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Laparoscopic Transperitoneal Infrarenal Para-Aortic Lymphadenectomy in Patients with FIGO Stage IB1-II B Cervical Carcinoma

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ABSTRACT

Background and Objectives: This study aimed to evaluate the safety, feasibility, and clinical outcomes of laparoscopic transperitoneal infrarenal para-aortic lymphadenectomy in patients with FIGO stage IB1-IIB cervical carcinoma.

Methods: Between August 1999 and April 2009, we performed 59 laparoscopic transperitoneal lymphadenectomies; specifically, 12 procedures were performed up to the level of the left renal vessels, and 47 procedures were performed up to the level of the inferior mesenteric artery. We retrospectively analyzed the pathology reports and clinical data and compared the 2 groups. The data were analyzed with a nonparametric Mann-Whitney test, Kaplan-Meier log-rank test, and Pearson's correlation analysis.

Results: The 2 groups did not significantly differ with respect to histologic type (P=.093), clinical stage (P=.053), tumor size (P=.383), time interval to start adjuvant therapy postoperatively (P=.064), and type of adjuvant therapy (P=.407). The blood loss (P=.131), operative time (P=.200), mean hospital stay (P=.417), and postoperative self-voiding (P=.306) did not significantly differ between the groups, with the exception of the number of harvested lymph nodes (P=.001). The disease-free survival was better in the group that underwent infrarenal para-aortic lymphadenectomy than the group that did not (P=.017); however, the 2 groups did not differ with respect to overall survival (P=.115).

Conclusion: We suggest that laparoscopic transperitoneal infrarenal lymphadenectomy for cervical cancer is feasible and safe. The rate of positive lymph nodes in infrarenal lymphadenectomy is very rare in patients with locally advanced cervical carcinoma. Infrarenal lymphadenectomy in patients with cervical cancer did not provide additional survival benefits in this study.

Key Words: Cervical carcinoma, Infrarenal para-aortic lymphadenectomy, Laparoscopy.

INTRODUCTION

Lymph node metastasis is not included in the clinical staging of cervical cancer among gynecologic malignancies. However, lymph node metastasis is one of the most important prognostic factors in patients with cervical cancer.[1] Although controversies exist regarding the range and effect of lymphadenectomy in patients with cervical cancer, lymphadenectomies are performed for radical treatment and surgical staging.[2] The purpose of performing a lymphadenectomy is to evaluate lymph node metastasis for planning the treatment and to obtain the debulking effect of removing metastatic nodes.[3] When extensive treatment is necessary for cervical cancer, a radical hysterectomy with pelvic lymphadenectomy, or para-aortic lymphadenectomy are performed. However, the range and effect of the para-aortic lymphadenectomy has not been determined.[4]

This study compared the surgical and clinical outcomes between 2 groups in which laparoscopic radical hysterectomy with lymphadenectomy was performed. One group underwent para-aortic lymphadenectomy with an infrarenal lymphadenectomy, and the other group underwent para-aortic lymphadenectomy without infrarenal lymphadenectomy.

PATIENTS AND METHODS

We retrospectively reviewed data from 59 cervical cancer patients registered in the Cancer Registry of Kyungpook National University Hospital (KNUH; Daegu, Korea) from August 1999 through April 2009. All patients underwent laparoscopic transperitoneal radical hysterectomy (type III [Meigs' hysterectomy]), bilateral pelvic lymphadenectomy, and bilateral para-aortic lymphadenectomy. Twelve patients underwent para-aortic lymphadenectomy up to

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the level of the renal vessels (group I), and 47 patients underwent para-aortic lymphadenectomy up to the inferior mesenteric artery (group II). When the laparoscopic transperitoneal radical hysterectomies were performed in early cases, the para-aortic lymphadenectomy was performed up to the inferior mesenteric artery, while in later cases the surgery was performed up to the renal vessels.

The medical records of patients in both groups were reviewed for patient characteristics, surgical results, and clinical parameters. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) software for Windows (version 15.0; SPSS, Inc., Chicago, IL, USA). The Mann-Whitney U test, Kaplan-Meier method, log-rank test, and Pearson's correlation analysis were used for comparing the 2 groups. $P<.05$ was considered significant. KNUH does not require approval from the Institutional Board for retrospective chart reviews; hence, this analysis was exempted from the approval process.

Surgical Procedure

The primary puncture was made using an 11-mm sharpened triple-edge pyramidal trocar after a skin incision along the lower margin of the umbilicus was made. CO_2 gas was used for insufflation of the abdominal cavity. The second puncture was made at the suprapubic area with a 5-mm trocar. The third and fourth punctures were made in the 2 lower quadrants with 5-mm trocars, and the fifth puncture was made in the left upper quadrant with an 11-mm trocar. The main procedure began after the pelvis was inspected for intraabdominal disease and biopsies of all suspicious lesions were obtained.

The lymphadenectomy began in the right para-aortic area by incising the peritoneum covering the upper part of the right iliac artery. The camera showed the aorta and vena cava horizontally, with the vena cava on top of the aorta. After identification and lateral displacement of the right ureter, the pre- and para-caval lymph nodes were dissected from the common iliac artery on the right side at the level of the right ovarian vein.

For a left-side para-aortic lymphadenectomy, the lymph nodes were dissected from the para-aortic and presacral areas after identification of the left ureter and inferior mesenteric artery, and an inframesenteric lymphadenectomy was performed (group II). The left para-aortic lymph node dissection extended up to the level of the renal vessels (group I). All dissected lymph nodes were removed through the 11-mm port site and enveloped in an endobag for prevention of port-site metastasis **(Figure 1)**. All dissected lymph nodes were sent for frozen section analysis. If the lymph nodes were negative, the next procedures were continued. After completion of the para-aortic lymphadenectomy, the pelvic lymphadenectomy and radical hysterectomy were performed.

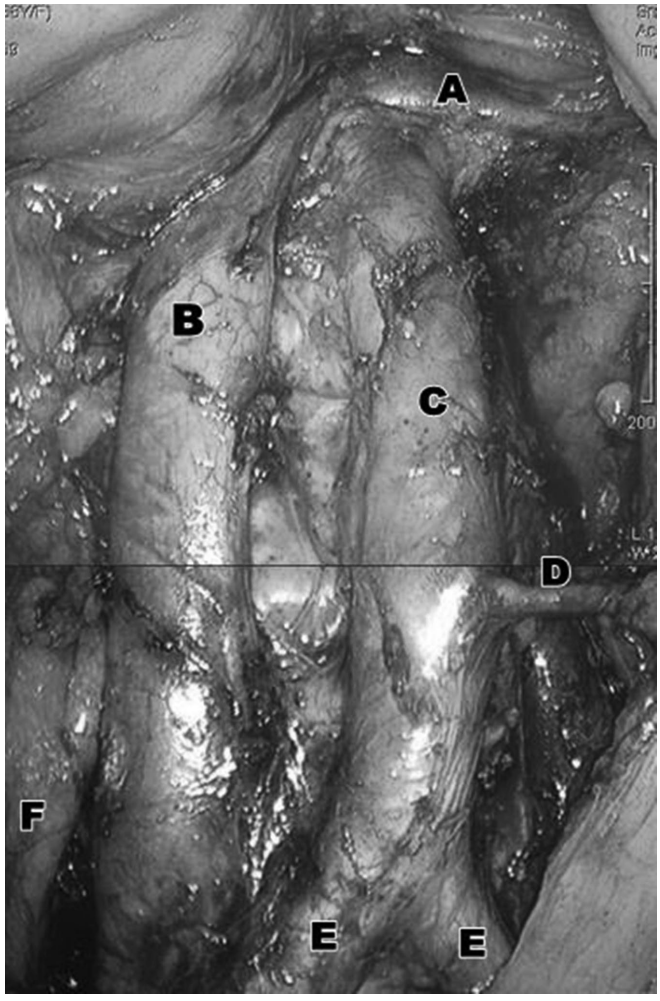

Figure 1. Para-aortic and pelvic lymphadenectomy. (A: left renal vein, B: vena cava, C: aorta, D: inferior mesenteric artery, E: both common iliac artery, F: right ureter)

RESULTS

Both groups were similar with respect to age and body mass index (45.0±8.6 [mean±SD] vs. 49.3±11.2 [mean±SD] years, P=.283; and 24.6±4.3 [mean±SD] vs. 24.0±3.4 [mean±SD] kg/m^2, P=.930, respectively). The most prevalent histologic type of cancer, squamous cell carcinoma, was found in both groups (67% vs. 85.4%, P=.093). The predominant FIGO stage was IB1 in both groups, (67% vs. 39.5%, P=.053). Tumor sizes in group I were 2 cm to 4 cm in 75% of cases and >4 cm in 25% of cases. In group II, 33.3% were

<2 cm, 16.7% were 2 cm to 4 cm, and 50% were ≥4 cm (P=.383). The time interval to adjuvant treatment in both groups did not differ significantly (47.8±38.1 [mean±SD] vs. 20.1±8.8 [mean±SD] days, P=.064). Before surgery, pelvic lymph node metastasis without para-aortic involvement was predicted based on computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET) for 4 patients in group I and 10 patients in group II (P=.385). The postoperative adjuvant treatment in group I consisted of concurrent chemoradiation (41.7%), chemotherapy (16.7%), radiation (8.3%), and no adjuvant therapy (33.3%). In group II, treatment consisted of concurrent chemoradiation (16.7%), radiation (22.9%), and no adjuvant therapy (60.4%). No statistical difference occurred between groups I and II (P=.407; **Table 1**). The surgical outcomes of both groups are summarized in **Table 2**. The total blood loss was 217.9±140.5 (mean±SD) mL in group I and 304.0±237.0 (mean±SD) mL in group II (P=.131). Compared with the postoperative hemoglobin (Hb) level, the Hb level without transfusion changed to 1.5±1.3 (mean±SD) g/dL in group I and 1.6±1.2 (mean±SD) g/dL in group II (P=.367). Two (16.6%) patients in group I and 26 (55.2%) in group II (P=.018) received transfusions. Intra- or postoperative complications occurred in 2 (16.6%) patients in group I and 15 (31.9%) in group II (P=.302). The total operative time was 271.3±50.2 (mean±SD) minutes in group I and 307.6±103.3 (mean±SD) minutes in group II (P=.200). The total number of harvested lymph nodes was 45.9±15.3 (mean±SD) in group I and 23.4±13.0 (mean±SD) in group II (P=.001). The total number of harvested para-aortic lymph nodes was 23.9±9.2 (mean±SD) in group I and 16.3±10.1 (mean±SD) in group II. The number of harvested pelvic lymph nodes was 21.3±7.7 (mean±SD) in group I and 11.5±7.2 (mean±SD) in group II. The median number of harvested infrarenal

Table 1.
Characteristics of the Patients

	Group I (n=12)		Group II (n=47)		P Value
Age, years	45.0 (±8.6)		49.3 (±11.2)		0.283
Body mass index, kg/m^2	24.6 (±4.3)		24.0 (±3.4)		0.930
Histologic type, (n, %)					0.093
Squamous	8	67	41	85.4	
Adenocarcinoma	4	33	6	12.5	
Small cell			1	2.1	
Clinical stage distribution, (n, %)					0.053
IB1	8	67	19	39.5	
IB2	3	25	13	27.1	
IIA	1	8.3	8	16.7	
IIB			8	16.7	
Tumor size					0.383
<2 cm	0		16	33.3	
2 cm ≤ <4 cm	9	75	8	16.7	
4 cm ≤	3	25	24	50	
Time interval, days	47.8 (±38.1)		20.1 (±8.8)		0.064
Positive LN in CT, MRI or PET					0.385
Paraaortic	0		0		
Pelvic	4		10		
Type of adjuvant therapy					0.407
CCRT	5	41.7	8	16.7	
Chemotherapy only	2	16.7			
Radiation only	1	8.3	11	22.9	
None	4	33.3	29	60.4	

Table 2.
Surgical Results of Lymphadenectomy in Locally Advanced Cervical Carcinoma

	Group I (n=12)		Group II (n=47)		P
Total blood loss, ml	217.9 (±140.5)		304 (±237.0)		0.131
Hb change, g/dL	1.5 (±1.3)		1.6 (±1.2)		0.367
Intra or post-op transfusion, n (%)	2	16.6	26	55.3	0.018
Intra or post-op complication, n (%)	2	16.6	15	31.9	0.302
Operation time, min	271.3 (±50.2)		307.6 (±103.3)		0.200
Harvested LN, n	45.9 (±15.3)		23.4 (±13.0)		0.001
Paraaortic	23.9 (±9.2)		16.3 (±10.1)		
Pelvic	21.3 (±7.7)		11.5 (±7.2)		
Infrarenal	7 (1-12)				
Patients with positive LN, n (%)	6 (50%)		10 (21.2.0%)		0.053
Paraaortixc	1		3		
Pelvic	5		7		
Infrarenal	0				
Hospital stay, days	8.3 (±3.7)		8.5(±3.1)		0.417
Self voiding (POD), days	8.6 (±7.0)		8 (±8.1)		0.306

Table 3.
Reports of Infrarenal Paraaortic Lymphadenectomy in Cervical Carcinoma

Author	N	Operation Type (LPS/LT)	Positive Infrarenal LN, % (n)	Isolated Positive Infrarenal LN, % (n)	Stage
Altintas et al (1995)	103	LT	4.8 (5)	0	NA
Michel et al (1998)	421	LT	4.7 (20)	1.9 (8)	Ib-IIb
Köhler et al (2003)	11	LPS	9 (1)	0	pT1b1L1 or higher
Current study	12	LPS	0	0	Ib1-IIa

[a]LPS: laparoscopy, LT: laparotomy, LN: lymph node, NA: none available.

lymph nodes was 7 (range, 1 to 12) in group I. All harvested infrarenal lymph nodes were negative for tumor. The number of tumor-positive lymph nodes was 6 (50.0%) in group I and 10 (21.2%) in group II (P=.053). The length of hospital stay was 8.3±3.7 (mean±SD) days in group I and 8.5±3.1 (mean±SD) in group II (P=.417). We routinely remove the Foley catheter on postoperative day 7; however, after a nerve-sparing technique was performed, the catheter was removed on postoperative day 5. The mean number of days to achieve a normal residual urine volume <100 mL or self-voiding was 8.6±7 (mean±SD) in group I and 8±8.1 (mean±SD) in group II (P=.306). In group I, the mean follow-up period was 41.4±18.0 (mean±SD) months. Four patients in group I had recurrences and 3 patients died. The 5-year disease-free and overall survival rates were 46% and 74.1%, respectively. In group II, the mean follow-up period was 77.6±33.2 (mean±SD) months. Seven patients in group II had recurrences and 5 patients died. The 5-year disease-free and overall survival rates were 91.3% and 91.3%, respectively. The disease-free survival was significantly different between the 2 groups (P=.017) but not the overall survival (P=.115; **Figure 2**). Based on regression analysis, the total operative time, blood loss, and number of harvested lymph nodes were not statistically different between the 2 groups during the study period **(Figure 3)**.

DISCUSSION

Laparoscopic pelvic lymphadenectomy was introduced in 1989 by Querleu[5] and laparoscopic inframensenteric para-

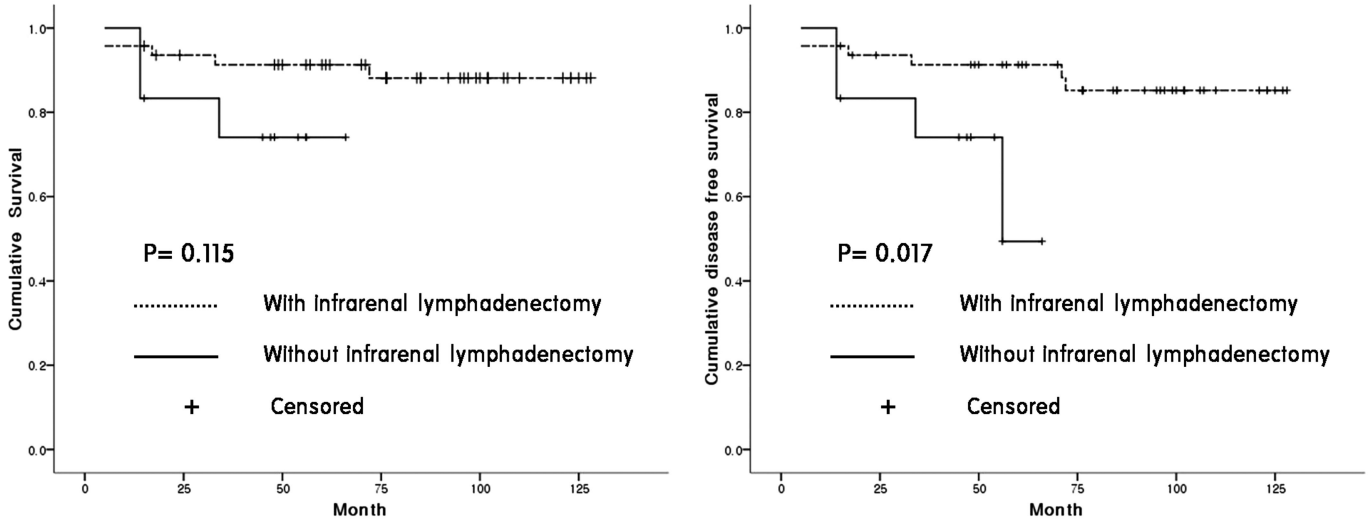

Figure 2. Cumulative overall survival and disease-free survival in groups that did and did not undergo infrarenal para-aortic lymphadenectomy.

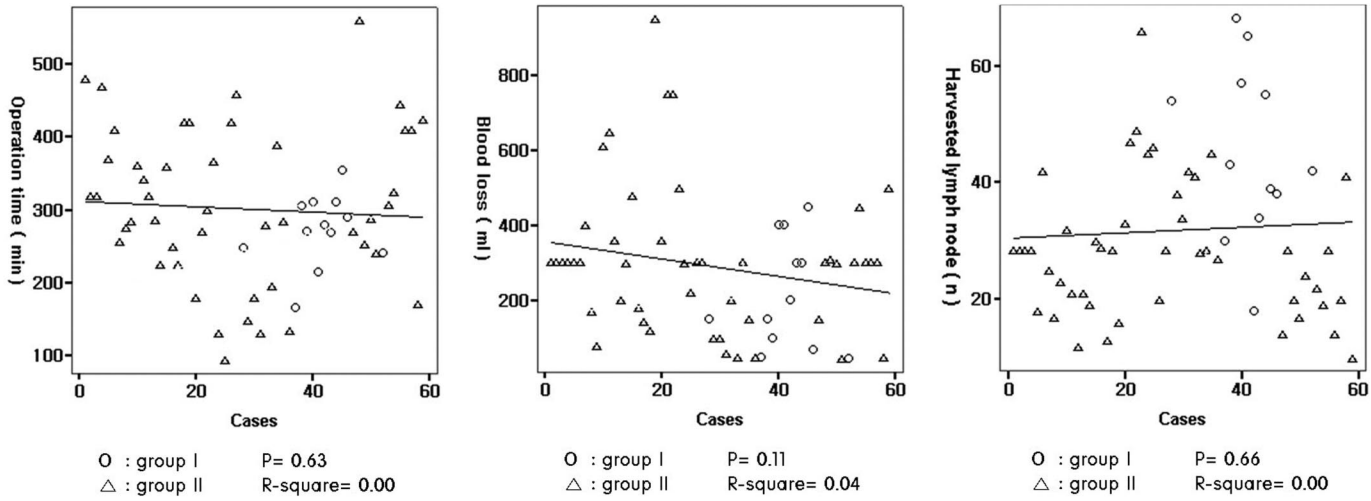

Figure 3. Regression analysis of operative on time, blood loss, and number of harvested lymph nodes relative to the increasing number of cases performed.

aortic lymphadenectomy was introduced in 1992 by Netzhat.[6] With the rapid development of laparoscopic operative techniques and instruments, laparoscopic lymphadenectomy has become a common procedure for the treatment of gynecologic malignancies. Laparoscopic surgery for advanced cervical cancer provides not only radical treatment but also the chance, by implementing staging, to benefit patients by adjusting treatment modalities according to the exact field of radiation and debulking nodal metastasis.[7] A recent advance has been robotic transperitoneal infrarenal aortic lymphadenectomy, which can be performed adequately and safely with the robotic column.[8]

A previous report described the increased survival in patients with macroscopic lymph node resected.[9] Another study also reported increased survival in patients without residual lymph nodes.[10] Marnitz et al[11] found that removal of more than 5 pelvic and/or 5 positive para-aortic lymph nodes was associated with significant improvement in overall survival. However, Goff et al[12] mentioned that without a randomized trial, it would not be possible to verify that surgical excision of grossly involved nodes provides a surgical advantage.

In this study, when the laparoscopic transperitoneal radical hysterectomy with lymphadenectomy procedure was

first performed, the surgeon was still in the learning phase, and lymphadenectomy was not performed up to the level of the renal vessel. As time progressed, an infrarenal aortic lymphadenectomy was performed.[13] When the 2 groups were compared, the differences were only in the intra- and postoperative transfusions, and harvested lymph nodes. Transfusions occurred frequently in the initial learning phase, and the larger number of harvested lymph nodes is considered a result of the more extended lymphadenectomy in group I. To examine the changes in surgical results relative to the increasing cases, a regression analysis was performed. The results showed there was no change over time with respect to blood loss, total harvested lymph nodes, and operative time; thus, the bias between the 2 groups can be minimized.

When considering the clinical and surgical results of this study, it was expected that the survival outcome would be poorer in group II, but the survival analysis showed the opposite results. Although there were limitations in comparison due to the small number of cases, the disease-free survival rate had a statistically significant decrease in group I.

Among the reported cases of cervical cancer, sufficient data on the results of infrarenal para-aortic lymphadenectomy are not available. Altintas et al[14] reported positive infrarenal lymph nodes in 5 of 103 cervical cancer patients (4.8%) and showed that omitting upper para-aortic lymph node dissection in the absence of malignant findings in the inferior para-aortic lymph node at frozen section must be considered. Köhler et al[15] reported positive infrarenal lymph nodes in 1 of 11 patients (9%). Michel et al[16] reported positive infrarenal lymph nodes in 20 of 421 stage Ib-IIb cervical cancer patients (4.7%), 8 of whom (1.9%) showed isolated positive infrarenal lymph nodes. This finding suggests that para-aortic lymphadenectomy should include removal of all of the left para-aortic chain and should be performed up to the level of the left renal vein. Michel et al[16] also recommended that because of the low frequency of para-aortic involvement when tumor size is <2 cm, such a procedure could be avoided in patients with small tumors. When the current and previous studies are comprehensively considered, the positive infrarenal lymph node rate is 4.7% (26/547), and the isolated lymph node rate is 1.4% (8/547). Of the aforementioned studies, laparoscopic lymphadenectomy was performed in our study and by Köhler et al,[15] whereas laparotomy lymphadenectomy was performed by Altintas et al[14] and Michel et al.[16]

No data are available for isolated infrarenal para-aortic lymph node recurrence after definitive therapy (staging procedure or radiation). The incidence, after definitive therapy for invasive cervical carcinoma, of radiographically detected isolated disease recurrence in para-aortic lymph node varies from 1.7% to 12%. In 2 larger series, with a combined total of 2087 patients, the incidence of isolated para-aortic recurrence was approximately 2%.[17–19] The 3-year survival rates after recurrence were 34%, 28%, and 5% for patients with para-aortic lymph node relapse alone, supraclavicular lymph node relapse with or without para-aortic lymph node relapse, and relapse other than para-aortic and supraclavicular lymph nodes. Of the patients with para-aortic lymph node relapse alone, 27% survived >5 years.[20] It was suggested that isolated para-aortic lymph node recurrence after primary irradiation due to cervical carcinoma is a curable disease. If diagnosed early with a normal SCC level or an SCC level <4 ng/mL, and no clinical symptoms or signs, the 5-year survival rate with concurrent chemoradiation was 51.2%.[18] The isolated para-aortic lymph node recurrence is very low and can be salvaged with concurrent chemoradiation after early detection.

CONCLUSION

This study showed that laparoscopic transperitoneal infrarenal lymphadenectomy is a feasible and safe procedure for gynecologic oncologists after a suitable learning phase. However, the extant literature and this study report that the ratio of isolated tumor-positive infrarenal or para-aortic lymph nodes was low, with better survival outcomes of isolated para-aortic lymph node recurrence with concurrent chemoradiation, and that the frequency of isolated infrarenal para-aortic lymph node metastasis without metastasis of inframesenteric lymph nodes was very low. Given that there is no evidence of greater survival benefits in patients who undergo infrarenal para-aortic lymphadenectomy, performing infrarenal para-aortic lymphadenectomy in patients with advanced cervical carcinoma should be withheld unless there is sufficient evidence of infrarenal lymph node metastasis. However, infrarenal lymphadenectomy can be a way to tailor postoperative ranges of radiation. This study has important limitations mostly stemming from its small sample size and retrospective design. Because of the weakness of this study, it is not reasonable to assume that high-level para-aortic lymphadenectomy might affect poor disease-free survival in group I. The poor disease-free survival might be caused by larger tumor size and greater number of positive lymph nodes. But infrarenal lymphadenectomy is not helpful in enhancing survival through debulking in this study.

Therefore, laparoscopic transperitoneal infrarenal lymphadenectomy in patients with cervical cancer is feasible and safe. However, this study showed that this procedure would not provide additional survival benefits. Further larger and randomized studies will be required to ascertain the role of infrarenal lymphadenectomy in survival outcomes.

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