ELSEVIER

JMIG
The Journal of Minimally Invasive Gynecology

Original Article

Laparoscopic Debulking of Enlarged Pelvic Nodes during Surgical Para-aortic Staging in Locally Advanced Cervical Cancer: A Retrospective Comparative Cohort Study

Berta Díaz-Feijoo, MD, PhD, Úrsula Acosta, MD, Aureli Torné, MD, PhD, Blanca Gil-Ibáñez, MD, PhD, Alicia Hernández, MD, PhD, Santiago Domingo, PhD, and Antonio Gil-Moreno, MD, PhD, on behalf of the Spanish Gynecologic Oncology Working Group *

From the Gynecology Oncology Unit, Institute Clinic of Gynecology, Obstetrics and Neonatology, Hospital Clínic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Faculty of Medicine - University of Barcelona (Drs. Díaz-Feijoo and Torné), Service of Gynecology, Hospital Universitari Vall d'Hebron, Universitat Autònoma de Barcelona (Drs. Acosta and Gil-Moreno), Barcelona, Department of Obstetrics and Gynecology, Hospital Universitario 12 de Octubre (Dr. Gil-Ibáñez), Spain, Department of Gynecology, Hospital Universitario La Paz (Dr. Hernández), Centro de Investigación Biomédica en Red de Cáncer, CIBERONC (Dr. Gil-Moreno), Madrid, and Department of Gynecology Oncology, Hospital Universitari i Politècnic La Fe, Valencia (Dr. Domingo), Spain

ABSTRACT **Study Objective:** To evaluate laparoscopic pelvic lymph node debulking during extraperitoneal aortic lymphadenectomy in diagnosis, therapeutic planning, and prognosis of patients with locally advanced cervical cancer and enlarged lymph nodes on imaging before chemoradiotherapy.

Design: Retrospective, multicenter, comparative cohort study.

Setting: The study was carried out at 11 hospitals with specialized gynecologic oncology units in Spain.

Patients: Total of 381 women with locally advanced cervical cancer and International Federation of Gynecology and Obstetrics 2018 stage IIIC 1r (radiologic) and higher who received primary treatment with chemoradiotherapy.

Interventions: Patients underwent pelvic lymph node debulking and para-aortic lymphadenectomy (group 1), only para-aortic lymphadenectomy (group 2), or no lymph node surgical staging (group 3). On the basis of pelvic node histology, group 1 was subdivided as negative (group 1A) or positive (group 1B).

Measurements and Main Results: False positives and negatives of imaging tests, disease-free survival, overall survival, and postoperative complications were evaluated.

In group 1, pelvic lymph node involvement was 43.3% (71 of 164), and aortic involvement was 24.4% (40 of 164). In group 2, aortic nodes were positive in 29.7% (33 of 111). Disease-free survival and overall survival were similar in the 3 groups (p = .95) and in groups 1A and 1B (p = .25). No differences were found between groups 1 and 2 in intraoperative (3.7% vs 2.7%, p = .744), early postoperative (8.0% vs 6.3%, p = .776), or late postoperative complications (6.1% vs 2.7%, p = .252). Fewer early and late complications were attributed to radiotherapy in group 1A than in the others (p = .022).

* Spanish Gynecologic Oncology Working Group: Berta Díaz-Feijoo (principal coordinator) and Aureli Torné, Hospital Clínic de Barcelona; Antonio Gil-Moreno and Vicente Bebia, Hospital Universitari Vall d'Hebron, Barcelona; Álvaro Tejerizo, Blanca Gil-Ibañez and José F. Pérez-Regadera, Hospital Universitario 12 de Octubre, Madrid; Virginia Benito and Amina Lubrano, Complejo Hospitalario Universitario Insular-Materno Infantil, Las Palmas de Gran Canaria; Alicia Hernández and Cristina González, Hospital Universitario La Paz, Madrid; Santiago Domingo and Víctor Lago, Hospital Universitari i Politècnic La Fe, Valencia; Rubén Ruiz and Paloma Cobos, Hospital Universitario Donostia, Donostia-San Sebastián; Rocío Luna- Guibourg and Ramón Rovira, Hospital de la Santa Creu i Sant Pau, Barcelona; Juan Gilabert Estelles and Anca Chipirliu, Hospital General Universitario de Valencia, Valencia; Antoni Llueca and Lola Piquer, Hospital General Universitari de Castelló, Castelló de la Plana; and Pluvio Coronado and Miriam Gracia, Hospital Clínico San Carlos, Madrid, Spain.

The authors declare that they have no conflict of interest.

Corresponding author: Berta Díaz-Feijoo, MD, PhD, Institute Clinic of Gynecology, Obstetrics and Neonatology, Hospital Clinic, C/ Villarroel 170, E-08036 Barcelona, Spain.
E-mail: bdiazfe@clinic.cat

Submitted May 2, 2021, Revised June 26, 2021, Accepted for publication June 28, 2021.
Available at www.sciencedirect.com and www.jmig.org

https://doi.org/10.1016/j.jmig.2021.06.027

Conclusion: Laparoscopic pelvic lymph node debulking during para-aortic staging surgery in patients with locally advanced cervical cancer with suspicious nodes allows for the confirmation of metastatic lymph nodes without affecting survival or increasing surgical complications. This information improves the selection of patients requiring boost irradiation, thus avoiding overtreatment of patients with negative nodes. Journal of Minimally Invasive Gynecology (2022) 29, 103−113.

Keywords: Aortic lymphadenectomy; Locally advanced cervical cancer; Pelvic lymph node debulking; Surgical staging

Lymph node involvement is a prognostic factor that has a major impact on the survival of patients with locally advanced cervical cancer [1]. Therefore, the prognosis of patients with locally advanced cervical cancer is closely related to the severity of the lymph node involvement (number of lymph nodes affected, pelvic and/or aortic dissemination, extracapsular involvement) [2]. The presence of suspicious pelvic lymph nodes assessed by positron emission tomography (PET)−computed tomography (CT) in patients with locally advanced cervical cancer varies between 37.6% and 56% [3,4]. In cases histologically confirmed by systematic pelvic lymphadenectomy, it reaches 47% [5]. The prognostic importance of lymph node involvement has led to the modification in 2018 of International Federation of Gynecology and Obstetrics (FIGO) staging, which includes 2 new subgroups based on pelvic and aortic node involvement (stages IIIC1 and IIIC2, respectively) and whether the involvement is suspected on the basis of imaging or confirmed by histology (IIICr or IIICp, respectively) [6].

Most studies on surgical staging before chemoradiotherapy (CRT) in patients with locally advanced cervical cancer have focused on aortic lymphadenectomy to determine areas for extended field radiotherapy (RT) [2]. There is no prospective randomized literature on the possible benefit of cytoreductive pelvic lymphadenectomy, although the Spanish Society of Gynecology and Obstetrics [7], the European Society of Gynecology and Obstetrics [8], and the National Comprehensive Cancer Network [9], consider the possibility of performing a pelvic lymph node debulking in the case of enlarged pelvic nodes by magnetic resonance imaging (MRI) or CT and/or metabolically positive by PET-CT. These recommendations are based on previous studies suggesting that pelvic lymph node debulking could improve local pelvic control with RT and, secondarily, could lead to a decrease of distant metastases [10,11]. According to retrospective radiobiology studies on the relationship between lymph node size metastasis and the efficacy of RT, 60 Gray (Gy) are needed to sterilize lesions ≥2-cm [12,13]. For this reason, pelvic lymph node debulking was proposed with the objective of increasing the response rate and reducing pelvic recurrence after treatment with CRT [14,15]. However, to our knowledge, there are no recent studies evaluating the prognostic and therapeutic value of pelvic lymph node debulking in patients with locally advanced cervical cancer [16].

In addition, the imaging tests used to evaluate para-aortic lymph node involvement in patients with locally advanced cervical cancer, especially PET-CT, show false-negative rates between 12% and 20% and false-positive rates of 16% to 29% [4,17]. However, there is little information on the accuracy of imaging tests of pelvic lymph node involvement in these patients.

Pelvic lymph node debulking and aortic lymphadenectomy in patients with enlarged nodes could lead to increased survival. In this retrospective study, the author concluded that debulking of tumor-involved lymph nodes significantly improves overall survival (OS) and should be performed before primary chemoradiation [18]. However, these surgical procedures can have complications (reported rates of 9%−10%), mostly owing to lymphatic drainage impairment and to a lesser degree vascular or urinary tract injuries [19]. Such complications can potentially cause a delay in the initiation of primary CRT treatment [19].

Our hypothesis was that debulking of enlarged pelvic nodes in patients with locally advanced cervical cancer can allow (1) accurate selection of patients with metastatic involvement of the pelvic nodes (stage IIIC1p FIGO 2018); (2) accurate indication to perform pelvic boost irradiation, with the reduction of complications owing to overtreatment in patients with falsely positive nodes by imaging tests; and (3) assessment of the possible effects of cytoreduction on the survival of these patients.

The aim of the present study was to evaluate the diagnostic and therapeutic implications, and the prognostic impact, of performing pelvic lymph node debulking during staging aortic lymphadenectomy in patients with stage IIIC1r or higher according to FIGO 2018 classification before CRT.

Materials and Methods

This was a multicenter, retrospective, comparative cohort study that included patients with histologic diagnosis of locally advanced cervical cancer in stages IIIC1r and higher (FIGO 2018) and recipients of primary CRT. A total of 11 Spanish reference hospitals in gynecologic cancer participated in the study. Patients were recruited between 2000 and 2016, although not all hospitals included patients from the beginning of the study as they did not introduce the surgical technique until 2010. The inclusion criteria were (1) histologic confirmation of squamous, adenosquamous, adenocarcinoma, or undifferentiated cervical cancer; (2) evaluation with imaging tests (PET-CT and/or MRI: MRI was the gold standard in the 2000s and PET-CT incorporated into clinical practice since 2009) of the tumor and

lymph node extension; (3) suspicion of pelvic nodal involvement in imaging tests; and (4) treatment with CRT (pelvic irradiation field). The exclusion criteria were (1) age >80 years; (2) Eastern Cooperative Oncology Group ≥2; (3) presence of carcinomatosis at the time of laparoscopy; and (4) lack of relevant data for statistical analysis or loss to follow-up during the first 2 years.

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. Written informed consent was obtained from the patients.

Data from the patients were obtained retrospectively from their medical records [2]. The clinical, histopathologic characteristics, type of treatment, and oncologic results of 3 cohorts of patients with pelvic lymph node involvement by imaging tests were compared: group 1, patients who underwent laparoscopic pelvic lymph node debulking during staging extraperitoneal aortic lymphadenectomy; group 2, patients who only underwent extraperitoneal aortic lymphadenectomy for pretherapeutic staging; and group 3, patients without pretherapeutic surgical staging. The criteria for performing pelvic debulking and/or aortic lymphadenectomy depended on the protocols of each hospital [2].

Subsequently, group 1 patients were divided for post-surgery analyses in 2 groups: group 1A included patients who underwent pelvic debulking, and the pathology report of the pelvic lymph nodes was negative; and group 1B included patients for whom the pathology result was positive.

Regarding imaging tests, they were reviewed by a single radiologist in each hospital participating in the study. Enlarged pelvic nodes were considered those larger than 1 cm in their short diameter by MRI, especially in the presence of other nodal features suggestive of involvement, such as round appearance or necrosis. In the PET-CT, the areas of increased uptake of the 18F-fluorodeoxyglucose tracer were qualitatively evaluated: positive nodes were those that lit up more than the background. Enlarged lymph nodes found until the bifurcation of the common iliac artery were considered pelvic.

Surgical Procedure

Para-aortic lymphadenectomy was performed by extraperitoneal laparoscopy or robotic, following procedures already described [2,20].

Pelvic lymph node debulking: in group 1, extraction of the enlarged pelvic nodes was carried out, directed by previous imaging techniques, using an extraperitoneal or transperitoneal approach depending on the node location and at the discretion of the surgeon after performing extraperitoneal aortic lymphadenectomy [21]. The nodes were removed in endoscopic bags and without fragmentation to avoid potential tumor spread. In addition to imaging enlarged nodes, intraoperatively enlarged nodes were also removed. However, a systematic lymphadenectomy was not performed in any case.

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 [2,22].

The Clavien-Dindo classification was used to categorize postoperative complications [23].

Chemoradiation Treatment

All patients received external radiation therapy up to a total dose of 45 Gy in 25 fractions in 5 weeks, concomitantly with cisplatin 40 mg/m^2 weekly. All patients received brachytherapy 30 to 35 Gy at point A without exceeding 20 Gy at the bladder point or 15 Gy at the rectal point. An additional boost was administered up to a maximum of 85 Gy in cases of suspected pelvic nodes by imaging in groups 2 and 3 or in cases of histologically confirmed macroscopic or microscopic positive nodes in group 1B. In the cases in which intensity-modulated radiation therapy was performed, the integrated and simultaneous boost was performed with the same previous criteria in doses of 57.7 Gy in 25 fractions. Groups 1 and 2 received extended-field RT in cases in which aortic lymph node involvement was histologically confirmed and group 3 in cases in which there was suspicion of aortic lymph node involvement by imaging.

CRT complications were registered using the *Common Terminology Criteria for Adverse Events v4.0* (US Department of Health and Human Services, National Institutes of Health National Cancer Institute; Bethesda, MD*)* [24] and classified as early or late depending on their occurrence before or after 90 days post-treatment, respectively.

Once the treatment was completed, follow-up was carried out as previously published [2,20,22].

Statistical Analysis

Categoric variables were expressed as frequencies and percentages, and quantitative variables as median and interquartile range (IQR) (25th−75th percentile). Categoric variables were compared using the chi-square (v2) test or Fisher exact test and continuous variables using Student's *t* test or Mann-Whitney U test for groups of 2 continuous data and analysis of variance or Kruskal-Wallis test for groups of 3 or more continuous data. Outcome data were described by the Kaplan-Meier method, and survival curves were compared using the log-rank test. Cox models were used to analyze the factors studied as risk factors for mortality using the risk estimation as hazard ratio (HR) and its 95% confidence interval (CI). Statistical significance was set at $p < .05$. R statistical software (version 3.6.1) was used for data analysis.

Results

From a total of 414 eligible patients, 381 were included: 164 patients in group 1, 111 patients in group 2, and 106 in group 3 (Fig. 1). Table 1 shows the clinical, diagnostic, and pathologic characteristics of the patients in each group. No information is available on the ethnicity of the patients since it was not collected.

Surgical Staging

The surgical data for groups 1 and 2 are shown in Table 2. There were no statistically significant differences in length of hospital stay or estimated blood loss, but in the group undergoing pelvic debulking, the surgery lasted a median of 82 minutes longer than in group 2 (215 minutes [IQR 170−240] in group 1 vs 132.5 minutes [IQR 113 −150] in group 2). There were no differences between the 2 surgical groups in intraoperative (3.7% in group 1 vs 2.7% in group 2, p = .744), early postoperative (8.0% vs 6.3% respectively, p = .776), or late postoperative complications (6.1% vs 2.7%, p = .252).

The median number of pelvic nodes removed during debulking was 8.5 (IQR 3−13), with a median size of 13 mm (IQR 8−18). Extracapsular invasion was present in 32.8% of metastatic lymph nodes. According to MRI, the median diameter of affected pelvic lymph nodes was 12 mm (IQR 10−15) in group 1, 12 mm (IQR 10−18) in group 2, and 11 mm (IQR 10−15) in group 3.

In group 1, pelvic lymph node involvement was confirmed (group 1B) in 71 patients (43.3%). The median number of aortic nodes removed was 12 (IQR 9−18) in group 1 and 14.5 (IQR 10.2−19.0) in group 2. Aortic nodes were positive in 40 patients (24.4%) of group 1 and in 33 (29.7%) of group 2 (p = .398). Table 2 describes the distribution of isolated and concomitant pelvic and aortic lymph nodes involvement as determined by pathologic analysis.

Concordance between Imaging and Pathology for Detection of Lymph Node Metastasis

Fig. 2 shows the distribution of lymph node involvement of the pelvic and aortic nodes according to the initial imaging analyses of group 1. The combination of MRI and/or PET-CT for the detection of metastases in pelvic nodes had a positive predictive value of 46.4 (95% CI, 36.95−56.1). When the pelvic lymph nodes were negative for metastasis, the aortic involvement was 6.7%.

Chemoradiation Treatment

Table 3 shows the details of CRT, as well as early and late toxicity, of the 4 groups under study. All patients received external pelvic RT, with pelvic boost irradiation in groups 1B, 2, and 3. Extended RT was performed at the aortic level in 9.9% of group 1A, 51% of group 1B, 28.2% of group 2, and 71.6% of group 3.

In the patients undergoing pelvic lymphadenectomy, there were fewer complications from radiation therapy when the nodes were negative (group 1A), especially in relation to early and late urinary complications.

Fig. 1

STROBE diagram. ECOG = Eastern Cooperative Oncology Group; E IIIC1r FIGO staging; LACC = Locally advanced cervical cancer

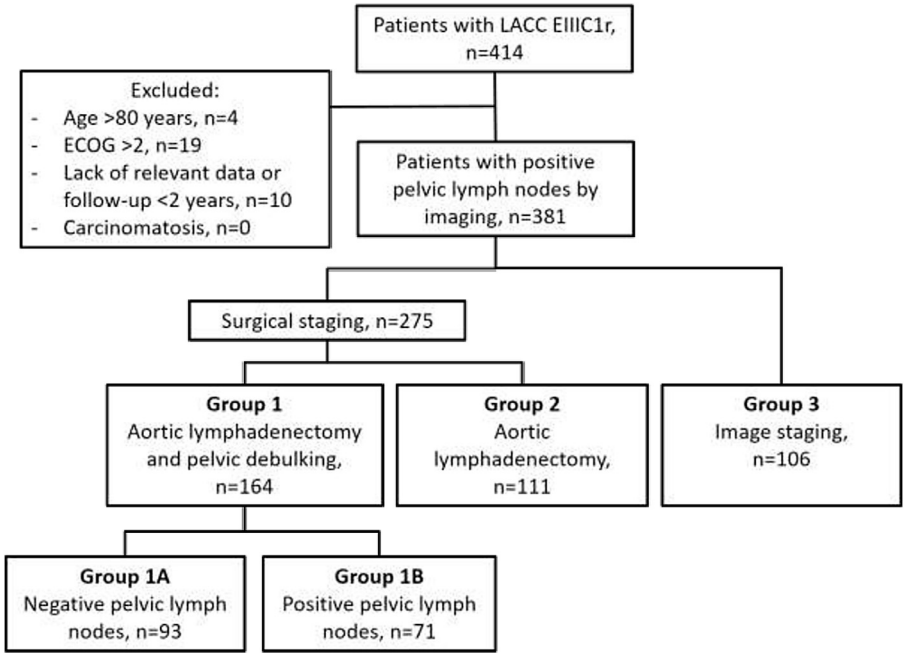


Table 1

Clinical characteristics of the patients

Variables	All patients n = 381	Group 1* n = 164	Group 2† n = 111	Group 3‡ n = 106	p-value
Age at diagnosis, yrs	49 [41−58]	48.5 [40−58]	49 [41−55]	51 [44−61]	.113
Body mass index, kg/m^2	25.9 [22.4−29.5]	26.0 [22.2−29.5]	25.3 [21.7−29.4]	26.2 [23.1−29.6]	.422
ECOG performance status					
0	263 (69.1)	129 (78.6)	93 (83.7)	41 (38.7)	<.001
1	118 (30.9)	35 (21.3)	18 (16.2)	65 (61.3)	
Histologic subtype					
Squamous	308 (83.5)	132 (83)	99 (91.7)	77 (75.5)	.007
Adenocarcinoma	61 (16.5)	27 (17)	9 (8.3)	25 (24.5)	
Adeno-squamous	5 (1.3)	3 (1.8)	1 (0.9)	1 (0.9)	
Undifferenced	7 (1.8)	2 (1.2)	2 (1.8)	3 (2.8)	
Tumor grade					
G1 well differentiated	22 (5.7)	6 (3.6)	6 (5.4)	10 (9.4)	.167
G2 moderately differentiated	83 (21.7)	41 (25)	26 (23.4)	16 (15.1)	
G3 poorly differentiated	110 (28.8)	50 (30.4)	33 (29.7)	27 (25.5)	
Not available	166 (43.5)	67 (40.8)	46 (40.5)	53 (50.9)	
FIGO stage (2009)					
IB2	64 (16.7)	43 (26.2)	12 (10.8)	9 (8.5)	
IIA2	22 (5.8)	9 (5.5)	11 (9.9)	2 (1.9)	
IIB	200 (52.5)	82 (50)	65 (58.6)	53 (50)	
IIIA	7 (1.8)	1 (0.6)	3 (2.7)	3 (2.8)	
IIIB	75 (19.7)	29 (17.7)	18 (16.2)	28 (26.4)	
IVA	13 (3.4)	0 (0)	2 (1.8)	11 (10.4)	
Imaging studies					
MRI,	359 (94.7)	156 (96.3)	108 (97.3)	95 (89.6)	.034
Positive pelvic and/or para-aortic nodes	292 (81.3)	110 (70.5)	96 (88.9)	86 (90.5)	<.001
Positive pelvic nodes	280 (78)	99 (63.5)	96 (88.9)	85 (89.5)	<.001
Positive para-aortic nodes	32 (8.9)	15 (9.6)	2 (1.9)	15 (15.8)	.001
Size of positive pelvic nodes, mm	12 [10−15]	12 [10−15]	12 [10−18]	11 [10−15]	.925
PET-CT,	175 (46.2)	51 (35.1)	56 (50.5)	68 (64.2)	<.001
Positive pelvic and/or para-aortic nodes	141 (80.6)	37 (72.5)	46 (82.1)	58 (85.3)	.207
Positive pelvic nodes	138 (78.9)	35 (68.6)	46 (82.1)	57 (83.8)	.102
Positive para-aortic nodes	36 (20.6)	10 (19.6)	6 (10.7)	20 (29.4)	.037
SUV[i] of tumor in PET-CT	16.9 [12−22.4]	14.7 [11.9−20.9]	16.1 [11.8−21.5]	18.5 [13−23]	.511

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

Values are given as median [IQR range] and number (%).

* Group 1: Aortic lymphadenectomy and pelvic debulking.

† Group 2: Aortic lymphadenectomy.

‡ Group 3: Nonsurgery.

Recurrence and Persistence

Table 4 shows the characteristics of disease persistence and recurrence. There were a greater number of regional recurrences at the pelvic level in patients in group 1B (14%) compared with the other groups (p = .015) and a greater number of distant recurrences, although not statistically significant.

Prognostic Impact and Analysis of Survival

Lymph node involvement presented a significant risk of death (HR = 1.93, 95% CI, 1.28−2.89; p = .001) and of recurrence (HR = 1.93, 95% CI, 1.28−2.89; p = .001). With a median follow-up period of 3.7 years (IQR 1.7−6.2), 148 patients (39.4%) had died at the last follow-up date (37.4% in group 1A, 50.7% in group 1B, 37.6% in group 2, and 35.2 % of group 3; p = .182). Of the 228 patients alive at the last follow-up date, 206 (90.7%) were disease-free (92.9% in group 1A, 94.3% in group 1B, 88.2% in group 2, and 89.7% in group 3; p = .772).

The OS at 5 years was 69.06% (95% CI, 0.59−0.80) in group 1A, 55.41% (95% CI, 0.44−0.69) in group 1B, 63.27% (95% CI, 0.53−0.75) in group 2, and 67.69% (95% CI, 0.58−0.77) in group 3. There were no differences in OS or disease-free survival (DFS) among the 3 groups or between groups 1A and 1B (Figs. 3 and 4).

Table 2

Surgical data of groups 1 and 2

Variables	All n = 275	Group 1* n = 164	Group 2† n = 111	p-value
Conventional laparoscopy approach	261 (95.3)	155 (94.5)	107 (96.4)	.57
Robotic assisted	13 (4.7)	9 (5.5)	4 (3.6)	
Conversion to laparotomy	9 (3.3)	6 (3.7)	3 (2.7)	.743
Intraoperative blood loss, mL	50 [20−78.8]	40 [20−50]	50 [32.5−147.5]	.05
Marsupialization	194 (75.8)	120 (76.4)	74 (74.7)	.875
Drain	55 (21.6)	40 (26.1)	15 (14.7)	.043
Blood transfusion	13 (4.9)	7 (4.4)	6 (5.6)	.889
Operative time, min	180 [130−240]	215 [170−240]	132.5 [113.8−150]	<.001
Length of hospital stay, d	2 [2−3]	2 [2−3]	2 [1−3]	.554
Hemoglobin decrease	1.3 [0.3−2.2]	1.4 [0.4−2.4]	1.2 [0.2−2.1]	.336
Pelvic lymph nodes excised	—	8.5 [3−13]	—	
Para-aortic lymph nodes excised	13 [9−18]	12 [9−18]	14.5 [10.2−19]	.123
Findings in pathologic anatomy:				
Pelvic lymph nodes				1
Negative	—	93 (56.7)	NA	
Positive	—	71 (43.3)	NA	
Size of positive pelvic lymph node, mm	—	13 (8,18)	NA	
Para-aortic lymph nodes				.398
Negative	202 (73.5)	124 (75.6)	78 (70.3)	
Positive	73 (26.5)	40 (24.4)	33 (29.7)	
Both pelvic and para-aortic lymph nodes positive	—	29 (17.8)	NA	
Both pelvic and para-aortic lymph nodes negative	—	82 (50.3)	NA	
Pelvic positive and para-aortic negative lymph nodes	—	42 (25.7)	NA	
Pelvic negative and para-aortic positive lymph nodes	—	11 (6.7)	NA	
Intraoperative complications	9 (3.3)	6 (3.7)	3 (2.7)	.744
Postoperative complications within 30 d	20 (7.3)	13 (8)	7 (6.3)	.776
Postoperative complications after 30 d	13 (4.7)	10 (6.1)	3 (2.7)	.252

IQR = interquartile range (25th−75th percentile); NA = not applicable.
Values are given as median [IQR range] and number (%).
* Group 1: Aortic lymphadenectomy and pelvic debulking.
† Group 2: Aortic lymphadenectomy.

Discussion

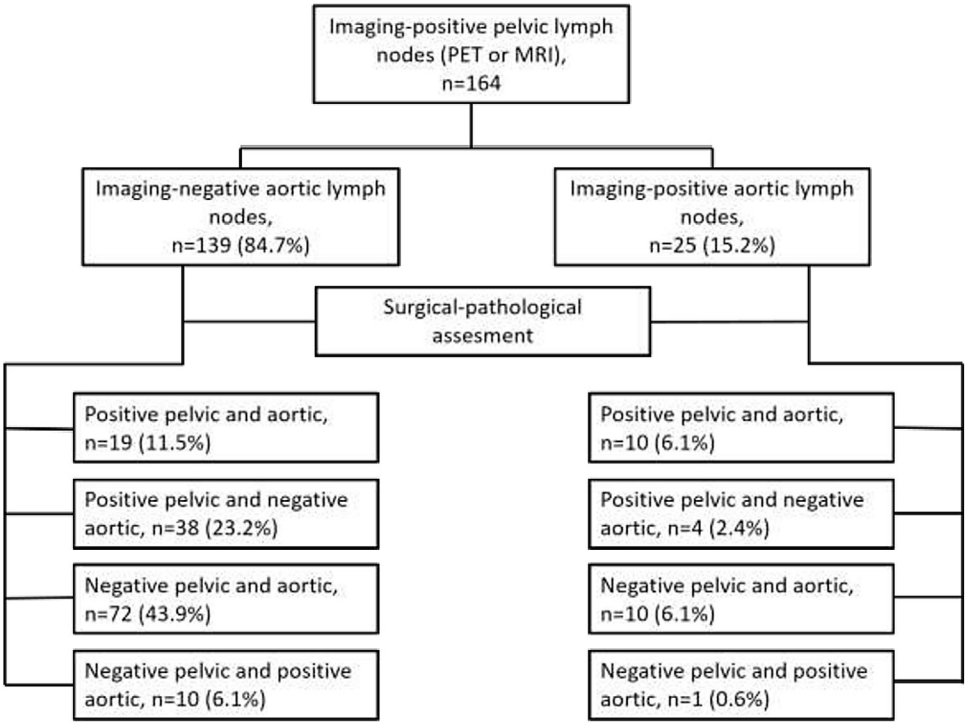
In this study, laparoscopic pelvic lymph node debulking confirmed the presence of metastases in approximately half of the patients with suspected pelvic lymph node involvement on imaging tests. This procedure did not significantly increase the morbidity of para-aortic staging surgery. Patients who did not have histologically confirmed pelvic lymph node metastasis had significantly fewer complications from radiation therapy, especially urinary. The OS and DFS in the patients with histologically confirmed pelvic nodal involvement were equivalent to that of the patients with no pelvic nodal involvement.

Although surgical staging in locally advanced cervical cancer has traditionally been considered only at the aortic level to determine areas for extended field RT, its routine performance is controversial [2]. A Cochrane review concluded that the decision to offer surgical pretherapeutic assessment of para-aortic lymph nodes in locally advanced cervical cancer needs to be individualized [25], since from the available randomized controlled trial there was insufficient evidence to demonstrate a benefit of surgical staging [26]. The recent results of the prospective trial Uterus-11 showed no differences in OS and progression-free survival globally, although a significant benefit in DFS was found for patients with FIGO stage IIB and, in a post-hoc analysis, a cancer-specific survival benefit in favor of laparoscopic staging [27]. However, in this study aortic lymphadenectomy was performed at the same time as pelvic lymphadenectomy, even in those cases that presented bulky pelvic nodes, and therefore, the effects only at the pelvic level were not evaluated. Performing pelvic lymph node debulking during pretherapeutic aortic staging may still be more controversial owing to the lack of studies studying its impact on diagnosis, treatment, and survival outcomes.

Overall, approximately 34% of patients with locally advanced cervical cancer have pelvic lymph node involvement [28]. Since the pelvic lymph node area is included in the irradiation field, most surgeons do not perform routine pelvic lymphadenectomy. For this reason, there is little information on the accuracy of pelvic lymph node

Fig. 2

Distribution of metastatic involvement of the pelvic and aortic nodes according to initial imaging tests. MRI = magnetic resonance imaging; PET = positron emission tomography.



involvement based on imaging tests. Some series, such as the Uterus-11 [29], in which CT is used for preoperative evaluation presented false negative rates at the pelvic level of 27.8% and false positives of 29% after performing systematic pelvic lymphadenectomy. In our series, the selection of cases with suspected pelvic lymph node involvement was performed by MRI and/or PET-CT and confirmed a positive predictive value of 46.4%. Although the best test for lymph node evaluation in patients with locally advanced cervical cancer is PET-CT [30], it is possible that concomitant tumor-related inflammatory processes may explain the high false-positive rates in the pelvic nodes. However, PET-CT evaluation of positive nodes in the para-aortic region is clinically more accurate since reactive tumor-related phenomena are less likely in this area [30]. Given the low accuracy of the imaging tests in the analysis of pelvic lymph nodes and awaiting a study that evaluates PET-CT vs staging surgery specifically, prospectively, and randomly, it seems acceptable, in conjunction with aortic lymphadenectomy, to perform pelvic lymph node debulking.

The surgical morbidity derived from performing laparoscopic pelvic lymph node debulking should also be considered. In our study, no significant increase in surgical complications was observed in group 1 compared with group 2. These data are consistent with the percentage of intraoperative and postoperative complications described in pelvic lymph node staging from 1.6% to 5.9% and para-aortic from 7.3% to 10.4% [5,31]. The slight increase in intra- and postoperative complications in group 1 compared with group 2 reflects the surgical difficulty involved in some cases in the removal of bulky nodes [20], in accordance with what was reported by other groups that describe a complication rate of up to 9% for pelvic lymph node debulking [19]. However, in these studies, morbidity did not condition a delay in the initiation of CRT. In centers with a good multidisciplinary organization, the delay of treatment owing to surgery should be minimal, as described by some authors [29].

The benefit of confirming pelvic lymph node metastases allows individualized RT treatment to be performed in patients with locally advanced cervical cancer, thus minimizing or eliminating patients who are overtreated because of false negatives in imaging tests. In our study, this information allowed us to design the specific irradiation fields by performing a concomitant pelvic boost in the areas of lymph node involvement in patients in groups 1B, 2, and 3 and to avoid such treatment and its morbidity in patients with confirmed negative pelvic nodes (group 1A). This may explain a decrease in early complications, and especially late complications owing to urinary radiation therapy observed in group 1A compared with the other groups. Although new technologies

Table 3

Treatment and toxicity

Variable	Total patients n = 381	Group 1A* n = 93	Group 1B† n = 71	Group 2‡ n = 111	Group 3§ n = 106	p-value
EBRT technique						
3D conformal radiation therapy	211 (55.3)	71 (76.3)	20 (28.1)	40 (36)	80 (75.5)	
IMRT	51 (13.4)	5 (5.3)	5 (7)	27 (24.3)	14 (13.2)	
IMRT/VMAT-SIB	75 (19.7)	9 (9.6)	39 (55)	22 (19.8)	5 (4.7)	
Not available	44 (11.5)	8 (8.6)	7 (9.8)	22 (19.8)	7 (6.6)	
Initial tumor and elective volume						
Pelvis	229 (60.1)	84 (90.1)	35 (49)	80 (71.8)	30 (28.3)	<.001
Pelvis + aortic	152 (39.9)	9 (9.9)	36 (51)	31 (28.2)	76 (71.6)	
Time from diagnosis to starting radiotherapy, d	57.5 [41−81]	59 [46−79.5]	63 [50−89.5]	73.5 [54−93]	39 [21.8−54.2]	<.001
Time from surgery to starting radiotherapy, d	31 [22.2−45]	28 [18.8−38.2]	30 [24.5−42]	39 [26−53]	—	<.001
Chemotherapy treatment	364 (95.8)	91 (97.8)	70 (100)	102 (91.9)	101 (95.3)	.038
Cycles concurrent with radiotherapy						
≥5	314 (87)	77 (86.5)	58 (84.1)	92 (90.2)	87 (86.1)	.675
<5	47 (13)	12 (13.5)	11 (15.9)	10 (9.8)	14 (13.9)	
Brachytherapy	337 (88.5)	86 (92.5)	62 (87.3)	100 (90.1)	89 (84)	.268
Type of brachytherapy						
LDR	54 (16.6)	20 (23.3)	24 (40.7)	2 (2.1)	8 (9.2)	
PDR	83 (25.5)	33 (38.4)	13 (22)	20 (21.3)	17 (19.5)	
HDR	189 (58)	33 (38.4)	22 (37.3)	72 (76.6)	62 (71.3)	
Acute toxicity	61 (16)	9 (9.7)	10 (14.1)	25 (22.5)	17 (16)	.091
Acute intestinal toxicity						.091
Grade 3	25 (6.6)	4 (4.3)	3 (4.2)	13 (11.7)	5 (4.7)	
Grade 4	1 (0.3)	1 (1.1)	0 (0)	0 (0)	0 (0)	
Grade 5	1 (0.3)	0 (0)	1 (1.4)	0 (0)	0 (0)	
No	354 (92.9)	88 (94.6)	67 (94.4)	98 (88.3)	101 (95.3)	
Acute rectal toxicity						.6
Grade 3	3 (0.8)	1 (1.1)	0 (0)	2 (1.8)	0 (0)	
Grade 4	1 (0.3)	0 (0)	0 (0)	1 (0.9)	0 (0)	
No	377 (99)	92 (98.9)	71 (100)	108 (97.3)	106 (100)	
Acute urinary toxicity						.003
Grade 3	5 (1.3)	0 (0)	0 (0)	5 (4.5)	0 (0)	
Grade 4	1 (0.3)	0 (0)	1 (1.4)	0 (0)	0 (0)	
No	375 (98.4)	93 (100)	70 (98.6)	106 (94.4)	106 (100)	
Acute hematologic toxicity						.228
Grade 3	31 (8.1)	3 (3.2)	6 (8.5)	10 (9)	12 (11.3)	
Grade 4	6 (1.6)	2 (2.2)	0 (0)	2 (1.8)	2 (1.9)	
Grade 5	3 (0.8)	0 (0)	2 (2.8)	1 (0.9)	0 (0)	
No	341 (89.5)	88 (94.6)	63 (88.7)	98 (88.3)	92 (86.8)	
Late toxicity	58 (15.2)	6 (6.5)	9 (12.7)	23 (20.7)	20 (18.9)	.022
Late intestinal toxicity						
Grade 3	13 (3.4)	3 (3.2)	3 (4.2)	5 (4.5)	2 (1.9)	.914
Grade 4	13 (3.4)	2 (2.2)	3 (4.2)	4 (3.6)	4 (3.8)	
No	355 (93.2)	88 (94.6)	65 (91.5)	192(91.9)	100 (94.3)	
Late rectal toxicity						
Grade 3	14 (3.7)	1 (1.1)	2 (2.8)	4 (3.6)	7 (6.6)	.347
Grade 4	8 (2.1)	2 (2.2)	3 (4.2)	1 (0.9)	2 (1.9)	
No	359 (94.2)	90 (96.8)	66 (93)	106 (95.5)	97 (91.5)	
Late urinary toxicity						
Grade 3	14 (3.7)	0 (0)	4 (5.6)	4 (3.6)	6 (5.7)	.007
Grade 4	10 (2.6)	0 (0)	0 (0)	7 (6.3)	3 (2.8)	
Grade 5	1 (0.3)	0 (0)	0 (0)	0 (0)	1 (0.9)	
No	356 (93.4)	93 (100)	67 (94.4)	100 (90.1)	96 (90.6)	

3D = 3-dimensional; EBRT = external beam radiotherapy; HDR = high dose rate; IMRT = intensity modulated radiation therapy; IQR = interquartile range (25th−75th percentile); LDR = low dose rate; PDR = pulsate dose rate; VMAT-SIB = volumetric modulated arc therapy-simultaneous integrated boost.

Values are given as median [IQR range] and number (%).

* Group 1A: Aortic lymphadenectomy and pelvic debulking with positive pelvic nodes.

† Group 1B: Aortic lymphadenectomy and pelvic debulking with negative pelvic nodes.

‡ Group 2: Aortic lymphadenectomy.

§ Group 3: Nonsurgery.

Table 4

Persistence and recurrences

Variable	All n = 381	Group 1A* n = 93	Group 1B† n = 71	Group 2‡ n = 111	Group 3§ n = 106	p-value
Complete response						
Yes	290 (76.1)	72 (77.2)	57 (80)	82 (73.6)	79 (75)	.782
No	91 (23.9)	21 (22.8)	14 (20)	29 (26.4)	27 (25)	
Local persistence	59 (15.5)	15 (17.2)	11 (15.5)	14 (12.6)	18 (17)	.779
Regional persistence	21 (5.5)	4 (4.3)	3 (4.2)	8 (7.2)	6 (5.7)	.826
Pelvic node persistence	11 (2.9)	0 (0)	2 (2.8)	5 (4.5)	4 (3.8)	.174
Aortic node persistence	10 (2.6)	3 (3.2)	1 (1.4)	3 (2.7)	3 (2.8)	.946
Progressive disease	25 (6.6)	2 (2.2)	2 (2.8)	14 (12.6)	7 (6.6)	.014
Recurrence	123 (32.3)	29 (31.2)	28 (39.4)	33 (29.7)	33 (31.1)	.502
Local recurrence	34 (8.9)	9 (9.7)	4 (5.6)	7 (6.3)	14 (13.2)	.253
Regional recurrence	47 (12.3)	10 (10.8)	16 (22.5)	13 (11.7)	8 (7.5)	.025
Pelvic node recurrence	25 (6.6)	5 (5.4)	10 (14.1)	8 (7.2)	2 (1.9)	.015
Aortic node recurrence	21 (5.5)	5 (5.4)	6 (8.5)	5 (4.5)	5 (4.7)	.676
Remote recurrence	74 (19.4)	14 (15.1)	17 (23.9)	23 (20.7)	20 (18.9)	.532

Values are given as number (%).
* Group 1A: Aortic lymphadenectomy and negative pelvic debulking,
† Group 1B: Aortic lymphadenectomy and positive pelvic debulking,
‡ Group 2: Aortic lymphadenectomy,
§ Group 3: Nonsurgery.

Fig. 3

Overall survival of groups 1, 2, and 3 and overall survival of groups 1A, 1B, 2, and 3. SS = surgical staging.

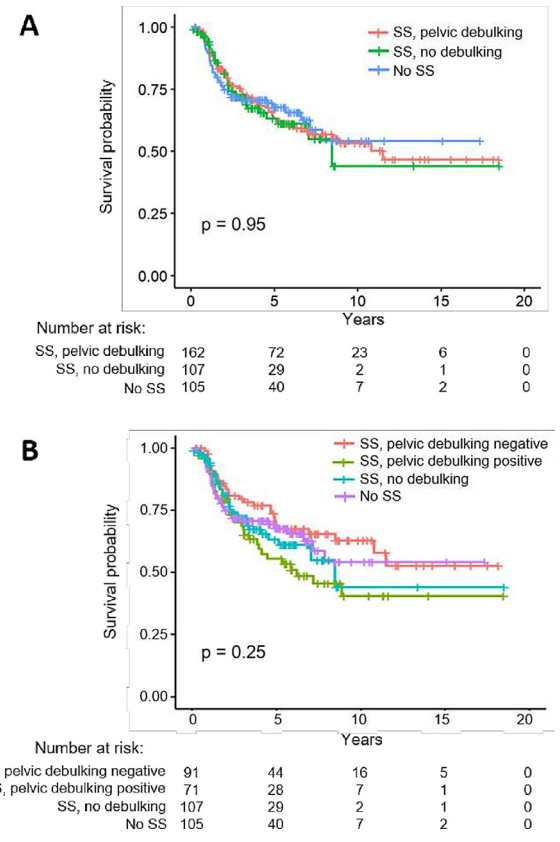
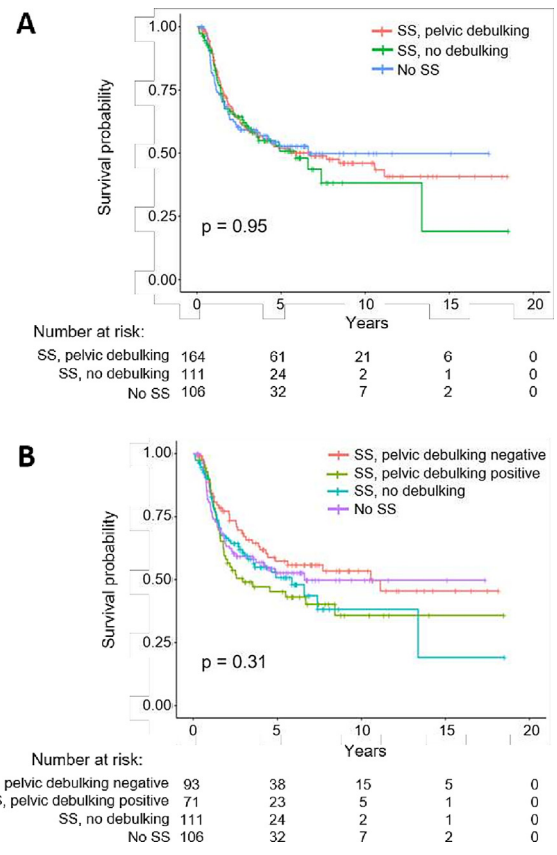


Fig. 4

Disease-free survival of the 3 groups under study and groups 1A, 1B, 2, and 3. SS = surgical staging.



in RT have allowed a considerable decrease in complications, the improvement in the indications and in the design of the radiation field are important to avoid unnecessary toxicities [32,33].

In our study, the possible therapeutic effect of pelvic lymph node debulking that facilitated the action of CRT and targeted radiation therapy, may explain why the OS and DFS among patients with and without pelvic metastatic involvement is equivalent. The FRANCOGYN group [34] compared para-aortic lymphadenectomy with pelvic plus para-aortic lymphadenectomy in 314 patients with locally advanced cervical cancer and found no difference in survival. However, in the subgroup of patients with confirmed pelvic lymph node metastases, better DFS was evident, with no differences in OS. This is in agreement with data from other series in which pelvic lymph node involvement was an independent prognostic factor for OS, so it might be warranted to confirm its involvement histologically [2,35,36].

There is controversy over whether pelvic lymph node debulking contributes to improving the radioresistance of bulky nodes [37]. According to Kupets et al [16], a randomized study to assess the theoretic beneficial effect of pelvic lymph node debulking is not feasible because of the high number of patients required [16]. In contrast, Tammela et al [38], on the basis of the calculation that the survival benefit would reach up to 43%, indicated that a trial would be feasible with fewer patients included [38]. In any case, randomized studies are needed to assess the therapeutic effect of pelvic lymph node debulking.

This study specifically evaluated the prognostic impact of pelvic debulking in locally advanced cervical cancer with a significant sample size, the largest published to date. However, it had major limitations inherent to its retrospective and multicenter design and the absence of a fully unified action protocol for the management of patients, such that the completion of the pelvic debulking was up to each center, or the lack of centralized review of imaging and pathology results. The 3 groups were unbalanced, such that there were more staged patients with PET-CT in group 3 but in turn, more patients in Eastern Cooperative Oncology Group 1 and more adenocarcinomas, a fact that could affect survival data, which should therefore be evaluated with caution. In addition, as the study collected cases spanning 16 years, not all were evaluated by PET-CT, currently considered the gold standard, as some hospitals began performing PET-CT and staging aortic lymphadenectomy only since 2010. Finally, the pelvic nodes removed were only those enlarged by imaging and intraoperatively, so this was not a study aimed at knowing the pelvic node status systematically but rather the effect of lymph node debulking. In addition, to be able to observe the effects of node debulking on OS and progression-free survival, all patients should have had pathology-confirmed metastasis because of the high rate of false negatives and false positives in imaging tests.

In conclusion, laparoscopic debulking of enlarged pelvic nodes together with staging para-aortic lymphadenectomy in patients with locally advanced cervical cancer allows for the confirmation of metastatic involvement without increasing surgical morbidity. This information is useful to accurately indicate whole-pelvic RT with nodal boost and to avoid radiation complications from overtreatment of women with negative nodes. This surgical procedure may contribute in part to explain the similar OS and DFS observed in patients with metastatic and negative pelvic nodes. Additional studies are needed to confirm the prognostic impact of pelvic lymph node debulking surgery in patients with locally advanced cervical cancer.

Acknowledgments

The statistical analysis has been carried out in the Statistics and Bioinformatics Unit of the Research Institute of the Vall d́ Hebrón Hospital. The authors thank Francisco López de Saro (Trialance SCCL) for medical writing support in the preparation of this manuscript.

References

1. Marth C, Landoni F, Mahner S, et al. Cervical cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up [published correction appears in *Ann Oncol*. 2018;29:iv262] [published correction appears in *Ann Oncol*. 2018;29:iv262]. *Ann Oncol*. 2017;28:iv72–iv83.
2. Díaz-Feijoo B, Torné A, Tejerizo Á, et al. Prognostic value and therapeutic implication of laparoscopic extraperitoneal paraaortic staging in locally advanced cervical cancer: a Spanish multicenter study. *Ann Surg Oncol*. 2020;27:2829–2839.
3. Martínez A, Voglimacci M, Lusque A, et al. Tumour and pelvic lymph node metabolic activity on FDG-PET/CT to stratify patients for para-aortic surgical staging in locally advanced cervical cancer. *Eur J Nucl Med Mol Imaging*. 2020;47:1252–1260.
4. Ramírez PT, Jhingran A, Macapinlac HA, et al. Laparoscopic extraperitoneal para-aortic lymphadenectomy in locally advanced cervical cancer: a prospective correlation of surgical findings with positron emission tomography/computed tomography findings. *Cancer*. 2011;117:1928–1934.
5. Mezquita G, Muruzabal JC, Pérez B, Aguirre S, Villafranca E, Jurado M. Para-aortic plus pelvic lymphadenectomy in locally advanced cervical cancer: a single institutional experience. *Eur J Obstet Gynecol Reprod Biol*. 2019;236:79–83.
6. Bhatla N, Berek JS, Cuello Fredes M, et al. Revised FIGO staging for carcinoma of the cervix uteri [published correction appears in *Int J Gynaecol Obstet*. 2019;147:279−280]. *Int J Gynaecol Obstet*. 2019;145:129–135.
7. SEGO publications. Clinical practice guideline of gynecological and breast cancer; 2018, http://www.seor.es/wp-content/uploads/2019/10/Cancer_cervix_2018_5.pdf. Accessed February 17, 2020.
8. Cibula D, Pötter R, Planchamp F, et al. The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology guidelines for the management of patients with cervical cancer. *Int J Gynecol Cancer*. 2018;28:641–655.
9. National Comprehensive Cancer Network. Clinical practice guidelines in oncology (NCCN Guidelines). Cervical Cancer; 2020. 1.2021 version https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed July 14, 2021.

10. Cosin JA, Fowler JM, Chen MD, Paley PJ, Carson LF, Twiggs LB. Pretreatment surgical staging of patients with cervical carcinoma: the case for lymph node debulking. *Cancer*. 1998;82:2241–2248.
11. Hacker NF, Wain GV, Nicklin JL. Resection of bulky positive lymph nodes in patients with cervical carcinoma. *Int J Gynecol Cancer*. 1995;5:250–256.
12. Withers HR, Peters LJ, Taylor JM. Dose-response relationship for radiation therapy of subclinical disease. *Int J Radiat Oncol Biol Phys*. 1995;31:353–359.
13. Wakatsuki M, Ohno T, Kato S, et al. Impact of boost irradiation on pelvic lymph node control in patients with cervical cancer. *J Radiat Res*. 2014;55:139–145.
14. Ferrandina G, Legge F, Fagotti A, et al. Preoperative concomitant chemoradiotherapy in locally advanced cervical cancer: safety, outcome, and prognostic measures. *Gynecol Oncol*. 2007;107: S127–S132.
15. Wei LC, Li X, Zhang Y, et al. Individualized pelvic lymphadenectomy should follow neoadjuvant concurrent chemoradiotherapy for locally advanced cervical cancer. *Medicine (Baltimore)*. 2018;97: e0331.
16. Kupets R, Thomas GM, Covens A. Is there a role for pelvic lymph node debulking in advanced cervical cancer? *Gynecol Oncol*. 2002;87:163–170.
17. Gouy S, Morice P, Narducci F, et al. Nodal-staging surgery for locally advanced cervical cancer in the era of PET. *Lancet Oncol*. 2012;13: e212–e220.
18. Marnitz S, Köhler C, Roth C, Füller J, Hinkelbein W, Schneider A. Is there a benefit of pretreatment laparoscopic transperitoneal surgical staging in patients with advanced cervical cancer? *Gynecol Oncol*. 2005;99:536–544.
19. Tozzi R, Lavra F, Cassese T, et al. Laparoscopic debulking of bulky lymph nodes in women with cervical cancer: indication and surgical outcomes. *BJOG*. 2009;116:688–692.
20. Diaz-Feijoo B, Luna-Guibourg R, Cabrera S, Manrique S, Gil-Moreno A. Laparoscopic extraperitoneal pelvic lymph node debulking in locally advanced cervical cancer. *J Minim Invasive Gynecol*. 2019;26:366.
21. Del Pino M, Fusté P, Pahisa J, et al. Laparoscopic lymphadenectomy in advanced cervical cancer: prognostic and therapeutic value. *Int J Gynecol Cancer*. 2013;23:1675–1683.
22. Díaz-Feijoo B, Franco S, Torné A, et al. Implications of extraperitoneal paraaortic lymphadenectomy to the left renal vein in locally advanced cervical cancer. A Spanish multicenter study. *Gynecol Oncol*. 2020;158:287–293.
23. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240:205–213.
24. *Common Terminology Criteria for Adverse Events (CTCAE)*. 2010, Children's Hospital of; Philadelphia, PAPhiladelphia Version 4.0
25. Brockbank E, Kokka F, Bryant A, Pomel C, Reynolds K. Pretreatment surgical para-aortic lymph node assessment in locally advanced cervical cancer. *Cochrane Database Syst Rev*. 2013;2013: CD008217.
26. Lai CH, Huang KG, Hong JH, et al. Randomized trial of surgical staging (extraperitoneal or laparoscopic) versus clinical staging in locally advanced cervical cancer. *Gynecol Oncol*. 2003;89: 160–167.
27. Marnitz S, Tsunoda AT, Martus P, et al. Surgical versus clinical staging prior to primary chemoradiation in patients with cervical cancer FIGO stages IIB-IVA: oncologic results of a prospective randomized international multicenter (Uterus-11) intergroup study. *Int J Gynecol Cancer*. 2020;30:1855–1861.
28. Chemoradiotherapy for Cervical Cancer Meta-analysis Collaboration (CCCMAC). Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: individual patient data meta-analysis. *Cochrane Database Syst Rev*. 2010;2010:CD008285.
29. Tsunoda AT, Marnitz S, Soares Nunes J, et al. Incidence of histologically proven pelvic and para-aortic lymph node metastases and rate of upstaging in patients with locally advanced cervical cancer: results of a prospective randomized trial. *Oncology*. 2017;92:213–220.
30. Lee SI, Atri M. 2018 FIGO staging system for uterine cervical cancer: enter cross-sectional imaging. *Radiology*. 2019;292:15–24.
31. Köhler C, Mustea A, Marnitz S, et al. Perioperative morbidity and rate of upstaging after laparoscopic staging for patients with locally advanced cervical cancer: results of a prospective randomized trial. *Am J Obstet Gynecol*. 2015;213. 503.e1−503.e7.
32. Dang YZ, Li P, Li JP, et al. Efficacy and toxicity of IMRT-based simultaneous integrated boost for the definitive management of positive lymph nodes in patients with cervical cancer. *J Cancer*. 2019;10:1103–1109.
33. Lazzari R, Riva G, Augugliaro M, et al. Intensity modulated radiation therapy boost in locally-advanced cervical cancer in the absence of brachytherapy. *Int J Gynecol Cancer*. 2020;30:607–612.
34. Bendifallah S, de Foucher T, Ouldamer L, et al. Comparison of pelvic and para-aortic lymphadenectomy versus para-aortic lymphadenectomy alone for locally advanced FIGO stage IB2 to IIB cervical cancer using a propensity score matching analysis: results from the FRANCOGYN study group. *Eur J Surg Oncol*. 2018;44:1921–1928.
35. Rose PG, Java J, Whitney CW, et al. Nomograms predicting progression-free survival, overall survival, and pelvic recurrence in locally advanced cervical cancer developed from an analysis of identifiable prognostic factors in patients from NRG oncology/Gynecologic Oncology Group randomized trials of chemoradiotherapy. *J Clin Oncol*. 2015;33:2136–2142.
36. Touboul C, Uzan C, Mauguen A, et al. Survival and prognostic factors after completion surgery in patients undergoing initial chemoradiation therapy for locally advanced cervical cancer [in French]. *Gynecol Obstet Fertil*. 2011;39:274–280.
37. Dargent D, Lamblin G, Romestaing P, Montbarbon X, Mathevet P, Benchaib M. Effect of radiotherapy on pelvic lymph node metastasis in cervical cancer stages IB2-IVA: a retrospective analysis of two comparative series. *Int J Gynecol Cancer*. 2005;15:468–474.
38. Tammela J, Bundy B, Odunsi K. Reassessment of pelvic lymph node debulking in advanced cervical cancer. *Gynecol Oncol*. 2004;92:1014–1015.