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SURGICAL TECHNIQUE

Primary laparoscopic retroperitoneal lymph node dissection for clinical stage I nonseminomatous germ-cell testis tumor☆

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KEYWORDS
Testis cancer;
Non-seminomatous germ cell neoplasia;
Laparoscopy;
Retroperitoneal Lymph node dissection

Abstract

Introduction: This report is intended to retrospectively assess cancer control and morbidity of primary laparoscopic reproperitoneal lymphadenectomy (L-RPLND) in patients with clinical Stage I non seminomatous germ cell tumour (NSGCT).

Material and methods: One hundred and sixty-four patients with clinical Stage I NSGCT underwent primary diagnostic LRPLND between 1993 and 2006. Patients were operated unilaterally limiting the dissection to templates. Kaplan Meier curves were generated estimating time to recurrence.

Results: Of the 164 patients, 82 (48%) had embryonal components and 35 (20%) lymphovascular invasion in the orchiectomy specimen. The median (IQR) age, operative time, length of hospital stay, blood loss and number of lymph nodes retrieved was 28 years (24-33), 135 minutes. (120- 180), 48 hours (24-48), 50 cc (20-100) and 14 (10-18) nodes, respectively. All patients had negative serum markers preoperatively.

Presence of lymph node metastasis was identified in 32 (19.5%) patients. Follow-up was available in 15 of these. Fourteen received adjuvant chemotherapy and 2 of them had recurrence at 3 and 64 months. Absence of lymph node metastasis was diagnosed in 132 (80.5%) patients. Follow-up was available in 80 of these. Among them 7 recurred (5 retroperitoneum, 2 lung), one of them 33 months after L-RPLND. Median follow-up for patients without recurrence was 14 months (IQR:4-35). The cumulative 3-year recurrence free rate was 82% (95%CI: 64-91). Seventeen (10%) of 164 patients had intra or perioperative complications.

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Conclusions: This is the largest series of L-RPLND performed in a single institution. Both morbidity and oncologic safety of this technique needs to be prospectively evaluated in randomized trials.

PALABRAS CLAVE
Cáncer de testículo;
Neoplasia no seminomatosa de células germinales;
Laparoscopia;
Disección retroperitoneal de ganglios linfáticos

Linfadenectomía retroperitoneal laparoscópica primaria para el tumor testicular de células germinales no seminomatoso en estadio clínico I

Resumen

Introducción: El propósito de este informe es evaluar retrospectivamente el seguimiento de cáncer y la mortalidad en linfadenectomía retroperitoneal laparoscópica (LRL) primaria en pacientes con tumor de células germinales no seminomatoso (TCGNS) es estadio clínico I.
Materiales y métodos: Ciento sesenta y cuatro pacientes con TCGNS en estadio clínico I se sometieron a LRL diagnóstica primaria entre 1993 y 2006. Los pacientes fueron operados unilateralmente limitando la disección a áreas. Se generaron curvas Kaplan Meier estimando el período de recurrencia.
Resultados: De los 164 pacientes 82 (48%) tenían componentes embrionarios y 35 (20%) invasión linfovascular en la muestra de orquiectomía. La edad media (RI), tiempo operatorio, estancia en el hospital, pérdida de sangre y número de ganglios linfáticos recuperados fueron 28 años (24-33), 135 minutos (120-180), 48 horas (24-48), 50 cc (20-100) y 14 (10-18) ganglios linfáticos, respectivamente. Todos los pacientes tenían marcador sérico negativo antes de la intervención. La presencia de metástasis en ganglios linfáticos se identificó en 32 (19,5%) pacientes. Se hizo un seguimiento en 15 de ellos. Catorce recibieron quimioterapia adyuvante y dos de ellos sufrieron recurrencia a los 3 y 64 meses. La ausencia de metástasis en ganglios linfáticos se diagnosticó en 132 (80,5%) pacientes. Se hizo un seguimiento en 80 de ellos. Entre ellos 7 sufrieron recurrencia (5 retroperitoneo, 2 pulmonar), uno de ellos a los 33 meses de la LRL. El seguimiento medio de los pacientes sin recurrencia fue de 14 meses (RI: 4-35). La tasa acumulada de supervivencia libre de enfermedad a los tres años fue del 82% (IC 95%: 64-91). Diecisiete de 164 (10%) padecieron complicaciones intra o perioperatorias.
Conclusiones: Ésta es la serie más larga de LRL llevada a cabo en una única institución. Tanto la mortalidad como la seguridad oncológica de esta técnica deben ser evaluadas prospectivamente en ensayos aleatorios.

Introduction

The improved cure rates observed in patients with testis cancer have been based on the joint efforts of medical and surgical therapies.[1] Although surveillance or chemotherapy regimens are some of the possible therapeutic options for stage I nonseminomatous germ cell testicular tumors (NSGCT), open retroperitoneal lymph node dissection (O-RPLND) remains the most reliable method for detecting lymph node metastasis in this setting. However, perioperative morbidity and invasiveness are concerning issues that have been addressed by several authors.[2,3]

Laparoscopic RPNLD (L-RPLND) has been proved feasible with low complication rates in highly experienced hands.[4-6] Nonetheless, there is controversy regarding its therapeutic efficacy as an alternative to the open approach for the management of NSGCT.[4,5] Intermediate and long term oncologic results are lacking in the literature. Our objective was to assess retrospectively the cancer control and morbidity of primary L-RPLND performed in patients with clinical Stage I NSGCT over a 13-year period.

Material and methods

Patients

Clinical and pathologic data was prospectively obtained from 164 patients with clinical Stage I NSGCT undergoing primary L-RPLND between 1993 and 2006. Clinical Stage I NSGCT was defined as tumor limited to the testis in patients with normal computed tomography scans of the thorax, abdomen and pelvis and normalized serum tumor markers after the inguinal orchiectomy.

The L-RPLND was performed with diagnostic intent following a modified template dissection. Neither bilateral template dissections nor intraoperative lymph node frozen section was routinely performed. Patients with positive lymph nodes in the final pathology examination

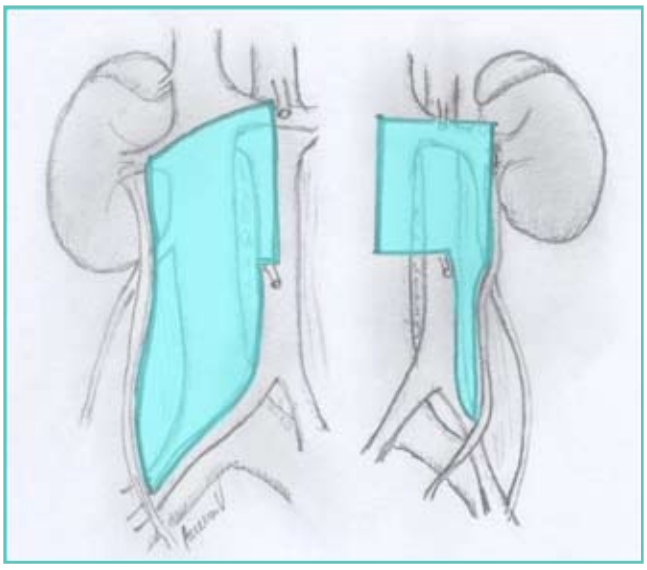

Figure 1 Modified templates with diagnostic intention in L-RPLND.

were treated with two cycles of adjuvant chemotherapy composed of Bleomycin, Etoposide, Cisplatin (BEP).

Surgical technique

Preoperative preparation and positioning

All patients received indication for liquid based diet the day previous the surgical procedure. A fleet enema was also administered before admission to hospital. Once under general anesthesia the patient was adequately positioned, with gastric and bladder drainage. Patients were placed in either right or left lateral decubitus position depending on the side indicated for the lymph dissection.

Operatory procedure

Pneumoperitoneum was created with Veress technique and intra-abdominal pressure is set at 15 mmHg. Port positioning varies with surgical side. As it has been demonstrated, the preponderance of early disease in the retroperitoneum metastasis for testis cancer lands ipsilateral and infrahilar.[7] The extent of the lymph node dissection in present series followed the templates described by Weissbach y Boedefeld,[8] with the sole modification being the inclusion of upper interaortocaval and precaval space on the left side (fig. 1). Sparing of the nerve fibers responsible for ejaculation was attempted in all cases. All procedures were performed with nerve sparing intention and during part of our experience we did not section the lumbar vessels to dissect underneath the great vessels with the believe that primary lymphatic metastatic spread in testis carcinoma occurs ventral to the lumbar vessels, and for diagnostic procedures the removal of this lymphatic tissue would not be necessary as it has been presented by Holtl et al.[9] More recently we are in the process of modifying our technique to do a therapeutic intent.

Right sided L-RPLND (fig. 2A). The right renal hilum delineates the upper border of the dissection and the caudal anatomical landmark for the template is the ureter-iliac vessels cross. To begin the dissection the right colon is extensively mobilized and also the duodenum is mobilized through a Kocher's maneuver. The flank position and the operating table tilt allow viscera to fall out the surgical field. Once the retroperitoneum is exposed, right iliac artery and ureter are identified, as well as the spermatic vessels, vena cava, aorta and renal hilum; caudal to cranial, dissections starts in the iliac bifurcation and goes upwards to the right renal artery. Lymphatic tissue is incised and dissected off the vena cava in its anterior surface and bilaterally. The interaortacaval space is carefully dissected with lumbar veins preservation. Surgical specimen includes paracaval, precaval and inter-aorta-caval nodes.

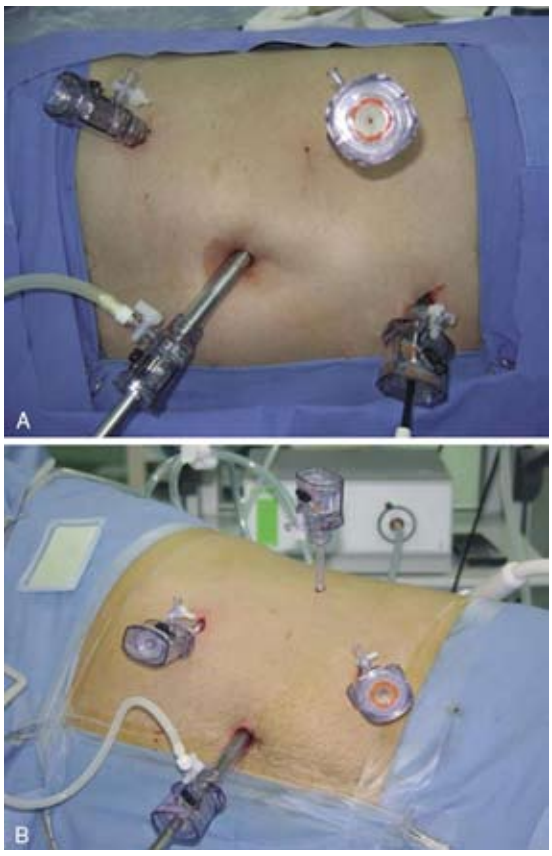

Figure 2 Trocar placement for right (A) and left (B) side L-RPLND.

Left sided L-RPLND (fig. 2B). Left colon is reflected medially. Dissection extents caudal to cranial from left common iliac artery upwards to the left renal vessels. Surgical specimen is limited to pre-aortic, para-aortic and the upper inter-aorta-caval lymphatic tissue, including nodes located inferiorly to the left renal vein. An extensive colon mobilization is essential at either side, as the first step of the procedure. We always perform dissection and resection of the spermatic cord, down at the area of the internal ring, which we consider an essential part of the technique as it was described by Chang et al.[10] In our series we have experienced three cord metastases and therefore we pay special attention to this part of the operation. Once

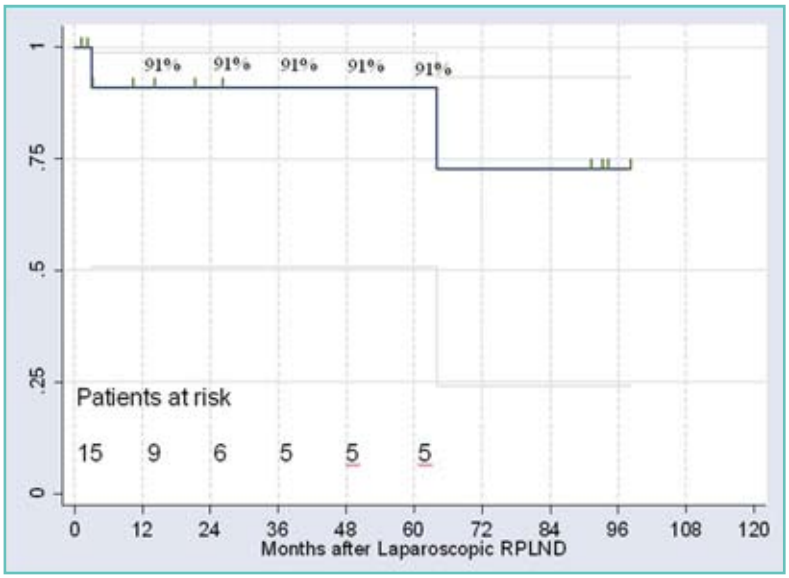

Figure 3 Recurrence-free survival for patients with positive nodes treated with L-RPLND and adjuvant chemotherapy.

the procedure is finished, surgical specimen is retrieved in an Endobag (Ethicon, Endosurgery).

Statistical analysis

Medians and interquartile (IQR) ranges (percentile 25-75) were estimated for each domain. Kaplan-Meier curves were generated estimating time to relapse. Statistical analyses were conducted using Stata 8.2 (Stata Corporation, College Station, TX). Relapse was defined as disease recurrence manifested by the presence of previously inexistent lymph nodes on imaging studies or by increase in serum tumor markers. We define perioperative complication as any medical or surgical adverse event taking place during or up to 30 days after the operation.

Results

A total of 164 patients with the diagnosis of non seminomatous germ cell carcinoma and negative serum markers were operated by laparoscopic retroperitoneal lymph node dissection. Of the 164 patients, 82 (48%) had any embryonal component in the orchiectomy specimen and 35 (20%) had lymphovascular invasion. The median (IQR) age, operative time, length of hospital stay, blood loss and number of lymph nodes retrieved was 28 (24-33), years 135 (120-180) minutes, 48 (24-48) hours, 50 (20- 100) cc and 14 (10-18) nodes extracted.

Thirty-two patients (19.5%) had metastasis to the lymph nodes. Follow-up was available in 15 of these 32 patients. Fourteen received adjuvant chemotherapy, 2 of whom suffered recurrence at 3 and 64 months (fig. 3). Both recurred in the retroperitoneum, with one also recurring in the port sites 3 months after surgery. Lymph nodes were negative in 132 (80.5%) patients. Follow-up was available in 80 of them; 7 of which had recurrence, one of them 33 months after L-RPLND. Median follow-up for patients without recurrence was 14 (IQR 4-35) months. Cumulative 3-year recurrence free rate for this group was 82% (95%CI 64-91) (fig. 4). Retroperitoneum was the site of 5 recurrences, one of them also associated with mediastinal disease, and two in the lungs.

Of the 164 patients, 17 (10%) had perioperative complications including injuries of vena cava (3), iliac artery (1), duodenum (1), lumbar vein (3), spermatic vein (1), lumbar artery (1), spermatic artery (1), lymphocele (3), postoperative hematoma (1), pulmonary edema (1) and port site recurrence (1). Only 4 (2.4%) patients required conversion to open surgery. Two patients (1.2%) needed blood transfusion. Retrograde ejaculation was registered in 3 (1.8%) patients. No perioperative deaths occurred.

Discussion

The retroperitoneum represents the first, and sometimes the only echelon in testis carcinoma spreading. Primary RPLND has the advantage of a minutely precise and effective pathological staging in germ cell tumors, and what is more it could be a curative procedure in 70% of the patients with stage B1 disease.[11] Besides, clinical understaging, significant relapse rate in surveillance protocols, and the presence of teratoma or viable carcinoma in resected tissue from patients exposed to chemoteraphy protocols constitute the reasons to prefer surgery over other therapeutical options in testis cancer.[12,]

Since its original description, RPLND has been modified in order to diminish morbidity while keeping the oncological standards required. Lessons learned after years of laparoscopic surgery and the advances in laparoscopic reconstructive techniques allowed us to attempt even more demanding procedures today. L-RPLND has emerged as a logical option for testis cancer surgery as it can be offered for management of clinical stage I NSGC testis cancer and low-volume retroperitoneal stage II disease.[7,9]

Figure 4 Recurrence-free survival for patients with negative nodes treated with L-RPLND alone.

There is no discussion that surgical management of retroperitoneal disease in testis carcinoma has changed since the early application of laparoscopy for testis cancer. Nelson et al published a retrospective review of 29 patients with clinical Stage I NSGCT who underwent transperitoneal L-RPLND, this series was performed by a single surgeon using a modified template in both right and left side. Positive retroperitoneal nodes were detected in 41% of patients. Among those with negative nodes (59%) only two patients relapsed, one in the chest and another biochemically. No evidence of disease recurrence was found in the retroperitoneum at a mean follow up of 65 months. Complications in this series included lymphocele in one patient and flank compartment syndrome in another one.[8] Bhayani et al reviewed the long term outcome of their series to verify that lymph nodes were negative in 17 of 29 patients. Of these 17 patients, 15 did not recur and were free of disease with 5.8 years of follow-up. Two patients had recurrence, one in the chest and another biochemically, and both were free of disease after chemotherapy. Twelve of 29 patients had lymph nodes with metastatic testicular cancer. Ten of these patients received adjuvant chemotherapy and were free of disease with 6.3 years of follow-up. One patient had a biochemical recurrence after positive RPLND and was salvaged with chemotherapy. One patient was observed after positive RPLND and was free of disease with 4.9 years of follow-up. The only long-term complication was retrograde ejaculation in a patient.[9]

In a series of 125 patients who underwent laparoscopic RPLND for NSGCT presented by Janetchek et al, 76 patients with stage I disease were treated with an operative time of 219 min, once the learning curve had been achieved. Only two patients were converted in this series and minor postoperative complications included asymptomatic lymphocele in 7 patients and chylous ascites in 6 cases. Mean postoperative hospital stay was 3.3 days. Mean follow-up for stage I group was 46 months. A false negative single retroperitoneal recurrence was observed and the rest of the patients remained disease free.[13]

The updated series of the Innsbruck group reported 162 patients with testicular cancer. Among them, 103 patients corresponded to clinical stage I. These authors also compared their data with the worldwide experience in L-RPLND. Oncologic outcomes were evaluated with a mean follow-up of 62 months. Only three conversions to open RPLND in clinical stage I were reported. The mean operative time was 217 minutes, mean blood loss was 144 mL and hospital stay was 3.6 days. Two retroperitoneal relapses (1.2%) and four distant relapses (2.5%) were observed during follow-up.[14]

An interesting study recently presented by Poulakis et al compared twenty-one patients with NSGCT who underwent transperitoneal L-RPLND with 29 patients who underwent O-RPLND. The mean follow-up time was 14 and 26 months for L-RPLND and O-RPLND groups, respectively. No major perioperative complications were verified. Nonetheless, early and late minor postoperative complications were significantly higher in the O-RPLND. L-RPLND patients showed significantly shorter hospitalization, greater quality of life scores, and a faster return to daily life.[15]

Abdel-Azis et al compared their experience with RPLND based on 28 patients who underwent O-RPLND (6 patients) or L-RPLND (22 patients) for clinical stage I NSGCT. Modified template dissection was employed in this series. The mean follow-up was similar in the two groups. The mean operative time was comparable (313 minutes for L-RPLND and 284 minutes for O-RPLND). The laparoscopic group had a significant shorter hospitalization (1.2 vs 8.5 days). A number of 33 vs. 17 lymph nodes were removed with open and laparoscopic, respectively. They have reported a single recurrence outside the modified template for both laparoscopic and open groups. In this series, L-RPLND was associated with less blood loss and a shorter hospital stay but O-RPLND showed a sustainable lymph-node yield.[16]

Herein, we have treated an important number of high risk patients (48% embryonal component and 20% lymphovascular invasion) with a final pathological specimen report of 132 patients being lymph node negative and 32 patients positive for testicular cancer metastases in the retroperitoneum. The median operative time of present series is 135 (120-180) minutes with a blood loss of 50 (20-100) cc, and this is encouraging when you take a look at the literature regarding L-RPLND. It must be clear that these numbers represent a long-term skill development in the technique.

Lymph nodes were negative in 80.5% of the patients and follow-up was available in 80 of these cases. Seven presented with recurrence, what represents an objective 8.7% recurrence rate in the series. In the literature an overall recurrence of less than 5% had been reported for laparoscopic RPLND.[17] The 7 patients with negative lymph nodes on final pathology who presented recurrence had a median number of lymph nodes of 16 (5-20) in the retroperitoneal specimen and all of them showed high-risk factors in the orchiectomy specimen of the primary tumor. This is a very important factor to objectively tailor therapeutic decisions. We have significant high-risk population in the present series and we believe this could explain our recurrence rate.

Our complication rate of 10 percent most often includes intraoperative lesions that in this operation almost always indicated conversion, as we experienced in 4 patients. The main limitation of our study resides in a high number of patients lost to follow-up, and that implies our recurrence-free rate should be interpreted with great care. The wide variety of cultural differences of our population might explain, at least in part, the loss for follow-up in many of them. This is another reason because of which surveillance is not easy to recommend as a therapeutic option in our population.

Another probable weak point in our series is how complications are reported. We do not consider L-RPLND a morbid procedure, and that is our main argument to perform it. However, despite the fact that our numbers conquered with the complications reported in the literature, we have realized that higher details are missing regarding patients´ discomfort and specific symptoms recording in the perioperative period.

Of course there is a great deal of controversy regarding L-RPLND. The work of Eggener and colleagues[18] strongly raises several issues about proper surgical treatment for clinical stage I NSGCT. This timely article must encourage laparoscopic groups to legitimate L-RPLND in terms of solid results reporting in cancer control and complications. Nielsen et al presented a retrospective multi-institutional study of 120 patients with NSGCT treated with L-RPLND. Median follow-up for the patients with pathologic Stage I (74 cases, 62%) was 28.5 months and 29 months (range 12-108) for those with pathologic Stage II (46 cases, 38%). No patient presented recurrence in this series.[19]

Conclusions

L-RPLND should be performed by highly specialized surgeons. Its morbidity and oncologic safety needs to be prospectively evaluated in randomized trials; even though there have been great efforts worldwide, not only to verify L-RPLND feasibility but also to comprehensibly validate its oncologic results. L-RPLND is today a reasonable option for the treatment of low stage testis NSGC neoplasia.

Conflicts of interest

The authors declare that they have no conflict of interest.

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