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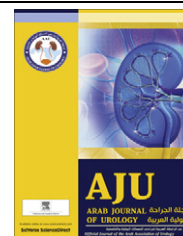
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REVIEW

Laparoscopic retroperitoneal lymph node dissection for testicular cancer

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KEYWORDS

Testicular cancer;
Lymph node
dissection;
Laparoscopy;
Retroperitoneal;
Germ cell tumour

ABBREVIATIONS

(N)(S)GCT, (non)
(seminomatous) germ
cell tumour;
(L-)RPLND, (laparo-
scopic-) retroperitoneal
lymph node dissection;
LOS, length of hospital
stay; SC, spermatic

Abstract Objectives: Laparoscopic retroperitoneal lymph node dissection (L-RPLND) was introduced over 20 years ago as a less invasive alternative to open node dissection. In this review we summarise the indications, surgical technique and outcomes of L-RPLND in the treatment of testicular cancer.

Methods: We searched MEDLINE using the terms ‘laparoscopy’, ‘laparoscopic’, ‘retroperitoneal lymph node dissection’, ‘RPLND’ and ‘testicular neoplasms’. Articles were selected on the basis of their relevance, study design and content, with an emphasis on more recent data.

Results: We found 14 pertinent studies, which included >1300 patients who received either L-RPLND (515) or open RPLND (788). L-RPLND was associated with longer mean operative times (204 vs. 186 min), but shorter hospital stays (3.3 vs. 6.6 days) and lower complication rates (15.6% vs. 33%). Oncological outcomes were similar between L-RPLND and open RPLND, with local relapse rates of 1.3% and 1.4%, incidence of distal progression of 3.3% and 6.1%, biochemical failure in 0.9% and 1.1% and cure rates of 100% and 99.6%, respectively.

Conclusion: There are no randomised controlled studies comparing L-RPLND with open RPLND. A review of case and comparative series showed similar

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cord; IVC, inferior vena cava; IMA, inferior mesenteric artery

perioperative and oncological outcomes. Patients undergoing L-RPLND on average have shorter hospital stays, a quicker return to normal activity and improved cosmesis.

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Introduction

In 2011, 8300 new cases and 350 deaths are estimated to occur due to testicular cancer [1]. The incidence of testicular cancer has increased by 50% since 1973 [2]. Fortunately, advances in multimodal therapy have resulted in survival rates of >90%. Despite the success of multidisciplinary management, surgery remains a critical treatment.

Most germ-cell tumours (GCTs) spread in a highly predictable manner via the retroperitoneal lymphatic channels. Mapping studies found that tumours from the right testis most commonly metastasise to the inter-aortocaval nodes followed by the precaval and paracaval nodes. Left-sided tumours spread to the para-aortic and pre-aortic lymph nodes. These patterns reflect the embryonic origins of the testes within the abdomen.

Seminomatous GCTs (SGCTs) differ from nonseminomatous GCTs (NSGCTs) by their exquisite radiosensitivity and more favourable prognosis. Infradiaphragmatic radiotherapy remains a standard treatment option for patients with stage I and low-volume stage II disease; surgery is rarely used before chemotherapy. NSGCTs are far less radiosensitive, and consequently, RPLND has a more prominent role in the management of patients with NSGCTs.

Following orchidectomy, patients with NSGCT and clinical stage I disease have many therapeutic options, which include active surveillance, multi-agent chemotherapy (bleomycin, etoposide and cisplatin) or RPLND. Surveillance has a relapse rate of \approx 13% and is best used in compliant patients with stage IA disease [3]. Chemotherapy has the lowest relapse rate. If a relapse does occur, it is less amenable to salvage therapy. Patients with stage II disease and a limited nodal burden might be treated with either chemotherapy or RPLND. Those with significant retroperitoneal adenopathy are best managed with chemotherapy followed by postchemotherapy RPLND in select residual masses.

RPLND has several advantages over both active surveillance and chemotherapy. Surgery most accurately stages the retroperitoneum and in patients with low-volume metastatic disease it can be curative. Consequently, selected patients can be spared the morbidity of chemotherapy and the potential risk of secondary malignancy associated with both chemotherapy and repeated CT while on active surveillance. RPLND is also therapeutic in patients with a teratoma, which due to its slow growth is resistant to chemotherapy. The long-term cancer-

specific survival rate after RPLND approaches 100% [4]. However, there is a 10% risk of extra-retroperitoneal recurrence, and therefore patients require long-term surveillance imaging, in particular of the chest and mediastinum [5]. An important concern with RPLND is the potential for overtreatment, as only 30% of clinical stage I patients are found to have positive nodes after RPLND [6].

RPLND has traditionally been performed via a large midline incision extending from the xiphoid process to pubic symphysis. First reported in 1992, laparoscopic RPLND (L-RPLND) was developed in an effort to reduce the morbidity of the procedure [7]. Advantages of a laparoscopic approach include decreased pain, shorter postoperative stay, improved cosmesis and a magnified view of delicate retroperitoneal structures, including the sympathetic plexus [8].

In this review we outline the indications for L-RPLND and the surgical technique, and review previous reports pertaining to perioperative and oncological outcomes.

Indications

After orchidectomy all patients with testicular cancer should receive a full metastatic evaluation. This examination includes repeat testing of serum tumour markers, serum chemistry, liver function tests, a chest X-ray and CT of the abdomen and pelvis. Additionally, CT of the chest, MRI of the brain and a bone scan can be used in selected cases. The tumour markers that should be obtained include α -fetoprotein, β -human chorionic gonadotrophin and lactate dehydrogenase. After orchidectomy, tumour markers should not be reassessed until sufficient time has passed to allow normalisation.

On completing the metastatic evaluation RPLND should be considered in patients with stage I, stage IIa and low-volume IIb NSGCTs. For patients who choose chemotherapy, RPLND can still be important in their treatment [9]. A residual retroperitoneal mass occurs in up to 30% of patients after induction chemotherapy for NSGCT [10]. These residual masses on excision will contain teratoma elements in 30–40%, viable tumour in 10–20% and necrotic tissue or fibrosis in 40–50% [11,12]. Post-chemotherapy RPLND is recommended in patients with residual masses of >1 cm, given that untreated retroperitoneal lymph node masses are associated with a low survival rate [13]. Although up to half of

the residual masses will only contain necrotic tissue, current imaging (including positron emission tomography) cannot reliably distinguish necrotic tissue from a teratoma or residual tumour.

For certain patients RPLND is not recommended; they include those with elevated tumour markers, which is indicative of systemic disease [14]. Similarly, the presence of markedly enlarged lymph nodes (> 5 cm) is predictive of systemic disease unsuitable for treatment with RPLND. An active peritoneal or abdominal wall infection is also a relative contraindication to RPLND. Lastly, patients with bleeding diatheses are best managed without surgery.

L-RPLND is a technically challenging operation and should only be attempted by experienced laparoscopic surgeons who are comfortable with advance vascular techniques and open RPLND, in case of conversion [15]. This is particularly true after chemotherapy, which is often associated with dense scar tissue that makes laparoscopic dissection challenging. Not surprisingly, conversion rates are higher for L-RPLND after chemotherapy [9].

Preparation

Patients should be counselled on the various treatment options available. The potential oncological outcomes and complications of each treatment method should be reviewed. For surgery, this discussion should include the possibility of inadvertent injury to the bowel, kidney, liver and pancreas. Postoperative lymph leakage should also be discussed. Patients should be aware that manipulation of the sympathetic chain could result in retrograde ejaculation. Preoperative sperm banking should be discussed with all patients.

It has been advocated that patients should be started on a low-fat diet 2 weeks before surgery [16], to decrease the risk of chylous ascites. Mechanical bowel preparation is used the day before surgery. In patients likely to have multiple adhesions, a full bowel preparation should be considered. All patients should be typed and crossed for packed red blood cells.

Induction chemotherapy regimens typically include bleomycin, which has been associated with pulmonary fibrosis; this can cause several postoperative respiratory issues, including respiratory distress syndrome [17]. Patients undergoing RPLND who received bleomycin benefit from preoperative consultation with a pulmonologist. Intraoperative intravenous fluids should be limited in these patients. The use of nephrotoxic medications should be minimised in patients who received cisplatin, given its deleterious effects on renal function. In addition, myelosuppression can occur after chemotherapy. Therefore, surgery should not be performed for at least 5 weeks from the last chemotherapy treatment, to allow for haematopoietic recovery [14].

Operating room set-up

An efficiently set up and organised operating room is critical for success. The surgeon stands on the contralateral side of the dissection. To prevent crowding from the surgical assistant, a self-retaining laparoscopic camera is recommended. To ensure that both surgeon and assistant have clear viewing angles, monitors should be placed on each side of the patient. The operating room staff should have a full laparoscopic tray, including vascular instruments, available. In addition, there should be an open vascular tray in the operating room should intraoperative haemorrhage necessitate a rapid conversion to open RPLND.

Patient positioning

A urethral catheter as well as an oral or nasogastric tube is placed after intubation. Some surgeons favour slightly elevating the ipsilateral flank when performing a unilateral template dissection. The authors prefer the supine position. Tilting of the operating room table is usually sufficient to passively retract the bowel away from the surgical field. Also, by keeping the patient supine the procedure can be converted to a full bilateral template with no need for repositioning.

After proper positioning, sequential compression devices are placed on the lower extremities, the patient's arms are tucked and all pressure points are adequately padded. The patient is secured to the operating room table with multiple layers of wide tape. A 'test roll' is then performed to ensure that the patient is properly secured to the operating room table. The patient is then prepared and draped from the xiphoid process to the upper thighs.

Laparoscopic access

Once pneumoperitoneum has been established, four 10–12 mm ports are placed (Fig. 1). The most superior port is placed 2 cm below the xiphoid process and the most inferior trocar 3 cm above the pubic symphysis. The remaining two ports are spaced equidistantly along the midline between the other two trocars. An additional 5-mm port may be placed laterally to assist with the spermatic cord (SC) dissection.

After placing the trocars the operating room table is rotated to elevate the side of dissection. The patient is also placed in slight Trendelenburg position to assist with passive bowel retraction. If additional bowel retraction is needed a paddle can be placed through the most inferior port.

Technique for right template dissection

The borders of the right modified template are the right renal vein superiorly, bifurcation of the right common

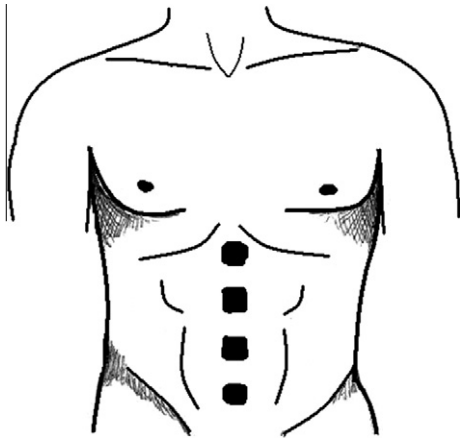


Figure 1 Trocar placement for L-RPLND four 10 mm trocars are placed in the midline evenly spaced from the xiphoid process to the pubic symphysis.

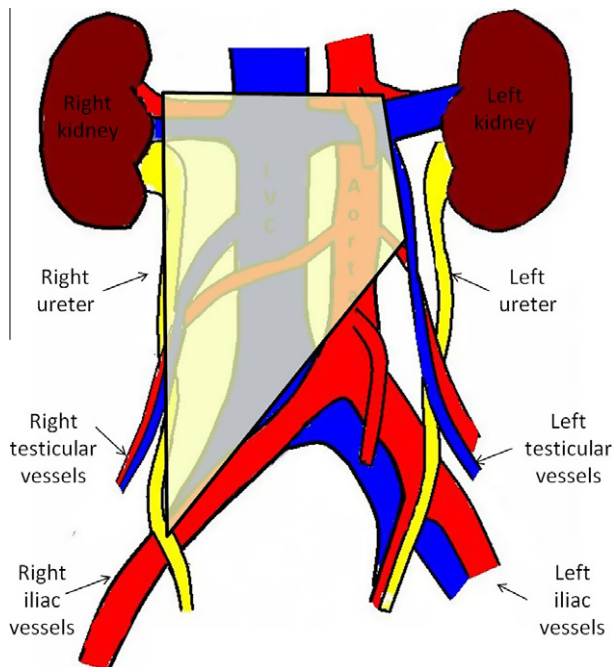


Figure 2 Right modified template.

iliac artery inferiorly, right ureter laterally and pre-aortic nodes medially (Fig. 2). In addition to the right SC, the right iliac, paracaval, inter-aortocaval and pre-aortic nodal packets are removed during the dissection.

After placing trocars the procedure begins with mobilisation of the ascending colon by incising the white line of Toldt from the hepatic flexure down to the medial umbilical ligament. Endoscopic monopolar scissors or a bipolar cutting device should be used judiciously to control bleeding, while minimising the risk of thermal injury to the bowel. The Kocher manoeuvre is then performed by mobilising the duodenum medially, exposing the retroperitoneum.

The next step is to identify the distal SC adjacent to the internal inguinal ring. The vas deferens is clipped

and divided. The dissection is continued distally, separating the SC from its attachments within the inguinal canal until the permanent suture from the previous radical orchidectomy is identified. Care is taken to avoid injury to the inferior epigastric vessels. The SC dissection then continues proximally. The gonadal vein is clipped where it enters into the inferior vena cava (IVC) and the gonadal artery is ligated where it arises from the aorta. Once completely dissected free, the SC is placed in an entrapment sac and removed.

The adventitia overlying the vena cava is then elevated and incised from the renal veins to the IVC bifurcation. Starting where the ureter crosses the iliac vessels, the paracaval nodes are 'split and rolled' away from the IVC towards the right ureter. Liberal use of clips when dividing lymphatic attachments is recommended. The dissection is continued up to the renal hilum. The ureter is retracted laterally, while the lymphatic tissue is freed medially. Finally, the entire packet is retracted anteriorly and separated from the underlying posterior body wall and sympathetic trunk. Use of cautery should be avoided to decrease the risk of damaging the sympathetic trunk.

Attention is then turned to removing the inter-aortocaval and pre-aortic nodal packets. The adventitia overlying the aorta is divided from the renal hilum down to the level of inferior mesenteric artery (IMA). The pre-aortic nodes are then retracted medially while the inter-aortocaval packet is elevated off of the posterior body wall. Multiple lumbar arteries can be encountered, which should be clipped. During the superior aspect of the dissection care should be taken to preserve the right renal artery, and if present, the accessory renal artery.

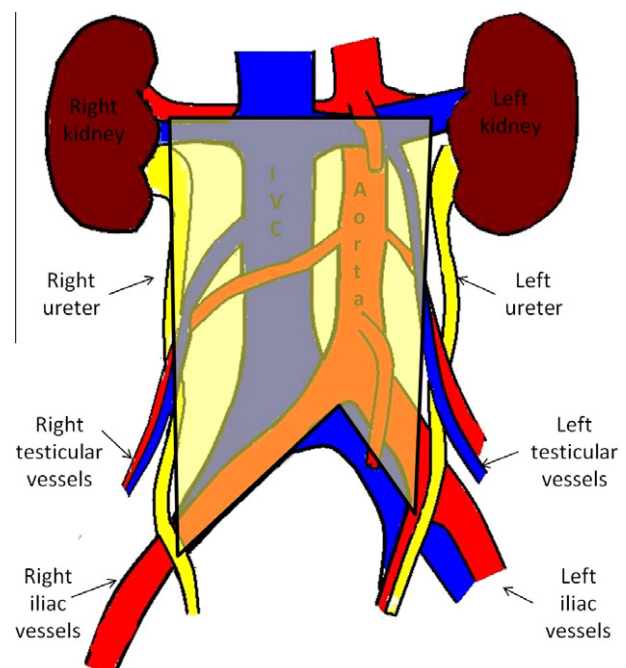


Figure 3 Bilateral template.

Up to 20% of patients can have an accessory renal artery that can be confused with lumbar vessels.

Lastly, the retrocaval dissection is performed. Lumbar veins are identified and ligated between metal clips, thereby allowing the IVC to be retracted anteriorly. After completing the retrocaval dissection, the nodal packets are placed in an extraction sac and removed.

If any grossly positive nodes are encountered during the dissection, then the operation is converted to a bilateral template resection (Fig. 3). If not, the lymphatic dissection ends here and the field inspected to identify any lymphatic leak. Any open lymphatic vessels should be clipped and any pooling of chylous fluid should prompt closer inspection. The peritoneum is surveyed one more time to exclude visceral injury. Closure of the fascia is required for all ports of ≥ 10 mm. Either a Carter-Thomason (Inlet Medical, Eden Prairie, MN, USA) or EndoClose (U.S. Surgical, Norwalk, CT, USA) fascial closure device may be used. The skin is then closed with a 4-0 absorbable suture.

Technique for left template dissection

The limits of the left modified template are the left renal vein superiorly, the bifurcation of the common iliac arteries inferiorly, the left ureter laterally and the vena cava medially (Fig. 4). The left iliac, pre-aortic and para-aortic nodes are cleared from the retroperitoneum during the left modified template dissection.

As on the right side, the dissection begins by incising the line of Toldt. The descending colon is mobilised from the splenic flexure to the bifurcation of the common iliac vessels. The tail of the pancreas is identified and moved medially. The splenophrenic and splenorenal

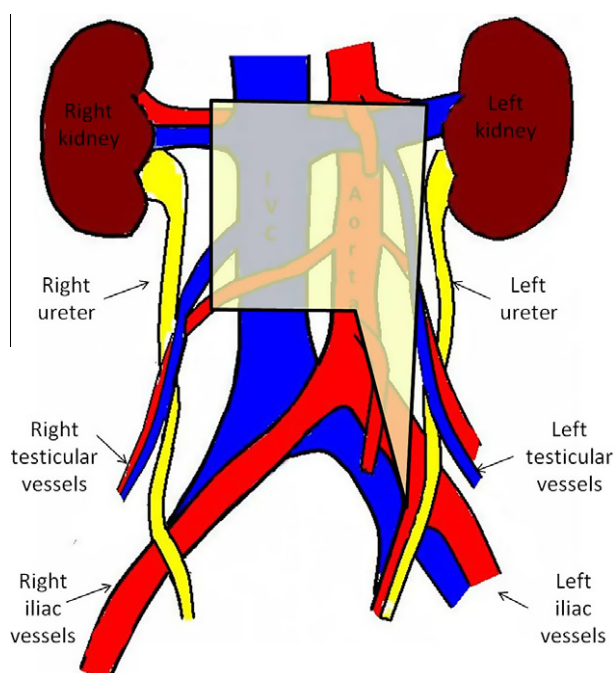


Figure 4 Left modified template.

attachments are divided to improve retroperitoneal exposure.

The left internal inguinal ring is identified and the distal SC is dissected free of the inguinal canal, as previously described. However, when performing the left-sided dissection, the left gonadal vein is followed to its insertion into the left renal vein and divided there. As on the right side, the SC is placed in an entrapment sac and extracted.

The aorta and ureter are then identified and para-aortic lymph node dissection is begun. The adventitia covering the anterior portion of the aorta is divided from the renal hilum to the IMA. After reaching the IMA the dissection shifts inferolaterally to where the left ureter crosses the iliac vessels. The para-aortic and iliac nodal packets are rolled laterally off of the aorta as the dissection continues up to the renal hilum. The pre-aortic nodes are swept medially from the renal hilum to the IMA separating them from the aorta and anterior spinous ligament. Lumbar arteries are ligated as the dissection moves caudally to permit clearing the retro-aortic space. Once again, care is taken to preserve the efferent sympathetic nerve fibres. Any remaining attachments to the posterior body wall are clipped and divided and the nodal packets are removed. The abdomen is then closed as described above.

Postoperative care

Peritoneal drains, although usually unnecessary, may be placed at the surgeon's discretion. In patients with no preoperative bowel issues, the nasogastric or orogastric tube may be removed. The urethral catheter is removed once the patient is ambulatory. Patients are eligible for discharge when their pain is under control with oral agents and they are tolerating a regular diet.

Results

No prospective, randomised studies have been reported comparing open with L-RPLND. Since 2000, only two retrospective comparative studies have been published, which are summarised in Table 1. Poulakis et al. [18] compared 21 patients undergoing L-RPLND to 29 treated with open RPLND. In a similar study, Abdel-Aziz et al. [19] reviewed 22 L-RPLND compared with six open RPLND procedures.

For perioperative outcomes, Poulakis et al. [18] found that the mean operative time (233 vs. 203 min, $P < 0.001$), estimated blood loss (270 vs. 422 mL, $P < 0.001$) and length of stay (LOS) (2 vs. 7 days) differed significantly between the laparoscopic and open groups, respectively. Similarly, Abdel-Aziz et al. [19] found that the laparoscopic group had less blood loss (159 vs. 254 mL, $P = 0.02$) and a shorter LOS (1.2 vs. 8.5 days, $P < 0.001$), but the operating times were not significantly different (313 vs. 284 min, $P = 0.17$).

Table 1 Comparative studies of L-RPLND vs. open RPLND.

Variable	[18] (<i>n</i> = 50)		[19] (<i>n</i> = 28)	
	L-RPLND	Open	L-RPLND	Open
N	21	29	22	6
Mean (SD)				
Operative time (min)	233 (17)	203 (25)	313 (31.5)	284 (29.3)
Estimated blood loss (mL)	270 (105)	422 (185)	159 (221)	254 (71.4)
Mean (range) LOS (days)	2 (1–3)	7 (5–8)	1.2 (1–3)	8.5 (5–21)
Complication rate, %	15	86	22	1/6
% Positive nodes	19	24	32	0

Items in bold are statistically significant.

The primary objective of the study of Poulakis et al. was to assess differences in health-related quality of life between laparoscopic and open RPLND. At 6 months after L-RPLND patients reported significantly higher levels of cosmetic satisfaction; this group also reported a shorter time needed to return to baseline quality-of-life scores (L-RPLND 29 days vs. open RPLND 51 days, $P < 0.001$).

The overall complication rate in the study of Poulakis et al. was significantly higher in the open RPLND group (86.2% vs. 15%, $P < 0.001$), but the vast majority of adverse events were minor postoperative complications, such as fever and paralytic ileus. In the study of Abdel-Aziz et al. the complication rate did not differ between the L-RPLND and open groups (18.2% vs. 16.7%, P value not provided).

The mean (range) follow-up in the study of Poulakis et al. was 14 (6–20) months in the L-RPLND group and 26 (8–38) months in the open RPLND group. Four patients (19%) in the laparoscopic and seven (24%) in the open group were found to have pN1 disease. All 11 patients received adjuvant chemotherapy. The authors reported that after a median follow-up of 18 months ‘all patients were alive with complete disease remission’. In the study of Abdel-Aziz et al. the mean oncological follow-up was 12 months in the L-RPLND group and 15 months in the open RPLND group. Seven patients at L-RPLND (32%) were found to have node-positive disease and five elected to undergo adjuvant chemotherapy. No patient was found to have positive retroperitoneal nodes in the open group. There was one in-template recurrence in the open RPLND group and one (5% L-RPLND, 1/5 open RPLND) recurrence outside the template in each group. All patients were free of disease at last follow-up. Both studies have several methodological limitations, including their retrospective design, few patients within each treatment group, short follow-up and high adjuvant chemotherapy rate in node-positive patients.

Given the scant comparative data, open and laparoscopic RPLND case series must also be analysed to draw meaningful conclusions about the relative efficacy of the two methods. Rassweiler et al. [20] reported a meta-analysis of 34 articles including >1000 patients

with clinical stage I NSGCT. The authors found significantly longer mean operating times for L-RPLND (204 vs. 186 min, $P < 0.05$), but shorter LOS (3.3 vs. 6.6 days, $P < 0.05$) and lower complication rates (15.6% vs. 33%, $p < 0.05$).

For oncological outcomes, Rassweiler et al. compared five laparoscopic (557 patients) series with five open (761 patients) series published between 2000 and 2008. The mean (range) follow-up from the L-RPLND series was 63 (30–84) months, compared to 54 (48–83) months from the open RPLND studies.

Of patients within both the laparoscopic and open groups 25% were found to have node positive disease. Ultimately, 29% of patients after L-RPLND received adjuvant chemotherapy, which was comparable to the 31% rate among patients after open surgery. Retroperitoneal relapse (1.4% vs. 1.3%) and biochemical failure (0.9% vs. 1.1%) rates were similar between the laparoscopic and open groups, respectively. Distant relapse was nearly twice as common in the open group (6.1%) than in the laparoscopic studies (3.3%). However, two of the open series had a ‘predominance of embryonal cell carcinoma and/or lymphovascular invasion’. Evaluating the therapeutic value of L-RPLND in patients with low-volume metastatic disease is difficult because most receive adjuvant chemotherapy. This is despite the National Comprehensive Cancer Network’s Guidelines recommending surveillance in compliant patients [21]. Some have argued that the high rate of adjuvant chemotherapy administration reflects an overall concern regarding the therapeutic efficacy of L-RPLND. However, reviewing previous reports shows that the chemotherapy rate is similar for node-positive patients undergoing both laparoscopic and open node dissections (29% and 31%, respectively) [22–31].

Another criticism of L-RPLND is related with nodal yield. Abdel-Aziz et al. [19] reported a significantly lower ($P = 0.005$) mean node count in their laparoscopic group (17 nodes) than in the open group (33 nodes). However, in a more recently published series of 137 patients, by Hyman et al. [32] the authors reported a mean (range) lymph node count of 26.1 (7–72), which is similar to yields seen in open series. They also found that when the nodes were submitted in individual packets the mean

yield was higher (44.3 nodes). Regardless, the optimal way to assess an adequate dissection is through oncological outcomes, which do not appear to differ [20].

Many small case series have been published on L-RPLND after chemotherapy [9,22,29,33,34]. In 2002, Palese et al. [9] reported seven cases of postchemotherapy L-RPLND with two conversions and a complication rate of 52%. A more recent study by Maldonado-Valadez et al. [33] in 2007, reported no conversions in 17 patients and no intra- and postoperative complications. Nevertheless, L-RPLND after chemotherapy is a technically very demanding procedure, particularly in patients with SGCT and should only be attempted by surgeons with extensive laparoscopic experience [35].

Although robotic surgery has become ubiquitous in urology, there have only been two studies published, with a total of seven patients, on robotic-assisted L-RPLND [36,37]. Until more studies are reported the utility of robotic-assisted L-RPLND cannot be reliably assessed.

Complications

Haemorrhage is the most frequent and serious complication encountered during L-RPLND. It has been shown by Kenney et al. [38] to occur in 2.2–20% of reported cases. Not surprisingly, haemorrhage is more likely to occur in patients after chemotherapy [9]. Minor vascular injuries can be repaired laparoscopically; major injuries require conversion to open surgery. Fortunately, this is a rare occurrence, as the conversion rate in recent studies has been estimated to be 3.3% [20].

Venous bleeding can usually be controlled by direct compression for 5–10 min. Temporarily increasing the pneumoperitoneum to 20 mmHg might also help to establish haemostasis. Various haemostatic agents can also be used, such as a gelatin matrix or oxidised cellulose. Bleeding from small arteries can be controlled with clips, or if the stump is too short a 5–0 suture can be used. Larger vascular injuries should be repaired with a 5–0 suture after compression.

Lymphatic leakage not recognised intraoperatively can manifest as flank pain, hydronephrosis from ureteric compression or chylous ascites. Meticulous clipping of lymphatic channels and careful monitoring of the peritoneal cavity during surgery is required to prevent this complication. Chylous ascites is rare (3%) and occurs due to damage to the cisterna chilli [14]. It can present with any combination of ileus, abdominal distension, chylous leakage from port sites and pleural effusion. The initial management is conservative. Patients should be placed on a low-fat, medium-chain triglyceride diet. If persistent, total parenteral nutrition and somastatin can be used, which reduce lymphatic flow [16,39,40]. If conservative measures fail, sclerosing therapy via lymphangiography can be used [16]. Surgical exploration and placement of a peritoneo-venous shunt are rarely required [16].

Bowel injury can occur during trocar placement and/or surgical dissection. If unrecognised, bowel injury can lead to significant morbidity and death. Disproportionate pain at a trocar site and/or prolonged ileus should raise a high level of clinical suspicion for bowel injury, prompting CT of the abdomen with oral contrast medium. Other causes of a prolonged ileus that should be considered include a urine leak, haematoma, abscess, lymphocele, chylous ascites and pancreatitis.

Sympathetic nerve injury has significantly decreased due to the use of modified templates. Like bowel injuries, sympathetic nerve damage often goes unrecognised during surgery and manifests soon afterwards. Retrograde ejaculation can occur in up to 5% of patients, even those treated in high-volume centres [41]. Injury to the ureter is rare and is easily preventable in patients not operated after chemotherapy. If unrecognised, it might present with a urine leak or hydronephrosis due to obstruction. Other rare complications include rhabdomyolysis, pulmonary embolism, leg paraesthesia and port-site metastasis.

Summary

L-RPLND is a feasible and effective procedure in patients with low-stage testicular cancer. Although comparative data are limited, L-RPLND appears to be comparable to open RPLND for perioperative complications and oncological efficacy, while providing patients with improved cosmesis and a faster recovery time. Nevertheless, L-RPLND is a technically demanding procedure, especially after chemotherapy and should only be considered by clinicians with extensive laparoscopic experience.

Conflict of interest

The authors have no conflict of interest to declare.

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