

Seminars article

Current controversies on the role of retroperitoneal lymphadenectomy for testicular cancer

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Abstract

Retroperitoneal lymph node dissection (RPLND) is an important component of the multimodal treatment which cures most patients diagnosed with testicular germ cell tumors. Considering the high cure rates achieved, research focus in recent years has been directed toward improving quality of life and decreasing long-term treatment related sequelae. Consequently, the role of RPLND has evolved over the past 3 decades in both low-stage and advanced testicular cancer.

The use of RPLND in clinically stage I and low volume stage II disease may offer the advantages of treating retroperitoneal teratoma which is present in 15% to 20% of patients, avoiding chemotherapy and reducing the need for frequent imaging during follow-up. Similarly, ongoing studies are evaluating the safety and effectiveness of RPLND for the treatment of early stage seminoma to avoid the long-term effects of chemotherapy and radiotherapy. RPLND is traditionally used for the treatment of residual masses >1 cm after completion of chemotherapy. Its role in subcentimeter residual masses remains somewhat controversial given the fact that 25% to 30% of these patients are found to harbor either teratoma or viable nonteratomatous germ cell tumors. The presence of teratoma increases the probability of teratoma in metastatic sites.

Modified unilateral templates were developed based on early mapping studies with the aim of preserving antegrade ejaculation. Recent data suggests initial mapping studies underestimated the risk of contralateral retroperitoneal metastases which may reach 32%. Furthermore, antegrade ejaculation may be preserved in >95% of patients undergoing bilateral nerve sparing primary RPLND and >80% undergoing nerve-sparing PC-RPLND, which, in our view is the more prudent oncologic approach.

Recently, multiple series have demonstrated the safety and short-term efficacy of minimally invasive RPLND; however, larger studies with prolonged follow-up are required to validate the long-term oncologic efficacy of newer techniques. © 2018 Elsevier Inc. All rights reserved.

Keywords: Testicular germ cell tumors; Retroperitoneal lymph node dissection; Postchemotherapy surgery; Minimally invasive surgery

Introduction

Retroperitoneal lymph node dissection (RPLND) is an essential part of the multimodal treatment of testicular cancer and contributes to the 95% overall cure rate [1, 2]. Historically, in the absence of effective chemotherapy, surgery was the best option for obtaining a durable remission [3]. The discovery of cisplatin in 1965 has revolutionized the treatment of testicular cancer, and has resulted in multiple controversies regarding the optimal integration of surgery

in the treatment of patients with testicular germ cell tumors (GCT) [1].

Surgery has an established role for the treatment of postchemotherapy residual masses in patients with nonseminomatous germ cell tumors (NSGCT) and select patients with seminoma [4]. However, the role of RPLND as the primary treatment of stage I and stage IIA/IIB NSGCT and for the management of patients with complete serological and radiographic response following chemotherapy remains controversial. Recently, there has been growing interest in the role of primary RPLND for the treatment of early stage seminoma.

Originally, RPLND performed in select centers included the resection of all nodal tissue surrounding the aorta and

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vena-cava extending cranially to the suprahilar region and caudally to the interiliac region. With the aim of decreasing surgical morbidity and preserving antegrade ejaculation, modified templates and subsequently, nerve sparing techniques were developed [3]. These changes have resulted in controversy regarding the appropriate limits of surgery.

Recently, multiple reports of minimally invasive RPLND have been published suggesting similar short- and intermediate-term results. However, it is still unknown whether these techniques will provide comparable long-term oncologic outcome.

In this seminar article, we will discuss current controversies associated with RPLND, and provide data delineating its evolving role in the treatment of testicular GCTs.

The role of primary RPLND for nonseminoma germ cell tumors (NSGCT)

Clinical stage I

Treatment options for clinical stage I NSGCT include active surveillance, chemotherapy, and RPLND, all of which obtain a long-term overall survival nearing 100%. Occult metastatic disease is present in 20% to 30% of patients; thus, 70% to 80% are cured by orchiectomy alone [5–8]. A recent study reported the excellent outcome of active surveillance for clinical stage I NSGCT with an overall relapse rate of 19% at a median follow-up of 62 months (range, 1–277 months), and a 5-year disease-specific survival of 99.4% [9]. The high rate of patients who do not require additional treatment following orchiectomy, and the morbidity associated with RPLND and/or chemotherapy, raise appropriate concerns regarding their role in this setting.

Numerous studies have identified risk factors for occult retroperitoneal metastases which include percentage of embryonal carcinoma in the primary tumor and presence of vascular invasion, a combination of which predicted either pathologic stage II or relapse on surveillance in 46.5% to 88% of clinical stage I patients [5–9]. The presence of these risk factors may therefore identify patients who will benefit from additional treatment following orchiectomy.

A randomized phase III trial comparing the outcome of primary RPLND vs. one course of bleomycin, etoposide, and cisplatin (BEP) for the treatment of clinical stage I NSGCT sought to address the issue of optimal treatment for patients not undergoing active surveillance. The 2-year recurrence free survival rate was 99.5% for chemotherapy and 91.9% for surgery with a significant hazard ratio of 7.94 (95% CI 1.81–34.48), supporting the use of one course of BEP over RPLND in the community setting [10]. While the exceedingly high recurrence free survival rate following one course of BEP standardized this chemotherapy regimen as a treatment option for stage I NSGCT, this trial was criticized for multiple reasons including the use of unilateral RPLND templates which likely contributed to the relatively high surgical failure rate within the retroperitoneum and scrotum.

Furthermore, as a multi-institutional study, it was performed by 61 centers with few procedures performed by most surgeons. Higher volume centers within this study have previously reported retroperitoneal relapse rates lower than 1%. In addition, the relatively short follow-up period of the study (median of 4.7 years), was insufficient to capture late relapses and relapses caused by slow-growing NSGCT and growing teratomas [11].

Advantages of performing RPLND for the treatment of clinical stage I NSGCT include treatment of retroperitoneal teratoma which is chemorefractory, present in 15% of patients with occult metastases, and amendable only to surgical treatment [12,13]. Patients are able to avoid chemotherapy and its associated long-term morbidity in more than 80% of cases (Table 1) [7, 10, 12–14]. Furthermore, the rate of retroperitoneal recurrences following a complete bilateral template is less than 1%, therefore we do not use frequent imaging of the abdomen during follow-up [13, 15, 16].

It is our current practice to perform active surveillance for patients with Stage I NSGCT who are at low risk for occult retroperitoneal metastases. For patients that are at high risk, especially in the presence of teratoma or yolk sac tumor in the primary lesion, we offer primary RPLND as a treatment option considering the advantages noted above.

Clinical stage IS

Clinical stage IS NSGCT is defined as persistently elevated serum tumor markers (STMs) after orchiectomy in the absence of radiographic evidence of metastatic disease. Historically, these patients were treated with RPLND however, several studies have clearly demonstrated that most patients with clinical stage IS have occult systemic metastases, reflected by a very high failure rate following surgery, and should therefore be treated initially with IGCCCG risk-appropriate chemotherapy [4, 17, 18].

Clinical stage IIA and IIB

Treatment options for patients with clinical stage IIA and small unifocal (<3 cm) IIB NSGCT include RPLND with adjuvant chemotherapy in select cases, or induction chemotherapy with or without PC-RPLND. Possible advantages of RPLND as a primary treatment are similar to those in stage I disease and include accurate staging of the disease, the treatment of teratoma which is present in approximately 20% of patients [19, 20], and the avoidance of chemotherapy in 13% to 35% of patients who have node negative disease [20–22]. Although no randomized trial exists comparing the two approaches in this setting, there are two nonrandomized studies [20, 22]. Weissbach et al. performed a prospective multicenter trial comparing 109 patients who received RPLND with 2 cycles of adjuvant chemotherapy with 78 patients who were treated with 3 to 4 cycles of primary chemotherapy. With a median follow-up of 36 months, 7% of patients receiving primary RPLND,

Table 1
Summary of articles evaluating the outcome of primary RPLND in different clinical stages of testicular germ cell tumors

Reference	No. Pts.	RPLND template	Adjuvant chemotherapy (%)	Follow-up (months)	Relapse rate (%)	Death rate (%)
Stage I NSGCT						
Richie 1990 [14]	85	Unilateral	15	38 (median)	6 PS I; 15 PS II	0
Donohue 1993 [12]	378*	Bilateral and unilateral	13	71.3 (mean)	12 PS I; 34 PS II without Cx; 0 PS II with Cx	0.8
Hermans et al. 2000 [7]	292	NA	12	46 (median)	10 PS I; 23 PS II without Cx; 0 PS II with Cx	0.3
Stephenson et al. 2005 [13]	297	Bilateral and unilateral	15	59 (median)	6 PS I; 19 PS II	0
Albers et al. 2008 [10]	173	Unilateral	18	56 (median)	9 Overall	0
Stage II NSGCT						
Donohue et al. 1995 [21]	140*	Bilateral and unilateral	42	132 (mean)	6 PS I; 37 PS II without Cx; 0 PS II with Cx	2
Weissbach et al. 2000 [22]	109	Bilateral and unilateral	88	36 (median)	23 PS I; 5 PS II-III with Cx	0
Stephenson et al. 2007 [20]	136	Bilateral and unilateral	49	63 (median)	21 overall at 5-year	2 at 5-year
Stage I-II Seminoma						
Warszawski and Schmucking 1997 [28]	45 CS I; 18 CS II	Bilateral	0	79 (median)	7 PS I; 33 PS II	8 at 5-years
Mezvrishvili and Managadze 2006 [29]	10 CS I; 4 CS II	Unilateral	0	56 (mean)	0	0
Hu et al. 2015 [30]	4 CS II	Unilateral	0	25 (mean)	0	0

CS = clinical stage; Cx = chemotherapy; NA = not available; NSGCT = nonseminoma germ cell tumor; RPLND = retroperitoneal lymph node dissection; PS = pathologic stage.

*Include patients treated after 1979.

and 11% of patients receiving primary chemotherapy suffered a disease relapse. The authors concluded that primary RPLND should be considered in patients with clinical stage IIA/ IIB NSGCT since fewer cycles of chemotherapy, and consequently a lower rate of chemotherapy-induced complications, were required when RPLND was used as the primary treatment. Furthermore, surgery in the primary setting was associated with fewer complications compared to the PC-RPLND [22]. In a nonrandomized comparison by Stephenson et al., 252 patients with clinical stage IIA and IIB NSGCT were treated with primary RPLND ($n = 136$) or induction chemotherapy with PC-RPLND ($n = 116$). When analyzed by primary treatment intervention, induction chemotherapy followed by PC-RPLND was associated with a significantly improved 5-year recurrence free survival compared to primary RPLND (98% vs. 79%, $P < 0.001$, respectively). However, 5-year cancer-specific survival were not significantly different (100% vs. 98%, $P = 0.3$), and patients treated with primary RPLND received fewer chemotherapy cycles, 51% of whom avoided chemotherapy altogether (Table 1) [20].

Currently, most patients with bulky retroperitoneal (>3 cm) disease and any patient with persistently elevated STMs are treated with IGCCCG risk-appropriate induction chemotherapy. Excluding patients with elevated postorchietomy STMs or clinical stage IIB disease from primary RPLND significantly increased the 4-year progression free survival from 83% to 96% [13]. Furthermore, patients with teratoma in their primary tumor have a significantly higher risk of teratoma in their retroperitoneal nodes. These patients may benefit from primary RPLND considering the higher tendency for an incomplete response to primary chemotherapy [19, 23, 24].

Primary RPLND as an emerging treatment for early stage seminoma

RPLND is traditionally reserved for the treatment of NSGCT, and its current utilization for seminoma is limited mostly to large postchemotherapy residual masses [25]. However, the long-term side effects of radiotherapy and chemotherapy, each of which is associated with an elevated risk of cardiovascular disease and secondary malignancies (particularly if both are required) resulting in an increased mortality, has led to growing interest in the use of RPLND for the treatment of earlier stage seminoma [26, 27].

Three retrospective reports support the efficacy of primary RPLND in the treatment of seminoma with low volume retroperitoneal disease (Table 1) [28–30]. In an early report, Warszawski and Schmucking treated 63 patients with stage I/II seminoma with primary RPLND (45 stage I, 7 stage IIA and 11 stage IIB/C), which was the preferred treatment for seminoma in their institution up until the year 1985. With a median follow-up of 79 months, recurrence rates were 7% for stage I disease, all of which were outside the RPLND template. There were no relapses for patients

with stage IIA disease. However, a 55% infield recurrence was reported for patients with stage IIB/IIC disease [28]. Two more recent retrospective reports evaluated the use of primary RPLND for seminoma in small cohorts of patients [29, 30]. Mezvrishvili and Managadze reported of 14 patients with pure seminoma who underwent modified template RPLND including 10 stage I patients at a high risk for disease relapse (primary tumor ≥ 6 cm), and 4 patients with clinical stage IIA. No adjuvant treatment was given and the patients remained free of disease at a follow-up of 56 months [29]. Hu et al. reported of 4 pure seminoma patients with isolated, low volume, retroperitoneal disease (3 stage IIA and 1 stage IIB) who were treated with modified template RPLND. No patient experienced disease recurrence with a mean follow-up of 25 months [30]. Despite the concern of the desmoplastic reaction associated with seminoma, both studies reported a minimal number of minor complications, and all patients maintained antegrade ejaculation [29, 30]. These studies suggest primary RPLND may be safe as the initial treatment of stage I and stage IIA seminoma with minimal side effects, and acceptable short-term oncologic outcomes.

Recently, two phase II, single arm, trials evaluating the outcome of RPLND without adjuvant treatment for low stage seminoma were initiated [31, 32]. The SEMS trial (NCT02537548), an American multi-institutional trial, aims to enroll 46 patients with isolated retroperitoneal disease, 1 to 3 cm in size, or stage I disease with an isolated retroperitoneal relapse within 3 years [31]. The PRIMETEST trial (NCT02797626), a single center trial from Germany, aims to enroll 30 patients, and will include patients with an initial clinical stage IIA/IIB disease, and patients with recurrent disease after surveillance for clinical stage I who may have received one dose of carboplatin after orchiectomy. The patients will undergo a modified template RPLND with ipsilateral nerve-sparing when feasible using an open, laparoscopic or robotic-assisted approach [32]. The primary outcome for both studies will be recurrence free survival at either 2 or 3 years after RPLND, and secondary outcomes will include short- and long-term complication rates, quality of life, recurrence free survival at 5 years and overall survival [31,32]. Both studies are currently recruiting and will be completed by 2021. While these studies may assist in clarifying the role of primary RPLND in this patient cohort, a potential concern is the use of modified templates.

We use RPLND within the setting of seminoma for the treatment of residual disease following chemotherapy. While the use of primary RPLND for low volume stage II seminoma may be promising, it is not a standardized treatment and is not our current practice.

Postchemotherapy RPLND for patients with a complete response

There is a consensus regarding the importance of RPLND when treating NSGCT patients with postchemotherapy

residual masses larger than 1 cm [4]. This approach is supported by the substantial rate of teratoma (39%–42%) and viable malignancies (11%–17%) in resected specimens [33–35]. Teratoma is chemoresistant, and if left unresected has the potential for rapid growth, malignant transformation, and late relapse [36]. When completely resected, the 5-year overall survival of patients with viable nonteratomatous GCT following PC-RPLND is 72%. Durable remission rates are lower after chemotherapy if residual or relapsing disease was not completely resected [37].

The role of PC-RPLND in patients who achieve complete radiographic and serologic response is controversial. The rates of viable GCT and teratoma in patients with nodes ≤ 10 mm range from 20% to 35%. A meta-analysis of 588 men who underwent PC-RPLND for a subcentimeter residual mass reported pooled estimates of 71% necrosis, 24% teratoma, and 4% viable GCT in the resected specimen [38]. Several studies evaluated the outcome of active surveillance for men achieving complete remission after chemotherapy for NSGCT [38–40]. Ehrlich et al. reported the study with the longest follow-up. A total of 141 patients who achieved complete remission were followed for a median time of 15.5 years. Twelve patients (8.5%) relapsed at a median time of 11 months from completion of chemotherapy, 6 of which recurred within the retroperitoneum. A total of 4 patients died of their disease 2 of which had a retroperitoneal recurrence. Estimated 15-year recurrence free survival rates were 95% for good-risk patients and 73% for intermediate- or poor-risk patients ($P=0.001$) [39]. Kollmannsberger et al. evaluated 161 patients who achieved complete response following chemotherapy. At a median follow-up of 52 months, 10 patients (6%) relapsed all of whom initially presented with IGCCCG good risk disease. All 10 remained disease free at a median follow-up of 64 months since recurrence [40]. A similar overall relapse rate of 6.4% and a retroperitoneal-only relapse rate of 2.1% with a median follow-up of 5.4 years were reported by Ravi et al. [38]. The low relapse rates of 6% to 8.5% may favor the use of active surveillance in patients with a complete radiographic response to chemotherapy; however, a subset of patients may require avoidable second-line chemotherapy and suffer from the potential adverse outcome of unresected teratoma and/or late relapse. A properly performed nerve sparing bilateral RPLND is associated with a low rate of anejaculation, and a $<1\%$ rate of infield RP recurrence, eliminating the need for frequent CT scans during follow-up with their associated radiation exposure. While MRI may be a comparable alternative to CT in identifying involved lymph nodes without the associated radiation exposure; this advantage is limited to experienced users. Furthermore, both modalities may underestimate positive lesion especially in nodes ≤ 2 cm [41,42]. Although the follow-up for the latter two studies (Kollmannsberger et al. and Ravi et al.) is relatively short, the data suggests that IGCCCG good-risk patients, and those without

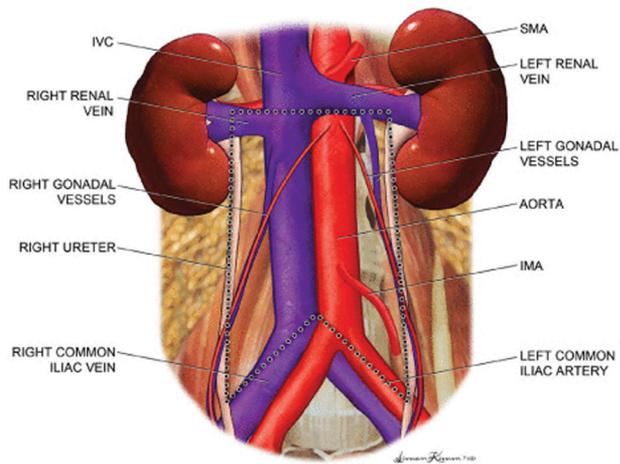


Fig. 1. Boundaries of full-template RPLND. The renal vessels form the superior boundary, the ureters form the lateral boundary, and the bifurcation of the iliac vessels forms the inferior boundary. IMA = inferior mesenteric artery; IVC = inferior vena cava; SMA = superior mesenteric artery. Obtained with permission from Thomas E. Keane, Sam D. Graham and Marc Goldstein, Glenn's Urologic Surgery 8th edition, Philadelphia: Wolters Kluwer, 2016.

teratoma in their primary tumor, who are at a lower risk for metastatic teratoma appear to be at lower risk for relapse [43].

Desperation RPLND

Patients with chemorefractory tumors who progress despite first- and second-line chemotherapy have a poor prognosis. Treatment options for these patients include third line systemic therapies or, for select patients, desperation RPLND. Suitable patients for desperation RPLND are those with slowly rising STMs and a limited volume of residual disease amenable to surgical resection [44].

Few studies evaluated the outcome of desperation surgery in this setting [45–47]. Histological findings at the time of resection were viable GCT in 76% of cases and teratoma or fibrosis in 24% [47]. Postoperatively, 47% to 60% of patients had normalization of their STMs [47]. At a median follow-up of 57 to 74 months 37% to 57% of patients were alive without evidence of disease [45–47]. Significant predictors of a poor outcome included increasing serum HCG and AFP levels, redo RPLND, and germ cell cancer in the surgical specimen [47].

These findings suggest that despite the overall poor outcome of desperation RPLND, it has a crucial role and can be the only way to achieve cure in this select group of patients.

Surgical complications and modified template RPLND

Complication rates in early RPLND series ranged from 30% to 36%, with major complications occurring in 12% to 19% of patients [48, 49]. These bilateral templates often extended into the suprahilar region, and resulted in nearly uniform retrograde ejaculation [50].

In an attempt to reduce the rates of retrograde ejaculation, and using mapping studies to define the lymphatic spread of testicular cancer, several investigators developed modified unilateral templates which were used in a select group of patients in both the primary and postchemotherapy setting (Figs. 1 and 2) [14, 15, 51–53]. Donohue et al. evaluated the use of modified templates in a large cohort of patients with clinical stage I NSGCT treated with a primary RPLND. Overall relapse rates were not significantly different between patients who were treated with a modified unilateral template and a bilateral template (15%–18% compared to 13% respectively), and all relapses occurred outside the retroperitoneum. The ejaculation rate of patients

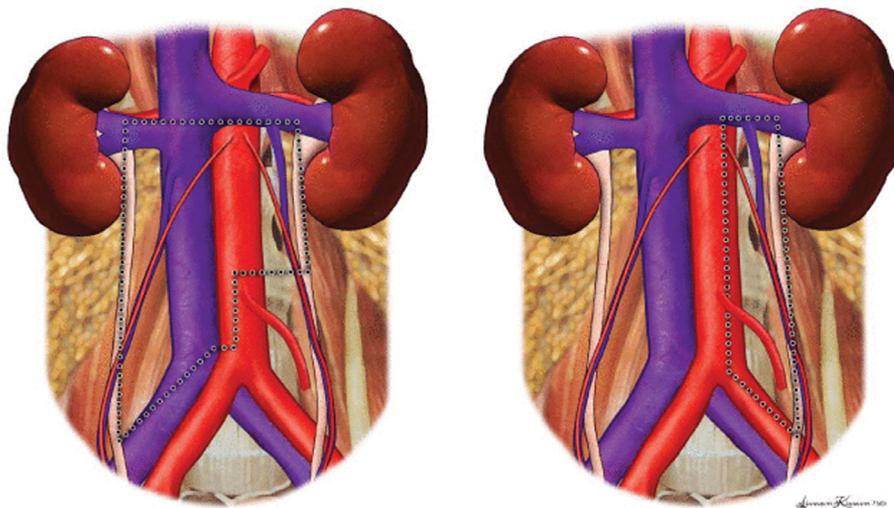


Fig. 2. Right and left modified templates for RPLND. Several side-specific modified templates for patients with low-stage NSGCT have been proposed, with each including ipsilateral lymph nodes inferior to the renal hilum extending to the bifurcation of the iliac arteries. Right-sided templates include the interaortocaval region, and both avoid dissection below the contralateral IMA. Obtained with permission from Thomas E. Keane, Sam D. Graham and Marc Goldstein, Glenn's Urologic Surgery 8th edition, Philadelphia: Wolters Kluwer, 2016.

who underwent unilateral modified template resection with prospective nerve sparing was very high approaching 98% [15]. Beck et al. evaluated the role of modified templates in a highly select subset of patients who underwent PC-RPLND for low volume tumors limited to the ipsilateral primary landing zone whose STMs normalized after cisplatin-based chemotherapy. With a median follow-up of 32 months, the estimated 2- and 5-year disease free survival rates were 95%. Four patients relapsed at a median of 8 months, all of which were outside the boundaries of a bilateral dissection [51]. In a follow-up study with a median follow-up of 125 months, the estimated 5- and 10-year recurrence free survival rates were 93% and 92%, respectively and the overall survival rate was 99% at 10 years. A total of 7 patients developed recurrent disease at a median time of 11 months, all of which occurred outside the boundaries of a full bilateral template RPLND [52].

A better understanding of the retroperitoneal neuroanatomy led to the development of the nerve-sparing RPLND. Jewett et al. and Donohue et al. both reported series of patients who underwent bilateral nerve-sparing RPLND. In these series, ejaculation was preserved in 90% to 100% of patients, and recurrence was observed in 5% of patients in one series, all of whom had node positive disease and did not receive adjuvant chemotherapy [54, 55].

When retrospectively comparing the two surgical approaches, an early study reported a lower complication rate associated with the modified unilateral procedure (9.4%) compared to a full bilateral dissection (19.3%) [53]. Other studies did not show a difference in complication rates between unilateral and bilateral nerve sparing RPLND, however the type of complications differed between the two [16].

Recent data has shown that the mapping studies supporting modified templates underestimated the extent of retroperitoneal metastases, and that the use of modified templates unnecessarily risks incomplete resection of contralateral metastasis. The reasons mapping studies underestimated the incidence of retroperitoneal metastases include lack of follow-up and the liberal use of postoperative chemotherapy [56, 57]. In the postchemotherapy setting 7% to 32% of patients had evidence of extratemplate retroperitoneal disease, depending on the boundaries of the modified template. Moreover, when using the Testicular Tumor Study Group templates, up to 26% of patients had extra template disease within the retroperitoneum despite having low volume postchemotherapy retroperitoneal masses, less than 2 cm in size [57].

Given the concerns regarding the early mapping studies which were used to support modified templates, the comparable overall complication rates in contemporary reports, and high rates of antegrade ejaculation achieved by both nerve-sparing and modified templates, the more prudent oncologic approach, in our view, is a bilateral template

performed in an experienced center, particularly in the post-chemotherapy setting.

Minimally invasive RPLND

The laparoscopic approach for RPLND was initially described in 1992, and introduced as a staging procedure [58]. Initial series included small cohorts of 6 to 29 patients with clinical stage I NSGCT. Perioperative complication rates ranged from 8% to 47% and conversion rates ranged from 6% to 13%. Six to 63% of patients had positive nodes and all were treated with chemotherapy [58, 59]. Cresswell et al. reported a series of 87 patients with clinical stage I GCT who underwent laparoscopic modified template RPLND, with the goal of pathological staging. A quarter of the patient were diagnosed with lymph node involvement and treated with 2 cycles of BEP. With a median follow-up of 84 months, 9% of patients with pathological stage I disease who did not receive chemotherapy relapsed, including 2 retroperitoneal recurrences outside the modified template, and one port site metastasis [60]. The technical difficulty associated with the procedure, and its initial diagnostic intent precluded wide applicability.

More recently, several investigators have reported the use of minimally invasive surgery with a curative intent in the pre- and postchemotherapy setting (Table 2) [61–63]. In a single center study, 91 patients with clinical stage I NSGCT underwent extended template laparoscopic RPLND. Twenty-one patients had pN1 disease and 7 had pN2. Adjuvant chemotherapy was given to 14/21 pN1 patients and all pN2 patients. With a median follow-up of 38 months, none of the patients with node positive disease recurred; however, 8% of patients with pN0 disease relapsed, including in the scrotum and the corpora [61]. The largest series of laparoscopic RPLND included 221 patients treated with a unilateral template for clinical stage I NSGCT. Twenty-nine patients (13%) had positive nodes, 7 of whom received adjuvant chemotherapy. With a median follow-up of 39 months, 6% of the patients relapsed, including 4% of pN0 patients and 27% of pN1 patients who did not receive chemotherapy. Over a third of the relapses occurred within the retroperitoneum [62]. Steiner et al. reported the long-term outcome of laparoscopic PC-RPLND for clinical stage II disease in a single center study. Patients with bulky disease (large tumors encasing vena cava, aorta, or renal vessels) after chemotherapy were not approached laparoscopically. A total of 71 patients underwent unilateral resection and 29 patients underwent bilateral resection. One patient with uncontrollable bleeding required open conversion. With a median follow-up of 59 months, one patient with a stage IIC disease managed by unilateral RPLND recurred within the retroperitoneum [63]. All three studies conclude that the present data supports the oncologic efficacy of laparoscopic RPLND. However, the findings are limited by a

Table 2
Summary of the main series evaluating the outcome of laparoscopic and robotic-assisted laparoscopic retroperitoneal lymph node dissection

Reference	No. Pts.	Clinical stage	PC-RPLND	RPLND template	Adjuvant chemotherapy (%)	Follow-up (months)	Relapse rate (%)	Death rate (%)
Laparoscopic RPLND								
Cresswell et al. 2008 [60]	87	I	No	Unilateral	24	84 (mean)	9 PS I; 0 PS II	0
Hyams et al. 2012 [61]	91	I	No	Bilateral	23	38 (median)	8 PS I; 0 PS II with or without Cx	0
Steiner et al. 2013 [63]	100	II	Yes	Unilateral and bilateral	2	59 (median)	1 Overall	0
Nicolai et al. 2017 [62]	221	I	No	Unilateral	3	39 (median)	4 PS I; 27 PS II without Cx; 0 PS II with Cx	0
Robotic-assisted laparoscopic RPLND								
Stepanian et al. 2016 [66]	19	I (11); II (6); III (2)	No (16); Yes (3)	Unilateral and bilateral	11	49 (median)	5 Overall	0
Pearce et al. 2017 [65]	47	I (42); IIA (5)	No	Unilateral	11	16 (median)	2 Overall	0

Cx = chemotherapy; PC-RPLND = postchemotherapy retroperitoneal lymph node dissection; PS = pathologic stage; RPLND = retroperitoneal lymph node dissection.

relatively short follow-up time, the common use of unilateral templates and the liberal use of adjuvant chemotherapy regardless of nodal volume of disease.

Robotic RPLND, initially described in the year 2006, is an additional approach for minimally invasive RPLND [64]. Multiple small cohorts with 3–47 patients suggest that robotic RPLND may be safely performed with a low complication rate and short hospital stay [64]. The largest series of primary robotic RPLND included 47 patients with clinical stage I-IIA NSGCT operated in multiple institutions. Modified unilateral templates were used in 96% of patients. Four percent of patients had intraoperative complications including one case of aortic injury which required conversion to open surgery; and 9% had an early postoperative complication. Five of 8 patients with node positive disease received adjuvant chemotherapy, and one patient had a pelvic recurrence at a median follow-up of 16 months (Table 2) [65]. While most series used a modified unilateral template, Stepanian et al. described a supine robotic approach used for bilateral template dissection; however, its use was limited to patients with a positive lymph node on frozen section or in the postchemotherapy setting [66]. Cheney et al. compared the surgical characteristics of robotic primary RPLND and robotic PC-RPLND performed in patients with residual retroperitoneal lymphadenopathy or persistently elevated tumor markers after primary chemotherapy. PC-RPLND was associated with higher complication and open conversion rates and longer operative times, however, the estimated blood loss, lymph node yield, and length of hospital stay were not significantly different [67].

While overall complication rates of MIS RPLND are comparable to those of open RPLND, several series suggest a higher rate of chylous ascites which appears in up to 6.6% of patients who undergo laparoscopic RPLND and 4.3% of patients who undergo robotic RPLND [65]. However, recent laparoscopic series had a relatively low rate of chylous ascites similar to that of open RPLND, possibly due to improved surgical technique and instrumentation associated with these series [61–63].

Few studies have compared the different treatment approaches [68, 69]. When comparing open PC-RPLND ($n=24$) and laparoscopic PC-RPLND ($n=43$), median operative time and major complication rates did not differ between the two approaches. Median postoperative hospital stay and duration of drainage was significantly shorter following laparoscopic PC-RPLND. Tumor recurrence rates were 8.6% for laparoscopic PC-RPLND and 14.2% for open PC-RPLND with mean disease-free survival rates of 76.6 months and 89.2 months, respectively. There was no significant difference in overall survival. These findings are limited due to the substantial selection bias as apparent by the median residual tumor size (2.2 cm for laparoscopic PC-RPLND and 6.8 cm for open PC-RPLND, $P=0.002$) and the reported outcomes [68]. A small series comparing laparoscopic and robotic RPLND using a modified template, has shown comparative intra- and perioperative

outcomes and failed to show any benefit to the robotic approach over the standard laparoscopic approach to justify the additional cost associated with this technique [69].

Concerns regarding the minimally invasive approach include the extent and thoroughness of dissection, the possible deleterious effects of the pneumoperitoneum with possible diffuse carcinomatosis, and the possibility of uncontrollable large vessel injury [61]. Furthermore, while both procedures were found to be safe, with low complication rates and short hospital stay, data regarding the oncologic outcome are limited by the small cohort size, short-term follow-up, the common use of modified templates and the liberal use of adjuvant chemotherapy which is often avoided in pN1, marker negative disease. Most importantly, considering the impressive cure rates associated with conventional RPLND, based on large patient cohorts with long-term follow-up, it is necessary to validate the long-term oncologic efficacy of newer techniques within a trial setting [70].

Summary

RPLND remains a critical component in the effective multimodal management of patients with testicular cancer. Its role has evolved significantly over the past 3 decades in both low-stage and advanced testicular cancer. RPLND is both a diagnostic and therapeutic procedure, but it must always be done with therapeutic intent, and not rely on effective cisplatin-based chemotherapy to compensate for suboptimal initial surgery. Studies addressing late relapse, re-operative surgery and contemporary mapping studies all suggest that a subset of patients undergoing either a primary or PC-RPLND will have unresected extratemplate disease if modified templates are utilized. Early mapping studies, which provided the basis for these modified templates have significant limitations and the need for re-operative surgery is an adverse and independent prognostic variable. In our view, when an RPLND is deemed to be an appropriate component in the management of a patient with testicular cancer, a bilateral nerve-sparing template is the most oncologically prudent approach and achieves comparable functional outcomes in high volume centers.

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None of the authors have anything to disclose.

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