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A comparison of extraperitoneal versus transperitoneal laparoscopic para-aortic lymphadenectomy for staging of endometrial carcinoma

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Abstract

Objective—The objective of our study was to compare the surgical outcomes of extraperitoneal laparoscopic, transperitoneal laparoscopic, and robotic transperitoneal para-aortic lymphadenectomy in endometrial cancer staging.

Methods—A retrospective review was performed from January 2007 to November 2012. Three groups were compared: extraperitoneal laparoscopic para-aortic lymphadenectomy and robotic hysterectomy and pelvic lymphadenectomy (“extraperitoneal group”; N=34); laparoscopic hysterectomy and transperitoneal pelvic and para-aortic lymphadenectomy (“transperitoneal laparoscopic group”; N=108); and robotic hysterectomy and transperitoneal pelvic and para-aortic lymphadenectomy (“transperitoneal robotic group”; N=52). Fisher’s exact test and Kruskal-Wallis test were used for statistical analysis, and statistical significance was defined as $P < 0.05$.

Results—Median number of para-aortic lymph nodes obtained was higher in the extraperitoneal group than in the transperitoneal laparoscopic and robotic groups (10, 5, and 4.5 nodes, respectively; $P < 0.001$). Among patients with BMI $< 35 \text{ kg/m}^2$, the median number of para-aortic nodes harvested was higher in the extraperitoneal group than in the transperitoneal laparoscopic and robotic groups (9, 4, and 5 nodes, respectively; $P < 0.01$). The same pattern was observed among patients with BMI $\geq 35 \text{ kg/m}^2$ (10, 6, and 3 nodes, respectively) ($P = 0.001$). There was no significant difference in median estimated blood loss between the extraperitoneal group and either

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the transperitoneal laparoscopic group (100 vs. 112.5 mL; $P=0.06$) or the transperitoneal robotic group (100 vs. 67.5 mL; $P=0.23$).

Conclusion—Extraperitoneal laparoscopic para-aortic lymphadenectomy resulted in a higher number of para-aortic lymph nodes removed than transperitoneal laparoscopic or robotic lymphadenectomy. The extraperitoneal approach should be considered for endometrial cancer staging.

INTRODUCTION

Endometrial cancer is the most common gynecologic malignancy in the United States, with 49,560 new cases and 8,190 related deaths estimated for 2013 [1]. The choice of treatment for endometrial cancer and the prognosis of patients depend on the extent of disease spread at the time of diagnosis, including spread to pelvic and para-aortic lymph nodes. The risk of spread to para-aortic lymph nodes is known to be higher in patients with lymphovascular space invasion, deep myometrial invasion, cervical involvement, or high-grade tumors [2].

Despite the prognostic value of spread to lymph nodes, the role of complete lymphadenectomy in endometrial cancer staging has been highly debated among gynecologic oncologists [3–6]. Laparoscopic surgery for endometrial cancer staging, including laparoscopic lymphadenectomy, has previously been validated and results in fewer postoperative complications and shorter hospital stay than laparotomy [8]. Additionally, prior studies have suggested that performing laparoscopic para-aortic lymphadenectomy via an extra-peritoneal approach, as opposed to a trans-peritoneal approach, likely decreases both intraoperative and postoperative complications [9,10]. These complications can include postoperative ileus, intestinal obstruction, and intraperitoneal adhesions.

In 2008, Dowdy et al. initially evaluated the feasibility of extraperitoneal laparoscopic para-aortic lymphadenectomy as compared to standard laparotomy staging in endometrial cancer [9]. In that study, there were 35 patients in the laparoscopy group and 167 in the laparotomy group. The median number of total nodes collected was similar in the 2 groups—16.5 nodes in the extraperitoneal laparoscopy group and 19.6 nodes in the laparotomy group. There was, however, a difference when the groups were stratified by BMI: among patients who underwent extraperitoneal para-aortic lymphadenectomy, the median total number of nodes harvested was higher in patients with a BMI ≥ 35 kg/m² than in those with a BMI <35 kg/m² (21.6 vs. 13.1 nodes). The authors concluded that extraperitoneal laparoscopic para-aortic lymphadenectomy was a practical option for staging, particularly in obese patients.

To date, however, there have been no studies directly comparing surgical outcomes of patients undergoing extraperitoneal laparoscopic para-aortic lymphadenectomy and transperitoneal laparoscopic lymphadenectomy. The aim of this study was to compare surgical outcomes of patients treated with these approaches.

MATERIALS AND METHODS

Following institutional review board approval, a retrospective chart review was performed in which databases from the Department of Gynecologic Oncology and Reproductive

Medicine at The University of Texas MD Anderson Cancer Center were queried to identify patients who underwent extraperitoneal laparoscopic or transperitoneal laparoscopic or robotic para-aortic lymphadenectomy for staging of endometrial cancer during the period from January 1, 2007, through November 30, 2012. Eighty-six patients were identified who underwent robotic hysterectomy for endometrial cancer staging. Of these, 34 had attempted or completed extraperitoneal laparoscopic para-aortic lymphadenectomy (the “extraperitoneal group”), and the remaining 52 patients underwent transperitoneal robotic pelvic and para-aortic lymphadenectomy (the “transperitoneal robotic group”). Both these groups were compared to 108 patients who underwent total laparoscopic hysterectomy and transperitoneal laparoscopic lymphadenectomy (the “transperitoneal laparoscopic group”). If the proposed surgery was attempted but unable to be completed, these cases were analyzed in the intended treatment group. A total of seven different surgeons took part in performing the extraperitoneal para-aortic node dissection.

The procedure for extraperitoneal laparoscopic para-aortic lymphadenectomy has previously been reported [11]. Briefly, a 10 mm incision is made 3 to 4 cm medial to the left anterior iliac spine in the midclavicular line, and the surgeon uses his or her index finger to open the space between the peritoneum and muscles of the abdominal wall. A 10 mm balloon-tipped trocar is then inserted and used to visualize the extraperitoneal space. Carbon dioxide is used to insufflate the extraperitoneal space to a maximum of 14 mm Hg. A second 10 mm trocar is placed at the subcostal margin along the external clavicular line about 5 cm above the prior incision, and a third 5 mm trocar is placed 3 to 4 cm superior to this second trocar. Lymph nodes are then removed from the bifurcation of the aorta to the renal vessels bilaterally. Once the extraperitoneal portion of the procedure has been completed, the previously placed 10 mm trocar in the subcostal margin is directed intraperitoneally and used as the assistant port. The 5 mm trocar is exchanged for an 8 mm robotic trocar placed intraperitoneally under direct visualization. Two additional 8 mm robotic trocars are placed under direct visualization in the right abdomen, 8 cm apart from each other. The total number of trocars placed is 6. The robotic hysterectomy and pelvic lymphadenectomy is then performed.

All node dissections were attempted to the level of the renal vessels regardless of approach. Extraperitoneal para-aortic lymphadenectomy was performed on high risk patients while transperitoneal para-aortic lymphadenectomy was done based on frozen section. There were no cases in this study of extraperitoneal laparoscopic para-aortic lymphadenectomy followed by a total laparoscopic hysterectomy and transperitoneal pelvic lymphadenectomy.

Fisher’s exact test was used to compare categorical variables between the study groups. Age at diagnosis, BMI, operative time, estimated blood loss, number of pelvic lymph nodes harvested, number of para-aortic lymph nodes harvested, number of positive lymph nodes, length of hospital stay, and follow-up time were compared using the Kruskal-Wallis test. If a significant difference was found among all 3 groups, each pair of groups was then tested for significance. Statistical significance was defined as $P < 0.05$.

RESULTS

Patient characteristics are summarized in Table 1. Median age was similar across the extraperitoneal, transperitoneal laparoscopic, and transperitoneal robotic groups (62, 61, and 62 years, respectively; $P=0.83$). BMI was higher in the extraperitoneal group than in the transperitoneal groups but did not differ between the transperitoneal laparoscopic and robotic groups. The most common histologic type in all groups was endometrioid adenocarcinoma. The extraperitoneal group had a higher rate of papillary serous histologic type than the other groups. The most common tumor grades were as follows: for the extraperitoneal group, grade 3 (79.4%); for the transperitoneal laparoscopic group, grade 2 (53.7%); and for the transperitoneal robotic group, grade 3 (51.9%).

Median numbers of lymph nodes harvested are summarized in Table 2. The median number of para-aortic lymph nodes harvested was significantly higher in the extraperitoneal group than in the transperitoneal laparoscopic or transperitoneal robotic groups (10, 5, and 4.5, respectively; $P<0.001$). There was no significant difference in the number of para-aortic nodes harvested between the 2 groups treated with transperitoneal lymphadenectomy ($P=0.78$). The median number of pelvic lymph nodes harvested did not differ significantly between the 3 groups ($P=0.47$). The extraperitoneal group was also found to have a higher percentage of total positive lymph nodes compared to the transperitoneal laparoscopic and transperitoneal robotic groups (18.2 vs. 16.7 vs. 13.5%, respectively), but this difference was not statistically significant ($P=0.80$).

The groups were then further divided into BMI categories of $<35 \text{ kg/m}^2$ and $\geq 35 \text{ kg/m}^2$. Among patients with a BMI $<35 \text{ kg/m}^2$, the median number of para-aortic nodes harvested was greater in the extraperitoneal group ($N=17$) than in the transperitoneal laparoscopic ($N=85$) and robotic groups ($N=40$) (9, 4, and 5 nodes, respectively; $P<0.01$) (Figure 1). The same pattern was observed among patients with a BMI $\geq 35 \text{ kg/m}^2$ (median 10, 6, and 3 nodes harvested, respectively; $P=0.002$). In individual group comparisons, for those with a BMI $\geq 35 \text{ kg/m}^2$, the number of para-aortic nodes harvested in the extraperitoneal group ($N=17$) was significantly greater than the number of nodes harvested in the transperitoneal robotic group ($N=12$) ($P=0.001$) but was not significantly different from the number of nodes harvested in the transperitoneal laparoscopic group ($N=23$) ($P=0.08$). There was no significant difference between the two laparoscopic groups ($P=0.07$) (Figure 1).

The median estimated blood loss was higher in the transperitoneal laparoscopic group (112.5 mL; range, 10–3500 mL) than in the transperitoneal robotic group (67.5 mL; range, 20–1800 mL) ($P<0.001$). However, there was no significant difference in median estimated blood loss between the extraperitoneal group and either the transperitoneal laparoscopic group (100 vs. 112.5 mL; $P=0.06$) or the transperitoneal robotic group (100 vs. 67.5 mL; $P=0.23$).

The median operative time also differed significantly between the groups. The median operative time was longer in the extraperitoneal group (339.5 minutes; range, 242–453 minutes) than in the transperitoneal laparoscopic group (286 minutes; range, 101–480 minutes) and the transperitoneal robotic group (297.5 minutes, range 182–633 minutes) ($P=0.01$). In individual group comparisons, the difference in operative time was significant

between the extraperitoneal and transperitoneal laparoscopic groups ($P=0.003$) and between the extraperitoneal and transperitoneal robotic groups ($P=0.01$). Median operative time did not differ significantly between the two transperitoneal groups ($P=0.64$).

Length of hospital stay was significantly longer in the transperitoneal laparoscopic group than in the extraperitoneal group (2 vs. 1 days; $P<0.001$) and the transperitoneal robotic group (2 vs. 1 days; $P=0.002$). There was no difference in length of hospital stay between the extraperitoneal group and the transperitoneal robotic group ($P=0.42$).

Three patients (8.8%) in the extraperitoneal group required conversion to transperitoneal laparoscopic lymphadenectomy. These patients were analyzed in the extraperitoneal group. For two of these patients, conversion was secondary to peritoneal entry during the extraperitoneal dissection, and in the third patient, conversion was secondary to suboptimal visualization. The rate of conversion to an open procedure was higher in the transperitoneal laparoscopic group (15.7%; $n=17$) than in the transperitoneal robotic group (3.9%; $n=2$) ($P=0.04$), but not higher than in the extraperitoneal group (8.8%; $n=3$) ($P=0.56$). The conversions in the transperitoneal laparoscopic group were secondary to suboptimal visualization (6/17, 35.3%), vascular injuries (4/17, 23.5%), adhesions (3/17, 17.7%), obesity (2/17, 11.8%), large or bulky lymph nodes (1/17, 5.9%), and inability to maintain Trendelenburg position (1/17, 5.9%). In the transperitoneal robotic group, there were only two conversions to an open procedure, one for suboptimal visualization and one for vascular injury. These cases were analyzed in the initial group classification.

Intraoperative complications included one vascular injury in the extraperitoneal group, seven vascular injuries in the transperitoneal laparoscopic group, and one vascular injury and one bowel injury in the transperitoneal robotic group. As for postoperative complications, the three groups did not differ with respect to postoperative transfusion rates, 30-day postoperative infection rates, or 30-day noninfectious complications (Table 3). The 30-day readmission rate was 8.8% ($n=3$) in the extraperitoneal group, 8.3% ($n=9$) in the transperitoneal laparoscopic group, and 0% ($n=0$) in the transperitoneal robotic group ($P=0.05$). In the extraperitoneal group, all three readmitted patients were secondary to abdominal infections. The main reasons for readmission in the transperitoneal laparoscopic group included vaginal cuff infection, respiratory infection, and trocar and wound infections.

DISCUSSION

The key findings from our study are that extraperitoneal para-aortic lymphadenectomy is a reasonable approach for endometrial cancer staging, and is the first study to directly compare extraperitoneal laparoscopic para-aortic lymphadenectomy to transperitoneal lymphadenectomy performed with both standard laparoscopy and robotic surgery. This study showed that extraperitoneal laparoscopic para-aortic lymphadenectomy resulted in a higher median number of para-aortic lymph nodes harvested than standard transperitoneal laparoscopic para-aortic lymphadenectomy or transperitoneal robotic para-aortic lymphadenectomy. In addition, this pattern held true within the subgroups of patients with BMI <35 kg/m² and patients with BMI ≥ 35 kg/m². This study also showed that extraperitoneal para-aortic lymphadenectomy was associated with few complications and

low failure rates. Only three cases required conversion to transperitoneal laparoscopic lymphadenectomy. This was similar to the Dowdy et al. [9] study, which had an extraperitoneal para-aortic lymphadenectomy success rate of 92% (35/38).

Our findings are in agreement with previous studies of the role of extraperitoneal laparoscopic para-aortic lymphadenectomy in gynecologic malignancies which have shown that this procedure is both safe and feasible [12–14]. This procedure has been shown to result in few complications and is associated with a low probability of conversion to transperitoneal laparoscopic or open lymphadenectomy [12,13].

In our study, patients in the extraperitoneal group had a significantly higher median BMI, at 35.1 kg/m². Dowdy et al. [9] found that among patients with a BMI of 35 kg/m², the total number of para-aortic nodes harvested was higher in the extraperitoneal group. Overall, our study showed similar rates of para-aortic nodal retrieval regardless of BMI. However, among patients with a BMI 35 kg/m², the median number of para-aortic nodes harvested was significantly higher in the extraperitoneal group than in the transperitoneal robotic group. There was also a trend toward a higher number of nodes in the extraperitoneal group than the transperitoneal laparoscopic group, although this was not significantly different. This validates the use of an extraperitoneal operative technique in patients with higher BMI, as well as in conjunction with a robotic-assisted hysterectomy and pelvic lymphadenectomy. With increasing BMI, transperitoneal lymphadenectomy may not be sufficient to adequately collect nodes up to the level of the renal vessels because of poor visualization due to increased intra-abdominal adipose tissue. The extraperitoneal approach provides an alternate means for complete para-aortic lymphadenectomy in this patient population.

In our current study, the percentage of positive nodes was slightly higher in the extraperitoneal group. This fact, combined with the increased total number of nodes collected in this group, argues for a more comprehensive para-aortic lymphadenectomy with dissection to the level of the renal vessels to aid in identifying patients with advanced disease. The increased proportion of positive nodes in the extraperitoneal group may be skewed, however, by the higher percentages of patients in this group who had papillary serous and grade 3 tumors. This likely reflects, in part, our institutional practice of staging all grade 3 and non-endometrioid tumors. Those in the extraperitoneal group were at higher risk prior to surgical staging, whereas, the transperitoneal groups were staged based on frozen section criteria including deep invasion or large tumor size. The higher rate of positive nodes does support an extraperitoneal approach in patients at increased risk for lymphatic spread, as there may be more nodal tissue collection. Additionally, some may argue that the extraperitoneal approach appears superior because of the low median numbers of para-aortic nodes harvested in the groups treated with transperitoneal lymphadenectomy. Although the median number of para-aortic nodes harvested in the transperitoneal groups was lower than expected, the para-aortic lymphadenectomy for all groups was performed at the same institution with similar surgical technique.

One of the disadvantages of extraperitoneal para-aortic lymphadenectomy demonstrated in this study is the operative time of 339.5 minutes (range, 242–453 minutes), which was approximately 50 minutes longer than the operating time in the standard transperitoneal

laparoscopy group and 40 minutes longer than the operating time in the robotic transperitoneal lymphadenectomy group. Some of the increased operating time may be explained by the time needed to transition from laparoscopy to the robotic portion of the procedure rather than actual operating time. Additionally, operation times were likely increased at baseline as these cases were done at a teaching institution with residents and fellows performing a large portion of the case. With increasing BMI and associated comorbidities, however, additional operative time may result in more anesthesia-related complications and higher operating-room costs. A cost analysis was not performed in this study, but likely has notable implications given the difference in operating-room-time among the three groups in this study and the cost of the robotic device. Additionally, other studies have shown laparoscopy to be less costly than robotic surgery in endometrial cancer staging [15,16].

The strengths of this study include the fact that to our knowledge this is the first study to directly compare extraperitoneal para-aortic lymphadenectomy to standard laparoscopic staging as well as robotic laparoscopic staging. In addition, the procedures were performed during the same time period by multiple surgeons within the same institution. The indications for para-aortic lymphadenectomy were consistent for all 3 groups. Weaknesses of this study include its retrospective nature, which means that selection bias might have affected the choice of surgical approach. We did not perform a cost analysis among the three groups. Lastly, given the retrospective nature of our study, we were unable to capture data on quality of life, particularly information on patient preference regarding the cosmetic results after the different surgical approaches.

In conclusion, our study has shown that extraperitoneal para-aortic lymphadenectomy resulted in higher total number of lymph nodes harvested than either laparoscopic or robotic transperitoneal lymphadenectomy. Extraperitoneal para-aortic lymphadenectomy should be considered for surgical staging of endometrial cancer.

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Figure 1.

Median number of para-aortic lymph nodes harvested by surgical approach in patients with body mass index of <35 kg/m² and ≥ 35 kg/m². Extraperitoneal Group, extraperitoneal para-aortic lymphadenectomy and robotic hysterectomy and transperitoneal pelvic lymphadenectomy. Transperitoneal Laparoscopic Group, laparoscopic hysterectomy and transperitoneal laparoscopic para-aortic and pelvic lymphadenectomy. Transperitoneal Robotic Group, robotic hysterectomy and transperitoneal robotic para-aortic and pelvic lymphadenectomy.

Table 1

Patient characteristics

Characteristic	Group 1: extra-peritoneal approach ^a (N=34)	Group 2: trans-peritoneal laparoscopic approach ^b (N=108)	Group 3: trans-peritoneal robotic approach ^c (N=52)	P value
Age at diagnosis, years				0.83
Median	62	61	62	
Range	32–76	24–92	36–80	
Histologic subtype, No (%)				<0.001
Endometrioid	13 (38.2)	86 (79.7)	32 (61.5)	
UPSC	9 (26.5)	6 (5.6)	4 (7.7)	
Clear cell	1 (2.9)	0 (0)	2 (3.9)	
Mixed	8 (23.5)	9 (8.3)	12 (23.1)	
MMMT	3 (8.8)	5 (4.6)	2 (3.9)	
Other	0 (0)	2 (1.9)	0 (0)	
Grade, No (%)				<0.001
1	0 (0)	19 (17.6)	1 (1.9)	
2	7 (20.6)	58 (53.7)	24 (46.2)	
3	27 (79.4)	28 (25.9)	27 (51.9)	
Unknown	0 (0)	3 (2.8)	0 (0)	
Stage, No (%)				0.70
IA	21 (61.8)	54 (50.0)	33 (63.5)	
IB	2 (5.9)	17 (15.7)	7 (13.5)	
II	3 (8.8)	3 (2.8)	3 (5.8)	
IIIA	2 (5.9)	11 (10.2)	3 (5.8)	
IIIB	0 (0)	0 (0)	0 (0)	
IIIC1	3 (8.8)	7 (6.5)	3 (5.8)	
IIIC2	3 (8.8)	11 (10.2)	3 (5.8)	
IVA	0 (0)	4 (3.7)	0 (0)	
IVB	0 (0)	1 (0.9)	0 (0)	
Body mass index, kg/m ²				0.02
Median	35.1 ^{de}	28.4 ^{df}	30.2 ^{ef}	
Range	20.6–47.4	17.5–53.8	19.1–51.2	

MMMT, malignant mixed müllerian tumor; UPSC, uterine papillary serous carcinoma.

^aExtraperitoneal laparoscopic para-aortic lymphadenectomy and robotic hysterectomy and transperitoneal pelvic lymphadenectomy.

^bLaparoscopic hysterectomy and transperitoneal laparoscopic para-aortic and pelvic lymphadenectomy.

^cRobotic hysterectomy and transperitoneal robotic para-aortic and pelvic lymphadenectomy.

^dGroup 1 compared to group 2, $P<0.01$.

^eGroup 1 compared to group 3, $P=0.04$.

^fGroup 2 compared to group 3, $P=0.38$.

Table 2

Median number of lymph nodes harvested by group

Nodal category	Group 1: extra-peritoneal approach ^a (N=34)	Group 2: trans-peritoneal laparoscopic approach ^b (N=108)	Group 3: trans-peritoneal robotic approach ^c (N=52)	P value
Para-aortic lymph nodes, total				<0.001
Median	10 ^{de}	5 ^{df}	4.5 ^{ef}	
Range	4–22	1–24	1–18	
Pelvic lymph nodes, total				0.47
Median	14	13	13.5	
Range	0–25	0–31	1–36	
Lymph node status, No (%)				0.80
Positive	6 (18.2)	18 (16.7)	7 (13.5)	
Unknown	1 (2.9)	0 (0)	0 (0)	

^aExtraperitoneal laparoscopic para-aortic lymphadenectomy and robotic hysterectomy and transperitoneal pelvic lymphadenectomy.^bLaparoscopic hysterectomy and transperitoneal laparoscopic para-aortic and pelvic lymphadenectomy.^cRobotic hysterectomy and transperitoneal robotic para-aortic and pelvic lymphadenectomy.^dGroup 1 compared to group 2, $P<0.001$.^eGroup 1 compared to group 3, $P<0.001$.^fGroup 2 compared to group 3, $P=0.78$.

Table 3

Postoperative Complications

Postoperative Complication	Group 1: extra-peritoneal approach ^a (N=34)	Group 2: trans-peritoneal laparoscopic approach ^b (N=108)	Group 3: trans-peritoneal robotic approach ^c (N=52)	P value
RBC Transfusion, No cases (%)	1 (2.9)	7 (6.5)	4 (7.7)	0.93
Infections <30 days, No (%)				0.15 ^d
Gastrointestinal	1 (2.9)	0 (0)	0 (0)	
Pelvic and vaginal cuff	0 (0)	2 (1.8)	0 (0)	
Respiratory	0 (0)	7 (6.4)	1 (1.9)	
Systemic	1 (2.9)	8 (7.3)	0 (0)	
Trocar and wound	4 (11.8)	8 (7.3)	1 (1.9)	
Urinary	1 (2.9)	6 (5.5)	1 (1.9)	
Non-Infections complications <30 days, No (%)				0.36 ^d
Hematoma/lymphocyst	1 (2.9)	2 (1.8)	2 (3.8)	
Cardiovascular	0 (0)	3 (2.8)	0 (0)	
Gastrointestinal	0 (0)	1 (0.9)	0 (0)	
Neurological	0 (0)	3 (2.8)	0 (0)	
Psychiatric	2 (5.9)	2 (1.8)	0(0)	
Pulmonary	1 (2.9)	3 (2.8)	0 (0)	
Trocar and wound	2 (5.9)	1 (0.9)	0 (0)	
Renal and urinary	0 (0)	4 (3.7)	2 (3.8)	
Vaginal	1 (2.9)	1 (0.9)	0 (0)	

^aExtraperitoneal laparoscopic para-aortic lymphadenectomy and robotic hysterectomy and transperitoneal pelvic lymphadenectomy.

^bLaparoscopic hysterectomy and transperitoneal laparoscopic para-aortic and pelvic lymphadenectomy.

^cRobotic hysterectomy and transperitoneal robotic para-aortic and pelvic lymphadenectomy.

^dP-value for comparing none vs. any.