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REVIEW

Oncological outcome and complications of post-chemotherapy retroperitoneal surgery in non-seminomatous germ cell tumours – a systematic review

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ABSTRACT

Introduction: Post-chemotherapy surgery constitutes an integral part of the management of patients with non-seminomatous germ-cell tumours with a residual mass in the retroperitoneum. Published data on recurrence rates and complications to bilateral retroperitoneal lymph node dissection (RPLND), unilateral template RPLND, and resection of residual mass only according to different surgical techniques (open, laparoscopic, and robotic surgery) were reviewed.

Material and methods: PubMed/Medline, Embase, and the Cochrane databases were searched systematically. The risk of bias was assessed with the Newcastle Ottawa Scale.

Results: In total, 28 studies were included. Eight studies reported on open surgery with the bilateral template, seven on the unilateral template, and three on resection of mass only. Median follow-up was 39, 39, and 70 months, respectively. Recurrences were found in 11, 12, and 14%, respectively. Major complications (Clavien–Dindo III or more) were observed in 18, 8, and 17%, respectively. Two studies reported on laparoscopic bilateral surgery, eight on unilateral, and two on residual mass only. A total of Median follow-up was 52, 29, and 55 months, respectively. Recurrences were found in 0, 1, and 9%, respectively. Major complications were not documented for bilateral but were observed in 4% for unilateral and 0% for resection of tumour only. Four studies on robotic bilateral surgery, three on unilateral and two on resection of tumour only were included. Follow-up was 18, 35, and 30 months, respectively. Recurrences were found in 0, 0, and 2%, respectively. Major complications were observed in 0, 10. and 2%, respectively.

Conclusions: When patient selection is made, recurrence rates for the open unilateral template are comparable to the bilateral template. The risk of complications is highest after an open bilateral template. Laparoscopic and robotic surgery should not be used as a standard procedure. More studies are required with larger patient populations and longer follow-up.

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Introduction

Post-chemotherapy (PC) surgery constitutes an integral part of the management of patients with non-seminomatous germ-cell tumours (NSGCT) with a residual mass in the retroperitoneum. The extent of surgery may, however, vary widely, ranging from excision of the residual mass only to bilateral retroperitoneal lymph node dissection (RPLND). The objective is to remove persistent lymph nodes as they contain teratoma in 30–40% of patients and vital cancer in 10–20% of patients [1]. Teratomas require special attention as they are chemotherapy-resistant [2], may occur many years after initial treatment [3,4], and have an inherent risk of transforming into somatic-type malignancy which is often not curable [5].

Several studies have investigated predictive criteria to accurately determine the histologic features of the residual mass preoperatively in order to avoid unnecessary surgery [6–10]. This strategy has so far proved disappointing as no diagnostic procedures have been able to discriminate between vital cancer, teratoma, and necrosis/fibrosis with acceptable precision. Thus, resection is recommended for any PC residual mass larger than 1 cm [11,12] in the axial plane on Computer Tomography (CT), and based on this, the extent of surgery has become the centre of the debate.

In the available literature, three main surgical principles exist: bilateral template RPLND, unilateral template RPLND, and resection of residual mass only (Figure 1). All can be conducted by open surgery (O-RPLND), laparoscopic surgery (L-RPLND), or robotic-assisted laparoscopic surgery (R-RPLND). Open bilateral PC-RPLND is considered standard of care in EAU and ESMO guidelines [11,12] and should preferably be performed as nerve-sparring procedure [11,12].

With the increased survival rates for patients with testicular cancer, the focus has shifted towards decreasing morbidity and treatment-related toxicities [13]. To assess the safety

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Supplemental data for this article can be accessed here.

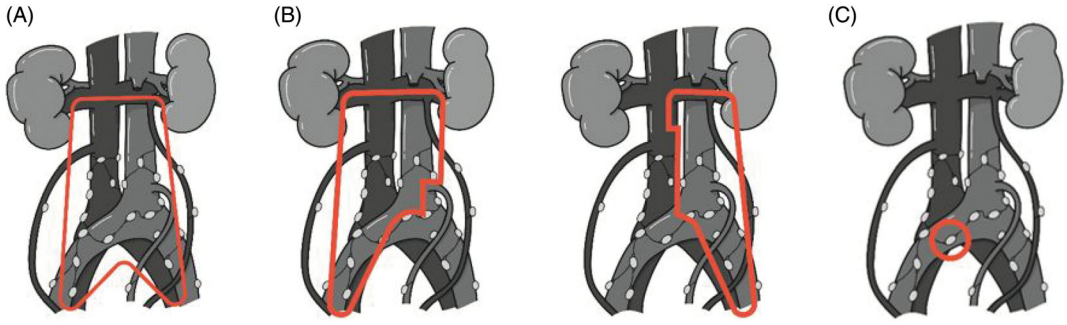

Figure 1. Illustration examples of retroperitoneal lymph node dissection (RPLND). (A) Bilateral RPLND: Involves all lymphatic tissue surrounding the aorta and vena cava, extending caudally to include the iliac regions with the crossing of ureter as the caudal boundary and cranially to the infrahilar regions, sometimes extended to include the suprahilar regions with the crura of the diaphragm as the cranial boundary. The ureters serve as lateral boundaries. It can involve a nerve sparing approach. (B) Unilateral RPLND: Different methods exist when conducting unilateral template. Right sided modified templates often include precaval, paracaval and interaortocaval lymph nodes and the right gonadal vein and most often preaortic and ipsilateral iliac lymph nodes. Sometimes paraaortic lymph nodes are included. The left sided template often includes preaortic and paraaortic lymph nodes, the left gonadal vein, precaval-/interaortocaval-/and ipsilateral iliac lymph nodes. (C) Residual mass only resection: Includes radical resection of the residual mass and surrounding macroscopically suspect tissue.

of patients undergoing surgery, standardized and reproducible classification of post-surgical complications has been adopted, the Clavien–Dindo Classification, validated in urological surgery [14,15].

The aim of this systematic review was to evaluate the incidence of surgical complications and recurrences after PC retroperitoneal surgery conducted with available surgical techniques.

Material and methods

Search strategy

We conducted a systematic literature search in PubMed/Medline, Embase, and the Cochrane Central Register of Randomised Controlled Trials database. The search was conducted with the filters: 'males', 'adults', 'humans' and published in the last 20 years. The search string is attached in Supplementary Appendix A3. The last search was conducted in October 2020. The systematic search was supplemented with a non-systematic manual search from cited references. Only literature in English was included. The literature obtained in the search was assessed by the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) criteria [16]. Abstracts and full-text screening, and data extraction was independently performed in duplicate (JJR and GLP) and disagreements were resolved by discussion or reference to an independent third party (GD). Figure 2 shows the flow diagram of evidence acquisition.

Study eligibility

We used Patient, Intervention, Comparator, and Outcome (PICO) [17] to determine the eligibility of the studies. To be eligible for inclusion, studies had to consist of the following: Patient cohorts with NSGCTs operated for a residual mass in the retroperitoneum after chemotherapy (P), with the use of bilateral, unilateral template or resection of residual mass only (I), no comparator was needed as it was not relevant for this study (C), they had one or more of the outcome of recurrence rates, recurrences inside bilateral template or complications classified by Clavien–Dindo [14] (O). The classification is listed in Supplementary Table A1. Studies with no distinction between seminomas vs. NSGCTs, primary RPLND vs. PC-RPLND, or no distinction between templates were excluded. Case reports were not included, but as some of the included cohort studies had patients treated with different templates the number of cases treated with each template was small.

Studies included

The search identified a total of 1123 studies after duplicates were removed. After selection, 28 studies reported on one or more of the following; recurrence rates, recurrences inside the bilateral template, and complication rates by Clavien–Dindo scale.

Risk of bias

The risk of bias was assessed by Newcastle Ottawa Scale with a maximum score of 9 where a study with a score $\geq$7 has been suggested as high-quality [18]. The assessment was done by two independent authors (JR and MB). Possible disagreements were settled by a third-party author (GD). Grading for the studies included is shown in Supplementary Appendix A2.

Results

In the studies included, 23 out of 28 were retrospective and only one study included a control group. Six out of 28 studies did not have a study group representing the general study population. Furthermore, six out of 28 studies had a follow-up period $>$ 5 years, four on open surgery and two on laparoscopic surgery. Only one study had a risk of bias score $\geq$7 suggesting high-quality (Supplementary appendix A2).

Open bilateral post-chemotherapy retroperitoneal lymph node dissection

Eight studies [19–26] on open bilateral PC-RPLND with a total of 408 patients were included (Table 1). Follow-up ranged

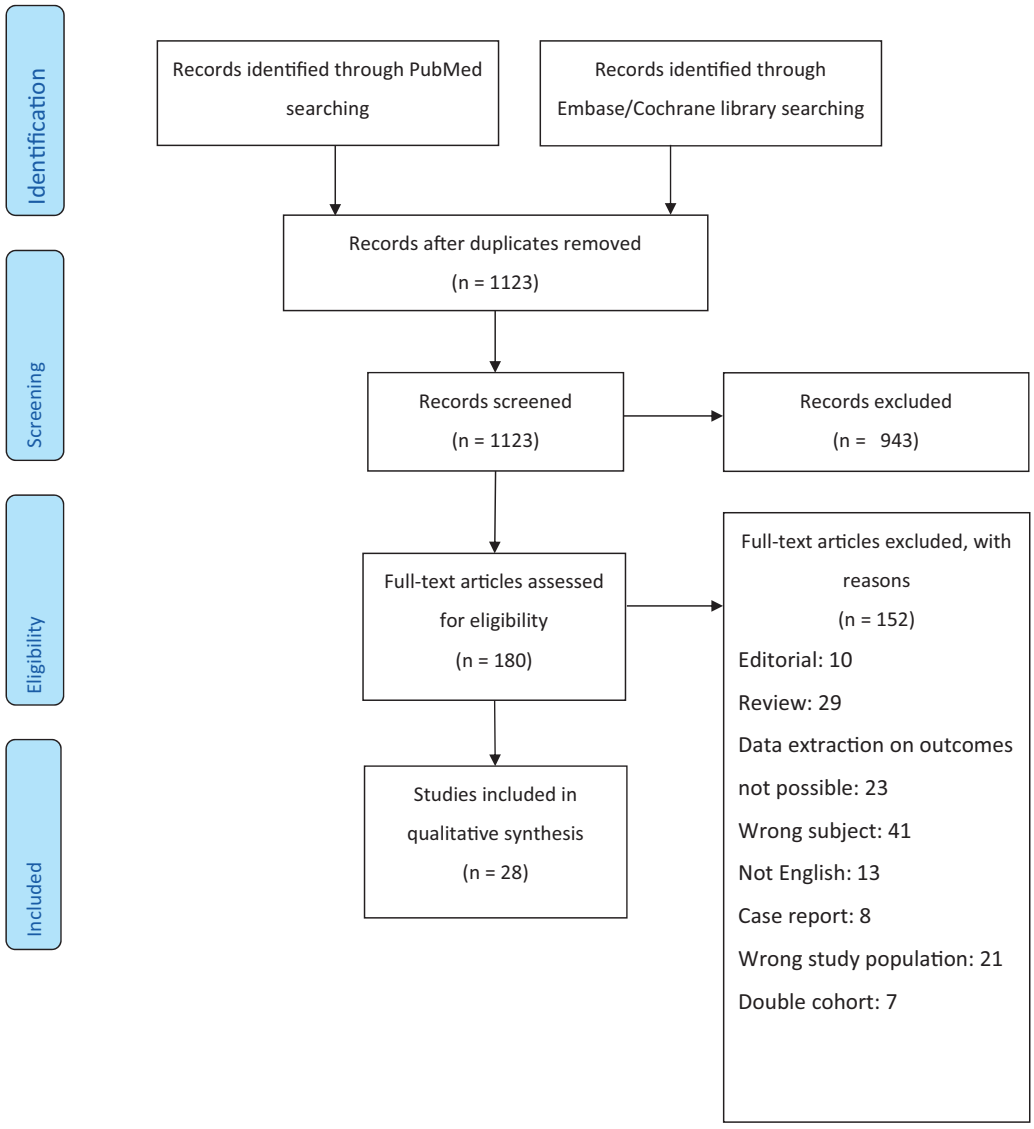

Figure 2. Flow diagram of evidence acquisition.

from 15–72 months with a median of 39 months. Four studies [19,20,23,24] documented prognostic groups according to The International Germ Cell Cancer Collaborative Group (IGCCCG). The proportion of patients belonging to the IGCCCG good prognostic group varied from 22–76%.

Seven studies [20–26] reported on recurrence rates with a total of 321 patients included. Recurrences were found in a total of 44 (11%) patients ranging from 0 (0%) to 18 (22%) and 6 (2%) patients experienced recurrence in the retroperitoneum. Four studies [19–21,23] reported on complications according to Clavien–Dindo. Of the 277 patients in those studies, 144 (52%) experienced complications, and 48 (17%) Clavien–Dindo grade III or above. In all the studies, four patients (1%) died of complications to surgery.

Open unilateral template

Eight studies on open unilateral PC-RPLND with a total of 779 patients were included [19,20,24,26–29,33]. Follow-up ranged from 15–125 months with a median of 39 months. The proportion of patients belonging to the IGCCCG good prognostic group ranged from 40–98% (Table 1). The selection of template was based on tumour size (<5 cm) and location (unilateral dissemination and not close to the large blood vessels).

Seven studies [20,24,26–29,33] reported recurrence rates, with a total of 522 patients included. Overall, 64 (12%) experienced a recurrence ranging from 3 (3%) to 45 (23%) and 16 (3%) inside templates in the retroperitoneum. Three studies with 347 patients included reported complications per Clavien–Dindo [19,20,33], 100 (29%) experienced complications, and 27(8%) experienced grade III complications or above. One death related to surgery was reported.

Open residual mass only resection

Three studies on PC resection of residual mass only with a total of 226 patients were included [30–32]. Follow-up

Table 1. Oncological outcome and complications from open surgery.

Studies included	Treatment period	No. patients	Median follow-up, months	IGCCCG			Recurrence, *n* (%)	Recurrence inside template, *n* (%)	Clavien–Dindo					
				Good, *n* (%)	Inter-mediate, *n* (%)	Poor, *n* (%)			I, *n* (%)	II, *n* (%)	IIIa, *n* (%)	IIIb, *n* (%)	IV, *n* (%)	V, *n* (%)
Bilateral template														
Gerdtsson et al. [19]	2007–2014	87	72	37 (43)	22 (26)	27 (31)	–	–	7 (8)	23 (26)	10 (11)	6 (7)	1 (1)	1 (1)
Hiester et al. [20]	2003–2018	81	15	18 (22)	24 (30)	39 (48)	18 (22)	3 (4)	8 (10)	34 (42)	3 (4)	0 (0)	3 (4)	1 (1)
Ariffin et al. [21]	2005–2015	36	35	–	–	–	2 (6)	1 (3)	5 (14)	5 (14)	6 (16)	3 (8)	0 (0)	0 (0)
Nowroozi et al. [22]	2006–2011	21	38	–	–	–	2 (10)	–	–	–	–	–	–	1 (5)
Luz et al. [23]	1994–2008	73	47	56 (76)	10 (14)	7 (10)	7 (10)	2 (3)	9 (6)	5 (7)	6 (8)	5 (7)	3 (4)	0 (0)
Heidenreich et al. [24]	1999–2007	54	39	26 (48)	12 (22)	16 (30)	6 (9)	0 (0)	–	–	–	–	–	1 (1)
Ehrlich et al. [25]	1996–2005	50	53	–	–	–	9 (18)	0 (0)	–	–	–	–	–	–
Tanaka et al. [26]	1992–2005	6	34	–	–	–	0 (0)	0 (0)	–	–	–	–	–	–
Total		408	39				44 (11)	6 (2)	29(11)	67(24)	25 (9)	14(5)	7(3)	4(1)
Unilateral template														
Gerdtsson et al. [19]	2007–2014	231	72	154 (68)	38 (17)	36 (16)	–	–	18 (8)	24 (10)	16 (7)	4 (2)	2 (1)	0 (0)
Hiester et al. [20]	2003–2018	90	15	36 (40)	29 (32)	25 (28)	5 (6)	0 (0)	11(12)	14 (16)	2 (2)	0 (0)	1 (1)	0 (0)
Cho et al. [27]	1991–2004	100	125	98 (98)	0 (0)	2 (2)	7 (7)	0 (0)	–	–	–	–	–	–
Heidenreich et al. [24]	1999–2007	98	39	57 (58)	26 (27)	15 (15)	3 (3)	1 (1)	–	–	–	–	–	–
Spiess et al. [28]	1980–2003	198	41	–	–	–	45 (23)	14 (7)	–	–	–	–	–	–
Tanaka et al. [26]	1992–2005	25	34	–	–	–	3 (12)	1 (0,5)	–	–	–	–	–	–
Sayed et al. [29]	1997–2002	11	38	–	–	–	1 (9)	–	–	–	–	–	–	1(9)
Total		753	39				64(12)	16(3)	58(18)	38(12)	18(6)	4(1)	3(1)	1(0)
Residual mass only														
Schmidt et al. [30]	1993–2013	109	124	59 (54)	29 (27)	20 (18)	10 (9)	2 (3)	27(25)	15(14)	5 (5)	13(12)	0 (0)	0 (0)
Ekenel et al. [31]	1991–2010	94	60	56 (64)	22 (25)	10 (11)	8 (9)	5 (5)	–	–	–	–	–	–
Öztürk et al. [32]	2005–2015	61	70	18 (29)	26 (43)	17 (28)	19 (31)	–	–	–	–	–	–	–
Total		264	70				37 (14)	7(3)	24(25)	15(14)	5(5)	13(12)	0(0)	0(0)

No.: number; IGCCCG: International Germ Cell Cancer Collaborative Group; -: not stated.

ranged from 60–124 months with a median of 70 months. Of these, 29–64% belonged to the IGCCCG good prognostic group (Table 1). No patient selection based on tumour size or location was made.

All three studies reported on recurrence rates and it was found that 37 (14%) experienced a recurrence with 7 (3%) in the retroperitoneum. One study [30] with 109 patients included reported complications by Clavien–Dindo, where 60 (55%) patients experienced complications and 18 (17%) grade III or above. No deaths were reported due to complications.

Laparoscopic bilateral retroperitoneal lymph node dissection

Two studies on bilateral L-RPLND with a total of 33 patients were included [34,35]. Follow-up ranged from 30–74 months with a median of 52 months. Information on IGCCCG prognostic group was documented in one study and all 4 (100%) patients included were in the good prognostic group (Table 2).

The reported recurrence rate was 0% in both studies. Complications by Clavien–Dindo were not reported.

Laparoscopic unilateral retroperitoneal lymph node dissection

Seven studies on laparoscopic unilateral L-RPLND with a total of 242 patients were included [34–40]. Follow-up ranged from 21–74 months with a median of 29 months. Information about IGCCCG prognostic group was reported in two of the studies (Table 2), and 50–93% belonged to the good prognostic group [34,36]. Patients were selected based on unilateral dissemination, residual tumour size (<5cm) and location (not close to large blood vessels). All seven studies reported recurrence rates with only 3 patients (1%) experiencing recurrences. The range of recurrences was 0–6%. Of the 3 patients with recurrence 2 (1%) were found in the retroperitoneum. Complication rates were reported in two studies [36,37] with 18 patients (21%) experiencing complications and 4 (5%) Clavien–Dindo III or above.

Laparoscopic residual mass only resection

Two studies with a total of 91 patients were included [32,41]. Follow-up ranged from 18–91 months with a median of 55 months. One study reported on the prognostic group and 81% belonged to the IGCCCG good prognostic group (Table 2). Recurrences were found in 8 (9%) patients, ranging from 0–9% with no recurrence found inside the template. None of the studies reported complications by Clavien–Dindo.

Robotic-assisted laparoscopic bilateral retroperitoneal lymph node dissection

Four small studies with a total of 9 patients were included (Table 3) [42–45]. Follow-up ranged from 10–22 months with a median of 18 months. Only one study documented criteria for patient selection and it was based on the location and size of the tumour [42]. One study [44] reported IGCCCG prognostic group and 2 (67%) were in the good prognostic group. No recurrences (0%) were found in any of the studies. One study reported complication by Clavien–Dindo, but only 1 patient was included. The patient experienced complications grade II.

Robotic-assisted laparoscopic unilateral retroperitoneal lymph node dissection

Three small studies with a total of 12 patients were included (Table 3) [42,44,45]. Follow-up ranged from 10–50 months with a median of 35 months. Only one study [44] documented IGCCCG prognostic group and 5 (83%) were in the good prognostic group. No recurrences (0%) were found during follow-up. Two studies [42,44] reported on complications by Clavien–Dindo, and 4 patients (40%) had complications to surgery. Only 1 (10%) experienced Clavien–Dindo III or above and no patients died due to complications in surgery.

Robotic-assisted laparoscopic resection of residual mass only

Two studies with a total of 48 patients were found [44,46]. Follow-up ranged from 3–41 months with a median of 30 months. Both reported on IGCCCG prognostic group and 67–85% were in the good prognostic group. Recurrence rates were reported in both studies with a total of 1 (2%) patient experiencing recurrence in the retroperitoneum. Only 2 patients (4%) experienced complications to surgery and only 1 (2%) Clavien–Dindo III or above.

Discussion

Templates and surgical modalities of PC-RPLND have been changing over time, from large open template operations [25] to less invasive templates and procedures [46]. With changing modalities large datasets on oncological outcomes and surgical complications evidence are critical to ensure the best possible care.

Open bilateral and unilateral surgery

Patient selection for bilateral or unilateral template surgery is a basic premise, but it creates a diverse study population and makes a direct comparison of recurrence rates and surgical complications difficult. All included studies selected patients for bilateral and unilateral templates based on size and location of the residual tumour [19,20,24,34,35]. Bilateral template surgery was used more frequently in patients belonging to the poor prognostic group compared to patients with a unilateral template operation.

When reviewing studies on open surgery we found that data on recurrence rates was quite similar between templates, including recurrences inside the template. For the two templates, the median follow-up was the same

Table 2. Oncological outcome and complications from laparoscopic surgery.

Studies included	Treatment period	No. patients	Median follow-up, months	IGCCCG			Recurrence rate (%)	Recurrence inside template (%)	Clavien–Dindo					
				Good, *n* (%)	Inter-mediate, *n* (%)	Poor, *n* (%)			I, *n* (%)	II, *n* (%)	IIIa, *n* (%)	IIIb, *n* (%)	IV, *n* (%)	V, *n* (%)
Bilateral template														
Kimura et al. [34]	2009–2012	4	30	4 (100)	0 (0)	0 (0)	0 (0)	0 (0)	–	–	–	–	–	–
Steiner et al. [35]	1993–2010	29	74	–	–	–	0 (0)	0 (0)	–	–	–	–	–	–
Total		33	52				0 (0)	0 (0)						
Unilateral template														
Nicolai et al. [36]	2011	67	21	62 (93)	3 (5)	2 (3)	0 (0)	0 (0)	1 (2)	1 (2)	1 (2)	1 (2)	0 (0)	0 (0)
Kimura et al. [34]	2009–2012	2	30	1 (50)	1 (50)	0 (0)	0 (0)	0 (0)	–	–	–	–	–	–
Steiner et al. [35]	2993–2010	71	74	–	–	–	1 (1)	1 (1)	–	–	–	–	–	–
Arai et al. [37]	2002–2010	20	45	–	–	–	0 (0)	0 (0)	13 (65)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)
Maldonado-Valadez et al. [38]	2002–2006	16	26	–	–	–	1 (6)	1 (6)	–	–	–	–	–	–
Calestroupat et al. [33]	2000–2006	26	27	–	–	–	0 (0)	0 (0)	1 (4)	5 (19)	1 (4)	0 (0)	1 (4)	0 (0)
Albqami et al. [39]	1995–2004	59	62	–	–	–	1 (2)	0 (0)	–	–	–	–	–	–
Palese et al. [40]	1996–2000	7	24	–	–	–	0 (0)	0 (0)	–	–	–	–	–	–
Total		268	29				3 (1)	2 (1)	15 (13)	7 (6)	2 (2)	1 (1)	1 (1)	0 (0)
Residual mass only														
Öztürk et al. [32]	2005–2015	89	91	72 (81)	12 (13)	5 (6)	8 (9)	–	–	–	–	–	–	–
Zambon et al. [41]	1999–2002	2	18	–	–	–	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total		91	55				8 (9)	0 (0)	0 (0)	0(0)	0(0)	0(0)	0(0)	0(0)

No.: number; IGCCCG: International Germ Cell Cancer Collaborative Group; -: not stated.

Table 3. Oncological outcome and complications from Robotic surgery.

Studies included	Treatment period	No. patients	Median follow-up, months	IGCCCG			Recurrence rate, *n* (%)	Recurrence inside template, *n* (%)	Clavien–Dindo					
				Good, *n* (%)	Inter-mediate, *n* (%)	Poor, *n* (%)			I, *n* (%)	II, *n* (%)	IIIa, *n* (%)	IIIb, *n* (%)	IV, *n* (%)	V, *n* (%)
Bilateral template														
Islamoglu et al. [42]	2017–2018	1	10		–	–	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Tamhankar et al. [43]	–	3	14	–	–	–	0 (0)	0 (0)	–	–	–	–	–	–
Kamel et al. [44]	2011–2016	3	22	2 (67)	1 (33)	0 (0)	0 (0)	0 (0)	–	–	0 (0)	0 (0)	0 (0)	0 (0)
Stepanian et al. [45]	2008–2014	2	22	–	–	–	0 (0)	0 (0)	–	–	–	–	–	–
Total		9	18				0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Unilateral template														
Islamoglu et al. [42]	2017–2018	4	10	–	–	–	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)
Kamel et al. [44]	2011–2016	6	35	5 (83)	1 (17)	0 (0)	0 (0)	0 (0)	1 (17)	1 (17)	0 (0)	0 (0)	1(17)	0 (0)
Stepanian et al. [45]	2008–2014	2	50	–	–	–	0 (0)	0 (0)	–	–	–	–	–	–
Total		12	35				0 (0)	0 (0)	1 (10)	2 (20)	0 (0)	0 (0)	1 (10)	0 (0)
Residual mass only														
Blok et al. [46]	2007–2019	45	41	28 (85)	6 (13)	1 (2)	1 (2)	1 (2)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)
Kamel et al. [44]	2011–2016	3	19	2 (67)	0 (0)	1 (33)	0 (0)	0 (0)	–	–	0 (0)	0 (0)	0 (0)	0 (0)
Total		48	30				1 (2)	1 (2)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)

No.: number; IGCCCG: International Germ Cell Cancer Collaborative Group; -: not stated.

(39 months). This suggests that a unilateral template is a viable option when patient selection is made.

Open residual mass only surgery

Only a few studies have looked at the feasibility and safety of removal of the residual mass only. None of the studies had a patient selection. The distribution of prognostic groups (Good 56%, intermediate 28%, poor 16%) corresponded to the distribution in the literature [12]. In a study by Schmidt et al. [30] the risk of recurrence inside the template appeared to be similar to bilateral and unilateral templates (3% vs 2% respectively), but redo surgery was needed in 13%[30]. This may reflect that patients undergoing desperation surgery and patients with prior retroperitoneal surgery were included in this study [30] while these patients were excluded in studies with the bilateral and unilateral template. In the same study, ten out of 109 patients (9%) had eleven relapses in total, nine were in the field of prior surgery and two were out of field [30]. In six patients, the bulky, locally advanced disease had compromised complete resection, and template resection of other areas would not have prevented these infield relapses. Seven out of 97 patients with no evidence of disease after PC surgery had recurrences (7%) but only one of them had recurrence within a template and would possibly have benefitted from template lymph node resection and avoided relapse.

Laparoscopic and robot-assisted surgery

Data on laparoscopic and robot-assisted PC-RPLND is hampered by limited follow-up data and small patient populations included in the available studies. Accordingly, it is difficult to make a meaningful evaluation of recurrence rates. The patient selection suggests that only patients with small tumours with specific locations were included and very few studies reported postoperative complications by Clavien–Dindo grade. It appears that both methods were equal in terms of blood loss, postoperative hospital stay, and serious complications compared to open PC-RPLND. According to the study by Nicolai et al. [36], 12% of the patients developed treatment-associated complications after laparoscopic surgery. Based on the number of complications, laparoscopic surgery seems to be a viable option, but the results cannot stand alone without long-term data on recurrences. In the study by Calaway et al. [47], patients treated with robotic RPLND had recurrences in unusual locations and which were associated with a high treatment burden. In order to gain important knowledge on the subject laparoscopic and robotic surgery should be conducted as part of a clinical trial with clear inclusion criteria and long follow-up.

Complications after open surgery

Because testicular cancer patients have long survival expectations after chemotherapy and surgery, focus on the quality of life is important in the management of the disease. When reviewing studies on open surgery, both intraoperative and postoperative complications were more frequent with bilateral template compared to unilateral and resection of residual mass only. This was also the case in the largest study with follow-up >5 years by Gerdtsson et al. [19] where postoperative complications were more common after bilateral PC-RPLND compared to unilateral (45% vs 25%, $p = 0.001$) with Clavien–Dindo grade IIIb reported in 8.3% and 2.2%, respectively ($p = 0.009$).

Irrespective of the selected template, the histological diagnosis of the surgical specimen is necrosis in 40–50% of patients undergoing PC resection [19,23,24,27,30,31,48]. Thus, in a substantial proportion of patients, adjunctive surgery offered no additional therapeutic benefit. Moreover, in the study by Luz et al. [23], patients with fibrosis in the residual tumour were more likely to have surgical complications This emphasises that in this patient group the surgical intervention should be minimised as much as possible.

Prediction models

In order to identify patients who would benefit from surgery (teratoma or other viable tumour cells in the residual tumour), studies have tried to make various prediction models [49–52]. Aprikian et al. [49] and Herr et al. [50] used intraoperative frozen-section analysis of residual tumours. If the resected mass demonstrated necrosis or fibrosis a limited resection was performed, whereas a bilateral RPLND was used in the presence of mature teratoma or viable cancer. Vergouwe et al. [51] used six predictors (histology of the primary tumour, prechemotherapy serum levels of a-fetoprotein, human chorionic gonadotropin, lactate dehydrogenase, residual mass size measured on CT, and change in mass size) in trying to determine residual tumour histology before surgery. Baessler et al. [51] used CT radiomics-based machine learning classifier in order to predict histopathology of residual tumours. Common for these different prediction models is that they all fail to identify all patients in need of surgery. False-negative cases are hard to accept without data on long-term oncological outcomes.

Conclusions

Selection of the optimal post-chemotherapy surgical method for residual tumours in the retroperitoneum in NSGCTs is complicated by the lack of large studies with clear entry criteria and description of operative complications. When clear patient selection is made, recurrence rates for open bilateral PC-RPLND is comparable to open the unilateral template. The risk of recurrence inside the template appeared similar with open resection of residual mass only, unilateral template, and for the bilateral template. The risk of complications after the bilateral template is higher than after the unilateral template and residual mass only resection. Studies on laparoscopic and robotic surgery are characterised by being small with short follow-up time and these techniques should not be used outside clinical studies with clear patient selection. High-quality studies are required with larger

patient populations and longer follow-up to ensure the quality of surgery in this group of patients.

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