) was detected in the L-RPLND group. Three patients who received only induction chemotherapy received two cycles of adjuvant chemotherapy.

For antegrade ejaculation, bilateral nerve-preserving L-RPLND or O-RPLND was performed in all patients. No disease recurrence was observed in both groups at the time of

writing. The median follow-up period was 46 months for the L-RPLND group and 71 months for the O-RPLND group.

The perioperative complications are summarized in Table 2. In the L-RPLND group, complications occurred in lymphocele in two cases but disappeared within approximately 1 month. Chyle leaks were observed in two cases (one in the L-RPLND group and the other in the O-RPLND group); however, the leaks disappeared within 1 week after consumption of a low-fat diet.

4. Discussion

L-RPLND began as a diagnostic tool for stage I germ cell tumors [6, 7]. After safety was confirmed, its indication was extended to include treatment [8–10]. The most common procedure for L-RPLND is composed of a unilateral modified template with an intraperitoneal approach. Some studies showed the viability of L-RPLND for post-chemotherapy residual masses, based on the results of operative time and rates of conversion, blood loss, and complications (Table 3) [11–14]. To the best of our knowledge, no prospective, randomized studies have been performed to compare L-RPLND with O-RPLND; only five retrospective comparative reports are available. Our report is also a retrospective study.

Poulakis et al. [12] compared 21 patients undergoing L-RPLND to 29 undergoing O-RPLND. In a similar study, Abdel-Aziz et al. [13] compared 22 patients undergoing L-RPLND with six patients undergoing O-RPLND. Nakamura et al. [14] compared 14 patients undergoing L-RPLND with 14 undergoing O-RPLND. Twenty-six patients were performed with a full bilateral template, with the exception of two patients of L-RPLND. The estimated blood loss and length of stay differed significantly between the L-RPLND and O-RPLND groups in these studies. Similarly, we found that estimated blood loss (165 mL vs. 403 mL, $p < 0.001$), and length of stay (8 days vs. 11 days) differed significantly between the L-RPLND and O-RPLND groups. In addition, Poulakis et al. [12] assessed differences in health-related quality of life between L-RPLND and O-RPLND. They found that patients who underwent L-RPLND reported significantly higher levels of esthetic satisfaction and a shorter time needed to return to baseline quality-of-life scores (29 days with L-RPLND vs. 51 days with O-RPLND, $p < 0.001$) [12]. In operation time, we found that the mean time (222 min vs. 453 min, $p < 0.001$) differed significantly between the L-RPLND and O-RPLND groups. Some studies showed the contrary results [11–14]. The significant difference in surgery time may be due to the difference in template dissection.

Table 2 Perioperative complications.

Clavien-Dindo classification grade	L-RPLND, <i>n</i> = 15			O-RPLND, <i>n</i> = 15		
	1	2	3a	1	2	3a
Lymphatic cyst, <i>n</i> (%)	0	1 (7)	1 (7)	0	0	0
Chyle leak, <i>n</i> (%)	0	1 (7)	0	0	1 (7)	0
Sub-ileus, <i>n</i> (%)	0	0	0	2 (14)	0	0
Surgical site infection, <i>n</i> (%)	0	0	0	2 (14)	0	0

L-RPLND, laparoscopic retroperitoneal lymph node dissection; O-RPLND, open retroperitoneal lymph node dissection.

Table 3 Comparative studies of laparoscopic versus open retroperitoneal lymph node dissection: Operative data.

Variable	Janetschek et al. [11]		Poulakis et al. [12]		Abdel-Aziz et al. [13]		Nakamura et al. [14]	
	L-RPLND	O-RPLND	L-RPLND	O-RPLND	L-RPLND	O-RPLND	L-RPLND	O-RPLND
Patients, <i>n</i>	29	30	21	29	22	6	14	14
Operative time, mean, min	390	252	233	203	313	284	439	408
Estimated blood loss, mean, mL	N/A	N/A	270	422	159	254	155	700
Length of stay, mean, day	4.7	10.6	2	7	1.2	8.5	7	10.5
Complication rate, %	41.4	30	15	86	18	17	50	35.7
Positive nodes, %	27.6	16.7	19	24	32	0	0	21.4

L-RPLND, laparoscopic retroperitoneal lymph node dissection; O-RPLND, open retroperitoneal lymph node dissection; N/A, not available.

Poulakis et al. [12] reported that the overall complication rate was significantly higher in the O-RPLND group than in the L-RPLND group (86.2% vs. 15%, $p < 0.001$). Conversely, Abdel-Aziz et al. [13] reported that the complication rate did not differ between the L-RPLND and O-RPLND groups (18% vs. 17%, p -value not provided). Nakamura et al. [14] reported that chyle leak was the most frequent complication, which was observed more frequently in the L-RPLND group than in the O-RPLND group. In the present study, one patient exhibited chyle leak in the L-RPLND group. In subsequent patients, we used a clip to seal the lymphatic vessels.

The median follow-up durations in the study by Nakamura et al. [14] were 36 months in the L-RPLND group and 70 months in the O-RPLND group; no patients in the L-RPLND group and three (21%) in the O-RPLND group had pN1 disease. Two out of three patients received adjuvant chemotherapy, and no disease recurrence was observed in either group. In our study, the median follow-up durations were 46 months in the L-RPLND group and 71 months in the O-RPLND group. One patient (7%) in the L-RPLND group and two patients in the O-RPLND group had node-positive disease. All three patients with node-positive disease elected to undergo adjuvant chemotherapy. All patients were free of disease at the most recent follow-up. The present study and the study by Nakamura et al. [14] both had methodological limitations, including a retrospective design, small sample size, and high rate of adjuvant chemotherapy in node-positive patients.

Rassweiler et al. [15] performed a meta-analysis of 34 studies published between 1992 and 2008 regarding clinical stage 1 nonseminoma germ cell tumors. They reported that, compared with the O-RPLND group, the L-RPLND group had a significantly shorter length of stay (3.3 days vs. 6.6 days, $p < 0.05$) and lower complication rate (15.6% vs. 33%, $p < 0.05$), but a longer mean operative time (204 min vs. 186 min, $p < 0.05$). For oncological outcomes, they compared five L-RPLND articles with five O-RPLND articles published between 2000 and 2008. The mean (range) follow-up of L-RPLND was 63 (30–84) months, compared to 54 (48–83) months of O-RPLND. The oncologic data were nearly identical with respect to retroperitoneal relapse (1.3% vs. 1.4%) and biochemical failure rates (0.9% vs. 1.1%) in the L-RPLND and O-RPLND groups. They concluded that

L-RPLND requires a slightly longer operative time, lowers the overall rate of complications, results in similar positive node rates, and provides similar oncologic outcomes with comparable numbers of chemotherapeutic cycles, compared to O-RPLND. We believe that L-RPLND after chemotherapy is a technically very demanding procedure and should only be attempted by surgeons with extensive laparoscopic experience. The involvement of these surgeons may reduce the time of surgery.

Data from the first report of robotic RPLND (R-RPLND) were encouraging; the findings included reduced blood loss, shorter hospital stays, and lower morbidity [16]. However, comparisons of the efficacies of R-RPLND and O-RPLND or L-RPLND series are lacking. The R-RPLND procedure should be used with caution until long-term efficacy and safety data are reported.

5. Conclusion

In this study with a small number of patients, we found that L-RPLND allowed more rapid recovery with a shorter hospital stay, as well as complications comparable to those of O-RPLND. L-RPLND is a feasible and efficient procedure with the benefits of minimally invasive surgery. Furthermore, L-RPLND and O-RPLND had similar oncological outcomes, following a similar number of chemotherapy cycles.

Author contributions

Study design: Toshihide Shishido, Takatsugu Okegawa, Hiroshi Fukuhara.

Date acquisition: Satoru Taguchi, Yu Nakamura, Mitsuhiro Tambo.

Data analysis: Kenjiro Hayashi, Kazuki Masuda.

Drafting of manuscript: Takatsugu Okegawa.

Critical revision of the manuscript: Toshihide Shishido, Takatsugu Okegawa.

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