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Laparoscopic Retroperitoneal Lymph Node Dissection After Chemotherapy: A Review

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Context: To review and summarize the literature regarding the current status of postchemotherapy laparoscopic retroperitoneal lymph node dissection (PCL-RPLND) in patients with testicular germ cell tumor.
Evidence Acquisition: A comprehensive review of the English literature was performed using the PubMed database using the terms "laparoscopy" or "laparoscopic", retroperitoneal lymph node dissection, and "postchemotherapy" or "chemotherapy".
Results: PC L-RPLND is more challenging than primary L-RPLND. However, morbidity, operative time, and complications have improved as surgical experience has increased.
Conclusions: PCL-RPLND is a technically demanding procedure and should be performed in high volume-centers. It has been shown that PCL-RPLND is a feasible and effective procedure in experienced hands. The oncological efficacy of this approach is similar to the results of open series.

Keywords: Testicular Neoplasms; Laparoscopy; Chemotherapy

1. Context

Testis cancer is the most common solid malignancy in young men. Cure rate of patients with testicular cancer has increased with both medical and surgical therapies (1). Retroperitoneal lymph node dissection (RPLND), active surveillance, and chemotherapy are treatment options for non seminomatous germ cell tumors (NSGCTs). Patients with advanced metastatic NSGCT are treated with cisplatin-based chemotherapy followed by postchemothapy RPLND, if needed. Postchemotherapy RPLND has a staging benefit because active tumors are discovered and supplemental chemotherapy can be applied and a therapeutic benefit, as any residual chemotherapy-resistant tumor (e.g. teratoma and sarcoma) is removed surgically. Traditionally, RPLND was performed through an open incision. But in the last decade, many centers have performed laparoscopic RPLND (L-RPLND) (2). L-RPLND was first performed on a patient with stage 1 testis cancer in 1992 (3). Thereafter, several reports about L-RPLND, its outcomes and complications have been published. It has been shown that L-RPLND is an appropriate alternative approach for stage 1 disease with a low complication rate in experienced hands (4). L-RPLND compared with open technique reduced postoperative morbidity and provided equal diagnostic accuracy (5). L-RPLND has been also applied in patients with higher stage disease after chemotherapy. Since fibrosis and desmoplastic reaction caused by the chemotherapy obliterates the natural tissue planes, L-RPLND is technically challenging in this setting. Here, we review the literature and summarize the outcomes and complications of postchemotherapy L-RPLND (PCL-RPLND).

2. Evidence Acquisition

To review the English literature about PCL-RPLND, we performed an extensive electronic search with no date restriction using the PubMed database. We used the terms "laparoscopy" or "laparoscopic", "retroperitoneal lymph node dissection", and "postchemotherapy" or "chemotherapy". We included all studies that reported series of patients who underwent PCL-RPLND, either in comparison with the open technique or in an isolated series. Due to the data scarcity in the field, we did not drop out any reports.

3. Results

We found 12 articles addressed the outcomes and complications of PCL-RPLND (6-17). Ten studies were case series (6-15), one was a case report (redo PCL-RPLND) (16), and one was a comparative study evaluating laparoscopic versus open postchemotherapy RPLND (17). All of the studies were retrospective.

Overall PCL-RPLND was reported in 258 patients. Mean (or median) diameter of retroperitoneal postchemotherapy masses ranged from 2 to 6 cm. Clinical evaluation revealed that clinical stage was IIA, IIB, IIC, and III in 60, 119, 34, and 33 patients, respectively. PCL-RPLND was performed in a bilateral template in 18 patients, and in a modified template in 228. In 2 patients, only mass resection was performed. Surgery was successfully completed in 240 (93%) patients, and converted to open surgery in 18, because of bleeding in 11 and desmoplastic reaction in 7 patients. All patients who underwent open surgery because of desmoplastic reaction were in the first reported series of PCL-RPLND. Mean (or median) operative time varied from 116 to 397 minutes. Mean (or median) blood loss ranged from less than 50 to 1050 cc. There were intraoperative major complications in 24 patients including 2 vena cava injuries, 3 renal artery injuries, 2 external iliac injuries, 1 duodenal injury, 1 intestinal injury, and 15 vascular injuries (site was not mentioned). Postoperative complications were minor and included lymphocele and chylous ascite. Mean (or median) postoperative hospital stay was between 1.2-6 days. There was retrograde ejaculation in 7 (2.7%) patients; 4 of them had undergone bilateral RPLND. Pathological evaluation of the final specimen revealed teratoma in 78 patients, active tumor in 33, and necrosis in 145. (Table 1) During a mean follow-up of 12-74 months, recurrence occurred in 7 (2.7%) patients.

4. Conclusions

Studies that have compared laparoscopic and open RPLND demonstrate advantages with the laparoscopic approach in terms of less blood loss, shorter convalescence, and improved cosmetic results. Janetschek et al. reported that the laparoscopic approach was superior to open RPLND in all measured parameters except operative time (18). The surgical cost is higher with laparoscopy, but the costs associated with hospital stay are higher for open surgery. When recovery time is taken into consideration, laparoscopy offers a clear cost advantage over open surgery (19, 20). There are some data in the literature suggesting improved quality of life after the laparoscopic procedure compared to open surgery (21). However; there are no prospective randomized studies comparing laparoscopic and open RPLND. Most of the comparative studies between open and L-RPLND are in clinical stage I patients; comparative data between open and laparoscopic PC-RPLND is scarce.

It is noticeable that reduced short- and long-term morbidity should not be achieved with the cost of decreased oncologic efficacy. Since there is no highly reliable parameter or combination of parameters to rule out residual retroperitoneal tumor after chemotherapy, bilateral RPLND is the standard procedure in the setting. The use of modified templates usually applied for stage I disease is controversial in the postchemotherapy setting and is often considered an incomplete procedure (22-24). Ehrlich et al. (22) reviewed 50 patients with metastatic germ cell tumor (GCT) who underwent bilateral PC-RPLND. There was teratoma in 28 patients (56%), viable carcinoma in three (6%) and necrosis or fibrosis in 19 (38%). In patients with clinical stage Is, IIA or IIB left primary tumors, the pattern of spread was predictably limited to a modified left side template. In clinical stage IIC and III, or right-sided primary tumors, metastatic pattern was less predictable, showing metastases to the contralateral side. They concluded that bilateral RPLND is the standard procedure in patients with metastatic NSGCT and residual postchemotherapy retroperitoneal mass. Nevertheless, a modified template could be used in postchemotherapy patients with left-sided primary tumors and limited nodal involvement at presentation. Carver et al. (24) reported 532 men who underwent PC-RPLND for metastatic NSGCT. There was no radiographic evidence of disease beyond the applied modified template in their patients. However, the incidence of extra template metastasis was 8%, 18%, 29%, and 25% in men with residual retroperitoneal masses of less than 1, 1 to 2, 2 to 5 and more than 5 cm, respectively. They concluded that bilateral RPLND is essential for the management postchemotherapy metastatic NSGCT. Because of the considerable recurrence of disease resection of the residual mass suggested by some authors is not sufficient (25-27). Heidenreich et al. (28) evaluated PC-RPLND using a bilateral or modified template resection. They concluded that bilateral RPLND is the procedure of choice for huge residual masses. However, in well-defined masses (located in the primary landing zone of testis cancer and measured ≤ 5 cm) a modified template RPLND could maintain the oncologic efficacy and reduce morbidity of the procedure.

Rassweiler and associates (6) first reported laparoscopic RPLND after primary chemotherapy in seven patients. Steiner and colleagues (17) reported laparoscopic PC-RPLND for low-volume, stage II, NSGCT in 100 patients (stage IIC: 16 patients; IIB: 68; and IIA: 16). Mean diameter of postchemotherapy retroperitoneal masses was 1.4 cm. Seventy one and 29 patients underwent unilateral and bilateral resection, respectively. Conversion to open surgery was needed in one patient because of bleeding. Recurrence was found in only one patient, which was outside the surgical field. No patient died of tumor progression. Antegrade ejaculation was preserved in 95.2% of patients who underwent bilateral nerve-sparing laparoscopic PC-RPLND. They mentioned that laparoscopic PC-RPLND is feasible and associated with high oncologic efficacy and low morbidity, if performed by experienced hands. Permpongkosol and associates (13) performed successful postchemotherapy laparoscopic RPLND in 14 patients. In their series, all intraoperative complications were vascular injuries and occurred at the beginning of their experience (1996 to 2000); with no intraoperative complication in the second half of the series (2000 to 2005). They concluded that complications and morbidity can be reduced with increased experience.

Table 1. Reported Series for PCL-RPLND [a]

Author	Rassweiler et al 1996	LeBlanc et al. 2001	Palese et al. 2002	Hara et al. 2004	Lima et al. 2005	Correa et al. 2007	Valadez et al. 2007	Permpongkosol et al. 2007	Colestroupat et al. 2009	Buch et al. 2012	Arai et al. 2012	Steiner et al. 2013
No. of Patients	7	5	7	3	1	9	16	16	26	46	20	100
Maximum Tumor Diameter After Chemotherapy, cm	NR	NR	4.5	4	2	NR	4	5	6	3.9	4.2	4
Clinical Stage; No. (%)												
IIA	0	5	2	NR	-	NR	2	3	16 (62)	6 (13)	10	16
IIB	0	0	3	NR	1	NR	6	8	10 (38)	14 (30)	7	68
IIC	7	0	1	-	-	NR	2	2	0	6 (13)	0	16
III	0	0	1	-	-	NR	6	3	0	20 (44)	3	0
Approach	Transperitoneal	Extraperitoneal	Transperitoneal	Extraperitoneal	Extraperitoneal	Transperitoneal	Transperitoneal	Transperitoneal	Transperitoneal (24);Extraperitoneal (2)	Transperitoneal	Extraperitoneal	Transperitoneal
Resection Template; No (%)												
Bilateral	0	0	1 (17)	0	0	0	0	2	0	12	0	3
Modified template resection, No (%)	9 (100)	5 (100)	6 (83)	3 (100)	0	0	16	14	26	32	20	97
Only mass resection	0	0	0	0	0	0	0	0	0	2	0	0
Mean (or Median) Operative Time, min (range)	348	230	397 (188-700)	255-310	116	358 (240-540)	237 (125-270)	327 (116-700)	183 (120-260)	212 (145-298)	223 (137-399)	Unilat.:241 (120-480) Bilat:343 (300-480)
Mean (or Median) Blood Loss; mL	NR	< 50	1053 (75-2800)	< 50	100	400 (150-1500)	NR	903 (100-2800)	400 (100-600)	41 (< 100) 1 (100-500) 4 (> 500)	20 (10-520)	84 (10-1600)
Complications												
Intraoperative, Major	0	NR	3	0	0	1	0	3	4	12 (26)	0	1
Intraoperative, Minor	0	NR	1	0	0	o	o	o	4	1 (2.2)	0	NR
Postoperative, Major	0	NR	1	0	0	0	0	0	0	0	0	0
Postoperative, Minor	1	NR	0	1	0	0	0	4	1	4 (8.7)	14	3
No. of Conversions	7 (all of them were 2C)	0	2	0	0	0	0	2	3	3	0	1
Hospital Stay, d	3.5	1.2	2 (1-68)	NR	2	2.8 (1-5)	4.7 (3-14)$	2 (1-68)	5 (2-6)	6 (5-7.5)	NR	3.9 (2-8)
Retrograde Ejaculation	1	NR	0	0	0	0	0	2 (Bilat. RPLND in 1 of them)	NR	NR	0	4 (Radical Bilat. RPLND in 3)
Residual Tumor Pathology; No. (%)												
Necrosis	9	1	2	2	0	NR	7	6	14 (54)	28 (60.9)	16 (80)	60
Teratoma	0	0	3	3	4.5 cm	NR	6	5	9 (35)	12 (26.1)	2 (10)	38
Viable tumor	0	4	2	2	Small focus	NR	3	5	3 (12)	10 (21.7)	2 (10)	2
Mean (or Median) Follow up, M	29	15	24	12	17	12	26 ± 11	30.7 (4-108)	27 (14-36)	30.1 (12.1-47.1)	45 (24-112)	74 (1-222)
Recurrence	0	0	0	1	0	0	1 (viable tumor)	0	0	4 (8.6)	0	1 (IIC)

[a] Abbreviations: NR: Not reported. $: One patient experienced a bleomycin-induced interstitial pneumonia that required hospitalization for 14 days.

Busch and colleagues (15) have reported the only study comparing open (n = 24) and laparoscopic (n = 43) PC-RPLND in patients with advanced testicular cancer. Median operative time was 212 and 232 minutes for laparoscopic and open PC-RPLND, respectively. Median duration of postoperative hospital stay was shorter in laparoscopy group. Intraoperative complications occurred in 21.7% and 38.0% of patients in the laparoscopy and open group, respectively. No significant differences were observed in bleeding, major vascular injuries, postoperative complications and overall survival between two groups. Authors concluded that laparoscopic PC-RPLND is a safe approach for select patients in experienced hands.

To achieve an excellent oncological outcome, it is critical for the patients to be managed at centers of excellence that have specific expertise in the management of advanced GCTs and postchemotherapy RPLND. Integration in concepts of these centers is that postchemotherapy L-RPLND has to be performed by experienced laparoscopic surgeons only; otherwise, the morbidity of this procedure might be too high to be recommended. It has been shown that PCL-RPLND is a feasible and effective procedure in experienced hands. It is technically demanding and should be performed by high volume surgeons. The oncological efficacy of this approach is similar to the results of open series. Operative time, complications, and morbidity have been reduced as surgical experience has increased. Further well-designed comparative studies are needed to more precisely clarify oncological outcome, and complications of the procedure.

Author's Contributions

Study concept and design by Seyed-Amir-Mohsen Ziaee. review and interpretation of data by Akbar Nouralizadeh, Mohammad Hadi Radfar. Drafting of the manuscript by Mohammad Ali Fallah, Mohammad Ali Ghaed, Mahboobeh Mirzaee. Critical revision by Seyed Amir Mohsen Ziaee, Mohammad Hadi Radfar.

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