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Effectiveness of Laparoscopic Combined Retroperitoneal and Transperitoneal Approach in Para-aortic Lymphadenectomy for Endometrial Cancer

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Abstract. *Background/Aim: This study aimed to compare laparoscopy with laparotomy and evaluate the effectiveness of a laparoscopic combined retroperitoneal and transperitoneal approach for para-aortic lymphadenectomy in patients with endometrial cancer. Patients and Methods: In this single-center retrospective study, patients with endometrial cancer who underwent para-aortic lymphadenectomy between December 2016 and November 2019 were analyzed. The patient's clinical and pathologic data were procured from medical records. Statistical analyses were performed using Fisher's exact and the Mann–Whitney U-tests. Results: A total of 37 and 28 patients were included in the laparoscopic and laparotomy groups, respectively. The laparoscopic group had similar operative time, similar number of resected para-aortic and pelvic lymph nodes, less intraoperative blood loss and complications, lower rate of blood transfusion, and shorter postoperative stay than the laparotomy group. Conclusion: Laparoscopic combined retroperitoneal and transperitoneal approach for endometrial cancer is safe and effective compared to laparotomy.*

Para-aortic lymphadenectomy is the standard staging procedure for endometrial cancer, which is the most common gynecologic malignancy in developed countries (1). Endometrial cancer often initially metastasizes to the pelvic lymph nodes followed by the para-aortic lymph nodes. Para-aortic lymph node metastasis occurs in 11.9% and 23.8% of patients in the intermediate-risk and high-risk groups, respectively (2). According to the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology, para-aortic nodal evaluation of the inframesenteric and infrarenal regions could be useful in staging women with high-risk tumors, such as deeply invasive lesions, high-grade histology tumors, serous carcinoma, clear cell carcinoma, and carcinosarcoma (3).

With the development of endoscopic equipment and minimally invasive surgical techniques, the utilization of the laparoscopic para-aortic lymphadenectomy as an approach for the management of endometrial cancer has been increasing and has been covered by health insurance since April 2020. However, the effectiveness of laparoscopic procedures in endometrial cancer remains to be determined.

Although transperitoneal para-aortic lymphadenectomy has been widely adopted in the surgical staging of endometrial cancer in Japan, this approach does not address the difficulties of small bowel retraction, dissection of adhesions, and identification of the ureters (4). In contrast, retroperitoneal para-aortic lymphadenectomy reportedly decreases enteric complications (4, 5). Therefore, we performed laparoscopic para-aortic lymphadenectomy combined with retroperitoneal and transperitoneal approach in patients with endometrial cancer.

This study aimed to compare the safety and effectiveness of laparoscopy with those of laparotomy in the para-aortic lymphadenectomy of patients with endometrial cancer and to evaluate the effectiveness of the laparoscopic combined retroperitoneal and transperitoneal approach.

Patients and Methods

Patients. In this single-center retrospective study, we included patients with T1b-2 endometrial carcinoma or T1a-2 serous, clear, and other histological types of endometrial cancer, who underwent para-aortic lymphadenectomy between December 2016 and November 2019 at Mie University Hospital. The 2017 TNM classification system was used to classify the patients accordingly.

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Patients who underwent laparoscopic surgical staging (laparoscopy group) and those who had surgical staging using laparotomy (laparotomy group) were identified. In the laparoscopy group, surgical excision through laparoscopic combined retroperitoneal and transperitoneal para-aortic lymphadenectomy was performed. The laparoscopic group and laparotomy group received enoxaparin subcutaneously at 2000 IU every 12 hours starting 24 hours after the operation until discharge.

Clinical and pathologic data. Clinical and pathologic data were procured from medical records of patients. Clinical data included age, body mass index (BMI), nulliparity, endometrial cancer-associated history (*e.g.*, diabetes mellitus, hypertension, and hyperlipidemia), surgical procedures, peri- and post-operative complications, operative time, blood loss, postoperative stay, lymph node count, lymph node status, postoperative chemotherapy, and prognostic information. Pathologic data included histology, depth of myometrial invasion, presence of lymphovascular involvement, and results of peritoneal cytology. Endometrial cancer stage was estimated in accordance with the International Federation of Gynecology and Obstetrics system (6). The histology of endometrial tumors was based on the World Health Organization Committee classification of tumors (7). This study was approved by the ethics committee of the Mie University Hospital and was performed according to the ethical standards of the Declaration of Helsinki, revised in 2001.

Laparoscopic staging procedure. A 10 mm trocar was inserted in the supraumbilical region. An additional 10 mm balloon trocar was inserted using the Spacemaker™ Dissection Balloon: PDB™ (Medtronic, Minneapolis, MN, USA) opposite the McBurney's point into the retroperitoneal space. Subsequently, a 10 mm and 5 mm balloon trocars were placed in the left abdomen. After identifying the inferior mesenteric artery and the left ureter, retroperitoneal para-aortic lymphadenectomy was performed from the aorta to the level of the left renal vein. An additional 10 mm and two 5 mm trocars were placed in the right abdomen, as seen in Figure 1. Transperitoneal right-sided, middle para-aortic, and pelvic lymphadenectomies and modified radical hysterectomy were additionally performed. Thus, eight trocar incisions were used.

Statistical analysis. Statistical analysis was performed using the Fisher's exact and the Mann–Whitney *U*-tests. Survival was assessed using the Kaplan–Meier method and compared between the two groups using the log-rank test. Statistical significance was set at $p<0.05$. All statistical analyses were conducted using the GraphPad Prism software (version 7.03; GraphPad Software Inc. San Diego, CA, USA).

Results

There were 37 and 28 patients in the laparoscopy and laparotomy groups, respectively. Clinical and pathologic data are shown in Table I. The median ages, BMI, nulliparity and endometrial cancer-associated history were not significantly different between the two groups. The laparoscopy group was less likely to have T1b but more likely to have T1a than the laparotomy group and histologic type did not differ significantly between the groups when analyzed using the Fisher's exact test.

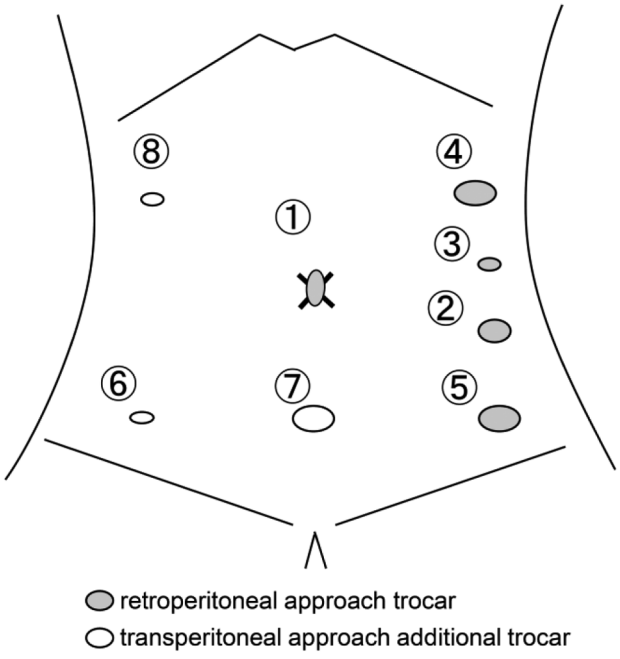

Figure 1. *Trocar placements for retroperitoneal and transperitoneal para-aortic lymphadenectomy. 10-mm balloon trocars were placed in ①②④⑤⑦ and 5-mm balloon trocars were placed in ③⑥⑧.*

Table II shows surgical findings and outcomes. The median operation times of the groups were not significantly different ($p=0.485$) when analyzed using the Mann–Whitney *U*-test. The laparoscopy group (median: 72 ml, range=18-280) had less ($p<0.0001$) intraoperative blood loss than the laparotomy group (median: 597 ml, range=386-883). The laparoscopy group (0%) had a lower ($p<0.0001$) rate of blood transfusion than the laparotomy group (42.8%). The number of resected pelvic lymph nodes was not significantly different ($p=0.301$) between the laparoscopy (median: 28, range=23.5-35.5) and laparotomy (median: 30, range=25.5-45.7) groups. The number of resected para-aortic lymph nodes was also not significantly different ($p=0.065$) between the laparoscopy (median: 20, range=14.5-33.5) and laparotomy groups (median: 29, range=20.2-36.0). Regarding operative complications within 28 days after surgery, the rate of bowel obstruction was lower ($p=0.030$) in the laparoscopy group (0%) than in the laparotomy group (14.2%), and the rate of operative complications was lower ($p=0.039$) in the laparoscopy group (8.1%) than in the laparotomy group (28.5%). The postoperative stay was shorter ($p<0.0001$) in the laparoscopy group (median: 7, range=6-10) than in the laparotomy group (median: 14, range=12-15). The median follow-up time was 32.0 months (range=24.0-38.5 months) for the laparoscopy group and

Table I. *Clinical and pathologic data*.

	Laparoscopy group (n=37)	Laparotomy group (n=28)	*p*-Value
Age (years old)	57.0 (49.5-63.0)	61.5 (54.0-67.5)	0.068
Body Mass Index	23.3 (20.3-26.1)	24.9 (20.9-29.0)	0.314
Nulliparous	2 (1-2)	2 (1-2)	0.561
Previous history associated with endometrial cancer*	17 (45.9%)	12(42.8%)	>0.999
Histologic type			
Endometrioid carcinoma G1/G2	22 (59.4%)	20 (71.4%)	0.433
Endometrioid carcinoma G3	6 (16.2%)	3 (10.7%)	
Serous carcinoma	5 (13.5%)	1 (3.5%)	
Carcinosarcoma	3 (8.1%)	3 (10.7%)	
Clear cell carcinoma	1 (2.7%)	1 (3.5%)	
Stage			
pT1a	26 (70.2%)	9 (32.1%)	0.002
pT1b	6 (16.2%)	15 (53.5%)	
pT2	5 (13.5%)	4 (14.2%)	
Lympho-vascular involvement	14 (37.8%)	13 (46.4%)	0.612
Positive peritoneal cytology	2 (5.4%)	1 (3.5%)	>0.999
Lymph node metastasis			
Pelvic nodes	3 (8.1%)	3 (10.7%)	>0.999
Para-aortic nodes	1 (2.7%)	3 (10.7%)	0.306

*Diabetes mellitus, hypertension, hyperlipidemia.

Table II. *Surgical findings and outcomes*.

	Laparoscopy group (n=37)	Laparotomy group (n=28)	*p*-Value
Surgery			
Radical hysterectomy	0 (0%)	2 (7.1%)	0.181
Modified radical hysterectomy	37 (100%)	5 (17.8%)	
Total hysterectomy	0 (0%)	21 (75.0%)	
Operating time (min)	386 (356-422)	372 (325-438)	0.485
Blood loss (ml)	72 (18-280)	597 (386-883)	<0.0001
Blood transfusion	0 (0%)	12 (42.8%)	<0.0001
Median of pelvic lymph nodes	28 (23.5-35.5)	30 (25.5-45.7)	0.301
Median of para-aortic lymph nodes	20 (14.5-33.5)	29 (20.2-36.0)	0.065
Number of operative complications	3 (8.1%)	8 (28.5%)	0.039
Vessel injury	1 (2.7%)	0 (0%)	>0.999
Bowel obstruction	0 (0%)	4 (14.2%)	0.030
Chyle or lymphorrhea	0 (0%)	1 (3.5%)	0.430
Compartment syndrome	1 (2.7%)	0 (0%)	>0.999
hydronephrosis	0 (0%)	1 (3.5%)	0.430
Re-operation	0 (0%)	1 (3.5%)	0.430
Venous thrombosis	0 (0%)	1 (3.5%)	0.430
Pulmonary embolus	1 (2.7%)	0 (0%)	>0.999

28.0 months (range=21.5-39.0 months) for the laparotomy group. The recurrence rate was not significantly different (p>0.999) between the laparoscopy (5.4%) and the laparotomy (7.1%) groups. The 2-year overall survival rates of the laparoscopy and laparotomy groups were 100% and 96.4%, respectively (p=0.239).

Discussion

Our findings are similar to those of the current literature (8-11). In the LAP2 study, a multicenter randomized controlled trial conducted by the Gynecologic Oncology Group comparing laparoscopy and laparotomy, the rate of

intraoperative complications was not significantly different between the laparoscopy (10%) and the laparotomy (8%) groups. The rate of postoperative complications was lower in the laparoscopy group (14%) than in the laparotomy group (21%). In the laparoscopy group, the rate of ileus and bowel obstruction was 5%, while the rate of all operative complications was 24% (10).

In the current study, the rates of bowel obstruction and operative complications were 0% and 8.1%, respectively, which were lower than those observed in the LAP2 study. Transperitoneal lymphadenectomy performed on patients with endometrial cancer has been widely adopted (12). Meanwhile, the retroperitoneal approach has been utilized for patients with cervical carcinoma to minimize the development of adhesions and potentially reduce the risk of radiation-related complications (13). However, this approach is not widely performed on patients with endometrial cancer in our country.

The advantage of the transperitoneal approach is the reproducibility of the laparotomy approach (14). On the other hand, retroperitoneal para-aortic lymphadenectomy has few complications and low failure rates (12, 15). Furthermore, difficulties in exposure that result from the overlying small bowel loops and obesity are reduced (16). As a result, the risk of electrosurgical bowel injury or enterotomy is reduced because the bowel and ureter are elevated out of the operative field by the peritoneal envelope (17). In a systematic review and meta-analysis, the retroperitoneal para-aortic lymphadenectomy was shown to have fewer intraoperative complications than transperitoneal lymphadenectomy (18).

The retroperitoneal approach seemingly allows better identification of the ureters and lumbar veins than the transperitoneal approach. However, the transperitoneal approach facilitates easier access to the right aortic nodes. In Mie University Hospital, the retroperitoneal approach followed by the transperitoneal approach allowed exposure of the surgical field after the retroperitoneal approach. Laparoscopic lymphadenectomy can thus be performed more safely.

The number of pelvic and para-aortic lymph nodes was not significantly different between the two groups in the LAP2 study (10). However, a retrospective multicenter study conducted in Japan found that the number of dissected pelvic and para-aortic lymph nodes was lower in the laparoscopy group than in the laparotomy group (8).

The median number of para-aortic lymph nodes is reportedly higher in the retroperitoneal group than in the transperitoneal laparoscopic and robotic groups in a review of 206 patients with endometrial cancer (12). In view of the previous study, we considered the combined retroperitoneal and transperitoneal approach for laparoscopic para-aortic lymphadenectomy because it leads to a higher number of resected lymph nodes. The retroperitoneal approach allowed better removal of the left-sided para-aortic and sacral lymph nodes than the transperitoneal approach. Compared to the retroperitoneal approach, the transperitoneal approach allowed removal of the right-sided and inter-aorto-caval para-aortic lymph nodes. In the current study, we found that the number of resected pelvic and para-aortic lymph nodes was not significantly different between the laparoscopy and laparotomy groups.

This study has several limitations. One limitation of the laparoscopic combined retroperitoneal and transperitoneal approach is the required training and experience in retroperitoneal lymphadenectomy. In the event of perforation of the peritoneum, dissection of the para-aortic nodes using the retroperitoneal approach becomes extremely difficult. In the current study, two patients (5.4%) in the retroperitoneal group required a change in approach to the transperitoneal laparoscopic lymphadenectomy. In our institute, the use of the PDB™ balloon could reduce peritoneal perforation, thus making the procedure easier. Another limitation of the combined retroperitoneal and transperitoneal approach is the requirement of more trocars than the other laparoscopic approaches. We adopted this procedure to improve the safety and usefulness of lymphadenectomy in patients with endometrial cancer. Finally, the follow-up time was short. Although in most patients, endometrial cancer has been reported to recur within 2 years (19), the median follow-up time for the laparoscopy group in our study was 32 months and the recurrence rate was not significantly different between the two groups.

In conclusion, the laparoscopy group had less intraoperative blood loss, lower rate of blood transfusion, fewer operative complications, shorter postoperative stay, and similar number of resected pelvic and aortic lymph nodes than the laparotomy group. The laparoscopic combined retroperitoneal and transperitoneal approach in para-aortic lymphadenectomy is thus as safe and useful as laparotomy in managing patients with endometrial cancer.

Conflicts of Interest

None of the Authors have any conflicts of interest to declare in relation to this study.

Authors' Contributions

Conception and design of the study: Michiko Kubo- Kaneda and Eiji Kondo; Analysis and interpretation of data: Michiko Kubo-Kaneda, Eiji Kondo, Ryo Nimura, Shintaro Maki, Masafumi Nii, Kenta Yoshida and Tomoaki Ikeda; Collection and assembly of data: Michiko Kubo- Kaneda, Ryo Nimura, Kenta Yoshida; Drafting of the article: Michiko Kubo- Kaneda and Eiji Kondo; Critical revision of the article for important intellectual content: Michiko Kubo-Kaneda; Final approval of the article: Eiji Kondo.

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