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ORIGINAL ARTICLE

A comparative study of peri-operative outcomes for 100 consecutive post-chemotherapy and primary robot-assisted and open retroperitoneal lymph node dissections

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Abstract

Purpose To describe and compare differences in peri-operative outcomes of robot-assisted (RA-RPLND) and open (O-RPLND) retroperitoneal lymph node dissection performed by a single surgeon where chemotherapy is the standard initial treatment for Stage 2 or greater non-seminomatous germ cell tumour.

Methods Review of a prospective database of all RA-RPLNDs (28 patients) and O-RPLNDs (72 patients) performed by a single surgeon from 2014 to 2020. Peri-operative outcomes were compared for patients having RA-RPLND to all O-RPLNDs and a matched cohort of patients having O-RPLND (20 patients). Further comparison was performed between all patients in the RA-RPLND group (21 patients) and matched O-RPLND group (18 patients) who had previous chemotherapy. RA-RPLND was performed for patients suitable for a unilateral template dissection. O-RPLND was performed prior to the introduction of RA-RPLND and for patients not suitable for RA-RPLND after its introduction.

Results RA-RPLND showed improved peri-operative outcomes compared to the matched cohort of O-RPLND—median blood loss (50 versus 400 ml, $p < 0.00001$), operative duration (150 versus 195 min, $p = 0.023$) length-of-stay (1 versus 5 days, $p < 0.00001$) and anejaculation (0 versus 4, $p = 0.0249$). There was no statistical difference in complication rates. RA-RPLND had lower median lymph node yields although not significant (9 versus 13, $p = 0.070$). These improved peri-operative outcomes were also seen in the post-chemotherapy RA-RPLND versus O-RPLND analysis. There were no tumour recurrences seen in either group with median follow-up of 36 months and 60 months, respectively.

Conclusions Post-chemotherapy RA-RPLND may have decreased blood loss, operative duration, hospital length-of-stay and anejaculation rates in selected cases and should, therefore, be considered in selected patients. Differences in oncological outcomes require longer term follow-up.

Keywords Retroperitoneal lymph node dissection · Robotic surgery · Testicular cancer

Introduction

Retroperitoneal lymph node dissection (RPLND) is an integral part of the multimodal treatment of testicular cancer, particularly non-seminomatous germ cell tumours (NSGCT) [1, 2]. In the United States, guidelines recommend using it as either primary treatment or if chemotherapy has failed to eradicate residual retroperitoneal disease [1, 3]. The European Association of Urology guidelines recommend RPLND only in the event of failed chemotherapy or when teratoma is found on orchidectomy pathology [2]. An exception is in select patients with high-risk oncological features or poor compliance with follow-up [2].

Open retroperitoneal lymph node dissection (O-RPLND) has been an established procedure performed since the mid-twentieth century and has the morbidity related to any major open surgery [4].

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Laparoscopic retroperitoneal lymph node dissection (L-RPLND) was first described in the early 1990s [5]. The laparoscopic approach proved to have fewer complications including less blood loss and reduced length of stay [6]. However, there were initial concerns about the ability to fully clear all appropriate lymph node areas with the laparoscopic approach [7]. As such, it was used for diagnostic rather than treatment purposes. However, this technique has since demonstrated efficacy as a treatment option, with reduced morbidity whilst maintaining satisfactory oncological outcomes [6]. Unfortunately, the uptake of L-RPLND has been limited due to its technically challenging nature and steep learning curve [8].

The first robot-assisted retroperitoneal lymph node dissection (RA-RPLND) was performed in 2006 [9]. This offered the advantages associated with minimally invasive surgery and a potential benefit in decreasing anejaculation rates due to increased magnification and three-dimensional vision. Ejaculatory disorders are one major drawback of RPLND. Anejaculation, resulting from affected innervation from the sympathetic nervous system [10] significantly worsens quality of life [11]. Furthermore, it affects fertility and interferes with family planning. This is of great importance as most of the patients are young with a long life expectancy. Until now, data on post-chemotherapy RA-RPLND ejaculatory disorders are limited.

Several recent case series reported favourable peri- and post-operative outcomes after RA-RPLND [7–9, 12–14], however, many of them have focussed entirely [8, 9, 14] on primary RA-RPLND. Post-chemotherapy RPLND is known to be more challenging than primary RPLND [6, 15, 16] due to the fibrosis associated with chemotherapy. As such, morbidity and complications rates are significantly higher [15, 16]. The evidence for post-chemotherapy RA-RPLND is gradually increasing [7, 12, 13, 17, 18] but remains limited and there is minimal comparison of outcomes to O-RPLND.

The aim of the present study is to describe early perioperative outcomes including post-operative anejaculation rates of RA-RPLND compared to O-RPLND in a predominant post-chemotherapy RPLND practice. To our knowledge, this is one of the largest post-chemotherapy comparative series of RA-RPLND and O-RPLND.

Materials and methods

Patient population and data collection

We performed a retrospective review of a consecutive single-surgeon series of 100 patients who underwent RPLND between 2014 and 2020. Chemotherapy was given as standard treatment for Stage 2 NSGCT with primary RPLND only considered where there was significant predominance of teratoma in the orchidectomy specimen or if there were certain patient factors that precluded chemotherapy. Peri- and post-operative data until last follow-up appointment were prospectively collected and submitted. Complications were graded according to the Clavien–Dindo Classification. Grade I–II complications were defined as minor and grade IIIa–V as major. Anejaculation was defined as an absence of the emission phase and no antegrade expulsion of ejaculatory products [10].

Patient selection criteria

RA-RPLND was considered for patients who presented with (i) unilateral retroperitoneal disease both before and after chemotherapy with their retroperitoneal disease consistent with the laterality of their orchidectomy (para-aortic retroperitoneal disease with left testicular cancer and interaortocaval disease with right testicular cancer), (ii) a discrete mass, (iii) a mass less than 10 cm and (iv) no previous retroperitoneal surgery.

Statistical analyses

Three separate comparative analyses were performed. The first comparison was between all RA-RPLND and O-RPLNDs to provide a general overview of the type of practice and cases. The second comparison was between all RA-RPLNDs and a matched cohort of O-RPLNDs which fulfilled the criteria for having a RA-RPLND prior to introduction of RA-RPLND (based on the four criteria above). The third analysis was a comparison of those patients having a post-chemotherapy RA-RPLND and those patients from the matched O-RPLND cohort in the second analysis who had previous chemotherapy.

The results for the O-RPLNDs and RA-RPLNDs for various parameters were then compared using a Mann–Whitney test and Fischer's exact test with $p < 0.05$ considered statistically significant.

Surgeon experience

The surgeon had completed two robotic fellowships and an open oncological surgery fellowship that included O-RPLND. He performs over 100 robotic cases per year including robot-assisted radical prostatectomy, radical cystectomy with intracorporeal urinary diversion, partial and radical nephrectomy, and nephroureterectomy. He had completed over 100 robotic cases and 47 O-RPLND when he commenced performing RA-RPLND.

Surgical technique

A left unilateral template included the para-aortic and pre-aortic tissue (Fig 1a of supplementary material). A lateral approach was used in these cases with port placement as shown in Fig. 1b of the supplementary material.

A right unilateral template included paracaval, precaval, interaortocaval and pre-aortic tissue (Fig 1c of supplementary material). A supine approach described previously by L'Esperance, Porter and Castle [19] was used with port-placements shown in Fig. 1d of the supplementary material. Retrovascular dissection was performed in all cases.

A da Vinci Si system was used for all cases (see supplementary Fig. 1). For left-sided templates, a fenestrated bipolar forceps, monopolar scissors and prograsp retractor were used. For right-sided templates, a single large needle driver was additionally used.

A template dissection was completed in all but one RA-RPLND case in this series with visual clearance of all tissue in the relevant template as seen in Fig. 1e and f of the supplementary material. In the one case where a template was not completed, a mass excision was planned pre-operatively as the patient had a cystic interaortocaval mass and previous history of a heart transplant. He was on significant immunosuppressive medications and was considered high risk from an anaesthetic perspective. He was excluded from the final two comparisons.

Results

One hundred patients had a RPLND for testicular cancer. RA-RPLND was introduced in 2016 with 28 robotic RPLNDs performed subsequently. Eighty-nine patients had a post-chemotherapy RPLND for residual retroperitoneal disease. Eleven patients had a primary RPLND—5 in the open group and 6 in the robotic group. Since the introduction of RA-RPLND, 54 RPLNDs were performed with 26 O-RPLNDs performed. These were for patients requiring bilateral template dissections, RPLND for significant retroperitoneal disease in seminoma and re-do RPLND.

Analysis 1: all robot-assisted versus all open RPLND

A comparison of the 28 patients who had RA-RPLND and the 72 patients who had O-RPLND is seen in supplementary Table 1. There was a statistically significant decrease in median operative duration (150 versus 240 min, $p<0.00001$), estimated blood loss (50 versus 800 mls, $p<0.00001$), transfusion rate (0 versus 14 cases, $p=0.009$), length-of-stay (1 versus 6 days, $p<0.0001$) and in anejaculation rates (0 versus 30 cases, $p<0.0001$) in the RA-RPLND group compared to all O-RPLND group. The median size of residual mass was higher in the O-RPLND group compared to the RA-RPLND group (30 versus 22 mm, $p=0.003$). There was no statistically significant difference in lymph node yields ($p=0.187$). These results are summarised in Table 1.

There were 2 patients (8%) in the RA-RPLND group and 5 patients (7%) in the O-RPLND group who had chylous ascites. These were managed with percutaneous

Table 1 All 100 RPLNDs: 28 RA-RPLND versus all 72 O-RPLND cases—peri-operative and post-operative data

	Robotic	Open	*p* value
Number of men, *n*	28	72	
Previous chemotherapy, *n*	22	67	0.0686
Body mass index [kg/m^2], median (range)	24.8 (18.4–32.9)	26 (17.4–43.6)	0.226
Size of mass (mm), median (range)	20 (12–80)	30 (11–390)	0.003
Operative duration (minutes), median, (range)	150 (105–275)	240 (135–330)	< 0.00001
Estimated blood loss (mls), median (range)	50 (25–400)	800 (150–4000)	< 0.00001
Transfusion, *n*	0	14	0.0093
Length of stay (days), median (range)	1 (1–2)	6 (2–21)	< 0.00001
Conversions, *n*	0		
Major complications (Clavien–Dindo ≥ 3a), *n*	2 (8)	6 (9)	1.0
Lymph node yield, median (range)	9 (1–22)	10 (2–53)	0.1868
Histopathology			0.4516
Necrosis, *n* (%)	4	16	
Teratoma, *n* (%)	19	39	
Viable cancer, *n* (%)	5	17	
Anejaculation, *n* (%)	0	30	< 0.00001

drainage (Clavien–Dindo 3a) and dietary modification with a medium-chain fatty acid diet. One patient (1%) in the O-RPLND group required an admission to the intensive care unit with acute respiratory distress syndrome post-operatively requiring intubation and ventilatory support (Clavien–Dindo 4a).

Analysis 2: all robot-assisted versus matched cohort of open RPLND

The O-RPLND group was further analysed to identify all patients who would now be considered for RA-RPLND—essentially a historically comparative matched cohort based on the criteria for RA-RPLND. A cohort of 20 patients with O-RPLND was identified and then compared to the RA-RPLND group. The results are seen in Table 2. There was a statistically significant decrease in median operative duration (150 versus 195 min, $p=0.005$), estimated blood loss (50 versus 400 mls, $p<0.0001$), length of stay (1 versus 5 days, <0.0001) and in anejaculation rates (0 versus 4 cases, $p=0.003$) in the RA-RPLND group compared to the matched O-RPLND group. There was no statistically significant difference in the number of post-chemotherapy cases (22 versus 18, $p=0.440$), median size of residual mass (22 mm versus 25 mm, $p=0.390$) or in lymph node yields (9 versus 13, $p=0.070$).

Analysis 3: post-chemotherapy robot-assisted versus post-chemotherapy matched cohort of RPLND

A final comparison was performed between patients in the second analysis, the RA-RPLND group and matched O-RPLND group, who had previous chemotherapy (Table 3). 21 patients from the RA-RPLND group and 18 patients from the matched O-RPLND group had a post-chemotherapy RPLND. There was again significant improvement seen in median operative duration (150 versus 195 min, $p=0.016$), estimated blood loss (50 versus 400 mls, $p<0.00001$), length of stay (1 versus 5 days, $p<0.00001$) and anejaculation rates (0 versus 4 cases, $p=0.019$). There was no significant difference in size of the residual mass (21 versus 24 mm, $p=0.384$) or lymph node yields (7 versus 13, $p=0.101$).

No recurrences were seen in either group with the median follow-up 36 months for the RA-RPLND group and 60 months for the matched O-RPLND group.

Discussion

The advantages of minimally invasive surgery have been evident in many different operations. In particular, there is a trend for decreased blood loss and length of stay [20]. This study shows that these benefits may also be evident in RPLND surgery. This study has shown that there is a statistically significant decrease in blood loss for RA-RPLND compared to O-RPLND in all the comparisons performed. The difference in blood loss whilst statistically significant

Table 2 Peri-operative and post-operative data of all 27 RA-RPLND versus matched cohort of 20 O-RPLND considered suitable for RA-RPLND

	Robotic	Open	*p* value
Number of men, *n*	27	20	
Previous chemotherapy, *n*	22	18	0.440
Body mass index [kg/m^2], median (range)	24.8 (18.4–32.9)	26.1 (17.4–41.4)	0.211
Size of mass (mm), median (range)	22 (18–80)	24 (13–74)	0.390
Operative duration (minutes), median (range)	150 (105–275)	195 (135–330)	0.005
Estimated blood loss (mls), median (range)	50 (25–200)	400 (100–2400)	< 0.00001
Transfusion, *n*	0 (0)	0 (0)	1.0
Length of stay (days), median (range)	1 (1–2)	5 (3–13)	< 0.00001
Conversions, *n*	0		
Major complications (Clavien–Dindo ≥ 3a), *n*	2	2	1.0
Lymph node yield, median (range)	9 (1–22)	13 (3–25)	0.070
Histopathology			0.748
Necrosis, *n*	4	3	
Teratoma, *n*	18	15	
Viable cancer, *n*	5	2	
Anejaculation, *n* (%)	0	4	0.025
Recurrence	0	0	1.0

Table 3 Peri-operative and post-operative data of matched cohort analysis of post-chemotherapy 21 RA-RPLND versus matched cohort of 18 O-RPLND considered suitable for RA-RPLND

	Robotic	Open	*p* value
Number of men, *n* (%)	21	18	
Body mass index [kg/m^2], median (range)	25.1 (18.4–32.9)	26.1 (17.4–41.4)	0.233
Size of mass (mm), median (range)	21 (12–60)	24 (13–74)	0.384
Operative duration (minutes), median (range)	150 (105–275)	195 (135–330)	0.016
Estimated blood loss (mls), median (range)	50 (25–200)	400 (100–2400)	< 0.00001
Transfusion, *n* (%)	0 (0)	0 (0)	1.0
Length of stay (days), median (range)	1 (1–2)	5 (3–13)	< 0.00001
Conversions, *n* (%)	0 (0)		
Major complications (Clavien–Dindo ≥ 3a), *n* (%)	2 (8)	2 (10)	1.0
Lymph node yield, median (range)	8 (1–22)	13 (3–25)	0.101
Histopathology			0.976
Necrosis, *n* (%)	4	3	
Teratoma, *n* (%)	16	15	
Viable cancer, *n* (%)	1	0	
Anejaculation, *n* (%)	0	4	0.019
Recurrence	0	0	1.0

is not necessarily clinically significant given that there is no significant difference in the transfusion rates for similar cases—the transfusion rate was significantly different for RA-RPLND compared to all O-RPLND, however, there was no significant difference to the matched O-RPLND cohorts (no transfusions).

In our series, all RA-RPLNDs were discharged on day 1 post-operatively apart from one patient who was discharged on day 2. The median length of stay for the matched O-RPLND group was 5 days with the lowest length of stay being 2 days. The patients having an O-RPLND take part in an enhanced recovery pathway and hence it is unlikely that the length of stay could be reduced much further than 2 days. The matched O-RPLND length of stay is based on the initial experience of O-RPLND for the surgeon and is hence slightly higher than compared to his later experience in which the median length of stay over the last 15 open cases is 3 days.

Additional benefits of RA-RPLND in our series included decreased operative duration and decreased anejaculation rates. This may be related to the increased magnification that enables easier nerve sparing within the template as well as the utilisation of unilateral templates in this series. It is also likely that less interaortocaval dissection was performed in the left-sided unilateral templates performed in the RA-RPLND group and perhaps explains the decreased lymph node yield in the RA-RPLND groups, albeit not statistically significant.

The reduction in operative duration in the robotic RPLND group appears contradictory to similar comparisons for other robotic surgery in comparison to open surgery. In studies for complex robotic surgery such as robotic radical cystectomy [21, 22] and partial nephrectomy [23], operative duration is generally increased due to the increased setup time regarding port placement and robot docking. However, in the only randomised controlled trial for open and robotic radical prostatectomy, operative duration was shorter in the robotic group [24]. Hence, the benefits in anatomical access and complex dissection may offset the additional setup time for certain operations.

To our knowledge, this is the largest series including post-chemotherapy RA-RPLND series that has reported post-operative ejaculatory function, and has a similar number of patients to the study of Li et al. [25], who reported outcomes of 93 patients having post-chemotherapy RA-RPLND and O-RPLND but which did not report post-operative anejaculation rates.

There have been multiple series that have reported their results of RA-RPLND and six studies have reported specifically on post-chemotherapy RA-RPLND [7, 12, 13, 17, 18, 25]. These are summarised in Supplementary Table 1 of the supplementary material. Cheney et al. [7] and Stepanian et al. [12] were pioneering studies and showed that post-chemotherapy robotic RPLND was feasible, although the proportion of post-chemotherapy cases was less than in the more recently published series. These studies also illustrated the supine approach and included bilateral template dissections. Kamel [17], Overs [13], Singh [18] and Li [25] only included post-chemotherapy RA-RPLND cases and their absolute numbers of post-chemotherapy cases were higher.

The comparison of these robotic series also shows evolution of technique and outcomes. Operative duration has improved with time although in our series, only unilateral templates were performed. Blood loss and transfusion rates were similar in all series. Length of stay was only one night for all but one patient in our series. This is likely to be related to the accumulated experience from the previous series and the use of enhanced recovery protocols. Lymph node yields were lower in two of the more recent series, Overs et al. [17] and our own series.

The role of lymph node yield as a quality control measure is of less value in the post-chemotherapy RPLND setting as many of the residual masses will consist of a conglomerate of fibrotic and necrotic lymph nodes that will only be counted as a single lymph node [7]. Lymph node yields are also highly susceptible to variability due to processing procedures [26]. Hence, the lymph node yields may be higher in series that included a higher proportion of primary RPLNDs and those series with bilateral template dissections.

Unilateral template dissections were utilised in this study. The determination regarding type of template performed was not altered by introduction of RA-RPLND as unilateral templates were utilised prior. A decision was made with the introduction of RA-RPLND to only consider RA-RPLND for lower risk cases given the infancy of the operation and importance of oncological outcomes. Hence, these were generally cases suitable for unilateral templates based on previous protocols.

There have been many studies that have analysed the suitability of unilateral templates in the post-chemotherapy setting. Concern has been raised regarding the oncological outcomes and risk of recurrence with such an approach. The advantage of such an approach is that it potentially decreases the risk of anejaculation by minimising the extent of dissection and the risk of injury to sympathetic nerves [27]. Nerve-sparing bilateral template dissections could be considered the gold-standard approach [28]. However, nerve sparing in the post-chemotherapy setting is difficult and inevitably there is likely to be a learning curve associated with effective adoption of such an approach. Unilateral template dissections have been adopted in high-volume centres [29, 30] and long-term follow-up has shown that oncological outcomes may not be affected at 10 years [29]. In particular, recurrence in the contralateral side of the retroperitoneum within the field of a bilateral template was not significantly different.

Bilateral RA-RPLND would be natural evolution of the procedure and would increase the patients suitable for RA-RPLND. It has been performed after the period of this study by the authors. This approach places a greater reliance on nerve-sparing technique to maintain emissary function which can be difficult in the post-chemotherapy setting and is likely to be dependent on surgical experience of the technique.

The learning curve for RA-RPLND is difficult to assess with this small series. Cases were selected on a case-by-case basis and although there were criteria for consideration of RA-RPLND, there was no absolute indication for performing a robotic approach. The main concern with such surgery is vascular injury and hence relationship of the residual disease to the great vessels was perhaps more crucial than the size of the mass. Inevitably, this introduces a selection bias in the robotic group as the alternative to perform O-RPLND was available. However, this series also includes the learning curve for O-RPLND of this surgeon since it includes all O-RPLND from the start of their practice (46 O-RPLND before the introduction of RA-RPLND). However, the selection bias in the O-RPLND group is less as no cases were abandoned or referred elsewhere during this time.

Further limitations with this study include the potential replication of outcomes. The consistent volume of RPLNDs at this surgeon's centre and previous experience in open and robotic retroperitoneal surgery is not easily reproducible. The retrospective nature of the study is an inherent bias with regards to the analysis.

There were no tumour recurrences observed in the RA-RPLND group which is indicative that this approach is safe from an oncological point of view in the short-term (median follow-up 36 months). However, the follow-up times remain too short to draw any conclusions on oncological outcomes. Further studies with larger numbers and long-term follow-up are necessary to truly determine the efficacy of RA-RPLND.

Conclusion

RA-RPLND offers comparable morbidity to O-RPLND with potential benefits including reduced length-of-stay, reduced blood loss and decreased operative duration. There may be benefits in anejaculation rates with a robot-assisted approach but not definitively in the post-chemotherapy setting. Therefore, RA-RPLND could be considered in selected patients.

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Author contributions PL and BT participated in conception and design, statistical analysis, analysis and interpretation of data, and manuscript drafting. AH, EL, HD, JS, CA, SS, DM, HW, NL and AW collected the clinical data and analysis and interpretation of data. MF contributed to analysis and interpretation of data, and manuscript drafting. DN participated in project supervision. All the authors read and approved the final manuscript.

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Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest Paul Lloyd, Anne Hong, Marc A. Furrer, Elaine WY Lee, Harveer S Dev, Maurice H Coret, James M Adshead, Peter Baldwin, Richard Knight, Jonathan Shamash, Constantine Alifrangis, Sara Stoneham, Danish Mazhar, Han Wong, Anne Warren, Ben Tran, Nathan Lawrentschuk, David E Neal and Benjamin C Thomas have nothing to disclose.

Ethical approval Approval was obtained from the local ethics committee. Informed consent was waived by the institutional review board in view of the retrospective nature of the study. All the procedures being performed were part of the routine care.

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