



Comprehensive laparoscopic lymphadenectomy from the deep circumflex iliac vein to the renal veins: Impact on quality of life[☆]



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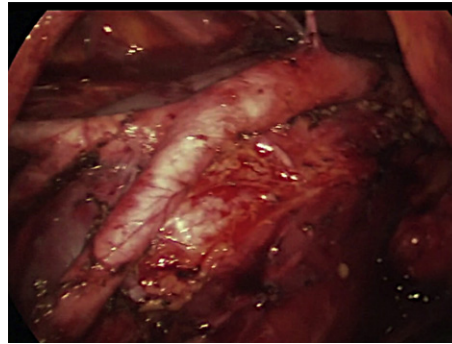
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HIGHLIGHTS

- Comprehensive lymphadenectomy does not harm patients' quality of life.
- Comprehensive lymphadenectomy does not cause lower extremity lymphedema.
- Comprehensive lymphadenectomy mildly contributes to lower extremity lymphedema after radiation and/or chemotherapy.
- Routine omission of the distal circumflex nodes may account for the low risk of lymphedema.
- Numbness and tingling may be caused by trauma to the genitofemoral nerve and should be avoided.

GRAPHICAL ABSTRACT



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ABSTRACT

Objective. Compare quality of life metrics for consecutive patients having total laparoscopic hysterectomy, bilateral salpingo-oophorectomy (TLHBSO) with and without comprehensive pelvic/aortic lymphadenectomy (CPALND) from proximal to the distal circumflex iliac nodes and vessels to the renal vessels.

Methods. Analysis of mailed survey responses with 25 validated questions regarding musculoskeletal/lower extremity, gastro-intestinal, abdominal, urological, and energetic/activities of daily living. Data analyzed with Chi-Square tests of Association, Mann-Whitney *U* tests and follow up regression analysis.

Results. Of 533 surveys mailed, 197 (37%) responded; 57 (28.9%) received CPALND. Age and parity were not different between groups, but the TLHBSO group had a higher BMI (31.4 v. 25.8, $p < 0.001$), and were less likely to receive chemotherapy (CT), radiotherapy (RT), or both (CT + RT). In the CPALND cohort, a mean of 47 nodes were removed, of which 26% were positive: 21% pelvic, 11% inframesenteric, 11% infrarenal. Both groups had similar total quality of life total scores of 86/92. Those having CPALND did not report more swelling but they did report more tingling/numbness (2.8 v. 3.5, $p < 0.001$). A series of hierarchical regressions confirmed that CPALND, per se, did not significantly reduce lower extremity scores apart from CT ($p = 0.402$) and CT + RT ($p = 0.108$). However, CPALND did predict for lower extremity swelling after receipt of CT, RT, or CT + RT. Node count, in total, or from each basin, did not correlate with any QOL decrement.

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Conclusions. CPALND did not cause lymphedema or a reduction in overall quality of life. Only after controlling for BMI, and receipt of radiation and/or chemotherapy were QOL scores mildly reduced. Routine omission of the distal circumflex nodes from the dissection may account for the low risk of lymphedema from the dissection. Larger prospective studies are needed to determine the optimal staging protocols that address all the likely sites of metastasis and recurrence, and optimize survival, while maintaining our patients' quality of life.

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1. Introduction

The treatment of both ovarian and endometrial neoplasia involves at least a laparoscopic hysterectomy with bilateral salpingo-oophorectomy (TLHBSO). However, many patients with clinically early high-risk endometrial and ovarian carcinoma must also undergo laparoscopic staging of their disease, including a comprehensive lymphadenectomy from the deep circumflex iliac vein in the lower pelvis to the renal veins, to assign an appropriately aggressive and accurately targeted postoperative therapy that will minimize risk of recurrence [1].

Understanding how each surgical procedure impacts quality of life after gynecologic cancer surgeries is important for surgeons as they weigh the risk-benefit ratio for each procedure under consideration in the individual patient's surgical plan and provide pre-operative counselling. The quality of life impact from TLHBSO is well-documented and minimal [2], but quality-of-life of patients receiving TLHBSO with a comprehensive laparoscopic pelvic and aortic lymphadenectomy (CPALND) from proximal to the deep circumflex iliac vessels to the renal vessels has never been reported. The additional impact of radiation and chemotherapy on their quality of life and on lower extremity lymphedema has not been well explored either. This is the first quality of life report of patients having a comprehensive lymphadenectomy from the pelvis to the renal vessels. This report also analyses the potentially confounding effects of age, body mass index, and post-operative chemotherapy and radiation therapy, using those patients undergoing laparoscopic hysterectomy/salpingo-oophorectomy as control subjects, for comparison with those also having a stringently defined laparoscopic lymphadenectomy from proximal to the distal circumflex pelvic nodes up to the renal vessels.

2. Patients and methods

With Investigational Review Board approval (BAY-2013.011) from Sequoia Hospital in Redwood City, CA, data was abstracted from hospital and office files for a consecutive series of patients who had laparoscopic surgeries for endometrial or ovarian neoplasia between January 1, 2002, when CPALND was introduced to this practice, until June 15, 2015.

Included in the study were patients with all types of endometrial neoplasia, from hyperplasia to clinically early carcinoma, so that the patients who had only TLHBSO could serve as controls for those receiving CPALND. Patients with endometrial lesions that were grade 3, or deeply invasive >50%, or invading the cervical stroma had TLHBSO with CPALND. Patients with all ovarian neoplasia, from benign ovarian mass to ovarian/tubal carcinoma, are included so that the portion who had only TLHBSO for an ovarian mass could serve as a control for those with malignant ovarian neoplasia who had TLHBSO with CPALND. Since the TLHBSO procedure was the same for both endometrial and ovarian neoplastic patients, all patients having only TLHBSO without CPALND will be grouped together as the study controls and called the TLHBSO group. All patients having TLHBSO with CPALND will be grouped together for comparison and referred to as the CPALND group.

Excluded from the study were patients referred with endometrial or ovarian carcinoma with radiographic evidence of metastasis, ascites or omental stranding, as these patients all had open laparotomy staging. Additionally, patients with BMI over 40 were excluded from this study because CPALND was not attempted in these patients.

2.1. Surgical technique

As reported elsewhere, a community gynecologic oncologist performed all procedures laparoscopically, assisted by a general gynecologist or a general surgeon, using a single field surgical prep technique [3], and a bipolar and monopolar vessel sealing device. A TLHBSO was performed in all cases [4,5]. CPALND was performed when laparoscopic staging was indicated, by either a transperitoneal or extraperitoneal approach.

CPALND consisted of a methodical *en masse* resection of the entire fibrofatty lymph-node bearing tissue surrounding each artery and vein, in six anatomic bundles, from three levels, bilaterally [6]. The distal surgical margins of the pelvic node dissections from proximal to the deep circumflex iliac vein crossing over the external iliac artery in the distal pelvis, medial to the genitofemoral nerve, cephalad to the ureter crossing the common iliac artery comprised the pelvic nodes, right and left. The distal-most, lateral external iliac nodes, also called the circumflex iliac nodes, were never removed because they are known to primarily drain the lower extremity [7], are not involved in pelvic malignancies absent widespread pelvic adenopathy [8,9], and are known to contribute to lower extremity lymphedema if removed. The systematic dissection continued from the ureter cephalic to the inferior mesenteric artery, for the Inframesenteric nodes (IM), right and left, and from the inferior mesenteric artery cephalad to the top of the bilateral renal vessels for the Infrarenal nodes (IR) [1]. In addition to the TLHBSO and CPALND, some patients had omentectomy, appendectomy, and other procedures as clinically indicated by their cancers (papillary serous or clear cell uterine, all tubal and ovarian primaries) for their staging. An appendectomy was encouraged for all patients in this practice, regardless of staging requirements, because the incidence of appendicitis is rising in the adult population, and the simple procedure takes about 2 min and requires only one pre-tied lasso vicryl suture [10,11].

A survey was sent to all eligible patients with a numbered return envelope that correlated their survey responses with their clinical history. This survey was adapted from the previously validated survey by Yost et al. [12] and from the validated EORTC questionnaire of quality of life, EORTC QLQ-C30 [13] (Table 1). This questionnaire has a total of 25 questions that addressed six categories of quality of life: energetic activity, abdominal problems, the lower extremities, genito-urinary problems, gastro-intestinal problems, and sense of general well-being. For most questions, the respondent indicated on a four-point scale any difficulties with a specific issue (e.g. having difficulty walking for long periods) with a maximum score of 92. The questions were randomly arranged in the survey, but for this analysis and manuscript, they are grouped into subcategories according to biological system: Energetic/Activities of daily living, abdominal symptomatology, musculo-skeletal/lower extremity, genito-urinary, gastro-intestinal, and overall. When significant differences were identified in the subcategories, sub-analysis of the individual questions in that group was performed to identify the specific QOL differences and their magnitude. Further impact of radiotherapy and chemotherapy were assessed using regression analyses.

Data was stored and analyzed on a Microsoft Excel Spread sheet using the IBM SPSS Statistical package version 24. Descriptive statistics including means, standard deviations, medians, and range were calculated. Correlation analyses, Pearson's R correlation, Man-Whitney *U* tests were used to compare overall and category scores and *t*-tests.

Table 1
Survey questions grouped for analysis of effect.

	Maximum scores
Energetic/activities of daily living	Total 16
Have you had difficulty walking for a long period of time?	4
Do you have any trouble taking a short walk outside of the house?	4
Do you need to stay in bed or a chair during the day?	4
Do you need help with eating, dressing, washing yourself or using the toilet?	4
Abdominal symptoms	Total 16
Have you had swelling in your lower abdomen?	4
Have you felt heaviness across your abdomen?	4
Have you had pain in your lower abdomen and/or pelvis?	4
Have you had a bloated feeling in your abdomen?	4
Musculo-skeletal/lower extremity	Total 20
Have you had swelling in one or both legs?	4
Have you felt heaviness in one or both legs?	4
Have you had pain in your lower back and/or legs?	4
Have you had tingling or numbness in your hands or feet?	4
Have you had aches or pains in your muscles or joints?	4
Genito-urinary	Total 16
When you felt the urge to pass urine, did you have to hurry to the toilet?	4
Have you passed urine frequently?	4
Have you had leaking of urine?	4
Have you had pain or a burning feeling when passing urine?	4
Gastro-intestinal	Total 16
When you felt you needed to have a BM, did you have to hurry to the toilet?	4
Have you had any leakage of stools?	4
Have you been troubled by passing wind?	4
Have you had cramps in your abdomen?	4
Overall	
How would you rate your overall health during the past week?	4
How would you rate your overall quality of life during the past week?	4
Total score from adding all of the above	92
Did you have radiation therapy for this cancer?	Y N
Did you have chemotherapy for this cancer?	Y N

Significance was preset at $p < 0.05$ with corrections for multiple testing where noted.

3. Results

The survey was mailed to 533 patients; 196 (36.8%) returned the survey with four or fewer missing responses, one person returned the survey missing half the responses, while 337 (63.2%) failed to return the survey. Because the period of data collection is so long, a Pearson's r correlation was employed to determine if those who had their surgeries more recently or more remotely had a different quality of life; no relationship was found ($r = 0.066$, $p = 0.360$). Additionally, a comparison was made of the demographics of those who did and did not return the survey to ascertain absence of respondent bias. Study participants were 3.1 years older than those who did not participate in the study, but BMI, parity, and weight class did not differ significantly (Table 2). Patients who underwent CPALND were more likely to return the survey.

Included for analysis are 139 (60.9%) patients who had TLHBSO only and 57 patients (29.1%) who also received CPALND (Table 3). Age and parity were not significantly different between groups, but those who had TLHBSO only had a significantly higher body mass index at the time of surgery than those who did receive CPALND (31.4 v. 25.8). BMI scores were controlled for in further regression analyses. Additional procedures included omentectomy in 29 patients who had either serous and clear cell uterine cancer or tubal/ovarian malignancy. Laparoscopic cystoscopy was performed for 41 patients to affirm urologic integrity [14]. 150 patients had an appendectomy on an incidental basis or for staging [11]. The systematic node dissections yielded a mean of 46.5

Table 2
Comparison of respondents and non-respondents.

	Respondents N = 197 M (SD)	Non-respondents N = 336 M (SD)	p-Value*
Characteristic at surgery			
Age (years)	62.3 ± 10.4	59.2 ± 12.0	0.002
Parity (#)	1.5 ± 1.4	1.6 ± 1.4	0.302
BMI (kg/m ²)	29.7 ± 8.7	30.6 ± 9.0	0.295
Surgical details			
EBL (cm ³)	107.9 ± 132.4	137.4 ± 204.9	0.859
Duration (min)	118.5 ± 75.5	121.1 ± 68.4	0.229
Days stay (day)	1.1 ± 0.7	1.1 ± 0.5	0.556
CPALND			
Total nodes removed	46.5 ± 14.2	47.0 ± 16.4	0.961
Total pelvic nodes	20.4 ± 7.6	22.7 ± 8.2	0.042
Total IM nodes	13.3 ± 7.4	11.7 ± 7.2	0.131
Total IR nodes	12.9 ± 7.9	12.6 ± 7.6	0.877

BMI, body mass index.

Data are mean ± standard deviation for continuous data; Nodal data includes only those patients who received CPALND.

p values < 0.005 (0.05/10) are considered statistically significant after Bonferroni correction for multiple comparisons.

* p values from independent samples t -test for age variable and from Mann Whitney U test for remaining continuous variables.

nodes, 20.4 from the pelvis and 26.2 from the aortic regions; 13.3 from the inframesenteric basin and 12.9 from the infrarenal basin. As expected, those who received CPALND were also significantly more likely to receive CT, RT, or both CT and RT than those who did not receive CPALND.

The scores for overall quality of life and all category scores were not normally distributed, so the Man-Whitney U tests were used. Table 4 lists the multiple comparisons.

3.1. Overall quality of life

Those who received CPALND did not have a significantly lower overall quality of life than those having TLHBSO only, with a total score of

Table 3
Comparison of those having TLHBSO only with those also having CPALND.

Characteristic	TLHBSO (N = 139)	CPALND (N = 57)	p value*
Age (years)	62.5 ± 10.8	61.9 ± 9.4	0.691
Parity	1.6 ± 1.4	1.4 ± 1.3	0.288
BMI (kg/m ²)	31.4 ± 9.5	25.8 ± 4.7	<0.001
	n (%)	n (%)	p value
Additional procedures			
Omentectomy	6 (4.3%)	23 (40.4%)	$p < 0.001$
Cystoscopy	26 (18.7%)	15 (26.3%)	0.234
Appendectomy	103 (74.1%)	47 (82.5%)	0.21
Lymphadenectomy data			
Total nodes removed, mean, SD	–	46.5 ± 14.2	–
# patients with positive nodes, n (%)	–	15 (26.3%)	–
Pelvic nodes removed	–	20.4 ± 7.6	–
# patients with positive nodes, n (%)	–	12 (21.1%)	–
Inframesenteric nodes, mean, SD	–	13.3 ± 7.4	–
# patients with positive nodes, n (%)	–	6 (10.5%)	–
Infrarenal nodes, mean, SD	–	12.9 ± 7.9	–
# patients with positive nodes, n (%)	–	6 (10.5%)	–
Post-operative therapy			
Chemotherapy	16 (11.5%)	44 (77.2%)	<0.001
Radiation therapy	15 (10.8%)	27 (64.3%)	<0.001
Both CT and RT	5 (3.6%)	18 (31.6%)	<0.001

* p values from independent samples t -test for age and remaining continuous variables report the p -values for Mann Whitney U tests. Categorical p values are from Chi-Square tests of association.

Table 4
Survey responses in comparison: Mann Whitney U comparisons.

Category total	TLHBSO		TLHBSO + CPALND		p value
	n = 139		n = 57		
	Mean	SD	Mean	SD	
Energetic/activities of daily living	14.47	2.65	15	2.16	0.17
Abdominal	14.67	2.17	14.35	2.65	0.469
Musculo-skeletal/lower extremity	17.16	3.16	16.12	3.4	0.024
Swelling in one or both legs?	3.6	0.69	3.26	1.04	0.062
Heaviness in one or both legs?	3.65	0.86	3.49	0.93	0.12
Pain in your lower back and/or legs?	3.32	0.9	3.39	0.77	0.926
Tingling or numbness in hands/feet?	3.46	0.84	2.75	1.15	<0.001
Aches or pains in muscles or joints?	3.13	1.01	3.23	0.96	0.51
Genito-urinary	13.32	2.64	13.35	2.55	0.99
Gastro-intestinal	14.56	1.91	13.77	2.83	0.136
General	6.85	1.17	6.63	1.08	0.174
Total	88.22	10.48	85.68	12.27	0.066

85.7 v. 88.2, out of 92 possible ($p = 0.066$). In all of the QOL categories, the scores were similar between the two groups, except for Musculo-Skeletal/Lower Extremity, which is further analyzed by each question.

3.2. Musculo-skeletal/lower extremity

Overall, those who received CPALND reported a slightly lower category score than those who only had TLHBSO (16.1 v. 17.2, $p = 0.024$) (Table 4). Those who received CPALND did not report significant swelling (3.3 v. 3.6, $p = 0.062$) or heaviness (3.5 v.3.7, $p = 0.114$) in their legs. They did report significantly more tingling or numbness in their hands or feet (2.8 v. 3.5, $p < 0.001$). The questionnaire did not include questions about the site of the numbness or tingling in the extremity, thus failing to distinguish between possible peripheral neuropathy and medial thigh numbness. There were no differences between groups with regard to low back or leg aches or pains in muscles or joints between the two groups.

3.3. Energetic/activities of daily living—no differences found

Both groups scored similarly in the energetic/activity category (15 v. 14.5, $p = 0.17$) with 31% having no or very little problem with a long walk, and 90% having little or no trouble with a short walk. 91% have little or no trouble getting out of bed in the morning. 95% need no or very little help with eating dressing, washing or using the toilet.

3.4. Abdominal symptoms—no differences found

CPALND appeared to have little or no significant effect on abdominal symptomatology (14.4 v. 14.7, $p = 0.469$). 96% had little or no swelling in or sense of heaviness across their abdomen. 96% reported little or no pain in their abdomen and/or pelvis. 94% reported no bloated feeling in their abdomen.

3.5. Genito-urinary—no differences found

Both groups reported similar scores (13.4 v. 13.2, $p = 0.99$) 94% reported no urinary urgency. 94% denied urinary frequency. 88% reported having no urinary incontinence. 97% reported no dysuria.

3.6. Gastro-intestinal—no differences found

There was no difference in GI symptomatology overall (13.8 v. 14.56, $p = 0.136$) 93% reported no need to rush to the toilet after feeling an

urge. Stool leakage was absent in 94%. Flatulence was equally rare with 92% having no gas problem. 95% reported no abdominal cramping.

There was no significant relation between total QOL or lower extremity QOL and number of pelvic, inframesenteric, infrarenal or total aortic, nodes resected after adjusting for multiple comparisons (Table 5).

A series of hierarchical logistic regressions were then undertaken to determine if CPALND, per se, was a specific predictor of any lower scores or whether the patients' significantly higher BMI's or variable receipt of chemotherapy or radiation therapy contributed to their disability (Table 6). Twelve different hierarchical regressions were run controlling first for: A) chemotherapy (CT) and BMI; B) for radiation therapy (RT) and BMI; and C) for receipt of both chemotherapy and radiotherapy (RT + CT) and BMI. Then, in each case, CPALND was further analyzed in the regression to see if the procedure, per se, caused further lowering of scores beyond the effects of BMI, CT or RT.

A statistically significant but clinically minor reduction in total QOL and swelling and numbness scores is attributable to BMI effects and to receipt of chemotherapy. Then, CPALND added significantly, but clinically minimally, to leg swelling ($p = 0.015$) (Table 6.A). Similarly, the effects of BMI and of radiation therapy contributed to decreased total QOL and specifically swelling and numbness. CPALND further decreased scores significantly, but clinically minimally in swelling and tingling in these cases, in particular (Table 6.B). As expected the combination of CT + RT with BMI effects was similar, with CPALND further contributing significantly to numbness and swelling, albeit minimally (Table 6.C). The adjusted r-squared change from radiation therapy alone was larger than those of chemotherapy alone or chemotherapy with radiation. The predictive percentage increased almost 4% when CPALND was added to RT, but <3% when taken with CT or CRT.

4. Discussion

Embryological and clinical experiments confirm that the lymphatic drainage route of the uterine fundus and the ovaries parallels the ovarian veins cephalad to the renal vein on the left and the high vena cava on the right [15,16]. Additionally, endometrial and ovarian cancers can have "skip" metastases that bypass the lower inframesenteric nodes and spread directly to the high infrarenal nodes [17,18]. Many reports confirm that resection of more nodes (basins not specified) increases the likelihood of finding metastatic deposits and/or confers improved survival in cases of endometrial and ovarian carcinomas [19,20]. Potentially small nodes that are radiologically and even pathologically negative can still harbor microscopic metastatic disease and foster recurrence if not removed, identified and used to indicate a more aggressive post-operative therapy. The data from sentinel node procedures with only cervical injection has not yet revealed a superior survivorship, and have not recognized the potential for aortic node

Table 5
Pearson's r correlations of symptoms with node counts.

Node count	Total QOL		Musculo – skeletal	
	Pearson's r	p value	Pearson's r	p value
Total nodes	-0.105	0.142	-0.117	0.103
Pelvic nodes				
Pelvic total	-0.052	0.465	-0.11	0.125
Positive nodes	-0.08	0.266	-0.069	0.146
Inframesenteric nodes				
IM total	-0.139	0.052	-0.146	0.041
Positive nodes	0.025	0.729	-0.023	0.745
Infrarenal nodes				
IR total	-0.116	0.107	-0.065	0.396
Positive nodes	0.004	0.951	-0.001	0.994
Total aortic (IM + IR) nodes				
IR + IM total	-0.135	0.06	-0.112	0.119
Positive nodes	0.015	0.839	-0.012	0.87

Table 6
Regression analysis to determine if CPALND contributed to effects after controlling for CT, RT, or both, with BMI.

A. CT, BMI	CT and BMI adjusted R-squared	CT and BMI p value	Adjusted R-squared change with addition of CPALND	CPALND change p value
Total QOL score	0.055	0.002	− 0.004	0.682
Lower extremity category	0.077	<0.001	− 0.002	0.402
Swelling in one or both legs	0.107	<0.001	0.027	0.015
Tingling or numbness	0.155	<0.001	0.011	0.104
B. RT, BMI	RT and BMI adjusted R squared	RT and BMI p value	Adjusted R-squared change with addition of CPALND	CPALND change p value
Total QOL score	0.041	0.006	− 0.002	0.509
Lower extremity category	0.049	0.003	0.019	0.05
Swelling in one or both legs	0.108	<0.001	0.038	0.004
Tingling or numbness	0.029	0.021	0.078	<0.001
C. CT + RT, BMI	CT + RT and BMI adjusted R squared	CT + RT and BMI p value	Adjusted R-squared change with addition of CPALND	CPALND change p value
Total QOL score	0.067	<0.001	− 0.004	0.732
Lower extremity category	0.084	<0.001	0.012	0.108
Swelling in one or both legs	0.14	<0.001	0.028	0.011
Tingling or numbness	0.073	<0.001	0.058	0.001

involvement [21–23]. It may be that either hysteroscopic or subserosal injections are needed to address the aortic nodes [22,23]. Todo and colleagues have shown that patients have a higher survival from endometrial carcinoma when aortic nodes, even if negative, are removed up to the renal vessels [20]. Even if a sentinel node protocol yields mature survival data, a comprehensive lymphadenectomy, such as the GOG described “high aortic” lymphadenectomy [24] to the renal vessels, will still be indicated for those patients with radiographic adenopathy, and for those found to have positive sentinel nodes and for patients with ovarian carcinoma. For now, comprehensive dissection of all the evidence-based nodal drainage basins is needed in high risk endometrial carcinoma and ovarian carcinoma patients to identify those who need more aggressive post-operative therapy. Among the patients selected for CPALND in this practice, 26% had occult nodal metastases: 21% in the pelvis, 10% in the lower aortics and 10% in the infrarenal aortics [6,20].

Although the BMI is higher in the TLH group, these patients were less likely to need any adjuvant treatment. This may relate to the biology of uterine cancer in that the high-BMI patients typically have a tumor biology that is less aggressive and does not indicate a lymphadenectomy. It does not appear to relate to a surgical decision to omit lymphadenectomy in high-BMI patients because it was technically more difficult, because the lower BMI patients required significantly more post-operative radiation, chemotherapy or both modalities. This lends support that the operative decision process did not shy away from performing the technically difficult lymphadenectomy due to the patients' BMIs.

In this survey report, the use of control patients with a relatively similar demographic and initial surgical care illuminates which post-operative symptoms might be attributed to just the TLHBSO per se, or other shared factors such as age, obesity or poor health. The absence of any significant impact from the CPALND in the categories of energetic/activities of daily living, abdominal or gastrointestinal, genito-urinary, and overall health quality was reassuring. This report confirms that CPALND may cause numbness and tingling in the lower extremities, but not swelling or heaviness. While the Mann Whitney U analysis did not identify any difference between lower extremity scores from patients who received CPALND and those who only received TLHBSO, the hierarchical regressions showed a decrement effect in those scores from the surgical procedure only in those patients having chemotherapy, radiotherapy or both. It is most lamentable that the questionnaire was not written to tease out the obvious differences between chemotherapy-induced neuropathy of hands and feet, and surgically induced dysesthesia of the medial thigh. The numbness and tingling that is attributed to CPALND is most likely due to incidental resection of the genitofemoral nerve with the common iliac inframesenteric nodes and should be

avoided in future dissections by identifying it and separating it from the lymphatic vessels.

Whether or not the patients received CPALND, the patients, as a whole, reported only “a little” swelling. While CPALND may significantly reduce lower extremity total scores after receipt of radiation or chemotherapy or both, the effects appear clinically minor with regard to swelling and heaviness, i.e. lymphedema.

Historically, many reports document that the pelvic portion of the lymphadenectomy can result in disabling lymphedema [25] and symptomatic pelvic lymphocysts [26]. Lower extremity lymphedema, in the absence of pelvic radiation and/or chemotherapy, was not seen in this cohort in which all dissections followed strict boundaries and were always comprehensive. The distal iliac nodes lateral to the genitofemoral nerve, described as the primary lymphatic drainage of the leg and not the pelvis, were never resected. We confirm the finding by Todo and colleagues that the singular factor that causes lower extremity lymphedema is removal of or radiation to those distal iliac nodes, which may explain the perception that pelvic lymphadenectomy carries significant risk of lymphedema [25]. This data also confirms that of Yost et al. [12], who found no association of a lower aortic lymphadenectomy with lower extremity edema or other symptomatology. Yost observed the self-reported lymphedema prevalence in patients treated with hysterectomy alone compared with hysterectomy with pelvic lymphadenectomy was 36.1% and 52.3% [12]. This large difference was not observed in the current study.

Beesly and Rowlands and the Australian National Endometrial Cancer Study Group observed a correlation between number of nodes resected, receipt of radiation and risk of lower extremity lymphedema [27,28]. They also noted that lower extremity lymphedema reduced the overall quality of life in physical, but not mental categories. In the Australian study, 38% of patients had 15 or more nodes resected, while in this report, the patients each had between 21 and 78 nodes removed. There were many surgeons in their study; and there was no mention of whether there was a focus to systematically omit the distal external iliac lateral nodes in the dissections. Additionally, in this current report, there was no correlation between scores on the lower extremity portion of the questionnaire and either number of pelvic nodes removed ($r = -0.11$, $p = 0.125$) or number with metastases ($r = -0.07$, $p = 0.146$).

Yost and colleagues at Mayo also observed no QOL correlation with number of nodes resected, and all patients had at least 15 nodes resected [12]. However, they only removed maximally 38 pelvic nodes and 15 aortic nodes, while in this study the mean number of pelvic nodes resected was 20, ranging up to 41; and the mean total inframesenteric and infrarenal aortic count was 26, maximally 51.

They also found that number of nodes resected does not reduce QOL or lower extremity scores. Yost reported the attributable risk of developing lower extremity lymphedema was 23% for patients with endometrial cancer who underwent lymphadenectomy compared with hysterectomy alone and that receipt of pelvic radiation therapy was a significant risk factor. In this current report, only 9–12% of CPALND patients report any significant swelling or heaviness, which may be due to our routine omission of the distal iliac lateral nodes.

Lymphatic mapping is a current strategy being studied to avoid lymphadenectomy due to the perception that it typically results in lymphedema. The current strategies for sentinel pelvic node sampling do not address the aortic nodes, and have not been reported to improve survival as lymphadenectomy has been reported [19,20]. It may be that with more widespread avoidance of the resection of the distal circumflex iliac nodes, lymphadenectomy will be more accurately perceived and found more useful in staging. Angioli and colleagues observed, as seen in the current study, that lymphedema did not impact the other categories of life quality, but did not specify from whence their reported maximal 21 nodes were removed [29].

Similar to other studies using mailed surveys, this report showed a relatively low response rate (37%) and, therefore, the findings may not relate well to the larger population of women with endometrial or ovarian cancer. The small number of patients may have limited our ability to detect other significant associations with quality of life issues. The retrospective design and the long study period are another limitation of our study. These patients have accrued over a 13-year period, and selection bias may have occurred if patients were too sick to answer, or too healthy to want to participate. It is possible that some patients with significant complications did not receive or did not respond to the survey. It also may be of concern that all surgeries were performed by one surgeon in a community hospital, which may not be easily reproduced. There may be other quality of life issues that were not addressed by the survey. The numbness and tingling that is suspected from the occasional incidental resection of the genitofemoral nerve should be further investigated. The strengths of this manuscript are that the same surgical methods and dissection boundaries were utilized in every case, and that the controls were women having similar laparoscopic surgeries as a baseline, with or without the CPALND.

Laparoscopic comprehensive lymphadenectomy to the renal vessels is feasible for patients with BMI up to 40, with clinically early locally advanced endometrial and tubal/ovarian carcinomas. We confirm that lymphedema is rare and minimal, even after radiation and chemotherapy, and that the impact of lymphadenectomy on quality of life is small. Avoiding resection of the distal iliac nodes and genitofemoral nerve appears critical to maintenance of quality of life for these patients. Larger prospective studies are needed to determine the optimal staging protocols that address all the likely sites of metastasis and recurrence, and optimize survival, while minimizing the impact on our patients' quality of life.

Conflict of interest statement

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

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