



Robot-assisted post-chemotherapy retroperitoneal lymph node dissection in germ cell tumor: is the single-docking with lateral approach relevant?

C. Overs¹ · J. B. Beauval² · L. Mourey^{2,3} · P. Rischmann² · M. Soulié² · M. Roumiguié^{2,3} · Nicolas Doumerc²

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Abstract

Introduction Surgical treatment of post-chemotherapy residual mass of germ cell tumor (GCT) may be performed in various techniques. We assess the feasibility, safety, and efficacy of single-docking with lateral approach robot-assisted retroperitoneal lymph node dissection (R-RPLND) in residual mass of GCT in our center.

Materials and methods A retrospective review of patients undergoing R-RPLND for residual mass of CGT was performed between January 2014 and April 2017. Patients with residual mass < 3 cm for seminoma or < 1 cm for non-seminoma were eligible. All surgeries were performed with single-docking RPNLD technique in lateral decubitus. We assessed preoperative characteristics (age, testicular pathology, template, chemotherapy regimen, lesion size, and clinical stage), peroperative (operative time, estimated blood loss, intraoperative complication, node count, pathology, and number of positive node), and postoperative outcomes (postoperative complications, hospital length of stay, recurrence-free survival at 2 year, and ejaculation dysfunction).

Results Eleven patients underwent R-RPLND with a median size of the residual mass of 20 mm. Median operative time was 153 min with 120 ml of estimated blood loss, without intraoperative complication. Median nodes count was 7 [1; 24]. Two patients had post-chemotherapy necrotic nodes and one no tumorous node. One patient had postoperative Clavien I complication (chyloperitoneum). We report 72.7% of antegrade ejaculation at 1 month from the surgery. Median clinical recurrence-free survival was 100% after 2 years from the surgery ($n = 6$).

Conclusion Lateral approach with single-docking R-RPLND for residual mass of GCT is feasible and safe, with satisfying functional and oncologic outcomes.

Keywords Robotic surgery · Testicular cancer · Retroperitoneal lymph node dissection · Single-docking · Post-chemotherapy residual mass

Introduction

Germ cell tumors are amongst the most curable solid cancer if managed appropriately [1]. Residual mass of germ cell tumor can be found after chemotherapy. A surgical approach is recommended for seminoma germ cell tumor (SGCT) with residual mass above 3 cm after 3–6 months from the chemotherapy with 18F-FDG PET-CT uptake [2, 3], or above 1 cm for non-seminomatous germ cell tumor (NSGCT), diagnosed after 4–6 weeks from the chemotherapy with a CT-scan [4]. The laparoscopic technique is feasible and sure but difficult because of perinodal fibrosis and adhesions [5, 6]. Robotic retroperitoneal lymph node dissection (RPLND) brings more comfort and dexterity to the surgeon. It allows an easier dissection around the vessels due to the 360° rotation of the

✉ Nicolas Doumerc
doumerc.n@chu-toulouse.fr

¹ Department of Urology, Andrology and Renal Transplantation, CHU Grenoble, La Tronche, France

² Department of Urology, Andrology and Renal Transplantation, CHU Rangueil, Paul-Sabatier University, 1, Av J Pouchès, 31059 Toulouse Cedex, France

³ Oncology Department, Cancer Institute of Toulouse (IUCT-O), Toulouse, France

instruments, with more oncologic and surgical security compared to the conventional laparoscopy. The feasibility of robotic technique has already been evaluated for staging testicular cancer [7–10], but only few studies had assessed its feasibility and effectiveness for residual mass [11, 12]. Herein, we present our experience with RPLND in residual mass of testicular cancer after chemotherapy using a lateral and single-docking approach.

Patients and methods

From January 2014 to April 2017, all medical charts of patients who underwent an RPLND of residual mass of testicular tumor by a single surgeon were retrospectively analyzed.

Population

After institutional review board approval, patients with germ cell tumor who had prior chemotherapy and residual mass on CT-scan (above 3 cm for seminomatous germ cell tumor or 1 cm for non-seminomatous germ cell tumor) were eligible (Fig. 1). Chemotherapy, according to the EAU guidelines, was 3 courses of BEP (cisplatin, etoposide, and bleomycin) or 4 courses of etoposide and cisplatin in case of contraindication for bleomycin. The indication of surgery was confirmed in multi-disciplinary oncologic meeting (with at least one urologist, one radiologist, one oncologist, or radiotherapist) and proposed to the patient. Patients who needed a vascular replacement were not eligible in this



Fig. 1 17 × 26 mm inter-aortico-caval residual mass and 21 × 25 mm laterocaval residual mass in a 49 year-old patient

mini-invasive approach. Patients' characteristics such as body mass index, ASA score, and prior surgery were not exclusion criteria.

Analyzed data

Evaluation of patients characteristics and operative outcomes were reviewed, such as demographic (age), pathological (testicular pathology, size, localization and clinical stage), intraoperative (operative time, estimated blood loss, intra operative complication, conversion, node count, pathology, and number of positive node), and postoperative outcomes (postoperative complication, follow-up, hospital length of stay, clinical recurrence(CR)-free survival at 2 year, and ejaculation dysfunction). The number of positive node corresponds to the number of node with residual tumor at the histological examination. Clinical stage follows the American Joint Committee on Cancer classification. CR was defined by the apparition of supracentimetric abdominal or pulmonary mass on thoraco-abdominal CT-scan with contrast enhancement. Imaging was performed once or twice the first year after chemotherapy, at 24 months the second year, at 36 months the third year and at 60 months the fourth year. Complications were reported using Dindo–Clavien classification (grade I included any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions; grade II included pharmacological treatment with drugs other than such allowed for grade I complications; grade III included surgical, endoscopic, or radiological intervention; grade IV included life-threatening complication requiring intensive care management; and grade V included death of the patient). Ejaculation function was evaluated by questioning the patient during the consultation at 1 month from the surgery.

Surgical technique

All patients had lateral approach with single-dock technique. Da Vinci™ Si HD surgical system was used (Intuitive Surgical Inc., Sunnyvale, CA, USA). Patients were placed in lateral decubitus position with the robot docked over the flank. Robotic port placement for right retroperitoneal lymph node dissection is described in Figs. 2 and 3. A 4-port transperitoneal robot-assisted laparoscopy was performed. First step was the mobilization of the colon, and for right template, the duodenum was kocherised until the inferior vein cava (IVC) was well visualized. Then we individualized the external iliac artery, the gonadal vein, and the ureter, which were the distal limit of the dissection. The nodal tissue and residual mass were cleaned off of the medial side of the IVC using the “split and roll” technique of Donohue starting by the dissection at the level of the renal vein, in the

Fig. 2 Robotic port placement for right RPLND. A Camera port (12 mm), B robotic arms (8 mm), a trocar assistant (12 mm), b additional trocar assistant (10 mm) and liver retractor (5 mm)

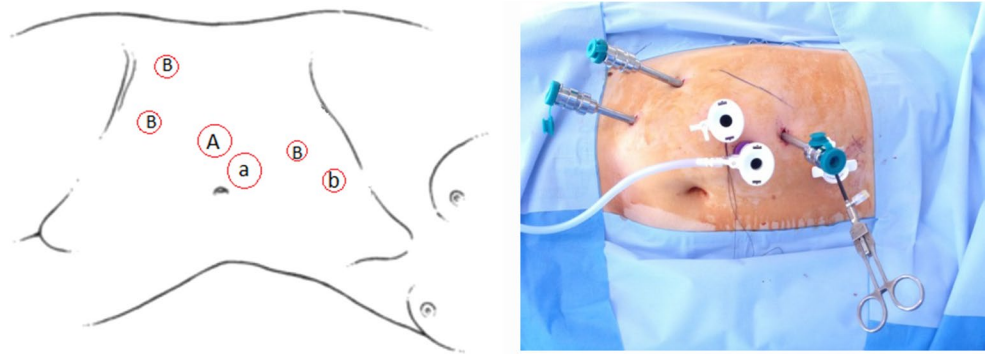


Fig. 3 Lateral single-docking for right RPLND

anterior midline of the cava medially towards the crossing of the external iliac artery (anterior split) and then dissecting the package off the great vessels medially and laterally (roll technique) [13]. The interaorticocaval LND was systematically performed for right testis tumor. For the left template, the dissection was performed from the external iliac artery, the common iliac artery, the aorta until the renal vein which was the proximal limit. The lymphostasis was progressively done using small clips (Challenger™, B-Braun Medical) or Hem-o-lok™ (Teleflex). Hemostasis was carefully controlled before patching a hemostatic gauze along the dissection. The gonadic vein was systematically removed with the retroperitoneal nodes in an endobag and delivered through the optic incision or a small muscle-splitting incision in the iliac fossa. Figure 4 describes the limits of unilateral modified retroperitoneal lymph node dissection for right and left templates.

Results

Preoperative data are described in Table 1.

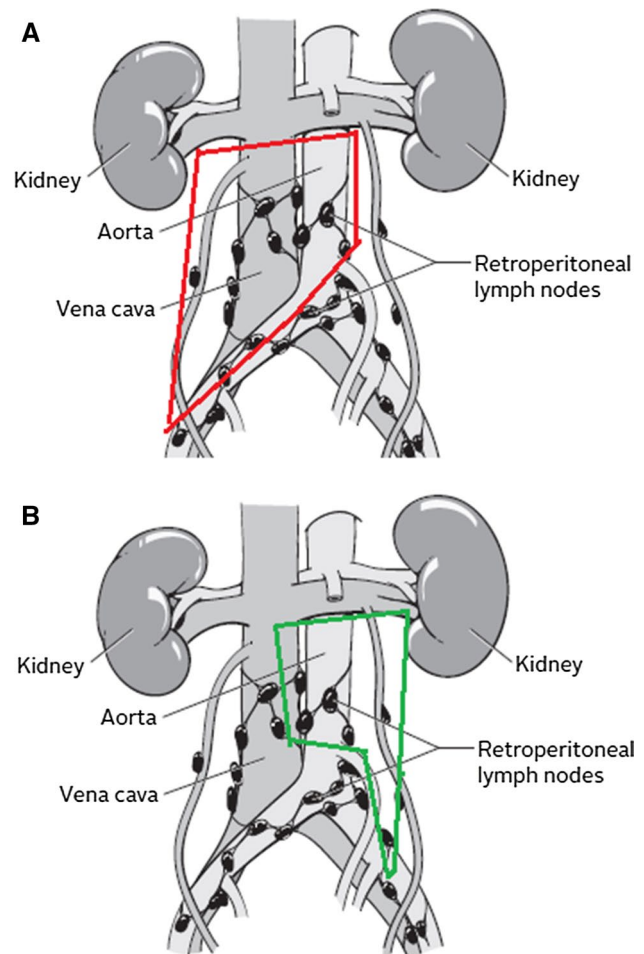


Fig. 4 Unilateral modified retroperitoneal lymph node dissection: right template (a) or left template (b)

All patients had NSCGT, except one with necrotic lesion with elevation of alpha foeto protein (AFP), and one with mixed lesion (SCGT and NGST). The median size of the residual mass was 20 mm, after commonly 3 cycles of BEP (bleomycine, etoposide or VP-16, platine). In 54.5% of the patients, clinical stage was IIa.

Table 1 Preoperative characteristics

Preoperative characteristics	
Median age (years)	33 [22;49]
Template <i>n</i> (%)	
Left latero aortic	6 (54.5)
Intra-aortocaval	3 (27.2)
Left para aortic	1 (9)
Laterocaval	1 (9)
Testicular pathology	
NSGCT	9 (81.8%)
Mixt	1 mixt lesion NSGCT/ SCGT
Other	1 necrotic lesion with elevation of AFP
Chemotherapy regimen <i>n</i> (%)	
3BEP	9 (81.8)
4BEP	1 (9)
2BEP then 2VIP	1 (9)
Median size of the lesion (mm)	20 [12.5; 40]
Clinical stage <i>n</i> (%)	
IIa	6 (54.5)
IIb	3 (27.2)
IIIb	1 (9)
II (Sx)	1 (9)

SGCT seminomatous germ cell tumor, NSGCT non-seminomatous germ cell tumor, AFP alpha foeto protein, BEP bleomycine, etoposide, platine

Median operative time was 150 min [(45–300), IQ25 = 120; IQ75 = 240], and estimated blood loss at 120 ml [(5–300) IQ25 = 30; IQ75 = 100]. No conversion was necessary; no intraoperative complication occurred during the procedure. Median node count was 7 (ranging from 1 to 24) and the number of positive nodes per patient was between 0 and 3.

Peroperative and postoperative outcomes are presented in Tables 2 and 3, respectively.

Regarding the postoperative outcomes, only one minor complication occurred (one chyloperitoneum which didn't need any drainage or surgery). Median hospitalization stay was 3 days (range). All the six patients operated before 2015 had recurrence-free survival at 24 months. Ejaculation status was collected in 9 patients out of 11 (81.8%) and was preserved in 8 patients (72.7%).

Table 2 Peroperative characteristics

Peroperative outcomes	
Operative time (min) mean (range)	150 [45; 300]
Estimated blood loss (ml) <i>n</i> (range)	50 [5; 300]
Node count <i>n</i> (range)	7 [1; 24]
Pathology <i>n</i> (%)	
NSGCT: teratoma	8 (72.7)
Tumoral necrosis	2 (18.2)
No tumor	1 (9)
Intraoperative complication or conversion	0
Positive nodes <i>n</i>	1 [0; 3]

NSGCT non-seminomatous germ cell tumor

Discussion

Retroperitoneal lymph node dissection is a challenging procedure and when performed in an open manner is associated with a significant morbidity and prolonged recovery [14]. Nevertheless, patients who have normal tumor marker level but residual mass in the retroperitoneum on CT should be strongly advised to a RPLND, as the risk of finding teratoma or viable germ cells on histopathological examination in such cases is 35 and 15%, respectively [15].

Laparoscopic retroperitoneal lymph node dissection for post-chemotherapy non-seminoma cell has been already evaluated, and can be considered as a standard option to open surgery in these patients. Nicolai et al. [16] assessed 67 patients undergoing laparoscopic surgery for residual mass between February 2011 and August 2015. Median size of the mass was 27 mm (15–31) and median operative time was 234 min (184–250). In his series, 3 patients (4.5%) needed conversion to open surgery. Sixty-six patients (98.5%) maintained antegrade ejaculation, and all patients were alive and event-free after a median follow-up of 21 months.

Robotic approach has been assessed as safe and reproducible in experienced hands [11]. It provides significant

Table 3 Postoperative outcomes

Postoperative outcomes	
Postoperative complication	1 Clavien I (9%) with 1 chyloperitoneum
Follow-up (month)	4 [1; 48]
Hospital length of stay (day)	3 [2; 4]
Recurrence-free survival at 2 years <i>n</i> (%)	6 (100)
<i>n</i> = 6	
Antegrade ejaculation <i>n</i> (%)	7 (77.8)
<i>n</i> = 9	
2 not disclosed	

advantages as enhanced 3D vision, higher dexterity with greater instrument precision, and ergonomic advantages for the surgeon. Specific advantages are found for RPLND including the ability to circumferentially dissect around structures owing the flexibility of the wristed instruments and to control bleeding from lumbar vessels. The robotic device allows to reproduce oncological principles of open RPLND with minimally invasive settings, permitting a posteriorly access to lymph node tissue to the great vessels, which can be challenging with the conventional laparoscopy approach [17]. While robotic RPLND is emerging as a viable alternative to open and laparoscopic approaches, it is associated with long operative times due to the learning curve but also to the robot intraoperative redocking [8, 11, 19]. The median operative time is 188–270 min with the open way, 185–291 min with the laparoscopic way, and 235 min with the robotic way [18–21].

Herein, we present our experience with a lateral single-docking approach. Out of this series of 11 patients undergoing RPLND for residual mass of germ cell tumor, no intraoperative complication or conversion was found, with a median operative time of 153 min and an estimated blood loss of 120 ml. One patient had a postoperative complication (chyloperitoneum) without any complementary procedure. Antegrade ejaculation was found in 72.7% of patients and recurrence-free survival at 2 years was at 100% for the six patients evaluated. Single-docking RPNLD for residual mass thus seems feasible and safe, with satisfying oncologic and functional outcomes.

Robot-assisted RPLND was first described by Davol et al. in 2006 [22]. Per and postoperative oncologic and functional outcomes of post-chemotherapy robot-assisted lymph node dissection of residual mass of germ cell tumor in the previous studies are described in Table 4.

Cheney et al. presented a series of RPLND in 18 patients with germ cell tumor, among those were 8 patients with post-chemotherapy residual mass [24]. There was no difference between the primary and post-chemotherapy RPNLD

for the lymph node yield, estimated blood loss, or length of stay, except for the operative time which was longer for the post-chemotherapy RPLND (311 vs 369 min, $p = 0.03$). In his center, they perform the surgery with two de-docking, with a mean operative time of 329 min. His higher lymph node yield rate (18 vs 7 in our series) can be explained by the fact that we performed modified unilateral lymph node dissection, unlike Cheney. Bora et al. also performed post-chemotherapy RPLND in a patient, with having to de-dock once the robot and change the patient's position, in 360 min, without intraoperative complication and with an estimated blood loss of 500 ml [11]. By comparison, our median operative time was inferior, because of not having to de-dock and then re-dock the robot. With this new approach (single-docking), we reduce the operative time. Stout et al. described a novel single-dock technique of post-chemotherapy bilateral retroperitoneal lymph node dissection in two patients, with an operative time of 470 and 300 min, without intraoperative complication, and no disease recurrence at 24 months [24]. Cheney et al. had higher blood loss (313 ml), but lymph node yield was also higher (18 nodes) [22]. The rate of antegrade ejaculate was 91% of patients. More recently, Kamel et al. reported a series of 12 patients with post-chemotherapy robotic retroperitoneal lymph node dissection for residual mass [25]. By comparison to our series, clinical stage was higher (50% stage III, 25% stage IIc, 16.7% stage IIb, and 8% stage IIa); masses were bigger (50% were ≥ 5 cm) and more lymph node count [12] which could explain a longer operative time (312 min) and more estimated loss (475 ml). The number of complication was similar, such as hospital stay and antegrade ejaculation.

Stepanian et al. described the supine approach to facilitate bilateral dissection for post-chemotherapy dissection, using a Da Vinci™ Xi platform [8]. We do think that the lateral approach is a more familiar way to perform this surgery. Indeed, total or partial robot-assisted nephrectomies are usually done in lateral decubitus position. Vascular and urologic landmarks are easily found in this position and do not require

Table 4 Studies regarding per and postoperative oncologic and functional outcomes of post-chemotherapy robot-assisted lymph node dissection of residual mass of germ cell tumor

Study	Number of patients	Operative time	Estimated blood loss	Peroperative complication	Antegrade ejaculation	Recurrence-free survival (month)
Cheney and al. [23]	8	369	313	2 conversions	100%	100% (1–18), mean = 11 months
Stout and al. [24]	2	385	150	0	100%	100% at 24 months
Kamel and al. [25]	12	312	475	0	66.7%	100% at 31 months
Bora and al. [10]	1	300	500	0	100%	100% at 12 months
Stepanian and al. [8]	4	324	137	0	90%	100% (12–51) mean = 40 months
Lee and al. [28]	1	420	ND	0	100%	ND
Dogra and al. [29]	1	210	450	0	yes	100% at 6 months

ND not disclosed

any learning curve. Moreover, most of patients do not need bilateral RPLND when post-chemotherapy residual mass are diagnosed.

We do not consider the sub-umbilical supine approach to be superior to ours, because the majority of robotic or laparoscopic urologic surgeries are performed with lateral approach, and we are more used to the anatomic landmarks in this way.

In the literature, only 15% of residual tumor after chemotherapy has viable germ cells [15]; therefore, in our series, patients with positive node were only followed-up without any complementary treatment.

Limitations of our study are the small number of patients of our cohort, probably due to the low incidence of patients with post-chemotherapy residual mass of germ cell tumor. It is a retrospective study, with only one surgeon performing the surgery as it is difficult and skillful, with a long learning curve. This specific approach is only possible for unilateral modified retroperitoneal lymph node dissection, with no need to access to right and left template during the same surgery. Bilateral access is usually chosen for staging RPLND and not recommended for post-chemotherapy residual masses surgery. Fertility rate was not assessed and it could have been an interesting issue.

For some authors such as Sheinfeld and Masterson [26], the technical feasibility is not a compelling argument for widespread applicability of a procedure. Indeed, in their referral centers for testicular cancer, they have noticed some rare and unusual late relapses after laparoscopic procedures (like port site recurrence, possibly diffuse carcinomatosis, or intrahepatic metastasis) which cannot be explained by the technique. The pathophysiology of the pneumoperitoneum is also incompletely understood. These relapses are challenging to manage, and responsible of additional treatment and risk of death from the disease. They point out as well that suboptimal RPLND can after lead to more treatment, late relapse, reoperation, and inferior survival. Thus, when the decision is made to perform an RPLND, its therapeutic potential should be maximized.

Minimally invasive RPLND approach has been criticized for oncological concerns. Incomplete resection can result in retroperitoneal recurrences, increased burden of therapy [27], and lower cure rates [25]. The robotic approach has demonstrated oncologic efficacy in various series [7, 8]. We should emphasize the necessity of high-quality complete surgical resection to reach high level of recurrence free. A rigorous selection of the patients elected to robotic approach is mandatory to guarantee good outcomes.

Conclusion

Post-chemotherapy RPLND is a challenging procedure for surgeons. Better vision and increased dexterity have placed robotic technology at the core of managing such patients.

R-RPLND by experienced robotic surgeons appears to be safe with acceptable perioperative morbidity. From our experience, RPLND with lateral approach and single-docking for residual mass of GCT seems feasible, safe, and reproducible with satisfying functional and early oncologic outcomes. Further studies are necessary to determine the long-term oncological outcomes of this approach.

Author contributions CO: data collection and management, data analysis, and manuscript writing. JBB: project development, data analysis, and manuscript writing. LM: project development. PR: project development. MS: project development. MR: project development, data management, and data analysis. ND: project development, data collection or management, and data analysis

Compliance with ethical standards

Conflict of interest Nicolas Doumerc is a consultant for intuitive surgical.

Research involving human participants Yes.

Informed consent Not concerned (retrospective study).

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