Platinum Priority – Testis Cancer

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Postchemotherapy Laparoscopic Retroperitoneal Lymph Node Dissection for Low-volume, Stage II, Nonseminomatous Germ Cell Tumor: First 100 Patients

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Abstract

Background: Retroperitoneal lymph node dissection (RPLND) is indicated after chemotherapy in case of radiologic incomplete remission or teratomatous elements in orchectomy specimens. Open RPLND is associated with considerable morbidity, but technical difficulty of postchemotherapy laparoscopic RPLND (L-RPLND) can be significant; therefore, literature concerning pc L-RPLND is sparse.

Objective: To evaluate feasibility and long-term oncologic outcome of postchemotherapy L-RPLND for clinical stage II disease at a single institution.

Design, setting, and participants: Records of patients with nonseminomatous germ cell tumor who underwent postchemotherapy L-RPLND between 1993 and 2010 were retrospectively reviewed. Unilateral template resection was used until a bilateral nerve-sparing approach was introduced in 2004. Follow-up investigations were performed at 3-mo intervals for the first 3 yr, every 6 mo for the next 2 yr, and annually thereafter.

Outcome measurements and statistical analysis: This was a descriptive analysis.

Results and limitations: The study cohort comprised 100 patients with stage II retroperitoneal disease (stage IIC: n=16; IIB: n=68; IIA with persisting tumor marker: n=16). Mean diameter of retroperitoneal masses before and after chemotherapy was 3.5 cm and 1.4 cm, respectively. Unilateral and bilateral templates were resected in 71 and 29 patients, respectively. Surgery was successfully completed in all but one patient, whose procedure was converted to open surgery due to bleeding. Mean operation time for unilateral and bilateral resection was 241 and 343 min, respectively. Mean blood loss was 84 ml. Postoperative complications were a large lymphocele in one patient and chylous ascites in another. Mean postoperative hospital stay was 3.9 d. L-RPLND specimens showed teratoma in 38 patients and active tumor in 2 patients. During a mean follow-up of 74 mo, one patient recurred. No recurrence was observed inside the applied surgical field. No patient died of tumor progression. After bilateral nerve-sparing postchemotherapy L-RPLND, 95.2% of patients reported antegrade ejaculation.

Conclusions: Postchemotherapy L-RPLND performed by experienced hands is feasible and associated with low morbidity and high oncologic efficacy.

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1. Introduction

Open retroperitoneal lymph node dissection (RPLND) is still frequently performed and represents a widely accepted diagnostic and therapeutic option in patients with non-seminomatous germ cell tumor (NSGCT). There is no doubt that RPLND is indicated after primary chemotherapy if remission is incomplete or teratomatous elements are detected in the orchietomy specimen [1]. Open RPLND is associated with considerable morbidity, particularly in terms of hospital stay and time to full recovery. Additionally, it requires a large incision that is cosmetically unfavorable in these mostly young patients. To overcome this, the laparoscopic approach to RPLND (L-RPLND) has evolved since 1992. It has repeatedly been criticized, however, for a small template in stage II patients and an unproven oncologic efficacy because, initially, all clinical stage I patients who were found to be lymph node positive at RPLND received additional chemotherapy. To overcome the potential drawback associated with templates, laparoscopic bilateral procedures have been developed, some of them including prospective identification and sparing of the sympathetic nerves [2,3].

On the other hand, technical difficulty of L-RPLND after chemotherapy can be significant; therefore, literature concerning postchemotherapy L-RPLND is very limited [4–9].

In the present retrospective study, we provide our single-institution experience of postchemotherapy L-RPLND with respect to surgical technique, and we evaluate the feasibility and, most importantly, the long-term oncologic outcome of this approach.

2. Materials and methods

2.1. Patients

After obtaining approval of the local ethical committee (study number UN3413), medical records of patients undergoing postchemotherapy RPLND due to a NSGCT at a single institution between March 1993 and December 2010 were retrospectively reviewed. Patients with bulky disease (large tumors encasing vena cava, aorta, or renal vessels) after chemotherapy were not approached laparoscopically at our department. As it is usually necessary to secure the vessels in these cases and to do minor or major vascular reconstruction during surgery, we believe these cases are not a good indication for laparoscopy. Patients who had undergone open RPLND and patients without chemotherapy before RPLND were excluded. In all patients, staging was performed according to the criteria recommended by the Workshop for Staging and Treatment of Testicular Cancer (Lugano 1979), including computed tomography (CT) of the thorax, abdomen, and pelvis, as well as determination of α-fetoprotein (AFP), beta human chorionic gonadotropin (βhCG), and lactate dehydrogenase (LDH). Another CT scan was performed 3 wk after cisplatin-based chemotherapy to assess patient response to the treatment. Whether or not the CT scan indicated complete or incomplete remission, patients treated by chemotherapy at our institution (n = 93) underwent L-RPLND 6 wk after chemotherapy to assess for residual active tumor or mature teratoma. An additional seven patients were transferred to our department for surgery because of persistent retroperitoneal mass after chemotherapy. To be included in the study, patients had to have normal tumor markers after first-line cisplatin-based chemotherapy.

Patient selection was not based on risk factors for histologic findings or body habitus. A 2-wk, preoperative, low-fat diet was continued for 3 wk after surgery because of reduced chylous ascites observed after implementation of this diet during the development of L-RPLND at our department [10]. Bowel preparation included a clear liquid diet and oral laxatives 1 d prior to surgery. Oral fluid intake started on the first day after surgery. Follow-up investigations were performed at 3-mo intervals over the first 3 yr, then every 6 mo until the end of the fifth year, and are planned to be done annually thereafter. Each follow-up includes a physical examination; complete blood count; blood chemistry with AFP, βhCG, and LDH levels; and imaging studies (ie, CT scan every third visit or chest radiography in combination with abdominal ultrasound). Admittedly, this scheme comprises short intervals and a frequent number of CT scans in patients with negative L-RPLND histology. Being increasingly aware of the potential risk of CT-related radiation, we changed our policy according to the current European Association of Urology guidelines at the beginning of 2012. Rate of antegrade ejaculation was interrogated by an urologist and an additional mailed questionnaire.

The surgical technique was performed as previously published for unilateral [10] and bilateral [3] templates; the unilateral template was used until the bilateral nerve-sparing approach was introduced in June 2004. Since that date, the unilateral approach has not been used. Hemostasis was obtained by clamping or sealing (LigaSure V; Covidien, Boulder, CO, USA). Statistical analysis was performed using descriptive analysis.

3. Results

Exactly 100 patients (mean age: 29.6 y; range: 11.4–52.0 y) with stage II retroperitoneal disease and who fulfilled the inclusion criteria were identified and included in this series. Of these, 16 had clinical stage IIC disease, 68 had stage IIB, and 16 had stage IIA (in combination with persisting elevated or rising tumor marker levels for stage IIA) at initial staging. Orchiectomy specimens yielded teratomatous elements in 36 patients. There was no patient selection concerning body habitus.

Prior to chemotherapy, the mean AFP level was 342 ng/ml (range: 1–10 000 ng/ml; median: 21 ng/ml), the mean βhCG level was 360 mU/ml (range: 0–11 890 mU/ml; median: 19 mU/ml), and the mean LDH level was 289 U/l (range: 127–850 U/l; median: 228 U/l). After cisplatin-based chemotherapy and before RPLND, all tumor marker levels were within normal limits.

The measurements of retroperitoneal masses before and after chemotherapy are listed in Table 1. L-RPLND was performed approximately 4–6 wk after chemotherapy. Two patients had a history of prior retroperitoneal surgery.

A unilateral template was resected in 71 patients (right side: 34; left side: 37), a bilateral template was resected in 29 patients; prospective identification and sparing of contralateral (depending on tumor location) sympathetic nerves was performed in 26 of these patients. Laparoscopic surgery was successfully completed in all but one patient, in whom conversion to open surgery was necessary due to bleeding from the posterior surface of the vena cava. This was also the only major intraoperative complication. No minor intraoperative complication occurred except eventual bleedings from lumbar vessels or vena cava that could all be managed laparoscopically by using bipolar forceps or endoscopic stapler devices (Fig. 1).
postchemotherapy RPLND and simultaneous resection of left, supraclavicular, residual lymph nodes. The latter complication included ligation of the thoracic duct; chylous ascites was refractory to conservative approaches and a peritoneal venous shunt was placed. The shunt was removed after 1 yr without recurrence of chylous ascites.

During histologic workup of the L-RPLND specimens, necrosis or fibrosis was seen in 60 patients and teratoma was found in 38 patients; small foci of active tumor (embryonal carcinoma) were found in two postchemotherapy L-RPLND specimens and both patients received additional chemotherapy (although surgery alone might have been curative in both patients and the use of additional chemotherapy has to be questioned in this setting).

During the mean follow-up of 74 mo (median: 59 mo; range: 1–222 mo), only one patient had recurrent disease. This was in a patient with left-sided stage IIC disease (prechemotherapy para-aortal lymph node metastasis only) managed by a unilateral, left-sided, postchemotherapy L-RPLND. The retroperitoneal recurrence was observed behind the vena cava outside of the initial template, and the patient was cured by additional chemotherapy and open RPLND clearing the complete right template. Most important, no retroperitoneal recurrence was observed inside the applied surgical field. All other patients have remained free of relapse; no patient died of tumor progression.

In unilateral template patients, antegrade ejaculation was not disturbed. After bilateral postchemotherapy L-RPLND, 20 patients reported antegrade ejaculation and 4 patients reported no antegrade ejaculation, including 3 in whom preservation of sympathetic nerve fibers was not performed for oncologic reasons. Ejaculatory function of another five patients was not documented because they were followed elsewhere.

### 4. Discussion

RPLND is indicated after primary chemotherapy if remission is incomplete, a marker-negative growing lesion is present, or teratomatous elements are detected in the orchietomy specimen (approximately 82% of these patients present with teratoma in the residual mass in the retroperitoneum) [1]. For the individual patient, postchemotherapy RPLND offers a staging benefit because active tumors are discovered and supplemental chemotherapy can be applied, and a therapeutic benefit, as any residual chemotherapy-resistant tumor (eg, teratoma, sarcoma) is removed surgically (in the present study, teratoma and active tumor were found in 38% and 2% of patients, respectively). Unfortunately, no single parameter or combination of parameters is reliable enough

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**Table 1 – Tumor measurements before and after chemotherapy**

<table>
<thead>
<tr>
<th>Tumor diameter</th>
<th>Before chemotherapy</th>
<th>After chemotherapy</th>
<th>Patients with residual disease &lt; 1 cm, no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Largest diameter</td>
<td>3.5 (1–20)</td>
<td>1.4 (0.3–10)</td>
<td>51</td>
</tr>
<tr>
<td>Largest transverse diameter</td>
<td>2.3 (1–6)</td>
<td>1.0 (0.3–4)</td>
<td>57</td>
</tr>
</tbody>
</table>

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to rule out residual retroperitoneal tumor. Approximately 20% of patients assumed to have necrosis or fibrosis actually harbor either teratoma or viable CCT. For this reason, it is our practice to perform postchemotherapy RPLND in all patients regardless of their postchemotherapy CT findings and their risk of teratomatous elements in the retroperitoneum; we are aware of that this does not represent a uniformly accepted approach.

The laparoscopic approach to RPLND is still very controversial; no prospective randomized studies exist and intermediate and long-term oncologic data are sparse. The reason for implementing laparoscopy to the armamentarium of testis cancer treatment was the intent to improve quality of life (QoL) and to reduce side effects in these very young cancer patients.

There are some data in the literature suggesting improved QoL after the laparoscopic procedure compared to open surgery: Hobisch et al. [11] and Poulakis et al. [12] report that L-RPLND patients had a significantly shorter hospitalization, increased QoL scores, and a faster return to normal activities than open-RPLND patients. We believe that, compared to open surgery, this benefit outweighs the admittedly longer operation time, which is an obvious disadvantage of the laparoscopic approach. Some authors have stated that the differences in QoL might be less pronounced when modern open-RPLND series are taken into account [13].

It is essential that the oncologic efficacy of RPLND must not be compromised by strategies aimed at reducing its short- and long-term morbidity. In this regard, anejaculation is the most common long-term morbidity of RPLND for low-volume metastatic disease. Facing the fact that many patients with testicular cancer have not yet fathered a child at the time they are diagnosed with testis cancer, nerve-sparing techniques have been developed to prospectively identify and spare the sympathetic postganglionic fibers, and other authors have proposed concepts for modified template dissection [14–17]. While a bilateral resection is considered standard, the use of modified templates, originally developed for stage I disease, in a postchemotherapy setting has been controversial and is often considered inappropriate [18–20]. Some reports even propose resection of residual masses only [21–26], which represents an inappropriate approach, in our opinion, because recurrences within the boundaries of a full bilateral or even a modified RPLND have been described in most of these series. This issue was addressed by Carver et al. [20], who reported 7% to 32% extratemplate retroperitoneal disease, depending on the boundaries of the modified template used. In our series with postchemotherapy L-RPLND, we experienced one recurrence within the boundaries of a full bilateral resection; in this patient with stage IIC disease, only a unilateral template (including the complete extent of the prechemotherapeutic mass) had been cleared of lymphatic nodes. We subsequently stopped performing postchemotherapy L-RPLND in larger residual tumors until we were capable of performing a laparoscopic bilateral (nerve-sparing, if indicated) procedure. With this bilateral nerve-sparing L-RPLND, we are now able to combine the advantages of the laparoscopic approach with the oncologic efficacy of a full bilateral resection, still being able to maintain a high rate of antegrade ejaculation. The observed antegrade ejaculation rate among our 21 postchemotherapy patients with performed nerve sparing and available data on functional follow-up was 95.2%, which compares very well to published data from open series [27,28].

Still, the laparoscopic approach is a challenging one. Literature concerning postchemotherapy L-RPLND comprise smaller series reporting significant difficulty compared to treatment in patients with stage I disease. A high rate of conversions (Table 2) and minor, but also severe, intra- and perioperative complications (e.g., lymphoceles, chylous ascites, vascular, bowel lesions) in up to 43.8% of patients have been described [4–6,8]. In contrast to these publications, we did not encounter increased intraoperative complications in postchemotherapy patients, although it has to be noted that dissection was more difficult in some patients with severe desmoplastic reaction after chemotherapy. We believe that this low complication rate is due to long experience with L-RPLND at our department and the limited number of surgeons involved.

From the oncologic view, the present results are encouraging because an excellent cure rate and a very low recurrence rate (1%) were achieved. Therefore, it appears that the bar set by the open approach can be reached.

As a matter of principle, it is critical for an excellent oncologic outcome that patients are managed at centers of excellence that have specific expertise in the management of advanced GCTs and postchemotherapy RPLND. Integrated 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. Quoting the data of improved QoL after the laparoscopic approach, we believe that L-RPLND has a role in low-volume stage II disease after chemotherapy.

### 5. Conclusions

In postchemotherapy NSGCT patients with residual masses, L-RPLND is feasible and associated with low morbidity if performed by experienced hands. The oncologic efficacy of this approach is promising and similar to the results of open series.

**Author contributions:** Hannes Steiner had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Steiner, Pichler, Peschel.

**Acquisition of data:** Steiner, Pichler, Stoehr, Leonhartsberger.

**Analysis and interpretation of data:** Steiner, Pichler, Stoehr, Leonhartsberger.

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Table 2 – Surgery conversion rates reported by different studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Conversion rate</th>
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<tbody>
<tr>
<td>Rassweiler et al., 1996 [6]</td>
<td>7 of 9 patients</td>
</tr>
<tr>
<td>Palese et al., 2002 [5]</td>
<td>2 of 7 patients</td>
</tr>
<tr>
<td>Pernpomkosal et al., 2007 [4]</td>
<td>2 of 16 patients</td>
</tr>
<tr>
<td>Calestroupat et al., 2009 [8]</td>
<td>3 of 26 patients</td>
</tr>
<tr>
<td>Present study</td>
<td>1 of 100 patients</td>
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</tbody>
</table>
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Critical revision of the manuscript for important intellectual content: Steiner, Pichler.

Statistical analysis: Steiner, Pichler.

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Supervision: Steiner.

Other (specify): Peschel.

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