

Systemic Laparoscopic Para-Aortic Lymphadenectomy to the Left Renal Vein

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ABSTRACT

Background: No large-scale clinical study has been done to show the standard surgical boundary and efficacy of laparoscopic para-aortic lymphadenectomy (LPAL).

Objectives: Therefore, this study aimed to evaluate the feasibility, efficacy, and standard surgical boundary of LPAL performed up to the left renal vein level in gynecological malignancies.

Methods: Medical records of 333 patients were retrospectively reviewed. All cases had gynecologic malignancies and had an operation including LPAL by a single surgical team between November 2003 and May 2018.

Results: Three hundred twenty-six patients underwent LPAL as part of their staging, restaging, or debulking surgery. Seven patients with isolated para-aortic lymph node recurrence underwent a repeat LPAL. The median age and body mass index were 54 years (range, 28–81 years) and 26.0 kg/m² (range, 20.3–37.2 kg/m²), respectively. The median operating time was 60 minutes (range, 24–135 minutes), and the median number of harvested para-aortic lymph nodes was 12 (range, 6–49). There were 11 cases of complications: 5 of major vessel injuries (3 inferior vena cava, 1 aorta, and 1 common iliac vein), 2

lymphocysts, 2 cases of chylous ascites, a cisterna chyli rupture, and 1 case of ureteric injury. There were 2 conversions to laparotomy: 1 left common iliac vein laceration that needed to be repaired and removal of an enlarged para-aortic lymph node completely.

Conclusion: It is feasible and efficient to perform LPAL to the left renal vein level for women with gynecologic malignancies by well-trained gynecologic oncology surgeons according to our suggested standard surgical boundary.

Key Words: Cervical Cancer; Endometrial Cancer; Laparoscopy; Lymphadenectomy; Ovarian Cancer; Para-Aortic Lymphadenectomy.

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INTRODUCTION

The status of lymph node involvement is one of the most important and independent factor affecting the prognosis in women with gynecological cancer. The pathology reports for the lymph nodes obtained from this surgery not only provide important information to predict the prognosis of the patient, but also provide more accurate information to assess the extension of the disease, enabling a tailored therapy.¹ Systemic retroperitoneal lymphadenectomy can be divided into pelvic and para-aortic lymph node dissection (PALND). The standard surgical boundary of the former is defined as the dissection of lymphatic tissue from the deep circumflex iliac vein to the midpoint of the common iliac artery. The latter is defined as the entire dissection and removal of fat and nodal tissues around the aorta, inferior vena cava, and renal vessels. The dissection level includes the left renal vein cranially and the midpoint of the common iliac vessels caudally.² The range of PALND can be classified into diagnostic, systematic and debulking dissection, depending on its radicality.³ Systemic PALND is considered a more complex and challenging surgical procedure compared to pelvic lymph node dissection that demands profound understanding of retroperitoneal surgical anatomy, advanced surgical technique, and abundant experience. Hence some gynecologic oncology surgeons choose to omit lymph node dissection, sample the lymph nodes, or per-

form lymphadenectomy to a reduced extent instead of complete retroperitoneal lymphadenectomy.^{4,5}

Para-aortic lymphadenectomy with laparoscopy is defined as laparoscopic para-aortic lymphadenectomy (LPAL) and para-aortic lymphadenectomy with open surgical procedure was defined as PALND. In the early 1990s, LPAL was introduced by some advanced laparoscopic surgeons.^{6,7} It offered advantages for women with gynecologic malignancies: shorter hospital stay, less blood loss, no increased complication rates. Shorter recovery periods in LPAL allowed the patients to start adjuvant therapy earlier than PALND.⁸ However, no large-scale clinical study has been done to show the standard surgical boundary and efficacy of LPAL since its introduction in the 1990s contrary to the well-established standard surgical boundary of PALND as indicated above.

This study aims to define the surgical boundary and evaluate the clinical efficacy of LPAL up to the left renal vein level for women with gynecologic malignancies based on the surgical outcomes by a single surgical team over a course of 12 years.

MATERIALS AND METHODS

Study Design and Patients

Medical records of 333 patients were retrospectively reviewed. All cases had gynecologic malignancies and had an operation including LPAL by a single surgical team between November 2003 and May 2018. The lymphadenectomies were performed by 5 expert gynecologic oncology surgeons. Patients' characteristics and surgical outcomes were analyzed including patients' age, body mass index, The International Federation of Gynecology and Obstetrics (FIGO) stage, change in hemoglobin concentration, estimated intraoperative blood loss, operating time, histopathological results, number of harvested lymph nodes and lymphadenectomy-related complications. Informed consent for potential complications and the possibility of conversion to laparotomy were provided to all patients before the surgery.

In this study, the surgical boundaries of LPAL were defined as caudally to the midpoint of the common iliac vessel, cranially to the left renal vein, posterior is the lumbar spine, bilaterally are the ureters and psoas muscles. Based on these surgical boundaries, systematic lymphadenectomy was performed on pre- and paraca-

val, aortocaval, preaortic, and left para-aortic lymph nodes.

The indications for LPAL include all patients with endometrial cancer, ovarian cancer, and patients with cervical cancers of FIGO stage IB1 with positive pelvic lymph node metastasis and stage IIA2 (**Table 1**). Inframesenteric lymphadenectomy up to the inferior mesenteric artery level was excluded from this study. The time required to perform lymphadenectomy starting from the peritoneal incision at crossing site of ureter over common iliac artery to the left renal vein was considered as an operating time for LPAL. This study was exempted from the Institutional Review Board approval because the chart review was conducted directly by the attending surgeon and thus the confidentiality of the participants' personal information was preserved. All values were given as medians and ranges. The statistical analysis was performed and recorded with Microsoft Excel 2013 (Microsoft Corporation, Redmond, WA).

A Sargis uterine manipulator (Richard Wolf Surgical Instrument Company, Vernon Hills, IL, USA) was transcervically inserted to manipulate the uterus easily. To prevent the possible transtubal spread of cancer cells in patients with endometrial cancer, the fimbrial portion of the fallopian tubes was ligated with a loop suture before inserting the uterine manipulator.

Surgical Techniques

All surgeries were undergone with patients in a dorsal lithotomy position and general anesthesia with endotracheal intubation. The operation room setup, patient positioning, and port-placement system for LPAL were as described previously.⁹⁻¹¹ The surgical boundaries of LPAL were posteriorly lumbar spine, bilaterally the ureters and psoas muscles. The caudal boundary was up to the midpoint of the common iliac artery and the cranial boundary was up to the left renal vein level, L2 vertebra.¹

Excluding 7 patients with isolated para-aortic lymph node recurrence who underwent repeated LPAL, 326 patients underwent LPAL as part of staging surgery, restaging surgery, or debulking surgery, where a bilateral laparoscopic pelvic lymphadenectomy from the deep circumflex iliac vein to the ureter that crosses the common iliac artery was performed before the LPAL. The positioning of the surgeon and monitor did not change during laparoscopic pelvic lymphadenectomy and LPAL. The methods how the LPAL was performed were introduced the previous studies.^{9,10,12,13} After laparoscopic pelvic lymphadenectomy, the first assistant rotated the telescope 90° clock-

Table 1.
Indications and Patients' Number of Laparoscopic Para-Aortic Lymphadenectomy up to the Left Renal Vein Level

Type of Cancer (Number)	FIGO Stage	Number of the Patients	Median Number of LNs (Range)	Number of the Patients with Positive LNs
Endometrial cancer (157)	IA	99	11 (6–21)	0
	IB	18	9 (6–15)	0
	II	13	11 (7–14)	0
	IIIA	4	9 (8–13)	0
	IIIB	1	18	0
	IIIC1	5	10 (6–15)	0
	IIIC2	17	13 (8–41)	17
Cervical cancer (117)	IB1 larger than 2 cm with negative pelvic LN metastasis	11	10 (6–32)	1
	IB1 with positive pelvic LN metastasis	36	11 (6–26)	1
	IB2	34	12 (10–15)	2
	IIA1	3	11 (10–12)	0
	IIA2	10	9 (8–13)	1
	IIB	15	15 (7–32)	2
	IIIB	6	14 (6–39)	2
Ovarian cancer (56) Tubal cancer (2) Primary peritoneal cancer (1)	Isolated para-aortic LN recurrence	2	6 (5–8)	2
	IA	14	10 (6–15)	0
	IB	5	15 (8–23)	0
	IC	8	13 (9–17)	0
	IIA	2	8.5 (8–9)	0
	IIC	1	15	0
	IIIA	2	16 (13–19)	0
	IIIB	2	20.5 (7–34)	0
	IIIC	17	18 (6–49)	14
	IV	3	10 (10–11)	1
	Isolated para-aortic LN recurrence	5	17 (10–27)	5

FIGO, Federation of Gynecology and Obstetrics; LN, lymph node.

wise so that the abdominal aorta and vena cava could be visualized in both parallel and horizontal positions and the LPAL was started from the right lower para-aortic region. After checking the path of the right ureter, it was pushed to the right side to make the right boundary of the LPAL. The right-sided LPAL was then started from the middle of the right common iliac artery. The left side para-aortic lymphatic tissue is dissected in the cephalad direction from the midpoint of the left common iliac ar-

tery. After lower para-aortic lymphadenectomy, the peritoneum is not incised further and the first assistant performs a ventral traction and tenting of the peritoneum at the level of the inferior mesenteric artery using a grasping forceps. The operator inserts an EndoGrab™ (Virtual Ports, Misgav, Israel) through a 5-mm trocar and anchors the peritoneum and falciform ligament to acquire sufficient retroperitoneal workspace (**Figure 1**). After completion of the LPAL, the surgeons checked if there was bleeding or

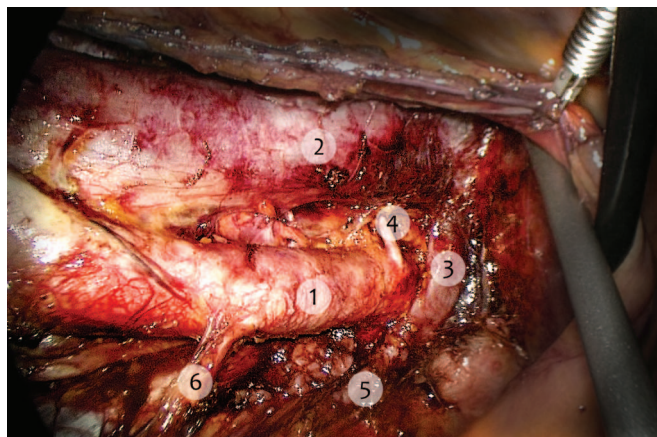


Figure 1. Laparoscopic image after systemic laparoscopic para-aortic lymphadenectomy. **1)** Abdominal aorta, **2)** inferior vena cava, **3)** left renal vein, **4)** right renal artery, **5)** left ovarian vein, **6)** inferior mesenteric artery.

leakage of lymphatic fluid. The resected lymphatic tissue was extracted through the 12-mm trocar using an endobag if hysterectomy was not performed, and through the open vaginal vault if hysterectomy was performed.

RESULTS

Three hundred twenty-six patients underwent LPAL as part of their staging, restaging, or debulking surgery. Seven patients with isolated para-aortic lymph node recurrence underwent a repeat LPAL. The surgical procedures accompanying the LPAL are as follows (**Table 2**). For endometrial cancers, 148 patients underwent laparoscopically assisted vaginal hysterectomy with bilateral salpingo-oophorectomy and 9 patients underwent laparoscopic radical hysterectomy with bilateral salpingo-oophorectomy. Six patients underwent laparoscopically assisted restaging surgery after hysterectomy at another institution. Three patients underwent a fertility-sparing laparoscopically assisted staging surgery followed by high-dose progestin therapy. One hundred fifteen patients with cervical cancer underwent laparoscopic radical hysterectomy. For ovarian cancers, 30 patients underwent laparoscopic primary staging surgery with laparoscopically assisted vaginal hysterectomy with bilateral salpingo-oophorectomy, appendectomy, omentectomy and multiple biopsy; 5 patients underwent interval debulking surgery and 16 patients who had previously received inadequate staging surgery at another hospital underwent laparoscopic restaging surgery. Two patients, both aged 23 years, and one patient aged 26 years underwent fertility-preservation surgery, including unilateral salpingo-oo-

phorectomy and contralateral ovarian cystectomy, along with LPAL. Seven patients with isolated para-aortic lymph node recurrence (2 cervical, 4 ovarian, and 1 peritoneal) underwent a repeat LPAL.¹³

The median age and body mass index of the patients were 54 years (range, 28–81 years) and 26.0 kg/m² (range, 20.3–37.2 kg/m²), respectively. The median number of harvested para-aortic lymph nodes was 12 (range, 5–49). The surgical outcome for each cancer type is listed in **Table 3**. Of the total study population, 48 patients (14.8%) were confirmed to have para-aortic lymph node metastases including 17 patients (10.8%) with endometrial cancer, 11 patients (9.4%) with cervical cancer, 19 patients (32.8%) with ovarian cancer and one patient with peritoneal cancer. Among the endometrial cancer patients with para-aortic lymph node metastasis, 10 patients (58.9%) had para-aortic lymph node metastasis with negative pelvic nodes and seven patients (41.1%) had para-aortic lymph node metastasis with positive pelvic nodes. In particular, 4 (2.5%) of the endometrial cancer patients were confirmed to have isolated para-aortic lymph node metastasis with less than 50% myometrial invasion. Most of the patients diagnosed with para-aortic lymph node metastases followed by cervical or ovarian cancer had concomitant pelvic lymph node metastasis (90.9% and 100%, respectively). The median operating time was 60 minutes (range, 24–135 minutes). There were 7 cases of intraoperative complications: 5 cases of major vessel injuries (3 inferior vena cava injuries, 1 aorta, and 1 common iliac vein), a cisterna chyli rupture and one case of ureteric injury. The aortic injury accidentally happened during the lymph node dissection with a harmonic shears (UltraCision Harmonic Scalpel®, Ethicon Endo-Surgery, Inc., Cincinnati, Ohio, USA). Repairing was done with interrupted suture with Prolene 5-0 and intracorporeal suture technique. There were 10 postoperative complications: 2 lymphocysts, 6 lymphedemas and 2 cases of chylous ascites. There were 2 conversions to laparotomy: 1 to repair a left common iliac vein laceration and the other to remove an enlarged para-aortic lymph node completely. In the former patient, bleeding from the lacerated site was so massive that a laparoscopic repair was impossible. Thus, an immediate midline skin incision was made, the bleeder was located and a vessel repair was performed with Prolene 5-0. The latter patient was a 50-year-old with ovarian serous adenocarcinoma IIIC3 in whom a vertically connecting enlarged node of around 5 cm was observed in the operation field during LPAL after laparoscopically assisted vaginal hysterectomy with bilateral salpingo-oophorectomy. A conversion was decided to completely

Table 2.

Surgical Procedures Accompanied by Laparoscopic Para-Aortic Lymphadenectomy up to the Left Renal Vein Level

Type of Cancer	Surgical Procedure	Number
Endometrial cancer	Staging surgery	148
	Restaging surgery	6
	Fertility-sparing staging surgery	3
Cervical cancer	Laparoscopic radical hysterectomy	115
	Resection of isolated LN recurrence	2
Ovary, tubal, and primary peritoneal cancer	Staging surgery	30
	Restaging surgery	16
	Interval debulking surgery	5
	Resection of isolated LN recurrence	5
	Fertility-sparing staging surgery	3

LN, lymph node.

Table 3.

Surgical Results of Laparoscopic Para-Aortic Lymphadenectomy up to the Left Renal Vein Level

	Endometrial Cancer	Cervical Cancer	Ovarian, Tubal, and PPC
Operating time, minutes, median (range)	60 (26–135)	68 (24–120)	50 (35–120)
Number of harvested LN, median (range)	12 (6–41)	11 (5–39)	12 (6–49)
LPAL-related complications (number)			
MVI	2	2	1
Chylous ascites	2	0	0
Ureteral injury	1	0	0
Symptomatic lymphocyst	1	0	1
Cistern chyli rupture	0	1	0
Lymphedema	1	1	4

LN, lymph node; LPAL, laparoscopic para-aortic lymphadenectomy; MVI, major vessel injury; PPC, primary peritoneal cancer.

remove and extract the enlarged node. Both of these patients were uneventfully discharged after conservative treatment.

DISCUSSION

Since the introduction of LPAL in the early 1990s,⁶ it has been reported as an efficacious alternative surgical technique to PALND using a laparotomic approach for women with gynecologic malignancies. Although LPAL is a more challenging procedure for surgeons than PALND, it is considered a state-of-the-art technique that gynecologic oncology surgeons must know and per-

form expertly.^{8,14,15} Lymph nodes extracted from PALND are sent for histopathologic analysis to confirm the metastasis of the lymph nodes, predict the prognosis, and provide important information for deciding on tailored adjuvant therapy.¹⁵ PALND at the time of staging surgery is the most reliable method of accurately determining lymph node status in a patient with gynecological cancers. It does not only allow for more accurate staging but also removed the involved lymph nodes compared to the imaging methods.^{16–18} The FIGO staging system for endometrial cancers and ovarian cancer includes retroperitoneal lymph node status,

the boundaries have been published and defined previously.^{15,19–21} The importance of this current study, in comparison with other studies, is that it includes only those patients who underwent a retroperitoneal systemic lymphadenectomy by complete bilateral LPAL in accordance with the definition of systematic para-aortic node dissection.²² We reviewed the intraoperative photos of LPAL, the number of the harvested para-aortic lymph nodes and the surgical outcomes from all study subjects.

Although preoperative studies to identify lymph node metastasis using a variety of radiological diagnostic techniques have been reported, their results are not satisfactory. An indirect preoperative evaluation of lymph node status with computed tomography, Magnetic Resonance imaging or positron emission tomography has low sensitivity and still has limits in replacing the operative staging procedure.^{16–18} In particular, a study on magnetic resonance imaging to evaluate para-aortic metastasis reported that when the size criterion of the short-axis diameter was set to 9 mm, the predictive value was only 14.3%, which is a far lower sensitivity than for pelvic lymph node status.¹⁷ The literature shows the rate of false-positive 18-fluoro-2-deoxy-D-glucose-positron emission tomography results to be 12.5%, suggesting that it cannot replace surgical staging in case of a positive result despite it being the most specific imaging method for nodal metastases.¹⁸ Hence the direct surgical removal of lymph nodes for histologic assessment remains the most accurate standard for staging and treatment plans in gynecological cancers.

The importance of PALND in patients with gynecologic malignancy is as follows. Although the therapeutic role of systemic PALND in gynecologic malignancies is still controversial, it allows accurate assessment of the presence of lymph node metastasis through surgical removal. It is recommended to perform systemic retroperitoneal lymph node dissection for efficient treatment because it is of significant benefit to remove the tissues highly likely to contain metastases and reduce tumor volume if metastasis is present.^{23–25}

In endometrial cancer patients, the group that received para-aortic lymphadenectomy combined with pelvic lymphadenectomy showed fewer deaths and longer overall survival compared with the group that received pelvic lymphadenectomy alone.^{26,27} The revised FIGO staging system in 2009 divided stage IIIC of endometrial cancer into C1 and C2, reflecting that para-aortic node involvement gave a worse prognosis.²⁸ For instance, 60% of stages IIIC1 endometrial cancer has a potentially

high rate of occult para-aortic node metastasis, requiring systemic para-aortic lymphadenectomy.²⁹ About 90% of the lymph node metastasis was observed in a “high” para-aortic lymph node, that is, in the lymph nodes between the renal vein and inferior mesenteric artery, and surprisingly, 35%–58% of those had confirmed metastasis only in the high para-aortic lymph nodes, without metastasis below the inferior mesenteric artery level.^{30–32} Patients with isolated para-aortic lymph node metastasis and without pelvic lymph node metastasis were reported to be 3% and among these patients, 67%–100% were reported to have high para-aortic lymph node metastasis.^{30–32} In our study, similar to previous studies, 10 patients (6.6%) had isolated para-aortic lymph node metastasis with negative pelvic nodes. All of them received appropriate adjuvant treatment and are currently without evidence of disease. Based on these results, systemic retroperitoneal PALND enables tailored adjuvant therapy which should not be missed and reduce unnecessary adjuvant therapy-related morbidity.

The importance and efficacy of PALND in epithelial ovarian cancer have been reported in many studies. This surgical procedure must be considered and at least 10 para-aortic lymph nodes should be removed when performing staging surgery for presumed early cancer and debulking surgery, as well as in cases where adequate optimal cytoreductive surgery is possible.³³ In addition, regardless of the grades and histologic types of cancer, the greater the number of harvested lymph nodes, the better the disease-specific survival. In particular, in the case of patients with stage IIIC disease and positive lymph nodes, when more than 20 lymph nodes are removed, the 5-year disease-specific survival increases to 51.1%.²³ In FIGO stage I ovarian cancer patients, lymphadenectomy also enhances the disease-specific survival and the greater the number of removed lymph nodes, the better the chances of survival.³⁴ In a randomized trial of 427 patients, systematic lymphadenectomy in advanced-stage ovarian cancer has a 7-month improved progression-free survival compared with the resection of bulky nodes (29.4 months vs. 22.4 months), but there was no difference in overall survival in amongst the patients and there was significant postoperative complications such as leg edema.³⁵

In the case of early-stage cervical cancer, radical hysterectomy with pelvic lymphadenectomy is the surgical standard.³⁶ The benefits of pretreatment laparoscopic surgical staging for patients with FIGO stage IB2 locally bulky tumor or advanced stage are deciding on necessity of extended-field radiation through the verification of para-aortic lymph

node metastasis, and reduction of the treatment-related morbidity following unnecessary treatment without actual para-aortic lymph node metastasis. For young patients, the laparoscopic transposition of the ovary outside the radiation field can be performed during LPAL to preserve the ovarian function. Even when conducting laparoscopic surgical staging, the time to commencing chemoradiation is only 9 days (mean \pm SD, 8.6 ± 3.3 days), which does not hamper postoperative treatment.³⁷ Debulking of tumor-involved lymph nodes in pretreatment laparoscopic staging surgery for locally advanced cervical cancer also enhances the overall survival.^{38,39}

Laparoscopic surgery is often applied to patients with complex benign conditions and malignant disease. However, hitherto LPAL has been a more challenging procedure than laparoscopic pelvic lymphadenectomy for surgeons because they face the risk of an increased lymphadenectomy-associated morbidity, as well as a lack of experience in LPAL. The most frequent complication is vascular injuries, excessive bleeding caused by a major vessel injury necessitated the conversion to laparotomy in 2.9% of the laparoscopic surgical staging for uterine cancer.^{8,40} It is the most frequent factor for conversion to laparotomy because of lack of experience in laparoscopic suture techniques, blood contamination in the telescope, the difficulty of sufficient exposure around the bleeding focus and the reduced volume of pneumoperitoneum from the frequent use of a suction device to find the bleeding focus. If surgery is performed taking into consideration the above mentioned methods, LPAL, which directly identifies para-aortic lymph node status and provides physicians with important information for prognosis as well as deciding tailored therapy for each individual, can be conducted successfully without increased morbidity. It is feasible and efficient for well-trained gynecologic oncology surgeons to perform LPAL to the level of the left renal vein for women with gynecologic malignancies.

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