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Infrarenal lymphadenectomy for gynecological malignancies: Two laparoscopic approaches☆

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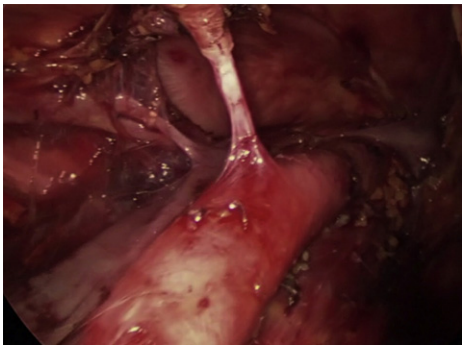
HIGHLIGHTS

- Extraperitoneal infrarenal lymphadenectomy yields more nodes in the aortic basins.
- Lymphadenectomy to the renal vein reveals occult metastases in 33% of patients.
- High aortic node dissection may improve survival by signaling enhanced therapy.

GRAPHICAL ABSTRACT



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ABSTRACT

Objective. Compare two approaches for laparoscopic infrarenal lymphadenectomy.

Methods. Retrospective chart review. Statistical analyses with SPSS.

Results. Patients: 4 stage II/III cervical carcinoma, 75 clinical stage I/II endometrial carcinoma, 36 clinically stage I/II tubal/ovarian cancer. 36 transperitoneal approaches; 79 extraperitoneal approaches. Both groups had similar age, 58 years (range 29–80), BMI of 25 (range 18–41), blood loss, 150 cm^3 (range 25–1500), and hospital stay, 1 day (range 1–6). The extraperitoneal surgery took longer (240 v 202 min; $p = .001$); yielded more nodes (50 v 41; $p = .004$). Extraperitoneal approach yielded more inframesenteric (14 v 10; $p = .036$), and infrarenal nodes (14 v 9; $p = .001$). 25% of cervical, 19% of endometrial and 14% of ovarian cancer patients had metastases in radiographically negative infrarenal nodes. 50% of cervical, 33% of endometrial and 17% of ovarian cancer patients had therapy altered by aortic lymphadenectomy. When the inframesenteric nodes were positive, 63% of endometrial and 80% of ovarian cancer patients had infrarenal metastases. More metastases were identified with increasing aortic node count. Extraperitoneal lymphadenectomy had no learning curve ($p = 0.320$), while transperitoneal lymphadenectomy did ($p = 0.016$). Higher BMI patients had lower aortic node yields by transperitoneal ($p = .057$) but not extraperitoneal approach ($p = .578$). Among the 14 patients whose BMI was 35–41, mean extraperitoneal total aortic nodal yield was 30; transperitoneal yield was 6.

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Conclusions. Infrarenal aortic lymphadenectomy may offer higher aortic nodal yields, even in patients with BMI's of 45. Larger prospective studies are needed to confirm whether this dissection in high-risk patients ensures more accurate therapy, and possibly improves cure rates.

1. Introduction

The Gynecologic Oncology Group confirmed that the transperitoneal laparoscopic approach for staging endometrial malignancies is a satisfactory method [1]. However, this approach is difficult in patients with BMI over 35, and often, dissections are terminated at the inferior mesenteric artery [2].

Metastatic lesions in the nodes above the inferior mesenteric artery up to the renal vessels have often been identified at both initial presentation and at recurrence of cervical, uterine and ovarian cancers, leading some to advocate for comprehensive pelvic-to-renal-vessel lymphadenectomy when staging is indicated [3–7]. In 2001, this gynecologic oncology practice began using the high-aortic lymphadenectomy margins of the renal vessels, as described in the Gynecological Oncology Group (GOG) Surgical Procedures Manual [8]. Initially, this series employed only the transperitoneal approach, but subsequently added the extraperitoneal approach, and now seeks to formally compare the risks and benefits of each. It is hypothesized that the extraperitoneal approach yields more aortic nodes regardless of BMI and may be easier to learn.

2. Patients and methods

With Investigational Review Board approval from Sequoia Hospital in Redwood City, CA, data was abstracted from hospital and office files for a consecutive series of patients who underwent comprehensive laparoscopic pelvic-to-infrarenal lymphadenectomy along with other indicated procedures from September 1, 2001 to June 1, 2015.

Patients with Stage II–III cervical carcinoma who had computed tomographic evidence of pelvic or aortic adenopathy had extraperitoneal lymphadenectomy. Patients with apical vaginal recurrence of endometrial carcinoma, and patients with the unexpected finding of Grade 3 or papillary serous histotype at hysterectomy by a general gynecologist, had laparoscopic staging. Patients with primary endometrioid uterine carcinoma grade 1 or 2 that was deeply invasive or had cervical spread, or any grade 3 or papillary serous carcinoma, had laparoscopic staging with hysterectomy and bilateral salpingo-oophorectomy. Patients with prior resection of a pelvic mass that revealed a clinically early stage ovarian cancer who were then referred by their gynecologist, and patients who were referred with complex masses found at frozen section to be malignant, had laparoscopic staging with appropriate extirpation of uterus and ovaries.

Excluded from the study were patients referred with ovarian carcinoma with radiographic evidence of metastasis, ascites or omental stranding. These patients had laparotomic staging and debulking. Additionally, patients whose BMI was over 45 were limited to laparoscopic hysterectomy with only clinical staging if their computed tomography confirmed that all pelvic and aortic nodes were smaller than 1 cm. The life-threatening risk of a serious vascular complication deep inside these massive patients from a laparoscopic lymphadenectomy far overshadowed any benefit of identifying and removing micrometastases.

A community gynecologic oncologist performed all procedures, assisted by a general gynecologist or a general surgeon, using a single field surgical prep technique [9]. Initially, the transperitoneal approach was used in all cases, with consistent dissection up to the inferior margin of the bilateral renal vessels. Once the extraperitoneal approach was introduced, it was performed for patients when lymphadenectomy was planned ab initio, such as for an established diagnosis of uterine papillary serous carcinoma or ovarian carcinoma. For patients at *known risk* of needing lymphadenectomy, but requiring frozen section of the uterus or ovary, the hysterectomy and salpingo-oophorectomy were performed through the umbilical port, suprapubic and right lower quadrant ports, thereby avoiding peritoneal perforation on the left, so that an extraperitoneal approach from the left could still be used if frozen section indicated lymphadenectomy. The transperitoneal approach continued to be essential in cases when lymphadenectomy was unexpectedly indicated during the surgery and a port had already breached the left peritoneal lining.

The pelvic-to-high-aortic lymphadenectomy dissection consisted of a methodical and complete *en masse* resection of the fibrofatty lymph-node bearing tissue surrounding each artery and vein, in six anatomic bundles, bilaterally, regardless of approach [10]. The surgical margins of the pelvic (PEL), inframesenteric (IM) and infrarenal aortic (IR) lymphadenectomy are described below.

The PEL lymphadenectomy margins include the genitofemoral nerve and pelvic sidewall laterally; the obturator nerve posteriorly, the ureter and superior vesical artery medially, the ureter crossing the bifurcation of the common iliac superiorly; and the crossing of the deep circumflex iliac vein over the external iliac artery inferiorly, conforming with page 9 in the GOG Surgical Procedures Manual [8].

The IM nodal bed inferior margin is the ureter crossing the common iliac artery at the bifurcation. The posterior margin is the psoas muscle and sacrum. The anterior margins are the peritoneal lining. The lateral margin is the ureter on each side. The superior margin is the level of the inferior mesenteric artery origin on the aorta, divided right and left by the middle of the aorta, conforming to the "para-aortic lymphadenectomy" on page 11 in the GOG Surgical Manual [8].

The IR nodes extend from the origin of the inferior mesenteric artery superiorly to the level of the branching of the renal veins off of the vena cava, with the psoas posteriorly on the left and the vena cava posteriorly on the right, the peritoneum and duodenum anteriorly, and each of the ureters laterally, divided right and left by the aortocaval margin, conforming to the "high para-aortic lymphadenectomy" on page 12 of the GOG Surgical Procedures Manual [8] (Fig. 1).

The pathologist submitted all nodal specimens into paraffin in their entirety, leaving no residual material. Ultrasectioning was not performed.

Patients had hysterectomy, salpingo-oophorectomy, omentectomy, appendectomy, and other procedures as clinically indicated for their staging. An appendectomy was encouraged for all patients because it is useful in staging, easily performed, and because the incidence of appendicitis is rising in the adult population [11,12]. Surgical duration was recorded from "cut-to-close" and included all additional procedures. Blood loss was from all procedures, and was measured in a graduated cylinder at the end of the suction irrigator.

Post-operative complications for this report were defined as any complication occurring up to 90 days after surgery and attributed to the lymphadenectomy. Data was stored and analyzed on a Microsoft Excel Spreadsheet. Statistical analyses were performed via the software program SPSS Statistics. Descriptive statistics including means, standard deviations, medians, and range were calculated along with correlation analyses, and t-tests. Significance was preset at $p < .05$.

3. Results

The series reflects the serial utilization of comprehensive laparoscopic lymphadenectomy over a 14-year period in a community practice and includes 115 consecutive patients (Table 1). A transperitoneal approach was utilized for 36 patients (31%), and the extraperitoneal approach was used for 79 patients (69%). There were no significant

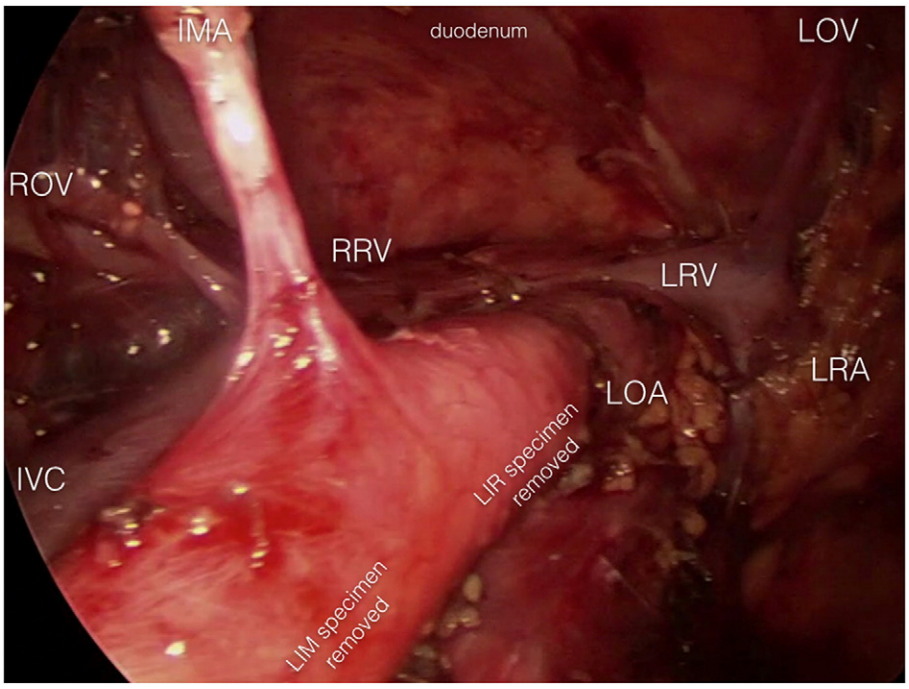

Fig. 1. View from the left sided extraperitoneal approach showing the stripped aorta with the duodenum as the roof of the dissection cavity and the left inframesenteric (LIM) and left infrarenal (LIR) specimens removed already. The inferior mesenteric artery (IMA) emanates anteriorly and divides the IR from the IM nodal basins. The inferior vena cava on the right side with right ovarian vein (ROV) originating superiorly, and the right renal vein (RRV) obscured, and the left renal vein (LRV) extending over the aorta and giving off the left ovarian vein (LOV). The left renal artery (LRA) typically originates from the aorta slightly more superiorly than the crossing of the left renal vein, and remains in a fatty investment. The left ovarian artery (LOA) slender stump remains visible midway up from the IMA.

differences in the mean ages, 57 years (median 58, range 29–80) or mean BMI at 26 kg/m^2 (median 25, range 18–41) between the two approach groups.

The patient cohort comprised 4 (3%) patients with stage IB2–III cervical carcinoma, 75 (65%) patients with clinical stage I or II endometrial carcinoma, and 36 (31%) patients with clinically early tubal or ovarian carcinoma (Table 1).

All 4 patients with Stage II/III cervical carcinoma had an extraperitoneal approach. Of the 75 patients with endometrial carcinoma, 22 underwent a transperitoneal approach and 53 had an extraperitoneal approach. Among the 36 patients who had tubal or ovarian carcinoma, 16 had a transperitoneal approach and 20 had an extraperitoneal approach.

The range of procedures performed is listed in Table 1. Simple hysterectomy was performed for 88 patients. Radical hysterectomy was performed for 18 patients with stromal spread to the cervix by endometrial carcinoma. Nine patients did not undergo hysterectomy: 4 patients with stage II/III cervical carcinoma and 5 patients with prior hysterectomy, 3 of whom had endometrial carcinoma and 2 with ovarian cancer. All endometrial and tubal/ovarian cancer patients underwent bilateral salpingo-oophorectomy and peritoneal washings for cytology, with 57 having total omentectomy. Laparoscopic cystoscopy was performed for 34 patients to affirm urologic integrity [13]. 91 patients had an appendectomy.

In order to analyze the surgical variables and outcomes of the comprehensive pelvic-to-renal vessel lymphadenectomy performed for these three pelvic carcinomas, the diagnostic groups are analyzed together and stratified only by surgical approach for node dissection.

The mean duration of the procedures, measured from cut to closure, was 36 min longer with the extraperitoneal approach (240 v. 202 min, $p = .001$). These durations included the simple or radical hysterectomy, any oophorectomy, variably performed appendectomy, and omentectomy, and in 9 patients, no hysterectomy. The durations of the procedures for the 9 patients without hysterectomy were not significantly different (mean 224, median 222, range 124–366 min). The duration of the pelvic-to-high-aortic lymphadenectomy portion of the procedure was not recorded; however, in a separate publication, the mean duration for a hysterectomy without node dissection for patients with uterine neoplasia or pelvic mass in this practice has previously been reported at 132 min [14], which suggests that the comprehensive lymphadenectomy might have added 72–108 min to the procedure time.

The average blood loss for both approaches was 217 cm^3, (median 150, range 25–1500 cm^3, $p = 0.449$). The average blood loss for the 9 patients not having hysterectomy was 156 cm^3, (median 105, range 50–300 cm^3). The mean blood loss previously reported from patients with in this practice having only hysterectomy/salpingo-oophorectomy, was 148 cm^3, [14] suggesting that 69 cm^3 may be attributed to the lymphadenectomy. While the blood loss from the lymphadenectomies was not recorded separately from the hysterectomy and other procedures performed, there was no catastrophic blood loss from the lymphadenectomy; and red blood cell transfusion rates were not different between the two approaches. Six patients required blood transfusions: 2 units each for 3 patients whose blood loss was over 1000 cm^3 and 1 unit each for 3 other patients, whose blood loss was 200–700 cm^3, but who presented for surgery with anemia. The mean and median duration of hospital stay was 1 day for both groups.($p = 0.110$).

Significantly more lymph nodes were resected via the extraperitoneal approach, with a total mean of 50 (median 46.5, range 20–90), compared to the transperitoneal approach total mean of 41 (median 40, range 9–83; $p = 0.004$) (Table 1). When analyzing each basin individually, the mean of 22 pelvic nodes (median 21, range 3–41; $p = .624$) was similar for both groups. However, significantly more inframesenteric nodes were obtained by the extraperitoneal approach than by the transperitoneal route: mean 14 nodes, (median 12, range 2–38) v. mean 11 nodes (median 8, range 0–38; $p = .036$). Also, significantly more infrarenal nodes were obtained by the extraperitoneal approach than by the transperitoneal route: mean 14 nodes (median 14, range 1–36) v. 9 nodes (median 8, range 1–37; $p = .001$).

Table 1
Patient demographics, diagnoses and procedures.

	Transperitoneal	Extraperitoneal		
	n = 36	n = 79		
Demographics	Mean, median (range)	Mean, median (range)	Statistic	p value
Age in years	57, 57 [29–80]	58, 58 [31–77]	t = −.552	p = 0.582
BMI in kg/m^2	26, 25 [18–38]	26, 25 [19–41]	t = −.270	p = 0.787
Carcinoma primary: n (%)	n	n		
Cervical, n = 4 (3%)	0	4		
Endometrial, n = 75(65%)	22	53		
Tubal/ovarian, n = 36 (31%)	16	20		
Hysterectomy performed	n (%)	n (%)		
Hysterectomy	33 (92%)	55 (70%)	c2 = 6.69	p = 0.035
Radical hysterectomy	2 (8%)	16 (20%)		
RPLND only	1 (2.7%)	8 (10%)		
Additional procedures	n (%)	n (%)		
Omentectomy	20 (55.6%)	37 (46.8%)	c2 = .752	p = 0.426
Cystoscopy	17 (47.2%)	17 (21.5%)	c2 = 7.846	p = 0.008
Appendectomy	26 (72.2%)	65 (82.3%)	c2 = 1.514	p = 0.322
Surgicopathological data	Mean, median, (range)	Mean, median, (range)		
Duration of surgery, minutes:	202, 195 [124–348]	240, 235 [141–406]	t = −3.575	p = 0.001
Measured blood loss, cc's	242, 266 [25–1200]	206, 150 [25–1500]	t = .759	p = 0.449
Red cell transfusions, units	0.08, 0 [0–2]	0.10,0 [0–3]	t = −.202	p = 0.840
Hospital stay in days	1.4,1 [1–6]	1.1,1 [1–5]	t = 1.635	p = 0.110
Lymph nodes resected				
Pelvic	21, 20 [6–41]^	22,21 [3–41]@	t = −.491	p = 0.624
Inframesenteric	10, 7.5 [0–38]^^	14, 12.0 [3–31]@@	t = −2.12	p = 0.036
Infrarenal	9, 8 [1–37]^^^	14, 14 [1–36]@@@	t = −3.506	p = 0.001
Total from all basins	41,40 [9–83]	50,47 [20–90]	t = −2.94	p = 0.004
Final FIGO staging	n	n		
Cervical carcinoma, clinically staged				
Stage IIB	0	2	Not surgically staged	
Stage IIIB	0	2		
Endometrial carcinoma, surgically staged				
Stage I and II	16	27		
Stage IIIA,B (adnexa, vaginal, parametrial)	2	5	c2 = 2.576	p = 0.327
Stage IIIC1,2 (pelvic or aortic nodes)	4	21		
Ovarian/Tubal carcinoma, surgically staged				
Stage IA-C/IF (tubal)-IIA-C	12	15		
Stage IIIA, B (abdominal mets)	1	2	c2 = 1.105	p = 0.641
Stage IIIC (nodal mets)	3	3		
Complications				
Conversion to laparotomy#	3	1		
Left renal artery transection repaired laparotomy#	0	1		
Obturator neurotmesis repaired laparoscopically	1	0		

*Fisher exact test. All other data analyzed by chi-square analysis.
#These four patients were not included in this report because their nodes were removed via laparotomy.
^5 had unilateral Pel nodes dissected: 1right only, 4 left only.
@6 had unilateral Pel nodes dissected: 2 right only, 4 left only.
^^8 had unilateral IM nodes dissected: 3 right only, 5 left only.
@@3 had unilateral IM nodes dissected: 2 right only, 1 left only.
^^^13 had unilateral IR nodes dissected: 8 right only, 5 left only.
@@@6 had unilateral IR nodes dissected: 1 right only, 5 left only.

There was a trend of decreasing nodal yield by the transperitoneal approach as patients' BMI increased (r = −.321, p = .057), but not with the extraperitoneal approach (r = .063 p = .578) (Fig. 2).

At the beginning of the series when only transperitoneal resections were performed, the number of aortic nodes resected increased significantly as experience was gained (r = .399 p = .016) (Fig. 3). When the extraperitoneal approach was adopted later in the series, a mean of 26 aortic nodes was obtained at the outset and maintained throughout the series (r = .113, p = .320).

Three of the 4 patients (75%) with cervical carcinoma had metastatic disease in pelvic nodes. However, 2 (50%) of cervical carcinoma patients had radiographically negative aortic metastases including 1 (25%) with infrarenal metastasis. Thus, the aortic lymphadenectomy altered the assignment of radiation therapy ports in 50% of the cervical carcinoma patient cohort (Table 2).

Twenty-five (33%) of the 75 "high-risk" (grade 3, or deeply invasive grades 1 or 2, or any stage II) endometrial carcinoma patients were found to have metastatic disease in radiographically negative nodes, which upstaged them, and indicated chemotherapy and pelvic radiotherapy. Twenty-two (29%) had metastases in the pelvic nodes. Among these 22, 14 (21% of total, and 64% of pelvic node positive patients) had inframesenteric metastases. Two patients (2%) had inframesenteric metastases with negative pelvic nodes. Of these 16 patients with inframesenteric metastases, 10 (13% of total and 63% of inframesenteric node positive patients) also had infrarenal metastases. An additional 4 patients (5%) were found to have isolated infrarenal metastases with 6–16 dissected negative inframesenteric nodes and no other metastatic foci. One patient among the four with isolated infrarenal adenopathy had a grade 2 carcinoma with 30 negative pelvic nodes, while three others with skip nodes to the infrarenals, two with

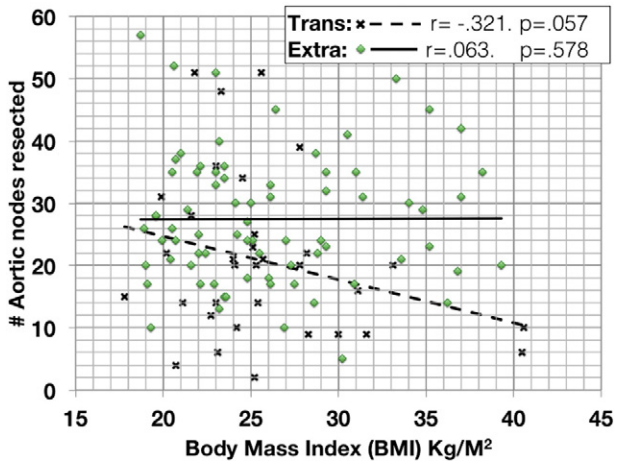

Fig. 2. Correlation of aortic nodal yields with increasing body mass index, stratified by approach. A trending decrement in nodal yield was observed in the larger patients with the transperitoneal approach ($p = .057$), but not with the extraperitoneal approach ($p = .578$).

grade 3 and one with grade 1 carcinoma, had only one positive pelvic node out of 10 to 19 nodes dissected. Thus, out of 75 patients with high-risk endometrial cancer, 20 (27%) had radiographically negative metastatic disease in the aortic nodes, and 14 (19%) had radiographically negative metastases in the infrarenal nodes, which indicated high aortic radiotherapy ports for optimal treatment.

Two (6%) of 36 ovarian/tubal carcinoma patients had metastatic deposits in the pelvic nodes. Six (17%) had radiographically negative aortic nodal metastases. 5 (14%) had inframesenteric metastases, and 4 of these (80%) also had infrarenal metastases. In addition, one patient (3%) with no other intraperitoneal disease, whose BMI was 38, had three positive isolated infrarenal nodes among 17 removed, with none of 18 inframesenteric nodes and none of 37 pelvic nodes involved. In all, 5 (14%) ovarian carcinoma patients with no radiographic evidence of adenopathy had metastases in the infrarenal basin.

In this cohort of patients with no radiological or preoperative clinical evidence of metastatic spread, there was a significant correlation between the total number of nodes resected and the chance of finding malignancy ($r = .332$, $p < 0.001$) (Fig. 4A). However, an analysis of this correlation by individual basin reveals that the significance was specific to the entire aortic basin, IM + IR, ($r = .366$, $p = 0.001$)(Fig. 4B) and not

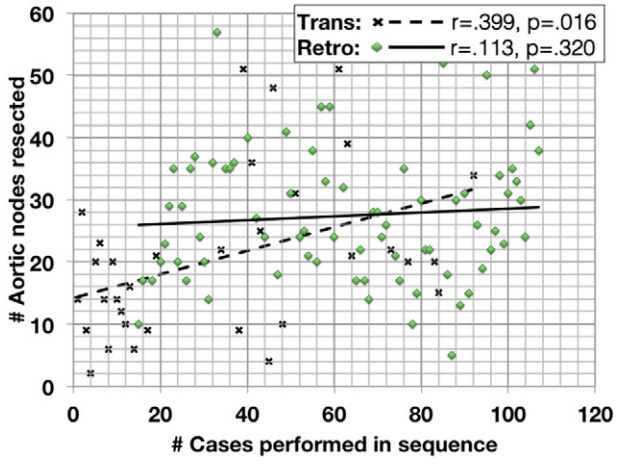

Fig. 3. Comparing aortic nodal yields with sequential case numbers, stratified by approach. Correlation of nodal yields from extraperitoneal and transperitoneal approaches in chronological sequence, a proxy for increasing surgeon experience, reveals a significant learning curve ($p = 0.016$) of increasing nodal yield for the transperitoneal approach. There was no significant learning curve ($p = 0.320$) effect with the extraperitoneal approach, which facilitated higher nodal yields from the outset.

the pelvic basin ($r = .094$, $p = .317$) (Fig. 4C). The removal of more inframesenteric nodes significantly increased the likelihood of finding cancer ($r = .483$; $p = 0.001$) (Fig. 2D), as did increasing numbers of infrarenal nodes ($r = .249$ $p = .007$) (Fig. 4E).

Complications from both lymphadenectomy approaches were rare but significant (Table 1). Four patients who are excluded from node count analysis were converted to laparotomy: three from a transperitoneal approach who had BMI's of 33, 41 and 48 respectively. One patient was converted to laparotomy from an extraperitoneal approach, despite having an ideal BMI, for intraperitoneal adhesiolysis causing peritoneal leaks. One extraperitoneal approach patient had transection of the left renal artery with immediate open laparotomy and saphenous vein transplant, with normal postoperative creatinine values. One patient had transperitoneal transection of her left obturator nerve with immediate laparoscopic repair and physical therapy.

4. Discussion

Embryologic and clinical experiments confirm that the cervix drains along the uterine vein to the pelvic nodes around the iliac veins, and that the fundus of the uterus and the ovaries drain through the lymphatic trunks that parallel the ovarian veins. [3,15] Additionally, cervical, endometrial and ovarian cancers can have "skip" metastases that bypass the inframesenteric nodes and spread directly to the infrarenal nodes. [16,17] For these reasons, this practice uses the renal veins as the superior margin for an indicated lymphadenectomy.

In 2008 Dowdy and colleagues compared the extraperitoneal route for lymphadenectomy to open laparotomy [18]. They reported a yield of 10 inframesenteric and 8 infrarenal nodes from 35 patients using an extraperitoneal approach. They also showed that the extraperitoneal route was superior to the open laparotomy approach in patients with BMI > 35. More recently, Pakish and colleagues studied 34 endometrial carcinoma patients who had extraperitoneal lymphadenectomies up to the renal vessels [7]. They combined the inframesenteric nodes with the infrarenal nodes and reported obtaining a mean of 5 nodes using a transperitoneal approach, and 11 nodes using an extraperitoneal approach. Akladios and colleagues also compared these two approaches to the aortic nodes in 21 cervical cancer patients. While their results show higher aortic nodal yields by the transperitoneal approach (17 by transperitoneal route v 13 by extraperitoneal route), their dissections stopped at the inferior mesenteric artery [19].

In this series of 115 patients having dissections up to the renal vessels, 79 had an extraperitoneal approach for the infrarenal lymphadenectomy, which yielded an average total of 25 lymph nodes from the two aortic levels, 12 nodes from the bilateral inframesenteric, and 13 nodes from the bilateral infrarenal regions. This is the largest series of extraperitoneal lymphadenectomy procedures up to the renal vessels presented in direct comparison to the transperitoneal approach. This study provides further suggestion that there may be a benefit to extending the superior margins of the aortic lymphadenectomy to the renal veins in locally advanced cervical, endometrial, and uterine/tubal carcinoma.

While there were only 4 patients with cervical carcinoma, one (25%) had infrarenal nodal metastasis. Similarly, Gil Moreno et al. found infrarenal node involvement in 16% of patients with locally advanced cervical carcinoma [5]. In this small series of patients with cervical carcinoma, the preoperative PET or CT studies did not identify the positive aortic (IM or IR) nodes in two of four patients that were only discovered by the lymphadenectomy. Both of these patients are alive at greater than two years, having received chemoradiotherapy targeted well above their pathologically identified nodal metastases. Gold and colleagues have also shown that including the infrarenal nodes in the staging lymphadenectomy for cervical carcinoma can increase survival by 12% [20], mainly by improving the accuracy of the radiation port assignment [10,21]. It is regrettable that there are only four patients with cervical carcinoma in this report. Larger prospective studies of patients

Table 2
Nodal involvement detected by comprehensive lymphadenectomy of 115 patients.

	Positive nodes/total (%)	Inframesenteric positive, pelvic negative/total (%)	Infrarenal positive, pelvic and inframesenteric negative/total (%)	Total aortic nodes positive/total (%)
Cervical carcinoma, n = 4				
Pelvic	3/4 (75%)			
Inframesenteric	2/4 (50%)			
Infrarenal	1/4 (25%)			
Total	3/4 (75%)	0	0	2/4 (50%)
Endometrial carcinoma, n = 75				
Pelvic	22/75 (29%)			
Inframesenteric	16/75 (21%)			
Infrarenal	14/75 (19%)			
Total	25/75 (33%)	2/75 (2%)	4/75 (5%)	20/75 (27%)
Ovarian/Tubal carcinoma n = 36				
Pelvic	2/36 (6%)			
Inframesenteric	5/36 (14%)			
Infrarenal	5/36 (14%)			
Total	6/36 (17%)	0	1/36 (3%)	6/36 (17%)

with cervical carcinoma with pelvic adenopathy are needed to document whether dissection of the aortic nodes up to the renal vessels significantly modifies the port assignments and improves survival.

Nearly 20% of patients with no intraperitoneal metastatic sites of endometrial carcinoma in this study had positive infrarenal nodes. Turan and colleagues also found the infrarenal nodes were involved in as many as 10% of their patients with clinically early endometrial carcinoma [22,23]. For endometrial cancer patients, resecting the infrarenal nodes in staging has been shown to add a 10% survival advantage [24]. In this study, comprehensive staging identified radiographically occult metastases in 33% of endometrial carcinoma patients, including 17% in the aortic basins, signaling need for radiation treatment aimed at these areas and higher for a goal of cure [25].

Among the patients with clinically early ovarian cancer, 14% had infrarenal metastases. Morice found that the infrarenal nodes were involved in 20% of clinical stage I ovarian cancer patients [26]. Aletti

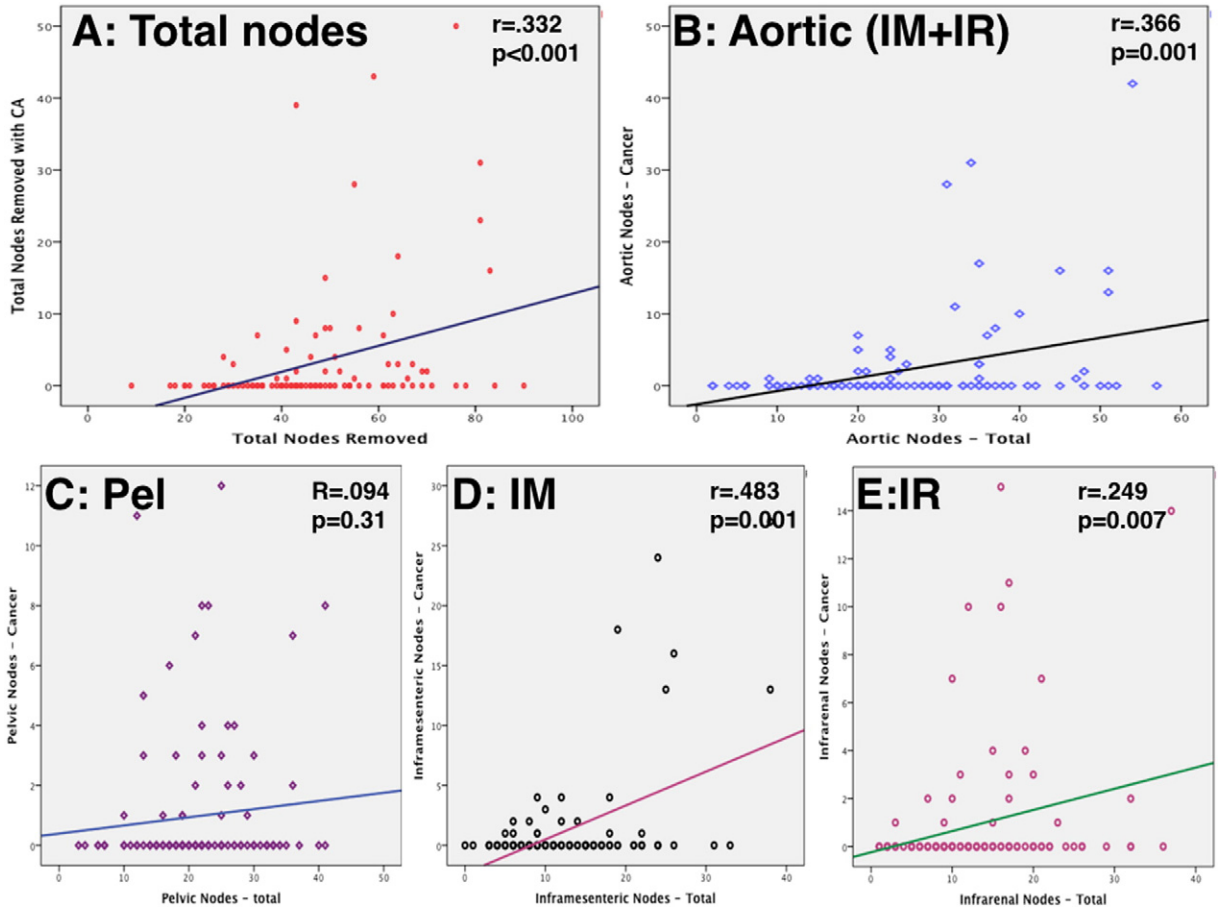

Fig. 4. Increasing nodal harvest increases detection of metastases in both aortic nodal basins. The total nodal yields from a comprehensive lymphadenectomy reveals a significantly increased chance of finding a metastatic deposit with increasing number of nodes removed (A). However, separating the three basins for specific comparison shows that only the aortic (IM + IR) basins are significant (B) and not pelvic nodes (C). Looking more specifically at each of the aortic nodal basins confirms that the more nodes harvested from each basin, (inframesenteric (D) and infrarenal (E)), the greater the chance of finding metastatic deposits. This confirms the importance of performing a comprehensive high aortic lymphadenectomy as described by the GOG Surgical Procedures Manual.

et al. found that performing the infrarenal lymphadenectomy for staging added a 21% overall survival advantage for these patients [27].

Both ovarian and endometrial carcinomas can recur in the infrarenal node basin unless these high aortic nodes are initially resected at staging [28,29]. In this study, when the inframesenteric aortic nodes were found to have endometrial or ovarian carcinoma metastases, 63% and 80%, respectively, will also have infrarenal metastases. This series also confirms that 5% of uterine, and 3% of ovarian carcinomas can metastasize directly to the infrarenal nodes skipping the inframesenterics, even in the very early stages [30,31].

Chan and colleagues found that resection of up to 25 total nodes (basins not specified) increased the likelihood of finding metastatic deposits and improved survival from both endometrial and ovarian carcinomas [32]. They further theorized that small nodes that are radiologically and even pathologically negative could still harbor microscopic metastatic disease and require more aggressive post-operative therapy [33–35]. This report demonstrates a similar significant relationship between the number of aortic nodes harvested from the inframesenteric and infrarenal basins, and the likelihood of finding nodal metastases in each of these basins. In this study, the comprehensive node dissection altered the primary plan of therapy in 50% of cervical, 33% of endometrial and 17% of ovarian cancer patients, as others have described [36].

There appeared to be a learning curve effect only with the transperitoneal approach; however, this approach was adopted before the extraperitoneal approach was included in the practice. While the transperitoneal approach for staging was first described and adopted by most oncologic surgeons, an extraperitoneal approach has more recently been shown to yield as many or more nodes in higher BMI patients and to provide more direct access to the high aortic lymph nodes at the renal veins [37,38]. In this study, the extraperitoneal approach yielded similar counts in patients across the BMI spectrum, in contrast to the trend of decreasing nodal yields with increasing BMI from the transperitoneal approach. This finding confirms other reports of the greater ease and efficacy of the extraperitoneal approach [7,18]. Among the 14 patients in the cohort whose BMI was over 35, two of whom had a BMI over 40, the mean nodal yield from the aortic basin was 31 by extraperitoneal approach, as compared to an average of 6 nodes by transperitoneal approach. The extraperitoneal approach also appears to be associated with reduced risk of bowel injury and adhesion formation [37].

Comprehensive lymphadenectomy is surgery directly on the major vessels, complicated by multiple anatomic variations, and compounded by patients' BMI and other comorbidities. Despite this, minimal blood loss was attributed to the lymphadenectomies, and major vascular complications were rare. Minor arterial bleeding such as avulsion of the right ovarian artery in two cases was treated with proprietary desiccated bovine cartilage coated with human thrombin. Minor venous complications such as avulsion of the perforators of the lower vena cava were also rare, but they were patched with a proprietary crushed equine cartilage matrix coated on one side with desiccated human thrombin and fibrinogen. The transected left renal artery was immediately repaired by open laparotomy and saphenous vein interposition and resulted in maintenance of normal creatinine. The transperitoneal injury to the obturator nerve could have been avoided by following the established standard in this practice of establishing the margins and landmark nerves of the pelvic node dissection well before any transection of tissue. Laparoscopic end-to-end repair resulted in normal ambulation and normal extremity function with no neuropathic pain. One challenge was failure of the extraperitoneal approach in obese patients following peritoneal perforation resulting in collapse of the posterior peritoneum, “the roof” into the retroperitoneal surgical field. The need to convert to laparotomy due to small peritoneal leaks of carbon dioxide was averted in many cases by use of a “liver retractor”: a 5 mm retractable metallic tubing that screw-tightens into a pretzel-shaped retractor, which can lift the posterior peritoneum even when a leak is present. However, this retractor does not help when a large rent develops and bowel falls through into the retroperitoneum, at which point a laparotomy, unfortunately, becomes necessary. None of these 115 patients have reported disabling lymphedema, but this report only encompasses the first ninety days after surgery. To address this issue, a retrospective Quality of Life survey of this same patient cohort is currently underway.

This retrospective case series has several weaknesses. Patient selection was not random, but consecutive. It also may be of concern that a single board-certified gynecologic oncologist in a community hospital performed all of the procedures, which may not be easily reproduced. The surgical durations and estimates of blood loss included many other procedures beside the comprehensive lymphadenectomy. Other complications are possible that were not encountered and reported in this series. Follow-up information was not rigorously solicited after three months from some of the patients who lived many hours away.

Soliman and colleagues surveyed members of the Society for Gynecologic Oncologists and reported that only 60% of gynecologic oncologists report routinely using minimally invasive approaches to endometrial carcinoma [39]. In their report, 50% of respondents said that when lymphadenectomy was required, they routinely dissect nodes only up to the inferior mesenteric artery, and only 11% reported routinely dissecting nodes up to the renal vessels [39]. The perception of a steep learning curve may initially dissuade some gynecologic oncologists from performing a high aortic lymphadenectomy, but all gynecologic oncologists can develop and incorporate these minimally invasive procedures into their oncologic surgery armamentarium [39].

We confirm that laparoscopic comprehensive lymphadenectomy to the renal vessels is feasible and beneficial for patients with BMI up to 45, with cervical, endometrial and tubal/ovarian carcinomas who require lymphadenectomy. Larger prospective studies are needed to confirm whether the more nodes harvested up to the renal vessels, the more accurate staging and more appropriate assignment of postoperative therapy, which may potentially confer a more optimal survival probability. The extraperitoneal approach may permit more direct access to infrarenal nodes, avoiding the anatomic obstacles that exist with transperitoneal lymphadenectomy.

Conflict of interest statement

No funding was received for this manuscript. No products are mentioned. No off label use described.

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