

Original Article





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The extent of aortic lymphadenectomy in locally advanced cervical cancer impacts on survival

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ABSTRACT

Objective: The prognostic impact of surgical paraaortic staging remains unclear in patients with locally advanced cervical cancer (LACC). The objective of our study was to evaluate the results of the surgical technique of preoperative aortic lymphadenectomy in LACC related to tumor burden and disease spread to assess its influence on survival.

Methods: Data of 1,072 patients with cervical cancer were taken from 11 Spanish hospitals (Spain-Gynecologic Oncology Group [GOG] working group). Complete aortic lymphadenectomy surgery (CALS) was considered when the lymph nodes (LNs) were excised up to the left renal vein. The extent of the disease was performed evaluating the LNs by calculating the geometric means and quantifying the log odds between positive LNs and negative LNs. The Kaplan-Meier method was used to estimate the survival distribution. A Cox proportional hazards model was used to account for the influence of multiple variables.

Results: A total of 394 patients were included. Pathological analysis revealed positive aortic LNs in 119 patients (30%). LODDS cut-off value of −2 was established as a prognostic indicator. CALS and LODDS <−2 were associated with better disease free survival and overall survival than suboptimal aortic lymphadenectomy surgery and LODDS ≥−2. In a multivariate model analysis, CALS is revealed as an independent prognostic factor in LACC.

Conclusion: When performing preoperative surgical staging in LACC, it is not advisable to

Keywords: Cervical Cancer; Survival Rate; Disease-Free Survival; Lymph Node Excision; Lymphatic Metastasis

take simple samples from the regional nodes. Radical dissection of the aortic and pelvic

regions offers a more reliable staging of the LNs and has a favorable influence on survival.

INTRODUCTION

Cervical cancer spreads primarily to regional lymph nodes (LNs) [1]. Recently, the International Federation of Gynecology and Obstetrics (FIGO) of 2018 has modified the



Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Conceptualization: L.A., D.F.B.; Data curation: B.V., H.A.; Formal analysis: E.J.; Methodology: L.A., G.M.A.; Software: E.J.; Supervision: L.A.; Writing - original draft: L.A.; Writing - review & editing: L.A., D.F.B.

staging of cervical cancer, including the LN status in the classification system that currently assigns patients with positive pelvic LN stage IIIC1 and women with aortic LN disease as stage IIIC2 [2].

Frequently, patients with cervical cancer are diagnosed in a locally advanced stage (FIGO IIA2-IVA and IB3). In these patients, the standard and most effective treatment is concomitant chemotherapy and pelvic radiotherapy. Aortic LN involvement is observed in 17%–24% of patients with locally advanced cervical cancer (LACC) [3].

Determination of aortic LN status is essential for planning the irradiation field in cases of LACC to avoid unnecessary irradiation and decrease associated morbidity [4].

The previous data justify the need to identify patients who present with aortic LN metastases, and are therefore tributary to receive treatment with extended field external radiotherapy in that region. However, a discussion about the best way to assess aortic LN status in patients with LACC remains open. Imaging studies, especially positron emission tomography-computed tomography (PET-CT), are less invasive but have low sensitivity for evaluation of aortic LN [5].

On the other hand, surgical staging is much more aggressive, although it provides more reliable information on the status of the aortic nodes. The prognostic and therapeutic value of paraaortic surgical staging remains unclear in patients with LACC, and there are some discrepancies in the scientific literature regarding this topic [6].

However, the risk of recurrence of other solid tumors according to the LN status suggests that the patient's prognosis or tumor recurrence may be influenced, not only by the nodal status in the paraaortic region, but also by the tumor burden in the LN, the number of positive or the location [7,8].

The number of regional nodes varies from one individual to another; therefore, it can lead to confusion. Underestimating the number of LN metastasis is a significant weakness of the staging system for cervical cancer. In an attempt to reduce this confusion, we have related the affected nodes with the volume of nodal disease through the log odds of positive LNs (LODDS).

The so-called LODDS, that is, the natural logarithm of odds between the number of positive and negative LNs, has also been described as a better discriminant prognostic factor than the simple positive LN count in some gastrointestinal cancers [9].

More recently, a LODDS major of –1.05 was defined as a dangerous independent prognostic indicator for disease free survival (DFS) in high-risk patients who underwent radical surgery followed by adjuvant treatment in cervical cancer. Among the various methods used for assessment of LN status, LODDS was the most powerful predictor associated with both, recurrence and overall survival (OS), as they are more discriminatory than the number of metastatic LNs to predict OS in cervical cancer with positive nodes (LOODS considers the tumor burden or the extent of the lymphadenectomy) [10].

Both pelvic and aortic surgical lymphadenectomies are performed to achieve better staging of the LN stage in cervical cancer. Furthermore, it allows reducing the extent of the therapeutic radiation field [11-13].



There is no evidence about which is the most appropriate technique to perform such lymphadenectomy—LN sampling or radical dissection—or whether finally, it has any influence on survival [14-16].

In this study, we evaluated the surgical technique of preoperative aortic lymphadenectomy in the LCC related to tumor burden and the extent of the disease to assess its influence on survival. In this context, a multicentric retrospective registry was carried out in a cohort of patients with (LACC), uniformly treated in specialized cancer units in tertiary hospitals in Spain (Spain-Gynecologic Oncology Group [GOG] working group).

MATERIALS AND METHODS

Data from patients with LACC from 11 Spanish hospitals with a high volume of gynecological cancers (Spain-GOG working group) were analyzed.

From 2000 to 2016 all cases were analyzed retrospectively after receiving Institutional Board approval of the Vall d'Hebron Universitari Campus Hospital (PR AMI 159/2015). For the purpose of this study, the cases in which the data on the surgical technique were completely filled were selected. At admission, we obtained an informed consent allowing the use of clinical data for research purposes from every patient included in the study.

LACC was defined as patients with at least stage IB2, according to the latest 2009 FIGO classification. Exclusion criteria were: patients with stage IVB, patients treated by radiotherapy only, and patients with missing data for surgical staging.

The clinical LN stage was studied by magnetic resonance imaging (MRI) and/or PET-CT. Any nodular image on the MRI with a size greater than 10 mm was considered suspicious for infiltration. In PET-CT studies, focal areas of abnormal uptake of F-18 fluorodeoxyglucose (FDG) were assessed qualitatively, with non-detectable FDG uptake defined as negative, and assessed as positive when there was a moderate uptake with a marked increase in absorption in relation surrounding tissues.

The kind of treatment applied to these patients was decided by each center within a multidisciplinary oncology committee considering the characteristics of the patient and the tumor.

During surgical paraaortic staging, all nodes from the bifurcation of the aorta to the left renal vein were removed. Pelvic lymphadenectomy was only performed when enlarged nodes were found on preoperative imaging tests. Complete aortic lymphadenectomy surgery (CALS) was defined as a complete and radical paraaortic dissection up to the left renal vein, and suboptimal aortic lymphadenectomy surgery (SALS) when only a sampling of the paraaortic or pelvic ganglia was performed. Minimally invasive surgery, laparoscopic, or robotic, was used in all patients at the surgeon's discretion and according to the availability of resources.

All patients were subsequently treated by chemoradiotherapy and received external pelvic radiotherapy at the total dose of 45 Gy (25 fractions) in 5 weeks with a concomitant weekly basis of 40 mg/m² of Cisplatin. They also received intracavitary brachytherapy (30 Gy) to complete external pelvic radiotherapy.



Follow-up of patients was made under the discretion of each center. Generally, with gynecological explorations every 6 months, and with imaging test at least every 12 months. The surgery date was used to calculate DFS and OS.

LODDS was defined as: log [(Number of positive LN retrieved+0.5)/(Number of total LN retrieved-Number of positive LN retrieved+0.5)]. The LODDS, considering both the number of positive LN and the number of negative LN retrieved in the lymphadenectomy, relate the extent of the lymphadenectomy and the burden of LN involvement.

1. Statistical analysis

The Geometric mean, due to their mathematical characteristics, is more representative than the arithmetic means when there are very extreme values in the variables as it happens with the number of dissected LNs, since the influence of the most extreme values of both the highest and the lowest decreases [17].

For all these reasons, we considered that the geometric mean of the number of dissected nodes (total, aortic, and pelvic) is an excellent approximation to the advisable number of nodes to dissect in the lymphadenectomy of each area, in cases where optimal surgery has been performed.

A cumulative sum (CUSUM) control chart of expected minus observed deaths was used between the value of the LODDS on a continuous scale and the vital status—alive or dead—to determine the optimal cut-off point for the LODDS variable [18].

Inferential statistical analysis was based on the Mann-Whitney test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables. The Kaplan-Meier method was used to estimate the OS distribution. Comparisons of survival were made using the log-rank test. A Cox regression was performed, including possible confounding factors for OS and the type of lymphadenectomy performed. Values of p<0.05 were considered to denote significant differences. Statistical analysis was performed using Stata Statistical Software Release 16 (StataCorp LLC, College Station, TX, USA).

RESULTS

From 2000 to 2016, 1,072 patients were treated for LACC in our institutions. Among them, 634 had undergone surgical staging, but only 394 had complete surgical records and met the inclusion criteria. The patients' main clinicopathological characteristics can be seen in **Table 1**.

CUSUM chart obtained for LODDS was monotonic, indicating that the higher the LODDS, the more deaths in the follow-up, with the prognostic cut at -2 (best prognosis below -2). Thus, a cut-off value of -2 was established as a prognostic indicator (**Fig. 1**).

The median age of patients at diagnosis was 50 years (range, 24 to 79 years). Most FIGO patients were IIb (53%), and the most common histology was squamous cell carcinoma (82.8%) and adenocarcinoma (15.8%). There were no FIGO IVB patients.

The characteristics of the surgical LN retrieved are shown in **Table 2**. The total number of LN recovered was 7,238, and 766 (11%) were N1. The 171 (43%) of patients were N1; 119 (30%) of



Table 1. Clinicopathological characteristics of the patients

Characteristics	Total (n=394)	SALS (n=11)	CALS (n=383)	p-value
Age	50.0±11.9	53.0±10.8	50.0±11.9	0.390
Body mass index (kg/m²)	26.0±5.1	29.0±5.7	26.0±5.1	0.100
Menopause				0.130
No	197 (50.0)	3 (27.3)	194 (50.7)	
Yes	197 (50.0)	8 (72.7)	189 (49.3)	
Tumor size	47.0±14.8	42.0±18.0	47.0±14.7	0.280
FIGO stage (2009)				0.570
Ib2	94 (23.9)	1 (9.1)	93 (24.3)	
II	229 (58.3)	7 (63.6)	222 (58.2)	
III	65 (16.5)	3 (27.3)	62 (16.2)	
IV	5 (1.3)	0	5 (1.3)	
Image LN (MRI-PET-CT)				0.320
Negative	165 (45.3)	3 (30.0)	162 (45.8)	
Positive	199 (54.7)	7 (70.0)	192 (54.2)	
Histological subtype				0.990
Squamous	323 (82.0)	9 (81.8)	314 (82.0)	
Adenocarcinoma	62 (15.7)	2 (18.2)	60 (15.7)	
Adenosquamous	5 (1.3)	0	5 (1.3)	
Undifferentiated	2 (0.5)	0	2 (0.5)	
Others	2 (0.5)	0	2 (0.5)	
Tumor grade				0.950
G1	20 (5.2)	1 (9.1)	19 (5.1)	
G2	111 (29.1)	3 (27.3)	108 (29.1)	
G3	103 (27.0)	3 (27.3)	100 (27.0)	
Unknown	148 (38.7)	4 (36.4)	144 (38.8)	
scc	10.0±21.7	11.0±22.7	10.0±21.7	0.830
CEA	13.0±61.1	6.0±10.4	13.0±61.9	0.800
CA199	84.0±265.1	48.0±14.6	85.0±268.0	0.850
Lymphadenectomy				0.730
Aortic	231 (58.6)	7 (63.6)	224 (58.5)	
Aortic and pelvic	163 (41.4)	4 (36.4)	159 (41.5)	
Chemoradiation treatment	` ,	,	, ,	0.310
Incomplete	14 (3.6)	1 (9.1)	13 (3.4)	
Complete	380 (96.4)	10 (90.9)	370 (96.6)	
Relapse	. ,			0.750
No	268 (68.0)	7 (63.6)	261 (68.1)	
Yes	126 (32.0)	4 (36.4)	122 (31.9)	
Last control status	- (- · · ·)	Ç)	(* · · ·)	0.024
Alive	236 (60.1)	3 (27.3)	233 (61.0)	
Dead	157 (39.9)	8 (72.7)	149 (39.0)	
Months of follow-up since surgery	40 (19-82)	18 (8-76)	40 (20-83)	0.069

Values are presented as mean±standard deviation, number (%) or median (interquartile range).

CA19.9, cancer antigen 19.9; CALS, complete aortic lymphadenectomy surgery; CEA, carcinoembryonic antigen; FIGO, International Federation of Gynecology and Obstetrics; LN, lymph node; MRI, magnetic resonance imaging; PET-CT, positron emission tomography-computed tomography; SALS, suboptimal aortic lymphadenectomy surgery; SCC, squamous cell carcinoma antigen.

patients have positive aortic LN; 92 (56%) of patients undergoing pelvic lymphadenectomy had positive pelvic LN. The median of positive LN in the aortic region was 2 (range, 0–31). Regarding the distribution of the aortic region, the aortic supramesenteric region, although a smaller number of LN was retrieved, a high number of positive LN were found (10%). In these series, the negative predictive value of imaging tests for aortic supramesenteric LN was 89%, 93% for aortic inframesenteric LN, and 50% for pelvic LN. These outcomes indicate that a negative image of LN involvement is only reliable for the aortic supramesenteric and inframesenteric region, but no for the pelvic region. The low positive predictive values of the imaging tests for aortic supramesenteric, aortic inframesenteric, and pelvic LN, were 25%; 16%; 56%, respectively. These values indicate that a positive image is not trustworthy for any region due to the high number of false positives.



Moreover, in 18% of LN retrieved, skip metastasis to the aortic supramesenteric region was found without the involvement of the aortic inframesenteric LNs. Similarly, 6.7% of positive aortic LNs and 3% in the supramesenteric region were found without pelvic LN in those cases where a pelvic lymphadenectomy was performed.

The geometric mean values of the total number of LNs retrieved are shown in **Supplementary Table 1** as an indicator of the advisable extent of lymphadenectomy in patients that received complete lymphadenectomy in LACC.

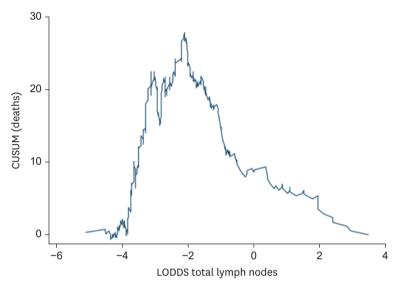


Fig. 1. CUSUM chart obtained for LODDS. CUSUM, cumulative sum; LODDS, log odds of positive lymph nodes.

Table 2. Characteristics of the surgical LN retrieved

Characteristics	Total (n=394)	SALS (n=11)	CALS (n=383)	p-value
LODDS total LN retrieved	-2.0±1.5	-1.0±2.3	-2.0±1.5	0.002
LODDS total LN cut-off -2				0.049
<-2	283 (71.8)	5 (45.5)	278 (72.6)	
≥-2	111 (28.2)	6 (54.5)	105 (27.4)	
Total No. of LN retrieved	17 (1–83)	15 (3-30)	17 (1-83)	0.310
Total No. of positive LN retrieved	1 (0-1)	0 (0-1)	1 (0-1)	0.280
Total LN status (pN)				0.047
Negative	223 (56.6)	3 (27.3)	220 (57.4)	
Positive	171 (43.4)	8 (72.7)	163 (42.6)	
LODDS aortic LN	-2.0±1.5	-1.0±2.3	-3.0±1.5	<0.001
LODDS aortic LN cut-off -2				0.030
<-2	291 (73.9)	5 (45.5)	286 (74.7)	
≥–2	103 (26.1)	6 (54.5)	97 (25.3)	
Total No of. aortic LN retrieved	13 (1–53)	10 (3-28)	13 (1–53)	0.110
Total No. of aortic positive LN retrieved	0 (0-31)	3 (0-8)	0 (0-31)	0.200
Aortic LN status (pN)				0.075
No	275 (69.8)	5 (45.5)	270 (70.5)	
Yes	119 (30.2)	6 (54.5)	113 (29.5)	
LODDS pelvic LN	-2.0±1.4	-1.0±1.9	-2.0±1.4	0.510
Total No. of pelvic LN retrieved	9 (1–31)	14 (2-20)	9 (1-31)	0.410
Total No. of pelvic positive LN retrieved	1 (0-18)	2 (1-3)	1 (0-18)	0.840
Pelvic LN status (pN)				0.075
Negative	71 (43.6)	0	71 (44.7)	
Positive	92 (56.4)	4 (100)	88 (55.3)	

Values are presented as mean±standard deviation, number (%) or median (minimun-maximum).

CALS, complete aortic lymphadenectomy surgery; LN, lymph node; LODDS, log odds of positive lymph nodes; SALS, suboptimal aortic lymphadenectomy surgery.



There were 16 (4.2%) and 39 (10.2%) patients with intra and postoperative complications, respectively. The most frequent intraoperative complications were hemorrhagic accidents mainly at the ports of entry in the abdominal wall and occasionally accidental injuries of major vessels. The majority of cases of postoperative complications consisted in the appearance of lymphocysts in first place and ureteral lesions in second place. No postoperative mortality was observed.

1. Analysis of survival

Medians OS for CALS and SALS were 18 and 139 months, respectively (**Fig. 2**). Medians OS for aortic LODDS minor of -2, and equal or major of -2, were 161 and 36 months, respectively.

Mean follow-up was 57.3 months (95% CI=52.5–62.2). During follow-up 157 patients (39.8%) died. One hundred and twenty-six patients experience recurrence during follow-up. CALS and LODDS <−2 were associated with better DFS and OS than SALS and LODDS ≥−2 (**Table 3**).

Table 4 describes the multivariate Cox regression, where the extension of preoperative aortic lymphadenectomy is shown as an independent prognostic factor in LACC.

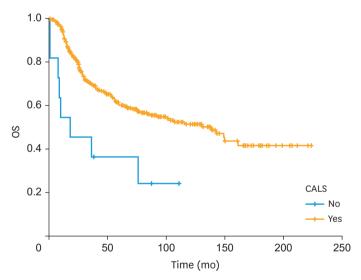


Fig. 2. Medians OS for CALS and SALS (p log-rank=0.003). CALS, complete aortic lymphadenectomy surgery; OS, overall survival; SALS, suboptimal aortic lymphadenectomy surgery.

Table 3. OS and DFS of LODDS and type of surgery

Characteristics	12 mo	24 mo	36 mo	48 mo	60 mo
% OS complete surgery*	94	81	70	66	60
% OS no-optimal	55	45	45	36	36
% DFS complete surgery [†]	88	75	70	68	65
% DFS no-optimal	88	74	59	59	59
% OS LODDS <-2 [‡]	94	85	76	73	68
% OS LODDS ≥-2	87	68	51	44	39
% DFS LODDS <-2§	88	80	75	72	70
% DFS LODDS ≥-2	88	59	55	53	50

DFS, disease free survival; LODDS, log odds of positive lymph nodes; OS, overall survival. $^*p=0.003; ^†p=0.33; ^‡p<0.001; ^§p=0.001.$



Table 4. Cox regression for overall survival

Characteristics	HR	95% CI	p-value
Lymphadenectomy			'
Complete	0.37	0.17-0.81	0.01
No-optimal (reference)	1.00		
Grouped FIGO stage			
II	1.43	0.88-2.33	0.15
III	1.72	0.94-3.15	0.08
IV	2.30	0.52-10.08	0.27
I (reference)	1.00		
Histology			
Adenocarcinoma	1.61	1.01-2.55	0.04
Others	0.62	0.15-2.54	0.51
Squamous (reference)	1.00		
Histologic grade			
G2	1.52	0.53-4.40	0.44
G3	2.31	0.81-6.60	0.12
Unknown	1.65	0.57-4.79	0.35
G1 (reference)	1.00		
Size long axis (mm)	1.00	0.99-1.01	0.65
Age	1.01	1.00-1.02	0.33
Body mass index (kg/m²)	1.01	0.98-1.04	0.54

CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio.

DISCUSSION

Our study describes the extent of lymphadenectomy as an independent prognostic factor in patients with LACC. Patients with CALS have a reduction in the risk of disease progression or death of 63%.

As mentioned in the introduction, the debate about LN assessment is still open. Our results demonstrate kind of confusion in the preoperative imaging, mostly CT scan and PET-CT, in the initial assessment of tumor spread to the aortic region, due to the high rates of false-positive LN retrieved. This fact coincides with other authors who reported similar results [19].

False-negative rates for PET CT in the aortic LN in patients with LACC have been reported as high as 13% with low sensitivity [20]. This coincides with our results, where a rate of 10% was obtained.

Contrarily, surgical aortic LN staging reveals a more realistic status of the aortic LN, as reveals the little concordance that generally exists between imaging tests and the most real LN stage obtained thanks to surgery.

One of the questions to be answered is the worth of performing a radical lymphadenectomy or a simply sampling, which we call suboptimal lymphadenectomy. Some authors reported a survival benefit in salvage and radical aortic lymphadenectomy either in recurrence or in surgical staging with negative imaging preoperative test [21,22]. In that line, our data demonstrate that a radical lymphadenectomy up to the renal vein improves both DFS and OS.

In rare cases, paraaortic LNs may be directly involved. A posterior cervical lymphatic trunk may drain lymph directly from the cervix into the paraaortic nodes, or rare cases of fusion between the cervical and uterine lymphatics may result in nodal metastases skipping to the L4 region via the gonadal vessels. Tumor emboli from the cervix can also reach the subaortic nodes directly via a posterior route [23-25].



In our data, we found nodal jumps from the inframesenteric zone or pelvis to the supramesenteric zone, 18% and 6.7%, respectively. In these cases, surgical aortic staging would also have a beneficial effect by acting as cytoreduction surgery in these cases, although these rates are not line with previous literature where the possibility of skipping metastasis to the supramesenteric region is rare [26].

However, the minimum number of LN that should be harvested to qualify a lymphadenectomy as "adequate" is still a matter of debate. The harvest of the LN retrieved from the aortic region is not well defined in the literature range from 3 to 20 LN in the aortic area [27,28]. In our opinion, the geometric mean of LN retrieved is the best approximation to the ideal number of LN to be retrieved in a CALS when there is absence of more evidence.

In most solid tumors, LN stages are classified according to the number of pathologic nodes found in the different regions and are generally well correlated with the prognosis. In this way, many groups have tried to assess the LN involvement of cervical cancer and its implication in the prognosis. Some authors noted the negative impact of 2 or more LN on survival after adjuvant radiotherapy, noting the importance of the location of positive LN, and showed that metastasis in higher LN was associated with a higher incidence of distant metastases (50% vs. 16%) [29,30].

The efficacy of LODDS in gastric and colorectal cancer has already been reported in large-scale studies, and Calero et al. [9] demonstrated the prognostic superiority of LODDS to classical LN staging. LODDS is a parameter that requires complex calculations and is less intuitive than the FIGO classification for cervical cancer. However, the strength of LODDS lies in their ability to discriminate patients with an equal LN stage by relating tumor burden to the number of LNs retrieved and thus distinguishes the different prognosis between patients with the same stage N, especially when there are no positive nodes.

Our data shows that a LODDS value major of -2 has a significantly higher risk of disease recurrence, specifically DFS, as well as worse OS. In the same line, Kwon et al. [10] found LODDS to be the strongest predictor for both recurrence and survival among the various methods used to assess LN status.

The indication for preoperative LN surgical staging in LACC is still controversial. The only prospective randomized study was conducted by Lai et al. [31] and concluded that there was no difference in DFS and OS between clinical and surgical staging. However, this study received much criticism for its design in which the compared groups were not homogeneous, and the study ended abruptly without reaching the primary endpoint. In the same line, our group (Spain-GOG working group), in a recent publication [13], has not been able to demonstrate an impact on survival for surgical staging compared to clinical ones. However, some other retrospective studies have found it [1]. On the other hand, the ongoing prospective study Lymphadenectomy in Locally Advanced Cervical Cancer Study (LiLACS) by Frumovitz et al. [32] should provide us with answers to all these questions. Meanwhile, our data demonstrate that in case of deciding to perform a preoperative aortic lymphadenectomy, it should be entirely up to renal vein since the extension of the lymphadenectomy has a favorable effect on the survival of patients with LACC.

This study has several limitations, such as the retrospective nature of the study or the absence of pre-established uniform protocol to manage these patients. Also, the small group sample



size in which LN sampling was performed. However, despite this, the comparison with the group subjected to radical dissection offers sufficient statistical power. On the other hand, the strengths of this study should be its multicenter nature and its ability to show a way of managing the LACC of tertiary hospitals in Spain over a long period.

It can be concluded that when the surgical staging of the LN status in LACC is undertaken, simple sampling of the regional nodes is not advisable. Radical dissection of the aortic and pelvic regions offers more reliable LN staging and has a favorable influence on survival. Overall, there is a moderate concordance between imaging tests and actual LN status.

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SUPPLEMENTARY MATERIAL

Supplementary Table 1

Geometric mean values of total number of lymph nodes retrieved in patients with optimal aortic lymphadenectomy surgery

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