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Implications of extraperitoneal paraaortic lymphadenectomy to the left renal vein in locally advanced cervical cancer. A Spanish multicenter study

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Abstract

Objective. Paraaortic lymph node involvement is an important prognostic factor in locally advanced cervical cancer (LACC) but anatomic limit of aortic lymphadenectomy is controversial. We assessed the impact of extraperitoneal paraaortic lymphadenectomy up to the left renal vein in patients with LACC undergoing pretherapeutic staging.

Methods. Retrospective multicenter study of patients with LACC stages FIGO 2009 IB2 and IIA2-IVA treated in 10 Spanish reference hospitals in gynecologic oncology between 2000-2016. Sites of metastatic paraaortic lymph nodes above or below the inferior mesenteric artery (IMA) were evaluated. Procedural-related intraoperative and early and late complications were assessed.

Results. We included 634 patients undergoing paraaortic lymphadenectomy, in 616 (97.2%) of which the left renal vein was the upper limit of dissection (laparoscopy 592, robotic-assisted 24). The median surgical time was 150 min (interquartile range, IQR 120-180), blood loss 50 mL (range 20-80), and length of stay 2 days (range 2-3).

Metastatic paraaortic involvement was found in 114 patients (18.5%), with infrarenal metastases in 73 (64%) of them. There were 11 patients (9.6%) with infrarenal metastases only, whereas in the remaining 62 (54.4%) concomitant infrarenal and inframesenteric metastases were observed. Intraoperative, early, and late postoperative complications occurred in 3.6%, 7.0%, and 4.5% of patients, respectively.

Conclusions. In this study of patients with LACC undergoing surgical staging, paraaortic lymphadenectomy up to the left renal vein detected skip or isolated infrarenal metastasis in 9.6% of the patients, with an acceptable surgical morbidity.

Keywords: Locally advanced cervical cancer, laparoscopic extraperitoneal paraaortic staging, left renal vein, inferior mesenteric artery, postoperative complications.

1. Introduction

Paraaortic lymph node involvement in locally advanced cervical cancer (LACC) has been reported in 18% to 37% of patients [1,2] and is a significant predictor of recurrence and death [3]. The debate about the most effective way (imaging or surgical) to assess paraaortic lymph node status is ongoing [4,5]. Determining paraaortic lymph node metastasis is of paramount importance to personalize the fields of radiation and to tailor chemoradiotherapy or other approaches with immunotherapy or treatment intensification [6]. Minimally invasive paraaortic staging surgery unveils the false-negative results of PET-CT imaging bug also may provide a therapeutic impact for patients with paraaortic nodal metastasis < 5 mm [7]. Moreover, lymph node density is a prognostic parameter in lymph-node positive LACC patients [8].

The limit of surgical dissection of paraaortic lymphadenectomy below or above the inferior mesenteric artery (IMA) [9] is still a matter of debate. Recent clinical guidelines of the European Society of Gynaecological Oncology [10], the National Comprehensive Cancer Network (NCCN) [11], and the Spanish Onco-guideline [12] recommend that paraaortic lymphadenectomy for surgical staging should be performed at least up to the IMA in LACC before chemoradiotherapy and brachytherapy, and only the NCCN guideline [11] suggests the possibility that cephalad extent of dissection can be modified based on clinical and radiological findings [11]. It has been shown that LACC has a similar pattern of aortic spread as some patients with endometrial and ovarian cancer, by bypassing the common iliac and inframesenteric nodes and affecting only the infrarenal nodes [13-16]. Although the usual lymphatic drainage takes place towards the pelvic nodes through the parametrium, there may be

accessory pathways, posterior cervical lymph trunk to the paraaortic lymph nodes [16] or via the ovarian lymphatic channels using the infundibulopelvic pathway directly to the infrarenal nodal group [17], which could explain the theory of skip metastasis in the infrarenal area without affecting the inframesenteric region.

The anatomical limit of the IMA in paraaortic staging for LACC is based on retrospective studies reporting a low rate of skipped metastases above the IMA and the potential additional surgical morbidity of extended dissection up to the infrarenal nodal basin in patients with negative preoperative PET-CT results [17-19].

We hypothesized that in patients with LACC, minimally invasive extraperitoneal paraaortic infrarenal lymphadenectomy may allow identifying a number of patients with isolated infrarenal nodal involvement, as well as patients with both infrarenal and inframesenteric metastatic lymph nodes, with minimal surgical morbidity. This study was conducted to assess the site of metastatic paraaortic involvement above or below the IMA and to determine the impact of paraaortic lymphadenectomy up to the left renal vein on surgical morbidity.

2. Materials and methods

2.1. Study design and participants

This was a multicenter retrospective study of patients with LACC, FIGO (2009) stages IB2 and IIA2-IVA [20] undergoing minimally invasive staging extraperitoneal paraaortic lymphadenectomy in 10 Spanish reference hospitals in gynecologic oncology between August 2000 and December 2016. Inclusion criteria were as follows: a) histological diagnosis of squamous, adenosquamous, adenocarcinoma, or undifferentiated carcinoma of the cervix; b) presurgical assessment of tumor extension and lymph node

involvement with MRI and/or PET-CT regardless of positive or negative nodal status (MRI was the gold standard in the 2000s and PET-CT incorporated into clinical practice since 2009); c) surgical staging with extraperitoneal paraaortic lymphadenectomy up to the left renal vein performed through minimally invasive surgery (conventional laparoscopy or robotic-assisted); and d) treatment with primary chemoradiotherapy (pelvic irradiation field). Exclusion criteria were as follows: a) age over 80 years; b) Eastern Cooperative Oncology Group (ECOG) performance status ≥ 2; c) paraaortic lymphadenectomy limited to the IMA; d) prior radiotherapy, neoadjuvant chemotherapy, and retroperitoneal surgery; e) peritoneal carcinomatosis; f) patients in whom a complete paraaortic lymphadenectomy could not be performed; and g) patients lost to follow-up during the first 2 years.

2.2. Ethics

The study was approved by the Clinical Research Ethics Committee of Hospital Universitari Vall d'Hebron (study protocol 159/2015) as the reference center and by the Institutional Review Boards of the participating hospitals. The study was carried out in accordance with the Declaration of Helsinki (7th revision) and the principles of Good Clinical Practice. Written informed consent was obtained from all who were alive at the beginning of the study.

2.3. Paraaortic lymph node surgical staging

Extraperitoneal paraaortic lymphadenectomy was performed laparoscopically or robotic-assisted with the da Vinci surgical system (Intuitive Inc., Sunnyvale, CA, USA) as previously described [21-23]. All patients underwent transumbilical diagnostic

laparoscopy for evaluation of the peritoneal cavity and after excluding peritoneal metastatic disease, extraperitoneal paraaortic lymphadenectomy through the patient's left side was performed. Lymph node bearing tissue from the aortocaval space, vena cava, and left paraaortic territories were completely removed up to the left renal vein and to the psoas muscle laterally. When all these lymph node groups were excised, the procedure was considered a complete lymphadenectomy. Pelvic lymph node dissection was not part of the routine procedure, as pelvic nodes are included in the radiation field but in some centers, their excision was selectively performed in patients in whom enlarged pelvic lymph nodes were suspected by MRI and/or PET-CT. In these cases, a pelvic lymph node debulking by either extraperitoneal or transperitoneal laparoscopy was performed. All excised lymph nodes were placed without fragmentation in endoscopic bags. The infrarenal (above IMA) and inframesenteric (below the IMA and up to primitive iliac vessels) nodes were submitted separately for histopathologic examination. The lymph nodes were carefully separated from adipose tissue by the pathologist, divided in multiple sections, and embedded in paraffin blocks. Sections of 5 µm were stained with routine hematoxylin eosin. Immunohistochemistry staining was required in one instance to identify nodal metastasis.

2.4. Outcomes

Intraoperative complications were recorded. Postoperative complications were graded using the Clavien-Dindo classification system [24] and divided into early (≤ 30 days) and late (> 30 days) complications. Major complications were defined as grade IIIb (any complication requiring surgery under general anesthesia) or more. Delayed initiation

of primary treatment was defined as the time interval from surgery to start chemoradiotherapy longer than expected. A delay in starting chemoradiotherapy was considered longer than 45 days or when radiation simulation has been already performed to initiate treatment and as a result of complications from surgery, radiotherapy could not be started.

Disease free survival (DFS) was defined as time from end of treatment to diagnosis of local recurrence or metastasis. Overall survival (OS) was defined as time from the end of treatment to date of death or last follow-up. Deaths from other causes not related to cervical cancer were censored at date of death. Local recurrence was considered when lesions were located in the vaginal or paracervical areas, and lymph node recurrence was divided into positive nodes in the pelvic or aortic regions.

2.5. Statistical analysis

Categorical variables are expressed as frequencies and percentages, and quantitative variables as median and interquartile range (IQR) (25th-75th percentile). The R statistical program (version 3.5.2) was used for the analysis of data.

3. Results

A total of 634 women with LACC were eligible for paraaortic lymphadenectomy but 18 patients (2.8%) were excluded for the following reasons: the limit of paraaortic dissection was the IMA in 11, complete left nodal removal was not possible due to extranodal metastatic spread to the left psoas muscle, left ureter, and/or the left lateral side of the aorta in 5, and confirmation of peritoneal carcinomatosis in 2. Therefore, the study population included 616 patients, with a median age of 49 years

(range 41-58). There were 144 (23.4%) patients with FIGO (2009) stage IB2, 43 (7.0%) stage IIA2, 329 (53.4%) stage IIB, 11 (1.9%) stage IIIA, 85 (13.8%) IIIB, and 4 (0.6%) stage IVA. Salient clinical and histopathologic findings are shown in Table 1.

Surgical staging was performed by conventional laparoscopy in 592 patients (96.1%) and robotic-assisted laparoscopy in 24 (3.9%). All paraaortic lymphadenectomies were performed by extraperitoneal approach. Lymph node debulking was performed in 169 (27.4%) patients by the extraperitoneal or the transperitoneal approach according to location of lymph nodes or preferences of the surgeon. The median operative time was 150 min (IQR 120-180), the median length of hospitalization 2 days (IQR 2-3), and the median amount of blood loss was 50 mL (range 20-80). The median number of aortic lymph nodes removed was 13 (IQR 9-17). Metastatic paraaortic involvement was found in 114 patients (18.5%) and positive infrarenal metastases in 73 (64%). Among patients with infrarenal paraaortic metastases, there were 11/114 (9.6%) with exclusive infrarenal metastases, whereas in the remaining 62/114 (54.4%) concomitant infrarenal and inframesenteric metastases were observed. In the 169 patients undergoing lymph node debulking, 96 (56.8%) had negative pelvic nodes together with negative paraaortic lymph nodes in 85. In the remaining 11 patients with negative pelvic nodes and positive paraaortic metastases, inframesenteric positive nodes were found in 7, both inframesenteric and infrarenal in 1, and infrarenal only in 3. Details of intraoperative variables are shown in Table 2.

All patients with positive paraaortic lymph nodes received extended-field radiotherapy (EFRT) (n = 114), including 3D conformal radiation therapy (n = 75), intensity-modulated radiation therapy (IMRT) (n = 14), and IMRT/volumetric modulated arc therapy-simultaneous integrated boost (VMAT-SIB) (n = 25). There was

a delay in starting chemoradiotherapy in 8 (1.3%) patients. The median number of days between surgery and starting chemoradiotherapy was 28.5 (IQR 21-42).

Intraoperative, early, and late postoperative complications occurred in 3.6%, 7.0%, and 4.5% of patients, respectively (Table 3). Intraoperative complications in 22 patients included operative bleeding in 11, ureteral injury in 5, peritoneal leak and termination of the transperitoneal route in 4, bowel perforation in 1, and anesthetic complication in 1. Only 2 lesions of the renal vein and 1 lesion of the renal artery were associated to dissection of the infrarenal space.

Forty-three (7.0%) patients experienced early postoperative complications, of which grade IIIb complications occurred only in 8 patients (1.3%) and grade IVa in 2 (0.3%). Among procedural-related complications, lymphocele occurred in 16 cases, reoperation due to bleeding in 3, chylous ascites in 2, trocar site hernia in 2, and sepsis secondary to bowel perforation in 2. Nephrectomy was required in 1 patient and renal dysfunction developed in 1 patient with lymphocele. Three patients with lymphocele developed infection of the collection (superinfection) with fever, positive culture of the drainage fluid, one of them with acute renal failure. Of early postoperative complications, the 2 cases of renal complications and probably the 2 cases of chylous ascites may be related to the infrarenal procedure.

Late postoperative complications were recorded in 28 (4.5%) patients, with grade IIIb in 3 (0.5%) and grade IVa in 1 (0.2%). Sixteen patients experienced procedural-related complications, including lymphocele in 7, trocar site hernia in 3, infected lymphocele in 2, renovascular hypertension due to hematoma in the renal pelvis in 1, port-site metastasis in 1, lymphedema in 1, and thrombosis of the left lower

limb in 1. Of late postoperative complications, renovascular hypertension due to renal pelvis hematoma may be attributed to infrarenal dissection.

After a median follow-up of 3.68 years (IQR 1.9-6.6), the disease-specific survival was 70.9% (95% CI 67.7-74.2) with a recurrence rate of 28.3% (177/616). Disease-specific survival was 77.2% in patients with stage IB2, 70.3% in stage IIA2, 71.5% in stage IIB, 47.1% in stage IIIA, 56% in stage IIIB, and 45.7% in stage IVA. Among patients diagnosed of recurrence, local recurrence was recorded in 52 cases (29.9%), pelvic and aortic recurrence in 70 cases (40.2%) (pelvic 23.6%, aortic 16.7%), and distant metastases in 98 (56.3%).

4. Discussion

The present study shows that extension of paraaortic lymphadenectomy above the IMA is feasible, with an acceptable surgical morbidity but, most importantly, dissection up to the left renal vein was able to detect isolated infrarenal paraaortic lymph node involvement in 9.6% of the patients out of the total 114 with paraaortic metastases. These patients otherwise would not have been treated with extended-field radiotherapy. In a series of 421 patients with stage IB or II, Guy et al. [14] reported infrarenal metastases in 8 (25%) of 32 patients with paraaortic positive nodes treated by surgery in combination with radiation between 1985 and 1994. Gil-Moreno et al. [9] showed in 98 patients evaluated, 16 had positive aortic lymph nodes (16.3%), 5 of which were at the infrarenal level only, which represents 31.2% of patients with aortic lymph node involvement.

The surgical pretherapeutic staging of paraaortic lymph nodes in LACC has been recently limited to the IMA based on the low rate of isolated skip metastasis above the

IMA, the potential surgical morbidity, and the absence of conclusive evidence regarding the survival benefits of the infrarenal dissection. The study of Leblanc et al. [18] in a series of 196 patients with LACC from two cancer centers in France has largely influenced the position of the inframesenteric dissection as an acceptable pattern for paraaortic lymphadenectomy. These patients with negative PET-CT imaging staging at the paraaortic level underwent extraperitoneal paraaortic lymphadenectomy, in which all nodes were removed from both common iliac bifurcations up to the left renal vein. Thirty patients had paraaortic lymph nodes metastasis, but only 1 (3.3%) had positive nodes exclusively located above the IMA (95% CI 0%-9.7%). In the study of Azaïs et al. [25] of 119 women with squamous or glandular LACC and negative PET-CT imaging, differences between infrarenal and inframesenteric paraaortic lymph node status were not found. The present study carried out in 616 patients undergoing surgical staging over a long period of 16 years is the largest series to address the incidence of isolated paraaortic lymph node spread above the IMA in patients with LACC.

Vandeperre et al. [17] compared surgical staging with imaging of the paraaortic lymph nodes in LACC and only performed a lower paraaortic sampling because of the rare incidence of infrarenal lymph involvement, which is justified by a low percentage of skip metastases to the superior part of the aorta reported in the systematic review of the literature of Ouldamer et al. [19]. However, in this review of 733 patients with LACC stages IB1-IV collected from five primary studies, 10 patients had lymph node metastasis above the level of the IMA exclusively with a rate of 1.36% (10/733), but the percentage increases to 16.1% when total number of 62 patients with paraaortic positive nodes is considered (10/62).

On the other hand, positive paraaortic lymph nodes located at both inframesenteric and infrarenal levels were found in 54.4% of the patients, which is agreement with a percentage of 46.7% reported in the study of Leblanc et al. [18]. In the retrospective study of 98 patients with LACC with no positive paraaortic nodes on PET-CT reported by Uzan et al. [26], the lymphadenectomy targeted the supra- and inframesenteric paraaortic space, but if suspicious nodes were found during the procedure, they were sent for frozen analysis, and if they were metastatic, the procedure was stopped and the radiation fields were extended to the paraaortic region. In addition, debulking of positive paraaortic lymph nodes of small size (< 5 mm) [7,27] or > 5 positive nodes removed [28] has been associated with improvement in survival. Limiting the dissection up to the IMA reduces assessment of the extension of the metastatic disease. Infrarenal paraaortic node information is thus important to reorient the management and establish a prognosis if positive nodes are found at this level.

Proponents of the extent of surgical staging below the level of the IMA cite technical difficulties of an infrarenal dissection, with an increase in the operative time and perioperative morbidity. In the present study, intraoperative complications were recorded in 22 cases (3.6%), 15 of which were related to paraaortic lymphadenectomy, but only 3 of them (2 lesions of the renal vein, 1 lesion of the renal artery) were associated to dissection of the infrarenal space. Other early and late complications possibly related to infrarenal dissection included 2 cases of renal complications, 2 cases of chylous ascites, and 1 case of renovascular hypertension due to renal pelvis hematoma. The group of Vandeperre et al. [17] reported 14 intraoperative complications among 179 patients undergoing inframesenteric paraaortic lymph node

sampling (7.8%), with peroperative bleedings of the retroperitoneal blood vessels in 10 cases. Petitnicolas et al. [29] in a comparison of the surgical morbidity of inframesenteric (n = 56) with infrarenal (n = 63) paraaortic lymph node dissections, no significant difference in intra- and postoperative complications were observed (1 vascular injury in the inframesenteric lymphadenectomy group and 4 vascular injuries in the infrarenal lymphadenectomy group). Leblanc et al. [18] in a longitudinal study of 196 patients treated between 2008 and 2013, two intraoperative significant bleedings occurred during the infrarenal dissection. In our study, patients were recruited since the year 2000, and include the learning curve of the surgical procedure for most of the participating hospitals. Probably, better experience with paraaortic infrarenal dissection and careful assessment of preoperative imaging findings to assess aberrations of retroperitoneal vessels [30] may reduce intraoperative morbidity during infrarenal lymphadenectomy [26]. In the most recently published series of the FRANCOGYN group [31] with 377 patients, there was a similar rate of intraoperative complications (4.8%) related to paraaortic lymphadenectomy, most of them vascular as in our series.

Lymphocysts or lymphoceles were the most frequent early and late postoperative complications after paraaortic lymphadenectomy, although preventive marsupialization to facilitate transperitoneal absorption of lymphatic fluid [1] was performed in up to 85.1% of cases. The rate of symptomatic lymphocele requiring drainage was 2.6% and 2.1% for early and late lymphoceles, respectively. It has been proposed that limiting paraaortic dissection to the inframesenteric area may reduce the lymphatic morbidity caused by transection of large perirrenal lymph channels [18]. In a prospective study to assess the incidence of lymphocele in 800 patients with

gynecological cancer who underwent pelvic and paraaortic lymphadenectomy, symptomatic lymphocele occurred only in 5.8% of patients [32]. Conservative management or CT-guided drainage of symptomatic lymphoceles does not usually cause a delay of primary treatment. However, in the comparison of surgical morbidity between inframesenteric and infrarenal paraaortic lymphadenectomy, no differences in the ratio of lymphoceles was found [29].

Another argument in favor of paraaortic lymphadenectomy limited to the IMA is an increase of operative time, but the median operative time of 150 min (range 120-180) and the length of stay of 2 days (range 2-3) reported in our study, considering that pelvic debulking was performed in 169 patients, seems reasonable if the goal is to identify infrarenal metastasis disease. In the comparison of inframesenteric and infrarenal surgical staging procedures, there was a difference of 35 min in favor of the inframesenteric technique, although the mean operative time of 206 ± 61 min for the infrarenal procedure was somewhat longer than in our study [29]. In this study, however, the number of lymph nodes obtained was considerable greater in the infrarenal lymphadenectomy group (22 vs. 13), and probably to extent paraaortic lymphadenectomy up to the left renal vein may have a high diagnostic reliability, with a minimal increase of operative time and surgical-related complications.

In the UTERUS-11 randomized clinical trial of the German GOG and Radiation Oncology Group, surgical staging was compared to clinical/radiological staging followed by chemoradiation in 240 LACC patients (FIGO2009 IIB-IVA), with disease-free survival (DFS) as the primary endpoint and overall survival (OS) as the secondary endpoint [33]. Differences in overall DFS and OS were not found, but surgical staging lead to superior disease-specific DFS and OS compared to clinical staging with

acceptable morbidity and no significant chemotherapy delay. In a recently published study of our group of 634 patients with LAAC, differences between surgical staging and imaging staging were not found neither in OS and DFS nor in the rate of systemic metastases (56.3% in the surgical group and 43.8% in the imaging group, $P = 0.089$) [34]. Also, the size of lymph node metastases (≤ 5 mm vs. > 5 mm) had no effect on OS.

The low incidence of cervical cancer in our country difficult the design and execution of comparative prospective studies. The present retrospective cohort included all LACC patients independently of preoperative imaging staging results. To our knowledge, this is the largest series published so far aimed to assess the site of lymph node paraaortic metastasis and, particularly, the rate of patients with isolated paraaortic metastases. However, the present results should be interpreted considering important limitations such as the retrospective design over a long time span of 16 years, the multicenter nature of the study, and the absence of centralization of histopathological studies. The median number of aortic lymph nodes was 13, which is lower than a mean of 22.3 reported in the series of Leblanc et al. [18] and a median of 17 nodes found in a previous study of our group [21]. Other limitations include the absence of systematic preoperative PET-CT to assess lymph node extension related to data recorded over a long period of time. It is important to consider that data collection for complications were recorded according to the time of occurrence (intraoperative, early, and late). The fact that complications were not evaluated in patients undergoing paraaortic lymphadenectomy alone and separated according to the type of procedure (inframesenteric or infrarenal) is also a limitation of the study.

In conclusion, this study shows that the left renal vein could be the optimal upper limit of paraaortic lymphadenectomy in patients with LACC undergoing

pretherapeutic surgical staging. Infrarenal paraaortic lymphadenectomy allows identifying patients with metastatic lymph nodes above the IMA only, as well as those with concomitant infrarenal and inframesenteric nodes with an acceptable surgical morbidity.

Conflict of interests: None

Author contributions:

Berta Diaz Feijoo: Conceptualization, methodology, software, validation, formal analysis, investigation, resource, data curation, writing-original draft, writing-review&editing, visualization, supervisión and Project administration.

Silvia Franco: Resource, data curation and writing-review&editing.

Aureli Torné: Resource, data curation, writing-original draft and writing-review&editing,

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Table 1. Clinical and histopathological characteristics of 616 women with LACC included in the study

Variables	Number patients (%)
Age at diagnosis, years, median (IQR)	49 (41-58)
Body mass index, kg/m^2, median (IQR)	25.4 (21.9-28.7)
ECOG performance status, n (%)	
0	505 (82.0)
1	111 (18.0)
Histological subtype, n (%)	
Squamous	504 (81.8)
Adenocarcinoma	85 (13.8)
Adenosquamous	13 (2.1)
Undifferentiated	14 (2.3)
Tumor grade, n (%)	
G1 well differentiated	48 (7.8)
G2 moderately differentiated	176 (28.6)
G3 poorly differentiated	178 (28.9)
Not available	214 (34.7)
Lymphovascular invasion	
No	90 (14.6)
Yes	33 (5.3)
Not available	493 (80)
FIGO stage (2009), n (%)	
IB2	144 (23.4)
IIA2	43 (7.0)
IIB	329 (53.4)
IIIA	11 (1.9)
IIIB	85 (13.8)
IVA	4 (0.6)
Imaging studies	
MRI	532
Negative aortic lymph nodes	510 (95.9)
Positive aortic lymph nodes	22 (4.1)
PET-CT (n = 164)	164
Negative aortic lymph nodes	147 (89.6)
Positive aortic lymph nodes	17 (10.4)

IQR: interquartile range (25th-75th percentile); ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; MRI: magnetic resonance imaging; PET-CT: positron emission tomography-computed tomography.

Table 3. Intraoperative, early, and late complications

Events	Number of patients (%)
Intraoperative complications	22 (3.6)
Related to paraaortic lymphadenectomy	15
Ureteral lesion	5
Common iliac vein injury	3
Inferior mesenteric artery section	2
Renal vein injury	2
Polar renal artery injury	1
Lumbar artery injury	1
Left renal artery injury	1
Related to the extraperitoneal approach	5
Parietal peritoneum perforation (procedure via transperitoneal)	4
Bowel perforation with marsupialization	1
Related to anesthesia	1
Hemothorax	1
Related to the diagnostic transperitoneal approach	1
Mesenteric bleeding	1
Early (30-day) complications	43 (7.0)
Clavien-Dindo classification	
Grade I	11
Grade II	14
Grade III	16
Grade IIIa	8
Grade IIIb	8
Grade IVa	2
Related to paraaortic lymphadenectomy	27
Lymphocele	13
Superinfected lymphocele	3
Retroperitoneal hematoma (reoperation)	3
Sepsis due to bowel perforation	2
Chylous ascites	2
Trocar site hernia	2
Left nephrectomy	1
Renal dysfunction	1
Late (> 30 days) complications	28 (4.5)
Clavien-Dindo classification	
Grade I	5
Grade II	6
Grade III	16
Grade IIIa	13
Grade IIIb	3
Grade IVa	10
Related to paraaortic lymphadenectomy	16
Lymphocele	7
Superinfected lymphocele	2
Trocar site hernia	3
Port-site metastasis	1
Lymphedema left lower limb	1
Thrombosis left lower limb	1
Renovascular hypertension due to renal pelvis hematoma	1

Table 2. Intraoperative variables and excised lymph nodes in 616 women with LACC undergoing paraaortic lymphadenectomy

Variables	Number of patients (%)
Type of lymph node surgical staging, n (%)	
Extraperitoneal paraaortic lymphadenectomy	447 (72.6)
Extraperitoneal paraaortic lymphadenectomy and/or pelvic debulking	169 (27.4)
Type of laparoscopy	
Conventional laparoscopy approach	592 (96.1)
Robotic-assisted	24 (3.9)
Marsupialization	509 (82.6)
Intraoperative blood loss, mL median (IQR)	50 (20-80)
Operative time, min, median (IQR)	150 (120-180)
Length of hospital stay, days, median (IQR)	2 (2-3)
Lymph nodes excised, median (IQR)	13 (9-17)
Pelvic lymph nodes excised, median (IQR)	8.5 (3-13)
Paraaortic lymph nodes, n (%)	
Negative	502 (81.5)
Positive	114 (18.5)
Inframesenteric lymph nodes	
Lymph nodes excised, median (IQR)	7 (5-12)
Negative	520 (84.4)
Positive	101 (16.4)
Supramesenteric lymph nodes	
Lymph nodes excised, median (IQR)	6 (4-9)
Negative	548 (89.0)
Positive	73 (11.8)
Pelvic lymph nodes (n = 169)	
Negative	96 (56.8)
With positive paraaortic lymph nodes	11
Inframesenteric only	7
Inframesenteric and infrarenal	1
Infrarenal only	3
With negative paraaortic lymph nodes	85 (50.2)
Positive	73 (43.2)
With positive paraaortic lymph nodes	31 (18.3)
Inframesenteric only	18
Inframesenteric and infrarenal	10
Infrarenal only	3
With negative paraaortic lymph nodes	42 (24.8)

IQR: interquartile range (25th-75th percentile).

Highlights

- 616 women with LACC underwent pretherapeutic extraperitoneal paraaortic lymphadenectomy up to the left renal vein.
- Of 114 patients (18.5%) with paraaortic lymph node involvement, 73 (64%) had supramesenteric metastases.
- There were 11 patients (9.6%) with isolated supramesenteric metastases.
- The left renal vein should be considered as the optimal upper limit of pretherapeutic paraaortic lymphadenectomy for LACC.

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