



Postchemotherapy robotic retroperitoneal lymph node dissection for non-seminomatous germ cell tumors in the lateral decubitus position: oncological and functional outcomes

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Abstract

Purpose Retroperitoneal lymph node dissection (RPLND) is recommended for residual masses following chemotherapy for non-seminomatous germ cell tumors (NSGCT). Recently, aberrant recurrence patterns were reported in patients who underwent robotic RPLND. We aimed to evaluate perioperative safety in addition to functional and early oncological outcomes of postchemotherapy robotic RPLND (pcR-RPLND) for NSGCT.

Methods A total of 25 patients with NSGCT who underwent a pcR-RPLND between January 2011 and June 2022 were evaluated retrospectively. Descriptive statistics were provided for demographics, clinical characteristics, intraoperative and postoperative parameters. Functional and oncological outcomes were recorded.

Results The median patient age was 28.9 years (IQR 21.5–32.4). The median retroperitoneal tumor size was 2.6 cm (IQR 1.5–3.5). Intraoperative complications occurred in only one case and the open conversion rate was 12%. There were seven cases with postoperative complications (Clavien grade II: 5 and IIIa: 2). Patients were followed for a median of 33.2 months (IQR 14.8–43.0). Antegrade ejaculation was preserved in 85.7% of the patients. Two patients (8%) relapsed and both had out-of-field recurrences at unusual sites (perinephric fat and omentum). Of those, one patient died (4%) of testicular cancer.

Conclusion pcR-RPLND is a feasible and technically reproducible procedure with favorable perioperative morbidity, low rate of complications, and acceptable postoperative ejaculatory function. Although the recurrence rate was low (8%), recurrences were observed at unusual sites. Further studies are required to investigate any association between the robotic approach and aberrant recurrence patterns.

Keywords Testicular cancer · Retroperitoneal lymph node dissection · Robotic surgery · Postchemotherapy · Minimally invasive surgery

Introduction

Cisplatin-based chemotherapy is highly effective as the first-line treatment for metastatic non-seminomatous germ cell tumors (NSGCT), but up to 40% of patients demonstrate residual retroperitoneal mass [1]. RPLND is mandated in all patients with normalized serum tumor markers and a residual mass > 1 cm following chemotherapy for metastatic

NSGCT [2]. Traditionally, RPLND was performed using an open approach through a large midline incision. A laparoscopic approach was first described in 1992 to decrease perioperative morbidity and improve recovery time after surgery [3]. Although promising results were reported in large series, the laparoscopic approach was not widely adopted due to the steep learning curve and technically demanding retroaortic and retrocaval dissections [4, 5]. A number of studies showed promising results for robotic RPLND following the initial report in 2006 [6], however, most of the data is based on primary robotic RPLND [7–11]. Postchemotherapy RPLND is known to be technically more challenging due to chemotherapy-associated desmoplastic reactions. Furthermore, concerns have been raised in the literature due to previously reported recurrence locations at unexpected sites after robotic RPLND such as peritoneal carcinomatosis,

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pericolic space, liver, and lymph nodes in the celiac axis [12, 13]. Data are limited regarding the oncological and functional outcomes of pcR-RPLND currently.

In this study, we aim to investigate perioperative safety, ejaculation rates, and early oncological outcomes in patients who underwent postchemotherapy robotic RPLND (pcR-RPLND). To our knowledge, this is one of the largest single-center pcR-RPLND series in the literature.

Patients and methods

Patient population

Following institutional ethics committee approval, we performed a retrospective review of all patients who underwent pcR-RPLND for NSGCT at our institution between January 2011 and June 2022. Patients who received platin-based chemotherapy and those with normal serum tumor markers (AFP, b-HCG, and LDH) before pcR-RPLND were included in the study. The decision to perform RPLND was made according to the size of the post-chemotherapy retroperitoneal residual mass and serum tumor markers as recommended by current guidelines [2]. Staging of the patients was done according to the 2016 TNM classification of the International Union Against Cancer (IUCC) [14]. Selection of the chemotherapy regimens was made at the discretion of the treating medical oncologist. Baseline clinicopathological characteristics such as age, body mass index (BMI), tumor laterality, clinical stage at first diagnosis, initial testicular tumor pathology, prechemotherapy serum tumor markers (S stage), and International Germ Cell Cancer Collaborative Group (IGCCCG) classification were recorded. Postchemotherapy retroperitoneal tumor sizes (greatest axial diameter at cross-sectional imaging) were evaluated in all patients.

Surgical technique and operative parameters

All surgeries were performed by one of two surgeons (T.E and Y.K) who have extensive experience with open and laparoscopic RPLND (more than 200 open RPLND and 30 laparoscopic RPLND in the last 10 years), as well as robotic surgery. The surgical approach (open or robotic) and the extent of the surgery were decided based on clinical characteristics and shared decision-making by the surgeon and the patient. Open postchemotherapy RPLND was recommended for patients with multiple previous abdominal surgeries, patients with residual lesions larger than 5 cm, and cases with a residual mass adhering to great vessels (Aorta and IVC) over 180°. The majority of the patients underwent unilateral modified template

dissection (20 out of 25 procedures, 80%). In five cases, residual mass resection was performed to avoid further surgical morbidity and to preserve ejaculation. Right-sided modified template resection included right common iliac, precaval, paracaval, retrocaval, interaortocaval, and preaortic lymph nodes to the level of the inferior mesenteric artery. The right renal vein represented the cranial boundary of the resection and the ipsilateral ureter represented lateral and caudal boundaries. Left-sided modified template resection included left common iliac, preaortic, paraaortic, interaortocaval, and retroaortic lymph nodes to the level of the inferior mesenteric artery. Cranial and lateral boundaries of resection were the left renal artery and ureter, respectively. The area below the inferior mesenteric artery was spared to preserve antegrade ejaculation.

The da Vinci Xi four-arm surgical systems (Intuitive Surgical, Sunnyvale, CA, USA) were used in all cases. All surgeries were performed in the lateral decubitus position using a transperitoneal approach. Surgical steps were performed as previously described [15]. Briefly, a camera port, three 8 mm robotic ports, and a 12 mm assistance port were placed. Afterward, the cecum, ascending colon, and duodenum on the right side or descending colon on the left side were mobilized by incision of the peritoneum to provide exposure to the retroperitoneum according to the preplanned template resection side. Once the dissection field margins were identified, the lymph nodes were removed using the “split-and-roll” technique. Whenever technically feasible, the nerve fibers of the hypogastric plexus were identified and preserved. A retroperitoneal drain was placed routinely in all cases.

Intraoperative parameters included dissection template, operation time, estimated blood loss (EBL), transfusion of blood, intraoperative complications, and auxiliary procedures. The conversion rates to open procedure and the reasons for open conversion were recorded. The pathological review included the number of dissected lymph nodes and the histology of resected residual mass.

Assessment of complications and follow-up

Postoperative complications were categorized using the Clavien–Dindo Classification system [16]. Length of stay (LOS) was documented for all patients. Follow-up protocol included physical examination, serum tumor markers, and computerized tomography scans as recommended by the European Association of Urology guidelines [2]. Recurrence was defined as an elevation of tumor markers or radiological progression. Time to recurrence was defined as the time between robotic RPLND and the date of recurrence. The treatments received after recurrence were also recorded.

Statistical analysis

Statistical analysis was performed using SPSS version 24 (IBM Corporation, Armonk, New York, USA). Descriptive statistics were provided using either mean and standard deviations (SD) or median and interquartile ranges (IQR) for continuous variables. Categorical variables were presented with frequency counts and percentages.

Results

Patient characteristics

A total of 25 patients underwent pcR-RPLND for residual masses following chemotherapy for GCT. The median age was 28.9 years (IQR 21.5–32.4). All patients had NSGCT at primary tumor histology. Mixed GCT was detected in 20 patients (76.9%). There were 3 patients (12%) with pure embryonal carcinoma and 2 patients (8%) with teratoma. One patient (4%) had a history of previous RPLND for primary testicular cancer. Prechemotherapy serum tumor marker elevation was detected in 17 patients (68%) but all had normalized serum tumor markers after chemotherapy. Baseline characteristics are summarized in Table 1.

Perioperative outcomes

The median tumor size at robotic RPLND was 2.6 cm (IQR 1.5–3.5). The median operation time was 180 min (IQR 150–325) and the median EBL was 150 mL (IQR 50–250). Only 1 patient (4%) received a postoperative blood transfusion. Intraoperative complication occurred in only one case (renal artery injury) and open conversion was decided upon due to significant bleeding (EBL was 3000 mL). The arterial injury was repaired and no auxiliary procedures such as nephrectomy were required. In two cases, poor exposure to the surgical field led to open conversion. The overall open conversion rate was 12% (3 out of 25 cases).

During the postoperative period, complications occurred in 7 patients (28%). Of those, only two (8%) had Clavien–Dindo \geq III major complications (Table 1). One patient required chest tube insertion due to postoperative pneumothorax. The chest tube was removed on the second postoperative day following pneumothorax resolution. In the other patient, chylous ascites resistant to conservative management led to a lymphangioembolisation. Lymphatic drainage decreased gradually and the drain was removed 10 days after the lymphangioembolisation. There were 5 Clavien–Dindo grade II complications. One patient (4%) received a blood transfusion and 4 patients (16%) received pharmacological treatment for prolonged lymphatic drainage. The median LOS was 4 days (IQR 3–6).

Oncological and functional outcomes

On pathological review, the mean nodal yield was 18.4 ± 12.3 in patients who underwent unilateral modified template dissection. Teratoma was identified in 16 patients (64%) and viable tumor was identified in one patient (4%). The remaining patients ($n=8$, 32%) had necrosis and/or fibrosis. The median follow-up duration was 33.2 months (IQR 14.8–43.0). One patient underwent an orchiectomy for a metachronous testicular cancer 10.5 years after pcRPLND. Pathological examination revealed mixed germ cell tumor (embryonal carcinoma, yolk sac tumor, teratoma, and seminoma). Two patients experienced recurrence during follow-up. One of them had IGCCCG good risk and the other had an intermediate risk disease. Both had normal serum tumor markers before RPLND and pathological examination revealed teratoma. In these patients, early recurrence was detected (time to recurrences were 5.16 months and 1.94 months, respectively) and open salvage surgery following further chemotherapy was performed. Metastatic deposits were observed in unexpected regions (perinephric fat and omentum) in both cases (Fig. 1). In the first case, pathological examination revealed primitive neuroendocrine tumor (PNET) differentiation of immature teratoma. Despite further dose-intensified chemotherapy (4 cycles of Vincristine, Doxorubicin, Cyclophosphamide, Ifosfamide, and Etoposide) and autologous stem cell support, the patient died from testicular cancer 14.8 months after the first RPLND. In the second case, elevated serum tumor markers were detected in early postoperative follow-up and further CT examination showed unusual recurrence at the omentum. Following dose-intensified chemotherapy (2 cycles of high-dose Cisplatin Etoposide and 5 cycles of Paclitaxel, Gemcitabine, and Oxaliplatin), salvage surgery revealed metastatic deposits composed of yolk sac tumor. After salvage surgery, the patient received further 8 cycles of Paclitaxel, Gemcitabine, and Oxaliplatin and is currently in complete remission with a follow-up of 33.9 months after the first RPLND. Overall two deaths (8%) took place during follow-up. The other mortality was related to cardiac problems.

Data on ejaculatory function was available in 21 patients. Among those, 18 (85.7%) preserved antegrade ejaculation after surgery. Of three patients who reported anejaculation, one patient had a recurrence and underwent salvage surgery and further dose-intensified chemotherapy. Both of the remaining patients underwent unilateral modified template dissection. None of the patients who underwent lumpectomy reported anejaculation.

Table 1 Demographics and tumor characteristics of patients who underwent postchemotherapy robotic RPLND and perioperative complications

Parameter	Mean (SD)/frequency (%)	Median (IQR)
Age (years)	29.1 ± 8.5	28.9 (21.5–32.4)
BMI (kg/m ²)	25.5 ± 3.0	25.2 (23.2–26.3)
Primary site of TGCT		
Right testis	8 (32%)	
Left testis	16 (64%)	
Extragonadal	1 (4%)	
Primary tumor histology		
Embryonal carcinoma	3 (12%)	
Teratoma	2 (8%)	
Mixed GCT	20 (80%)	
• Seminoma component	7/20 (35%)	
• Teratoma component	12/20 (60%)	
• Yolk sac tumor component	13/20 (65%)	
• Embryonal carcinoma component	18/20 (90%)	
• Choriocarcinoma component	2/20 (10%)	
Clinical stage		
IIA	4 (16%)	
IIB	12 (48%)	
IIC	1 (4%)	
IIIA	3 (12%)	
IIIB	4 (16%)	
IIIC	1 (4%)	
Prechemotherapy serum tumor markers		
S0	8 (32%)	
S1	13 (52%)	
S2	4 (16%)	
Prechemotherapy largest retroperitoneal tumor diameter (cm)	3.94 ± 3.26	2.8 (2.2–3.8)
IGCCCG classification		
Good	19 (76%)	
Intermediate	4 (16%)	
Poor	2 (8%)	
Received chemotherapy regimens		
3 cycles of BEP	14 (56%)	
4 cycles of BEP	8 (32%)	
Others ^a	3 (12%)	
Largest retroperitoneal tumor diameter at RPLND (cm)	2.73 ± 1.41	2.6 (1.5–3.5)
Complications		
Intraoperative complications		
Renal artery injury	1 (4%)	
Open conversion due to poor exposure	2 (8%)	
Postoperative complications		
Clavien–Dindo grade II	5 (20%)	
• Postoperative blood transfusion	1 (4%)	
• Somatostatin treatment for prolonged lymphatic drainage	4 (16%)	
Clavien–Dindo grade IIIa	2 (8%)	
• Chest tube insertion	1 (4%)	
• Lymphoembolisation	1 (4%)	

Abbreviations: *BMI* body mass index, *TGCT* testicular germ cell tumor, *IGCCCG* International Germ Cell Cancer Collaborative Group, *BEP* Bleomycin/Etoposide/Cisplatin, *EP* Etoposide/Cisplatin, *VIP* Etoposide/Ifosfamide/Cisplatin, *RPLND* Retroperitoneal Lymph Node Dissection, *SD* standard deviation, *IQR* interquartile range

^aOther chemotherapy regimens include 4 cycles of VIP ($n = 1$), 4 cycles of EP, 4 cycles of TIP ($n = 1$), and 2 cycles of BEP ($n = 1$). The case who received only 2 cycles of BEP did not receive further treatment due to severe chemotherapy-related side effects



Fig. 1 Representative images of metastatic lesions excised at salvage surgery. **A** Primitive neuroendocrine tumor (PNET) differentiation of immature teratoma localised at perirenal fat. **B** Large PNET extend-

ing through Gerota fascia and perirenal sinus. **C** Large tumor implant at omentum (consistent with yolk sac tumor)

Discussion

The advantages of minimally invasive surgery including decreased blood loss, reduced pain, shorter hospital stay, faster recovery, and smaller incisions were reported in many urological procedures. Such benefits can be more prominent in RPLND considering the young age of patients undergoing RPLND and the need for large incisions in open RPLND. However, laparoscopic RPLND is a very challenging procedure and oncological principles should never be compromised for the advantages of minimally invasive surgery. Advanced instrument maneuverability of robotic systems was hypothesized to enable meticulous dissection around blood vessels and may overcome the limitations of laparoscopic surgery.

Currently, most of the data for robotic RPLND is based on robotic RPLND for primary testicular cancer [7–11]. Excellent perioperative recovery and promising early oncological outcomes were reported. However, only a limited number of studies reported outcomes of pcR-RPLND [17–21] and showed favorable perioperative outcomes. To date, two different patient positions were defined to perform pcR-RPLND; lateral decubitus position (flank) [18, 21] and supine position [7, 11, 17]. Favorable outcomes and feasibility of both positions were reported for both techniques. Since robotic total-partial nephrectomies as well as adrenalectomy surgeries are commonly performed in the flank/lateral decubitus position, urologists are very familiar with this position and landmarks can be identified very easily. We believe this approach flattens the learning curve significantly for urologists to perform pcR-RPLND effectively. The lateral decubitus position provides better exposure to great vessels (IVC and aorta) and renal vasculature enabling meticulous dissection in the interaortocaval region as well as retroaortic and retrocaval space without any additional need for retraction of mesentery and ureter. Lateral decubitus position also

enables to reach contralateral template dissection area without any need for a change in position or redocking of the robot. However, extended dissection of contralateral pelvic lymph nodes is challenging and a change in patient position and redocking of the robot can be required. On the other hand, the supine position not only provides excellent exposure to both template sides at the same time but also enables to perform bilateral pelvic lymph node dissection. Therefore, we believe the supine position may be advantageous over the lateral decubitus position when an extended bilateral template resection including pelvic lymph nodes was intended.

In our series, intraoperative complications occurred in only one case (renal artery injury). Since prior chemotherapy is known to be associated with vascular complications, the low rate of vascular complications demonstrated the feasibility of the pcR-RPLND [22]. The open conversion was decided in three cases (12%) and the most common cause of open conversion was poor exposure. These results are consistent with previous studies reporting rates of open conversion between 10–25% and reporting poor exposure as the most common cause of open conversion [17, 18, 21]. Limited blood loss and short hospital stay demonstrated the benefits of the minimally invasive nature of pc-RRPLND in our study. The median operative time was 180 min which is comparable to or even shorter than previous reports [22]. The shorter operation times in our study are related to the performed dissection method (unilateral modified template and resection of only the residual mass) and the modest median size of retroperitoneal masses. Postoperative complication rates were also acceptable in our study. In a large open RPLND series, major complication rates were reported as 18% with chylous ascites being the most frequent cause of postoperative Clavien–Dindo \geq III complications [23]. Previously, a review suggested an association between laparoscopic and robotic approaches and increased chylous ascites rate and postoperative ileus after postchemotherapy

RPLND [24]. In our study, Clavien–Dindo \geq III major complication occurred in only two cases (one chylous ascites and one pneumothorax) (8%). Further studies are required to investigate any association between the laparoscopic and robotic approach and postoperative chylous ascites rates. During follow-up, the ejaculatory function was preserved in 85.7% of the patients despite no nerve-sparing technique being performed. These results indicate that good functional results can be achieved with the unilateral modified template without nerve-sparing technique in pcR-RPLND, as previously shown in the open RPLND series [25].

In recent years, inferior oncological outcomes have been reported for minimally-invasive surgical approaches compared to open surgery in patients with cervical cancer [26, 27]. Extrapelvic lymph node recurrences and peritoneal carcinomatosis were also found more frequently in robotic radical cystectomy compared to open surgery [28]. These results raised concern for a possible risk of peritoneal seeding in various malignancies treated with minimally invasive surgical approaches. Regarding testicular cancer, Calaway et al. reported five cases with aberrant recurrences following robotic RPLND [12]. Memorial Sloan Kettering Cancer Center (MSKCC) group also reported peritoneal carcinomatosis in three patients who underwent minimally invasive primary RPLND [13]. The authors discussed whether the tumor biology was altered with pneumoperitoneum and if the robotic approach changed the natural course and recurrence patterns of the disease. Besides the alteration of the tumor biology, tumor seeding resulting from pneumoperitoneum was also discussed as a possible cause of aberrant recurrence patterns in GCT [13]. In our experience, recurrence rates (2 cases, 8%) were acceptable at 33.2 months of follow-up but recurrences were indeed at unusual locations; perinephric fat and omentum. One of the cases showed PNET transformation of teratoma and died from testicular cancer 14.7 months after the first pcR-RPLND. PNET transformation of teratoma was previously reported in open RPLND series as well and is known to be associated with inferior oncological outcomes [29]. The other case presenting with increased tumor markers after pcR-RPLND and salvage surgery following systemic treatment revealed metastatic deposits composed of yolk sac tumor at the omentum. Despite such recurrences occurring in aberrant locations, they are not unique to robotic RPLNDs and have been reported in previous open RPLND studies as well [30]. Unusual recurrences are possibly under-reported regardless of the surgical approach. Therefore, further studies reporting recurrence sites after open, laparoscopic, and robotic RPLNDs are required to draw any conclusion on this potentially serious issue.

The present study has several strengths and limitations. The main strength is the homogenous nature of the patients included in the study; all patients received modern

chemotherapy regimens (BEP, EP, or VIP), all underwent pcR-RPLND by one of two very experienced urologists, and oncological/functional outcomes were evaluated at the same center. The main limitation is the retrospective nature of the study with its inherent shortcomings. Despite this being one of the largest single-center studies in the literature, the number of patients was still small and the follow-up duration was limited. Lastly, this is a descriptive study designed to report the outcomes of pcR-RPLND and no conclusions can be made about the comparison of robotic pcRPLND with other surgical approaches.

We conclude that pcR-RPLND is a feasible surgical procedure that demonstrates quick recovery, reduced blood loss, favorable perioperative morbidity, and low postoperative complication rates. Unilateral modified template resection provides acceptable postoperative ejaculation function even when a nerve-sparing technique is not administered. In our series, rates of recurrence were low, but recurrences were detected at unusual sites. Larger series with longer follow-up periods are required to investigate whether the robotic approach is associated with aberrant recurrence patterns in patients with testicular cancer.

Author contributions YK: project development, manuscript writing, and manuscript editing. EK: data collection and management, and manuscript writing. BE: data analysis and manuscript writing. AO: data collection, MCK: data collection and management, and manuscript editing. MK: data collection. TE: project development, and manuscript editing.

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Data availability All relevant data are stored in a password-protected drive. This data can be provided upon request.

Declarations

Conflict of interest B Esen is supported by European Urological Scholarship Programme through a 1-year research scholarship.

Ethical approval Institutional local ethics committee approval was obtained. Signed informed consent form were obtained from all patients.

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