



## Invited Review Article

# Retroperitoneal lymph node dissection: the past, present, and future, a review

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### Abstract

Testicular cancer is a malignancy that impacts young men worldwide. The modern treatment of testicular cancer has evolved due to innovations in medical approaches and surgical techniques. The retroperitoneal lymph node dissection (RPLND) is an integral component in the treatment of testicular cancer. We aim to highlight the advances in surgical approaches and oncologic considerations noted over the past century. Once recognized as a highly morbid procedure, innovations in the understanding of anatomy and minimally invasive approaches have greatly improved patient outcomes. In addition to surgical approaches, we describe oncologic principles associated with modern dissection templates for both non-seminomatous germ cell tumors as well as more recent indications for surgery in seminomatous germ cell tumors. The overall goal of this review is to provide a summary in the utility and recent advances in RPLND techniques.

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## Introduction

Testicular cancer is a rare malignancy but remains the most common solid organ malignancy in young men between the ages of 20 to 40 years. The annual rate of new testicular cancer cases was estimated to be 5.9 per 100,000 men in the United States,<sup>1</sup> with incidence rates ranging from ~7 per 100,000 in Europe and Oceania to < 2 per 100,000 men in Asia.<sup>2</sup> Germ cell tumors (GCT) comprise 95% of all testicular malignancies, further being categorized as seminomatous or non-seminomatous germ cell tumor (NSGCT). However, with a multimodal treatment approach including a combination of chemotherapy, radiation, or surgery, 5-year survival rates can be as

high as 95%, regardless of stage.<sup>3</sup>

When staging testicular cancer, computed tomography (CT) imaging has improved diagnosis of extragonadal spread. However, even with advances in CT imaging, up to 20-30% of patients can be understaged based on the size cutoffs used for lymphadenopathy (typically 1 cm in the short axis).<sup>4</sup> GCT has a predictable pattern of metastasis which follows lymph drainage, with right-sided tumors initially metastasizing to the nodes between the aorta and the inferior vena cava (interaortocaval nodes) and left-sided tumors initially spreading to the nodes lateral to the aorta (para-aortic).<sup>5,6</sup> Retroperitoneal lymph node dissection (RPLND) is an important

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surgical procedure for diagnosis and treatment of extra-testicular disease.

In this review, we will discuss the evolution of techniques for RPLND in its role for management in testicular cancer over time.

### Historical Technique

Dr. Most in 1898 was one of the first surgeons to note the extragonadal lymphatic spread of testicular cancer up to the paraaortic nodes near the renal hilum.<sup>7</sup> Surgeons then began performing techniques to treat these extragonadal metastasis. Some of the earliest reports of the RPLND were described by Frank Hinman in 1914.<sup>8</sup> He described RPLND being performed in France, England, and Italy between 1905 and 1914. His description of the technique involved a two-step procedure, starting with an inguinal incision for the radical orchiectomy and then extending the inguinal incision superiorly up towards the flank.

In the middle of the 20th century, mainly after World War II, there was an increasing number of patients treated with transabdominal RPLND after orchiectomy.<sup>9</sup> Around 1950, it was noted that unilateral RPLND was insufficient in up to one third of cases, leading to implementation of a bilateral template. In 1985, Farley et al. described their series of 98 patients who underwent extended supra-hilar RPLND through a midline incision.<sup>10</sup> Interestingly, they excised the renal fascia, perirenal fat, and adrenal gland on the side of the tumor. They performed unilateral dissection down to the bifurcation of the common iliac vessels. Reported complications from their study included ileus (most common), pleural effusion, and pneumonia. In terms of oncologic outcome, 16% of the 57 patients who had RPLND for stage I testicular cancer had relapse between 5-11 months after surgery requiring chemotherapy.<sup>10</sup>

The technique of the RPLND continued to evolve as surgeons turned their attention to variations in the surgical template. Donahue et al. described the evolution of their RPLND technique from 1965 to 1989 for stage I testicular cancer.<sup>11</sup> Their study highlighted the progression of their technique starting with the traditional bilateral supra-hilar extended RPLND to the bilateral infra-hilar RPLND and then to a modified unilateral RPLND in an attempt to preserve ejaculatory function. Almost 75% of patients who had modified unilateral template RPLND had preserved

ejaculation. This prompted further investigation into prospective nerve-sparing by pre-dissection identification of the lumbar postganglionic nerves and preservation of these nerve trunks to improve ejaculation outcomes. With this modification in technique, nerve-sparing (NS) modified template RPLND led to 98% preserved ejaculation.<sup>11</sup> There was no significant difference in relapse rate between supra-hilar, bilateral infra-hilar, and modified unilateral templates for these patients, with around 11% of patients with stage I disease having relapse for each template.

As the RPLND has developed, it has evolved to serve multiple roles. The RPLND serves a diagnostic role by providing pathology to allow for confirmation of staging as well as performing a therapeutic role in removal of disease. It can potentially cure patients with N1 nodal disease with surgery alone, thereby avoiding chemotherapy.<sup>12</sup> Additionally, if chemotherapy was primary treatment, RPLND can be performed to remove residual disease.<sup>12</sup>

### Full Bilateral Template RPLND

With the development of the RPLND over time, the variations in technique led to the development of the full bilateral template RPLND for oncologic control (Table 1). In a retrospective study of 283 patients who underwent RPLND, the retroperitoneal spread of primary testicular cancer was shown to vary between right and left primary testicular tumors.<sup>5</sup> Right-sided testicular tumors spread to the ipsilateral retroperitoneal lymph nodes 85% of the time, with 13% to ipsilateral and contralateral lymph nodes and finally only to the contralateral side in ~2%.<sup>5</sup> Left-sided testicular tumors had extragonadal spread to the ipsilateral retroperitoneum 80% of the time, with 20% in bilateral retroperitoneal lymph nodes.<sup>5</sup> As such, the standard full template RPLND involves dissection of the retroperitoneal lymph nodes between the following landmarks: renal vessels superiorly, ureters laterally, and the iliac vessels inferiorly.<sup>13</sup> Use of the 'split-and-roll' technique allows for careful dissection of lymph node tissue over the IVC and aorta. The technique involves splitting the lymphatics on the plane over the adventitia of the great vessels and rolling them to identify other branches of the vessels.<sup>13</sup> The RPLND is performed most commonly through a large midline incision with a transperitoneal

**Table 1.** Summary of studies over the development of the RPLND

Highlighted Papers	Number of Patients	Key Findings
<b>Anatomy and Templates</b>		
Ray et al. – 1973	283	Lymphatic drainage from testicles follows predictable patterns which set the stage for modern templates
Fraleys et al. – 1985	98	Suprahilar bilateral template RPLND with chemo led to survival rates of 88% in stage II disease and 100% survival in stage I disease.
Donohoe et al. – 1993	464	Evolution from the bilateral suprahilar to infrahilar bilateral template with nerve sparing and introduction of unilateral template over 25 years with comparable rates of relapse. Ejaculation preserved in 98% of patients.
<b>Extraperitoneal</b>		
Kim et al. – 2012	12	Extraperitoneal approach had greater lymph node yield, shorter operative times, lower blood loss, and shorter length of stay
Syan-Bhanvadia et al. – 2017	69	The approach was safely used in post-chemotherapy patients and confirmed prior results. 5.7 retroperitoneal relapse rate
<b>Robotic Assisted</b>		
Pearce et al. – 2017	47	Primary RPLND. 96% had modified unilateral template. Median OR time 235min, blood loss 50 mL, post-op length of stay 1 day. 2-year recurrence-free survival rate of 97%. Median of 26 nodes per patient.
Rocco et al. – 2020	58	Primary RPLND alone. Bilateral and unilateral templates used. Median OR times of 319 minutes, blood loss of 100 mL, and post-op length of stay of 2 days. 2 year recurrence-free survival rate of 91%. Median of 26 nodes per patient.
Ohlmann et al. – 2021	23	Bilateral and unilateral templates were feasible with appropriate lymph node yield. Approach can be utilized with primary and post-chemo patients. No recurrence at 16-month follow-up
<b>Prospective Trials in Seminoma</b>		
Daneshmand et al. – 2023	55	SEMS Trial. Stage I relapse or newly diagnosed stage II disease (Lymph nodes between 1-3cm, 2 maximum). 81 % recurrence-free survival at 2 years. 13% complication rate. 3 patients had long term anejaculation (all 3 did not have nerve sparing).
Hiester et al. – 2022	33	PRIMETEST Trial. Stage I relapse or newly diagnosed staged II disease (lymph nodes less than 5cm, no maximum). Unilateral template. Study showed progression-free survival of 70%. Did not meet endpoints and could not recommend primary RPLND for seminoma outside of clinical trial at this time
Heidenreich et al. – 2023	16	COTRIMS Trial. Stage II disease. Open or robotic approach. Varied template. Showed 8% recurrence-free survival. Salvaged with chemotherapy. No long-term complications noted.

approach. In a retrospective review of 157 patients who had full template bilateral primary RPLND for low-stage NSGCT, median total lymph node yield was 28 lymph nodes.<sup>14</sup> This study suggested that higher lymph node yield was associated with lower risk of relapse, with mean 5-year recurrence-free survival of 91% vs 79% for yields  $\geq 28$  vs  $< 28$  nodes respectively.

Complications of RPLND include ileus, small bowel obstruction (SBO), venous thromboembolism (VTE), chylous ascites, and ejaculatory dysfunction.<sup>15</sup> Ejaculatory dysfunction is a result of injury to the sympathetic nerves of the hypogastric plexus and lumbar post-ganglionic sympathetic fibers (especially L2-L4) since these nerves stimulate antegrade ejaculation.<sup>16</sup> In an effort



to improve nerve-sparing to reduce ejaculatory dysfunction, modified templates were developed since preservation of the ipsilateral sympathetic nerve trunks below the inferior mesenteric artery (IMA) was seen to improve antegrade ejaculation.

### Modified Unilateral Template RPLND Right

In patients with disease limited to right side on imaging, RPLND was performed with the following landmarks: right renal vessels superiorly, right ureter laterally, periaortic lymphatic above the IMA medially, and the right iliac vessels inferiorly.<sup>13</sup> The nodes resected include paracaval, precaval, interaortocaval, and preaortic lymph nodes.<sup>13,17</sup> The iliac nodes and ipsilateral gonadal vein are also removed.

### Left

The left modified unilateral template RPLND involves dissection of lymph nodes between the following landmarks: left renal vessels superiorly, left ureter laterally, periaortic lymphatic above the inferior mesenteric artery (IMA) medially, and the left iliac vessels inferiorly.<sup>13</sup> The nodes resected in this template include the paraaortic, preaortic, interaortocaval lymph nodes.<sup>17</sup> The iliac nodes and ipsilateral gonadal vein are also removed.

### Oncologic outcomes

However, as modified unilateral templates have evolved, their oncologic outcomes have been a key point of interest. Eggener et al. showed that the risk of disease outside of the modified unilateral templates ranged between 3 to 23% for patients with stage II testicular cancer.<sup>18</sup> They studied 5 modified templates, 3 of which were open (Testicular Tumor Study Group (TTSG), Memorial Sloan-Kettering Cancer Center (MSK-CC), and Indiana University), and 2 laparoscopic templates (The Johns Hopkins University and the University of Innsbruck). While extra-template disease was as high as 23%, they highlighted that if the right-sided dissection templates included preaortic, paraaortic and right common iliac nodes, residual disease outside of the right side template came down to 2%. For left template RPLND, inclusion of interaortocaval, precaval, paracaval and left common iliac nodes could lead to only 3% of missed extra-template disease.<sup>18</sup> The main point was that inclusion of these lymph

nodes in the bilateral infrahilar full template RPLND with nerve-sparing allowed for the best oncologic outcomes while still preserving fertility.

In a recent study of 274 patients, 94% of whom had RPLND using a modified unilateral template, there was no difference in recurrence-free survival between modified and bilateral template.<sup>19</sup> They described their left modified technique as dissection of the preaortic, paraaortic, retro-aortic and left common iliac lymph nodes and their right modified template included dissection of the preaortic, interaortocaval, retro-aortic, paracaval, retrocaval and right common iliac nodes. This study included 126 patients with pathologic stage II disease (46%). The use of primary RPLND for treatment of stage II NSGCT led to 81% who were cured through surgery alone. In 55 months after RPLND, 12% of patients had recurrence. Of these 33 recurrences, only 1.6% of these recurrences occurred in the contralateral retroperitoneum. There was concern that 4 out of the 7 relapses were extra-template, which could be avoided with a full template bilateral nerve-sparing RPLND while still preserving fertility.<sup>20</sup> Overall survival for the entire patient group was 98% regardless of surgical templates.

The use of modified unilateral templates is still debated, especially considering the fact that use of full bilateral template with nerve-sparing can achieve good rates of antegrade ejaculation without compromising on oncologic outcomes. With the risk of residual extra-template disease with use of modified unilateral templates, there is risk of late relapse, need for re-operative RPLND and the need for additional chemotherapy.<sup>18</sup> Importantly, the most common pathology during a repeat procedure is teratoma, which is resistant to both chemotherapy and radiotherapy.<sup>21</sup> Repeat RPLND increases the risks of surgical complications, which can be as high as 30% in the perioperative period.<sup>21</sup> Additionally, the long term risks of chemotherapy are becoming increasingly evident, including risk of secondary malignancy, cardiovascular dysfunction, and impaired mental function.<sup>22</sup> As such, use of modified unilateral templates is an area that is still being studied and remains controversial.

### Extraperitoneal RPLND

Another modification to the standard trans-abdominal RPLND technique is the development



of the extraperitoneal RPLND. The rationale for this technique arose from an attempt to reduce gastrointestinal complications such as ileus or small bowel obstruction as well as inadvertent bowel injury. A study in 2012 evaluated clinical outcomes of a single surgeon experience with 12 patients who underwent midline extraperitoneal RPLND compared to transperitoneal RPLND.<sup>23</sup> In this small series of patients, the extraperitoneal approach had decreased blood loss (mean 305mL vs 517mL for transperitoneal), shorter operative time (292 min vs 334 min for transperitoneal) and greater lymph node yield (44 vs 29 lymph nodes for transperitoneal).<sup>23</sup> They also showed statistically significant shorter return of bowel function (1.7 days vs 2.9 days for transperitoneal) and shorter length of stay (3.3 days vs 5.3 days for transperitoneal).<sup>23</sup> Their described technique starts with a midline abdominal incision from xiphoid to just cephalad to the pubic symphysis. Careful blunt dissection was performed to keep the peritoneum intact and then sweep the peritoneal contents medially. The authors emphasized caution with dissecting off the anterior peritoneum due to its relative thinness. The dissection of the peritoneum was continued until the peritoneum was mobilized up to the contralateral renal hilum. The remainder of the lymph node dissection was then performed in the standard fashion. The authors reported no evidence of retroperitoneal recurrence at a median follow-up time of 196 days. This presentation of technique was however, limited by small sample size and limited follow-up period.

In 2017, this group expanded on their initial series to evaluate 69 patients who underwent extraperitoneal RPLND between 2010 and 2015.<sup>24</sup> Primary extraperitoneal RPLND had extended ipsilateral templates for resection and their post-chemotherapy resections underwent full bilateral template vs extended ipsilateral templates. In the overall cohort, 1 out of 69 patients required conversion to the transperitoneal approach due to inability to progress through the case. Of the remaining 68 patients who successfully had extraperitoneal RPLND, primary RPLND was performed in 27 patients and 41 had post-chemotherapy RPLND. They showed a median length of stay of 3 days postoperatively and median of two days for return of bowel function.<sup>24</sup> They had a median yield of 36 nodes

for their extraperitoneal approach. In this series, 4 patients had retroperitoneal relapse, with one patient having relapse after post-chemotherapy RPLND. These patients had successful salvage treatment with chemotherapy and the authors felt that oncologic outcomes were not compromised with the extraperitoneal approach.

## Minimally Invasive Techniques

### Robotic-assisted laparoscopic RPLND

Robot-assisted laparoscopic RPLND was developed an effort to improve on the laparoscopic technique. Robotic RPLND has been mainly utilized in low clinical stage, low volume disease. While multiple studies have shown that factors such as blood loss, length of stay, and visualization are improved with robot-assisted RPLND,<sup>25,26</sup> there is still debate of this technique regarding oncologic outcomes. In a study of 23 patients who had robotic RPLND, with a mix of primary and post-chemotherapy RPLND (7 vs 16 respectively), median lymph node yield was 11 nodes.<sup>27</sup> When stratified by bilateral template, lymph node yield was 26 nodes compared to 12 nodes for modified unilateral template. At a median follow up time of 16 months, this study reported no recurrence or death.

In a multicenter institution series, Pearce et al. studied the outcomes of 47 patients who had primary robotic RPLND for low-stage NSGCT between 2011 and 2014.<sup>28</sup> Modified unilateral template was used in 96% of patients, with nerve-sparing performed per surgeon discretion. There was a median lymph node yield of 26 nodes per patient. Eight patients had node positive disease on RPLND, with 5 receiving adjuvant chemotherapy.<sup>28</sup> Their reported 2-year recurrence-free survival rate was 97%, however their median follow-up time was 16 months. One patient had conversion to open procedure due to aortic injury but overall complication rate was found to be 9% for early complications (< 30 days; chyle leak, ileus) and 0% for late complications. All patients had preserved antegrade ejaculation. The authors concluded that robotic RPLND has promising early oncologic outcomes and complication rates but long-term data was required to truly evaluate its use as a therapeutic procedure.

Rocco et al. studied the outcomes of primary robotic RPLND in low stage disease. In their 58 patients, performed between 2008-2019, they had



a 2-year recurrence-free survival rate of 91%.<sup>29</sup> Of note, the authors did initially use a modified unilateral template, but overall, 69% of their patients had full bilateral template dissection. In terms of the logistics of their robotic technique, their median operative time was 319 minutes, median blood loss was 100 mL, and they had a median yield of 26 nodes per case.<sup>29</sup> Their patients stayed for a median of 2 days after surgery. The use of a retroperitoneal 'hammock' is described in multiple studies as a method to secure the peritoneum to the abdominal wall.<sup>29-31</sup>

Based on these studies, robotic RPLND is still to be considered in select patients but should be performed by experienced surgeons. As more long-term data is acquired on surgical and oncologic outcomes from robotic RPLND, the implementation of robotic RPLND may increase, especially as robotic techniques improve as well.

### Primary RPLND for Seminoma

One area of increased interest is the use of RPLND as a primary mode of treatment for patients with seminoma. For stage I seminomas, EUA and AUA guidelines suggest the use of surveillance or chemotherapy, while management of stage II seminoma consists of chemotherapy or radiation.<sup>32</sup> RPLND has primarily been reserved in the post-chemotherapy setting for FDG-avid lesions.<sup>32</sup> While highly effective, these treatments are often associated with significant long-term cardiopulmonary, renal, and reproductive consequences from chemotherapy.<sup>22</sup> Recent prospective studies in stage II seminoma have shown utility in the use of RPLND for primary disease management.

The Surgery in Early Metastatic Seminoma (SEMS) trial looked at 55 patients across 12 sites between USA and Canada with isolated stage I relapse between 1-3 cm or newly diagnosed stage II disease with no more than two 1-3 cm lymph nodes on staging imaging.<sup>33</sup> These individuals underwent modified ipsilateral template or bilateral template RPLND per surgeon discretion (35% had bilateral RPLND). Extraperitoneal approach was utilized in 27% of patients had RPLND. Of the total cohort, 87% of their patients had nerve-sparing, with overall 5% of patients having anejaculation (notably in patients who did not have nerve-sparing). With a median follow-up time of 33 months, the 2-year recurrence-free

survival was noted to be 81%. Overall survival was noted to be 100% at 24 months. In the 12 patients who had a recurrence of disease, 75% had chemotherapy and 25% underwent additional surgery.

Another prospective trial, the PRIMETEST trial, examined outcomes of primary RPLND in 33 patients with stage I disease with relapse, or stage IIA/B disease with lymph nodes up to 5cm in size.<sup>34</sup> Compared to the SEMS trial, this study examined only unilateral templates (42% were open, 58% robotic approach). Their study showed 10 recurrences (30%), with progression free survival of 70%, 7 of which were outside of their operative field at their 32 month follow-up timeline.<sup>34</sup> Their study did not meet their primary endpoint of a recurrence rate less than 30%. However, they concluded that surgery with a unilateral template shows promise in highly selected patients but could not be recommended at this time outside of further clinical evaluations.<sup>34</sup>

The COTRIMS trial is a prospective clinical trial where primary nerve sparing RPLND was performed on 16 patients with stage II seminoma, where clinical stage was IIA (13 patients) or IIB (3 patients).<sup>35</sup> Open nerve-sparing RPLND was performed in 14 patients, with 2 of 16 having robotic-assisted procedures. Ejaculation was preserved in almost 88% of the cohort and the study noted no high grade surgical complications (greater than Clavien-Dindo grade 3A). Relapse was found on 4 and 6 month follow up out-of-field in 2 of 16 patients (12.5%), which was salvaged with chemotherapy.<sup>35</sup> While limited in sample size and long term follow-up, these trials suggest that nerve-sparing RPLND can be performed as a primary treatment in an effort to reduce treatment morbidity from chemotherapy or radiation with relatively low complication rate in the hands of experienced surgeons.

### Conclusion

RPLND is a diagnostic and therapeutic procedure that is continuing to evolve to improve patient outcomes from testicular cancer. Oncologic outcomes should be prioritized when determining template selection and technique for performing RPLND. Advances in techniques such as open extraperitoneal RPLND, nerve-sparing, and development of robotic-assisted laparoscopic RPLND have aimed to reduce surgical complication, preserve antegrade ejaculation, and maintain



oncologic outcomes. A new promising area of study is the use of primary RPLND for treatment in select patients with low stage seminoma, with the goal of limiting the side effects of chemotherapy and radiation in this young patient population. The indications for RPLND continue to expand, as it remains an integral component of the multimodal management of testicular cancer.

### Conflict of Interest

The authors declare no conflict of interest.

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