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PERSPECTIVES

Implementing High-Quality Retroperitoneal Lymph Node Dissection for Testicular Cancer at an Australian Tertiary Hospital: Challenging the Centralisation Paradigm in High-Need Areas

Prassannah Satasivam[1,2], Samith Alwis[1], Sudheshan Sundaralingam[2], Owen Niall[2]

[1]Department of Medicine, The University of Melbourne, Parkville, VIC, Australia; [2]Department of Urology, Northern Health, Epping, VIC, Australia

Correspondence: Prassannah Satasivam, Northern Hospital Department of Urology, 185 Cooper St, Epping, VIC, 3076, Australia, Email prassannah.satasivam@nh.org.au

Background: Retroperitoneal lymph node dissection (RPLND) plays an integral role in the curative management of metastatic testicular cancer. As a major surgery, RPLND poses a risk of significant complications, particularly in the post-chemotherapy (PC-RPLND) setting. We assessed the safety of introducing RPLND as a new service at an Australian tertiary hospital.

Methods: A strict protocol prioritising appropriate case selection, multidisciplinary surgical expertise and ready access to intensive care facilities was implemented to introduce RPLND. Prospective data was collected on patients who underwent PC-RPLND between October 2020 and October 2022 at the Northern Hospital in Melbourne. Primary and secondary endpoints were 30-day postoperative Clavien-Dindo (CD) classification complication rate and perioperative quality measures, respectively.

Results: Six patients (mean age 28.7 ± 4.3 years) underwent bilateral template open PC-RPLND. Median node count was 17 (IQR = 16) with metastatic germ cell tumour identified in all patients on histopathology. Median length of stay was 6 days (IQR = 3) with 1 day in intensive care. No blood transfusions were required, and no 30-day CD complications were encountered. Median follow-up was 22 months (IQR = 21) with no recurrences or significant delayed complications.

Conclusion: Following a strict protocol, RPLND has been safely introduced as a new service at our tertiary institution. Perioperative quality endpoints match those of high-volume international centres.

Keywords: testicular cancer, retroperitoneal lymph node dissection, postoperative complications

Introduction

Testicular cancer remains the most common solid malignancy in men between 20 and 34 years.[1] Advanced stages of testicular cancer are associated with retroperitoneal lymph node or distant metastases and are managed primarily with platinum-based chemotherapy. Retroperitoneal lymph node dissection (RPLND) may be required for residual disease in up to 30% of these patients, as determined by post-chemotherapy surveillance imaging and tumour markers.[2,3] Pathology from resection of residual disease may show necrosis, viable germ cell tumour, or teratoma, the latter being resistant to chemotherapy with the potential for malignant transformation.[4,5] In addition to identifying metastatic nodal disease, a complete resection has been associated with a low recurrence rate in low-volume residual disease, thereby signifying its curative potential.[6]

Despite its benefits, post-chemotherapy RPLND (PC-RPLND) presents a complex intraabdominal procedure. In addition to a significant operating time, chemotherapy-induced desmoplastic changes challenge the anatomical separation between vital abdominal structures.[7] Consequently, RPLND is associated with complications including lymphocele, ileus, haemorrhage and potential sympathetic nerve injury causing retrograde ejaculation.[8,9] Understandably, studies have found a greater operating time, length of stay and complication rate associated with PC-RPLND compared to primary

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RPLND.[8,10,11] Furthermore, adjuvant organ removal such as a nephrectomy may also be required at times to achieve oncologic control.[12] It is therefore recommended that this complex operation be performed only in appropriate candidates and at high-volume dedicated centres of excellence.[9,13]

The Northern Hospital is a rapidly-growing tertiary referral centre servicing the northern metropolitan and inner regional suburbs of Melbourne. Given an increasing volume of referrals and desire for local services, we identified the need to introduce an RPLND service at our tertiary institution. This paper evaluates our initial experience.

Methods

Patient Selection

Prospective data was collected from six patients (n = 6) receiving open PC-RPLND at the Northern Hospital, Victoria, Australia, between October 2020 and October 2022. These patients all had residual masses greater than 1cm on surveillance computed tomography (CT) of the chest, abdomen and pelvis, after completing at least three cycles of bleomycin, etoposide and platinum (BEP) chemotherapy. The six cases included all patients referred for RPLND during this time, and no cases were sent to other centres. Cases were referred from our medical oncology service and included patients who had undergone orchidectomy at other institutions. To provide an insight into case volume, our institution performed 77 radical orchidectomies for germ cell tumours in the ten years prior to study completion.

All patients underwent PC-RPLND according to a rigorous protocol involving appropriate case selection and surgical planning. All cases were discussed in our comprehensive multidisciplinary meeting with surgeons, medical oncologists, radiation oncologists, radiologists, pathologists and cancer care nurses in attendance. All patients personally met with the operating surgeon prior to surgery.

This study was approved by the Northern Health Office of Research and Ethics Committee.

RPLND Protocol

Preoperative

Patients underwent routine preoperative work-up, including pulmonary function testing. Routine planned postoperative intensive care unit (ICU) admission was also arranged. Imaging and serum tumour marker levels were performed a maximum of 6 weeks prior to planned surgery. Sperm banking was performed prior to chemotherapy.

Intraoperative

An experienced urologist with Fellowship training in RPLND from a major US high-volume centre performed all cases. This surgeon completed 14 RPLND surgeries during Fellowship, and assisted senior colleagues upon his return, prior starting this new service. An additional Fellowship-level first assistant was present for each case, as well as on-site vascular surgeons in an adjacent theatre. We intentionally did not undertake any cases that would require hepatobiliary or thoracic surgical input.

At our institution, RPLND utilises a full bilateral template dissection with adjuvant organ removal as necessary and nerve-sparing where possible, as previously described.[14] Paracaval, inter-aortocaval and paraaortic packets are sent off as separate specimens.

Postoperative

Patients were routinely admitted to ICU postoperatively for 24 hours. Opioid-based patient-controlled analgesia was utilised. Patients were initially kept nil by mouth with comfort measures, with oral intake gradually reintroduced upon passage of flatus. The indwelling catheter is routinely removed on postoperative day 4.

Data Collection and Analysis

We collected de-identified patient data prospectively and also conducted a retrospective chart review. The data collected included demographics, clinical stage, preoperative biomarkers – ß-human chorionic gonadotrophin (ß-hCG), alpha fetoprotein (AFP), and lactate dehydrogenase (LDH) – operative time, node count, histopathology, intraoperative blood loss, transfusion rates, length of stay (including in ICU), and preservation of antegrade ejaculation. Operative time was

noted from the initial skin incision until reversal of anaesthesia. Blood loss was measured from the total volume in the suction canisters at the case. Packs were not routinely used to stem bleeding due to risk of dislodging clips, and intraoperative irrigation was not required. Complications within 30 postoperative days were recorded using the Clavien-Dindo (CD) classification to grade surgical complications.[15] Descriptive statistics were used to summarise the data.

Results

Six patients with a mean age of 28.7 ± 4.3 years underwent bilateral template PC-RPLND over the October 2020 to October 2022 period. Patient clinical characteristics, including clinical stage and pre-orchidectomy tumour markers, are shown in Table 1.

Indications

The histopathology from the orchidectomy and RPLND specimens is shown in Table 2. Patients 1, 3 and 6 received three cycles of BEP. Patients 2 and 4 received four cycles. Patient 5 received one cycle of BEP, followed by three cycles of EP.

CT identified residual masses in all six patients. Patient 1 demonstrated involvement of three paraaortic nodes of approximately 2 cm size. A paraaortic 8 cm residual mass and a 1 cm pulmonary nodule were detected in Patient 2. A 1.5 cm paraaortic lymph node and a 3 mm hilar lymph node were seen in Patient 3. Patient 4 had a 4.8 cm paraaortic lymph node encompassing the left ureter, and which required preoperative stenting. Patient 5 had a 4 cm paraaortic lymph node that had grown from 3 cm on his prior imaging. Patient 6 had inter-aortocaval and paraaortic lymph nodes measuring up to 3cm.

All six patients received an open bilateral-template dissection. An adjuvant nephrectomy was required in Patient 2 (Figure 1). In Patient 4 the left ureter was wrapped around the paraaortic mass, and required a prolonged operative time in order to release it (Figure 2). Of the six patients, only one patient was suitable for nerve-sparing surgery (Table 2).

Perioperative Outcome Measures

Individual case-specific outcome measures are shown in Table 3. The mean operative time was 483 ± 101 minutes. A mean intraoperative blood loss of 808 ± 466 mL was recorded, with no blood transfusions required. Median operative times and intraoperative blood loss are conveyed in Table 4. The median length of stay following RPLND was 6 days (IQR = 3) with five patients requiring 1 day each in ICU.

At follow-up, recovery of antegrade ejaculation was absent in Patient 1. Antegrade ejaculation was not recorded in the charts of patients who received non-nerve sparing templates.

30-Day Clavien-Dindo Classification Complications

The median follow-up period for complications was 14 months (IQR = 10). No CCS2 or above complications were encountered within 30 postoperative days. Patient 6 had a CCS1 haemoserous wound strikethrough without deep

Table 1 Pre-RPLND Biomarkers and Clinical Stage for Patients Undergoing PC-RPLND

	Case					
Biomarker	**1**	**2**	**3**	**4**	**5**	**6**
Age (years)	27	23	25	32	29	36
Clinical Stage	3A Good risk	3C Poor risk	2A	3A Poor risk	2B	2B
AFP (ng/mL)	3.0	5.0	3.0	4.0	1.4	6.0
ß-hCG (IU/L)	20.2	7.6	0.2	49.6	1	0.2
LDH (IU/L)	185	312	181	180	195	318

Abbreviations: AFP, alpha-fetoprotein; ß-hCG, ß human chorionic gonadotrophin; LDH, lactate dehydrogenase.

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Table 2 Histopathology Findings and Follow-up in Patients Undergoing PC-RPLND

	Case					
	1	**2**	**3**	**4**	**5**	**6**
Testicular histology	95% EC <5% CC	95% MT 5% seminoma	100% YST	>90% EC, <5% CC <5% MT	80% MT 20% EC	50% MT 40% EC 5% YST 5% CC<1% seminoma
LVI	✓	✕	✕	✓	✕	✕
PC-RPLND						
Template	Bilateral	Bilateral	Bilateral	Bilateral	Bilateral	Bilateral
Nerve-sparing	✓	✕	✕	✕	✕	✕
Other	-	Adjuvant nephrectomy	-	-	-	-
RPLND histology	MT Treatment effect	MT	YST Treatment effect	MT	MT Treatment effect	MT YST
pNx stage	pN2	pN3	pN1	pN1	pN2	pN2
Duration of F/U (months)	38	39	22	2	22	21
Recurrence during F/U	No	No	No	No	No	No

Abbreviations: CC, choriocarcinoma; EC, embryonal carcinoma; LVI, lymphovascular invasion; MT, metastatic teratoma; PC-RPLND, post-chemotherapy retroperitoneal-lymph node dissection; YST, yolk sac tumour; F/U, follow-up.

dehiscence that was managed conservatively. Patient 3 had a delayed presentation with abdominal pain 72 days postoperatively, with no abnormality detected following a thorough evaluation. Patient 4 passed away from a motorcycle accident 42 days postoperatively.

Histopathology

The median lymph node count was 17 (IQR = 16). Teratoma was discovered in 4 paraaortic nodes from Patient 1. Teratoma was also found to encase the renal vessels of Patient 2. Patient 3 had metastatic yolk sac tumour in an inter-aortocaval node as well as evidence of treatment effect. Patient 4 had teratoma in 1 inter-aortocaval and 1 paracaval lymph node. Patient 5 had teratoma in 1 of 17 inter-aortocaval lymph nodes. Patient 6 had 95% teratoma and 5% yolk sac tumour in 1 inter-aortocaval lymph node.

Oncological Control

Including the patient who died in a motorcycle accidents 2 months post RPLND, the median follow-up for this series of patients was 22 months (IQR = 21). There were no cancer recurrences in the five surviving patients during follow-up, and no patients required adjuvant chemotherapy. Cases 1, 2 and 4 all had metastatic teratoma in the RPLND specimen, which was anticipated based on the orchidectomy histology and response to first-line chemotherapy. These patients remained disease-free post RPLND despite having preoperative ß-hCG levels above 2 IU/L.

Discussion

RPLND is recognized as a major surgery due to its technical complexity and risk of morbidity. Existing literature recommends that the procedure, particularly PC-RPLND, should be performed at high-volume centres of excellence.[9,13]

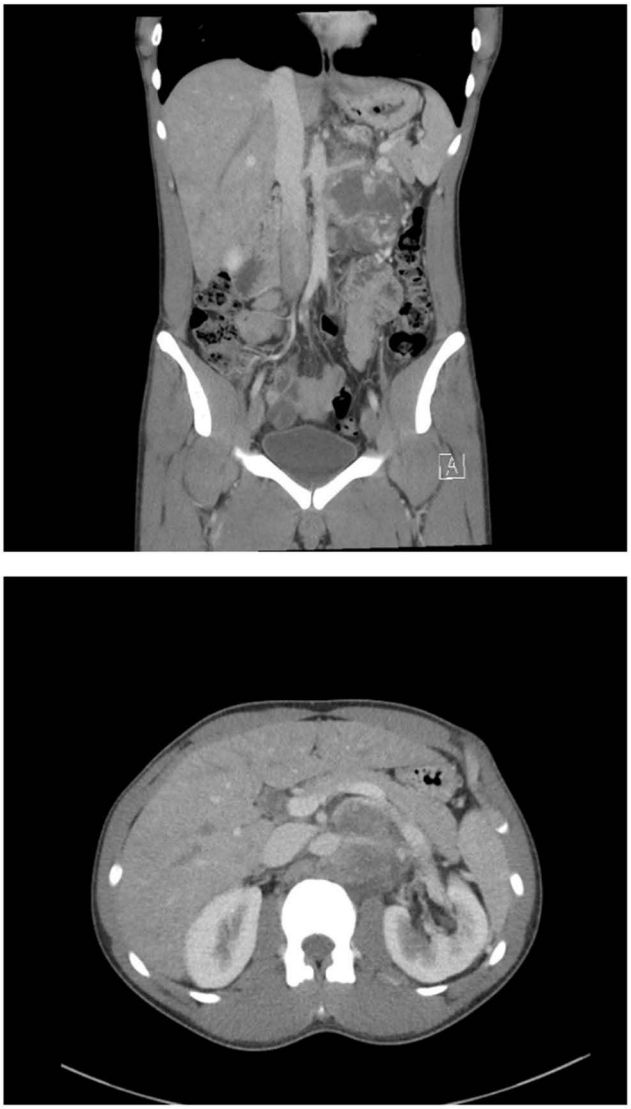

Figure 1 Patient 2 required concurrent left nephrectomy due to involvement of the left renal artery.

Although most cases are still conducted at low-volume institutions by surgeons with limited experience, improved survival outcomes and fewer complications have been recorded at high-volume institutions.[13]

There is marked variability in the different approaches used to perform RPLND. From the standpoint of open PC-RPLND, a recent systematic review summarised an average complication rate of 21.8%.[13] By contrast, our study demonstrated an absence of significant complications and no surgery-related perioperative mortality. Although perioperative mortality is uncommon with PC-RPLND,[9,11] the absence of 30-day complications in our study is promising. These results were attributed to the rigorous protocol implemented for each individual case. The findings support the hypothesis that PC-RPLND can be safely introduced at an Australian tertiary hospital with adherence to a strict protocol.

The protocol targeted several potential risk factors for complications that were proposed by past studies, broadly categorised into patient and service provider factors.[9,13] Firstly, appropriate case selection is required to identify features of the disease that may complicate the procedure. This was achieved through accurate staging and planning of vascular and general surgery involvement at multidisciplinary team meetings.

It must be noted that no cases were excluded at multidisciplinary meetings during this study period. However, the importance of case assessment is evident with patient 2, in whom seminoma was detected on primary staging. Seminoma has been associated with an increased desmoplastic response following chemotherapy and therefore an increased risk of

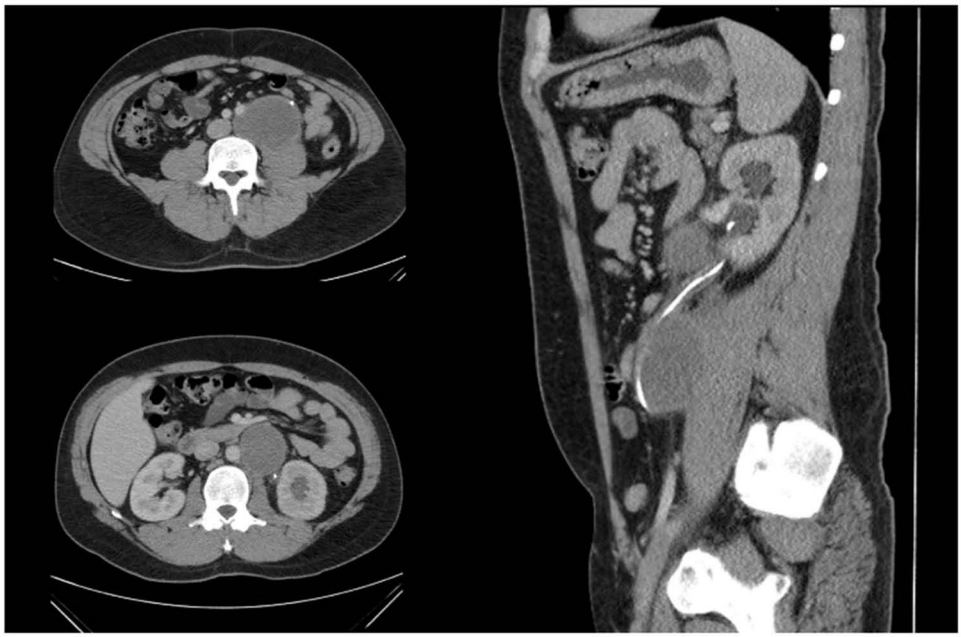

Figure 2 The left ureter was successfully preserved in Patient 4 (note ureteric stent in situ).

intraoperative procedures and postoperative complications.[16] We therefore recommend that cases with seminoma in the post-chemotherapy setting should be avoided, where reasonable, during the early stages of introducing RPLND as a new service.

Preoperative biomarkers also guide case assessment. A higher preoperative LDH – a marker of tumour bulk[17] – supported also by a larger residual mass on imaging are associated with a more difficult operation. It has previously been shown that tumour size can be predictive of increased adjunctive procedures.[18] Consistent with expectations, Patient 2 required an adjuvant nephrectomy for disease encasing the renal vessels and therefore recorded markedly higher operating time (570 minutes) and greater intraoperative blood loss (1300 mL). Similarly, Patient 4 had tumour completely encasing the left ureter. This was successfully excised without damaging the ureter or requiring nephrectomy, however this also required a longer operative time (655 minutes) and resulted in greater blood loss (1250mL). As such, case selection and appropriate team involvement is essential to minimise complications.

Desperation RPLND refers to patients who undergo surgery for rising serum tumour markers post cisplatin-based chemotherapy, and salvage chemotherapy is usually offered as second-line treatment in this setting. All cases were discussed in the MDM setting, and the decision to proceed to RPLND rather than salvage chemotherapy in patients 1, 2

Table 3 Case-Specific Perioperative Quality Measures of Patients Undergoing PC-RPLND

	Case					
Variable	**1**	**2**	**3**	**4**	**5**	**6**
LN excised	33	13	14	8	19	26
Operative time (mins)	360	570	390	655	465	460
Intraoperative blood loss (mL)	150	1300	650	1250	300	1200
Units transfused	0	0	0	0	0	0
Length of ICU stay (days)	0	1	1	1	1	1
Length of stay (days)	10	6	5	6	8	6

Abbreviations: ICU, intensive care unit; LN, lymph nodes.

Table 4 Perioperative Quality Measures of Patients Undergoing PC-RPLND

Variable	Median (n = 6)	IQR
LN excised	17	16
Operative time (mins)	463	209
Intraoperative blood loss (mL)	925	1000
Units transfused	0	0
Length of ICU stay (days)	1	0
Length of stay (days)	6	3

Abbreviations: ICU, intensive care unit; LN, lymph nodes.

and 4 was made in collaboration with our medical oncologists. Of note, all of these cases had metastatic teratoma in the RPLND specimen, which was anticipated based on the orchidectomy histology and response to first-line chemotherapy. Furthermore, none of these patients developed recurrences during follow-up.

Due to the complexity of the procedure, it is well recognised that RPLND should only be performed by experienced urologists.[13] In addition to the lead surgeon having consultant-level expertise with subspecialty Fellowship training, we ensured the availability of on-site vascular and general surgical expertise in adjacent theatres in case the procedure necessitated vascular repair or adjuvant organ removal. We also intentionally avoided cases that would require retrocrural or thoracic procedures in our initial experience. These requirements of the protocol follow recommendations in the literature for minimising the risks of RPLND and PC-RPLND. Furthermore, to reinforce safety, routine postoperative admission in the intensive care unit was also arranged preoperatively as a contingency in the event of a complicated procedure.

Residual metastatic disease was found on histopathology in all patients in the form of metastatic teratoma or yolk sac germ cell tumour. Although the modified template dissections using limited resections have been associated with reduced postoperative complications, shorter length of stay and better preservation of antegrade ejaculation,[5] the standard bilateral template dissection remains recommended in recent guidelines.[19] Particularly in post-chemotherapy patients, this avoids risking incomplete resection and subsequent out-of-template recurrence.[13,20] There were no recurrences in our 6 cases undergoing bilateral template dissection after a median follow-up of 22 months, which is consistent with these guidelines.

Perioperative quality measures also vary in the literature given clinical staging and heterogeneity of approaches and templates used. A recent study determined a mean operating time and intraoperative blood loss of 453 minutes and 403 mL respectively for open RPLND in 15 patients.[21] In comparison, our study of PC-RPLND noted a slightly higher mean operating time of 483 minutes and increased blood loss of 808 mL. The difference in the latter can be attributed to the increased complexity and therefore blood loss seen in Patients 2 and 4. Importantly, no patient required blood transfusion. With regard to histopathological outcomes, the median lymph node count of 17 in our series was identical to a recent population-based analysis of the National Cancer Database and Surveillance, Epidemiology, and End Results (SEER) database.[22] Although this count remains low by the standards of large US centres of excellence, we feel that the lack of recurrence during almost two years of follow-up acts as a further marker of the completeness and quality of RPLND performed at our centre.

Thankfully, there exists a recent large Australian series that can act as a comparator to our case series.[23] This single-surgeon, multi-centre series of 94 patients over 15 years included mostly post-chemotherapy residual masses (95.7%) undergoing open RPLND (93.6%). The median length of stay was 8 days and 61 patients (64.8%) had no CSS2 or above complications within the first 90 days of surgery. Bilateral templates were used in 86.2% of patients, and 26.6% required additional procedures. They did not report node count, however the cohort had a 91.5% recurrence-free survival at a median follow-up of 47.5 months. The results from our initial experience are certainly comparable, if not superior, to this larger series, and call into question the authors' contention that RPLND should remain centralised to specialised centres with high-volume surgeons.

Several limitations are present in this study. Firstly, given the timeline of this study, patients received variable periods of follow-up (median = 22 months) and therefore findings may not include delayed-onset complications occurring substantially beyond the 30-day postoperative period. However, in studies with patients receiving more extended follow-up (median = 51 months), complications occurred more frequently in the 30-day postoperative period (32%) compared to delayed-onset complications (7%).[11]

A small sample size of six cases is not sufficient for statistical comparison of performance. However, it must be noted that the objective was to demonstrate that RPLND can be safely introduced as a new service under a strict protocol with access to appropriate facilities and personnel. The comparative efficacy and longer-term safety outcomes with respect to high-volume institutions will be investigated in future studies.

Conclusion

RPLND plays an integral role in the multidisciplinary management of testicular cancer, albeit with a significant risk of complications, particularly in the post-chemotherapy setting. We have shown that implementing a rigorous protocol with appropriate personnel, facilities and case selection allowed for the safe introduction of RPLND at an Australian tertiary hospital. Our experience suggests that arguments for the centralisation of services in high-volume centres should not preclude establishment of new centres, particularly in areas of documented need.

Disclosure

The authors report no conflicts of interest in this work.

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