

Original Article

Symptomatic Lymphocele After Robot-Assisted Pelvic Lymphadenectomy as Part of the Primary Surgical Treatment for Cervical and Endometrial Cancer: A Retrospective Cohort Study

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ABSTRACT **Study Objectives:** Pelvic lymph node dissection (PLND) is part of the primary treatment for early-stage cervical cancer and high-intermediate risk or high-risk endometrial cancer. Pelvic lymphocele is a postoperative complication of PLND, and when symptomatic, lymphoceles necessitate treatment. The aim of this study was to investigate the incidence and risk factors of symptomatic lymphocele after robot-assisted laparoscopic PLND in cervical and endometrial cancer.

Design: Retrospective cohort study.

Setting: Single-center academic hospital.

Patients: Two hundred and fifty-eight patients with cervical cancer and 129 patients with endometrial cancer.

Interventions: Pelvic lymphadenectomy by robot-assisted laparoscopic surgery.

Measurements and Main Results: The authors retrospectively included all patients with early-stage cervical cancer and high-intermediate risk or high-risk endometrial cancer who underwent pelvic lymphadenectomy by robot-assisted laparoscopic surgery between 2008 and 2022. Medical records were reviewed for the occurrence of a symptomatic lymphocele. Univariate and multivariate logistic regression analyses were conducted to identify risk factors for developing a symptomatic lymphocele. In total, 387 patients, 258 with cervical cancer and 129 with endometrial cancer, were included in the study. The overall incidence of symptomatic lymphoceles was 9.6% with a median follow-up of 47 months [interquartile range 23–61]. For the entire cohort, smoking was the only significant risk factor for symptomatic lymphoceles identified in univariate (OR 2.47, 95% CI 1.19–5.11) and multivariate analysis (OR 2.42, 95% CI 1.16–5.07). For cervical cancer, body mass index (BMI) (OR 1.09, 95% CI 1.00–1.17) and prior abdominal surgery (OR 2.75, 95% CI 1.22–6.17) were also identified as significant independent risk factors. For endometrial cancer, age was identified as a significant independent risk factor (OR 0.90, 95% CI 0.83–0.97).

Conclusion: This single-center cohort study demonstrated an incidence of almost 10% of symptomatic lymphoceles after robot-assisted laparoscopic PLND for cervical cancer and endometrial cancer, with a higher risk observed among patients who smoke at the time of diagnosis. Furthermore, risk factors differ between the 2 populations, necessitating further studies to establish risk models. Journal of Minimally Invasive Gynecology (2024) 31, 243–249. © 2024 AAGL. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>)

Keywords: Lymphocele; Cervical cancer; Endometrial cancer; Lymph node dissection; Robotic surgery

This study was exempt for the need of informed consent by the institutional review board.

The authors declare that they have no conflict of interest.

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Background

In both cervical and endometrial cancer, lymph node involvement impacts treatment strategy and prognosis, highlighting the importance of accurate nodal assessment. Traditionally, pelvic lymph node dissection (PLND) is performed as a standard nodal assessment procedure in patients with early-stage cervical and clinically early-stage high-risk or high-intermediate risk endometrial cancer [1,2].

Common postoperative complications of PLND include lymphedema and the formation of pelvic lymphoceles [3], defined as a cystic lesion containing lymph fluid [4]. A large proportion of lymphoceles exists asymptomatic and regresses spontaneously [5,6]. Only large or symptomatic lymphoceles, causing infection, pelvic pain, leg edema, and symptoms related to compression of adjacent structure [5–7], necessitate treatment since their occurrence is associated with hospitalization and could cause treatment delays [8].

Existing literature reports an overall lymphocele incidence of 14% after PLND, with symptomatic lymphoceles at 3%. Incidence varies by surgical approach, with higher rates after laparotomic versus laparoscopic procedures (18% vs 7%), although the difference for symptomatic lymphoceles is smaller (4% vs 3%) [9]. Robot-assisted laparoscopic approach for PLND lacks extensive research, only Persson et al [10] reported an 8% lymphocele incidence, and 2 cohort studies reported a symptomatic lymphocele incidence ranging from 3% to 6% [11,12].

This retrospective single-center cohort study aims to report the incidence and risk factors of symptomatic lymphoceles after robot-assisted laparoscopic PLND in cervical and endometrial cancer patients.

Materials and Methods

Design

We performed a retrospective cohort study reporting on all women diagnosed with either early-stage cervical cancer or early-stage high or high-intermediate risk endometrial cancer who underwent robot-assisted PLND between January 1st, 2008, and February 1st, 2022, at the University Medical Center Utrecht. All patients in this study received standard medical treatment performed according to national and international guidelines. The need for informed consent was waived by the institutional review board for this study based on the retrospective anonymized use of data.

Inclusion criteria were age ≥ 18 , histologically proven primary malignancy of the cervix or endometrium, the International Federation of Gynecology and Obstetrics (FIGO) 2018 stage IA1–IB2 and IIA1 for cervical cancer, FIGO 2009 stage IA, IB or II for endometrial cancer and primary surgical treatment including PLND by robot-assisted laparoscopic surgery. Exclusion criteria were neoadjuvant treatment (in light of the EORTC 55994 study), sentinel lymph node (SLN) procedure only, conversion to laparotomy, and

conversion to debulking due to perioperative upstaging (in the case of endometrial cancer). Patients with suspicious nodes on pre-operative imaging did undergo additional imaging or histology (frozen section) to rule out nodal metastases first.

Procedure

All surgical procedures were performed by a surgical team consisting of 3 gynecological oncologists. For all procedures, the da Vinci (Si until 2017, and X/Xi from 2017 onwards) Surgical System (Intuitive Surgical, Sunnyvale, CA) was used. Surgical procedures regarding cervical cancer performed at our institution have been previously described [13,14]. In case of early-stage cervical cancer, an additional SLN procedure could be performed. The primary treatment of clinically early-stage high or high-intermediate risk endometrial cancer consisted of systematic PLND and para-aortic lymph node dissection (PAOLND) combined with hysterectomy and bilateral salpingo-oophorectomy (SLN procedure was not performed as this is not considered standard-of-care in high/high-intermediate risk endometrial cancer). PLND involves the resection of all lymphoid tissue located in the obturator fossa and surrounding the internal, external, and common iliac vessels. Hemostatic agents were not routinely used, and when used, not in the pelvic surgical area but mostly for vaginal closure. PAOLND involves the resection of lymphoid tissue located in the precaval and paracaval area up to the level origin of the left renal vein. In some cases, PAOLND was not performed because of technical reasons (e.g., BMI-related). In case of serous, clear cell, or uterine carcinosarcoma, additional omentectomy and peritoneum biopsies were conducted. All patients received antibiotic prophylaxis (cefazolin 2000 mg and metronidazole 500 mg IV) directly preoperatively. During the study period, no changes in use of uterine manipulator (McCartney tube, LiNA Medical, Glostrup, Denmark) or other surgical techniques occurred.

Oncological follow-up was performed according to guidelines. Patients were not routinely screened for the development of lymphoceles. In case of symptoms of a lymphocele, such as symptoms caused by compression of adjacent structures, pelvic pain, signs of infection, or deep vein thrombosis, imaging was used to detect lymphocele (ultrasound and/or computed tomography (CT) scan). Drainage of lymphoceles was done by interventional radiology. No sclerosing substances were used when performing drainage. In case of hospitalization, patients were referred back to routine oncological follow-up after discharge, with an additional check-up after 2 weeks in most cases.

Data Collection

Clinical data were extracted from the institutional medical records. Preoperative parameters collected included: age, BMI, in kg/m^2 , American Society of Anesthesiologists (ASA) classification, history of abdominal surgery, history

of hypertension, and smoking. Smoking was divided into actively smoking at the time of diagnosis, stopping before diagnosis, and having no history of smoking at all. Postoperative parameters for analysis included: operation time (start of incision until end of closure), number of pelvic lymph nodes dissected, additional PAOLND, presence of metastatic lymph nodes, and adjuvant external beam radiation therapy.

The primary outcome measure was development of a symptomatic lymphocele. Lymphoceles were defined as a retroperitoneal unilocular or multilocular cystic structure containing fluid visible on either ultrasound or CT-scan. Symptomatic lymphoceles were defined as a lymphocele visible on imaging with the presence of symptoms caused by compression of adjacent structures, pelvic pain, signs of infection, or deep vein thrombosis. Morbidity was graded using the Common Terminology Criteria for Adverse Events 5.0 grading system [4]. A symptomatic lymphocele was classified as grade 2 or 3 based on the requirement of medical intervention. Grade 2 symptomatic lymphocele was defined as a lymphocele with symptoms for which no invasive intervention or hospital admission was needed, whereas grade 3 symptomatic lymphoceles needed invasive intervention and/or hospital admission.

Statistics

Continuous data was presented as median with the lower and upper quartile range (median [lower quartile – upper quartile]) when not normally distributed. Mann–Whitney U test was conducted to check for significant differences in continuous outcomes between the 2 groups. Categorical data was presented as proportions. Chi-square test was performed to check for significant differences in proportions between the 2 groups.

Possible risk factors for developing symptomatic lymphoceles were analyzed using univariate and multivariate logistic regression. Variables yielding significant *p*-values by univariate analysis were included in a multivariate logistic regression model. In addition, risk factors reported in our previous meta-analyses were included to determine their independent association with development of symptomatic lymphoceles [9]. Sub-analyses for cervical cancer and endometrial cancer were performed. Statistical significance was defined as a *p*-value of <0.05. All analyses were made using SPSS version 28.0 (IBM SPSS Statistics for Mac, Armonk, NY).

Results

Baseline

In total, 387 patients underwent robot-assisted laparoscopic PLND. This cohort consisted of 258 patients with cervical cancer and 129 patients with endometrial cancer. In the cervical cancer group, 236 patients (91.5%) received an

additional SLN procedure. In the endometrial cancer group, 111 patients (86%) underwent PAOLND in addition to PLND. Median follow-up duration was 47 months [interquartile range 23–61]. In total, 349 patients (90.2%) had a follow-up duration of 12 months or longer. Of the remaining 38 patients (9.8%) with a follow-up duration of less than 12 months, 5 patients died within 12 months after surgery, 16 patients underwent surgery within 12 months prior to data collection and were therefore still in their first year of oncological follow-up, and 17 patients were lost to follow-up.

The demographic and surgical characteristics of the study population are summarized in Table 1. Baseline characteristics that exhibited significant differences between the 2 populations were controlled for in subsequent subgroup analyses. The additional characteristics of the cervical cancer and endometrial cancer populations can be found in Supplementary Table S1 and Supplementary Table S2, respectively.

Symptomatic Lymphocele

In the entire cohort, 37 patients (9.6%) developed a symptomatic lymphocele; 27 patients with cervical cancer and 10 patients with endometrial cancer. A symptomatic lymphocele is defined as a lymphocele visible on imaging with the presence of symptoms caused by compression of adjacent structures, pelvic pain, infection, or deep vein thrombosis. Median time until development of symptomatic lymphocele was 59 days [interquartile range 17–112]. Out of the patients who had a symptomatic lymphocele, 2 patients underwent ultrasound exclusively to confirm their diagnosis, one patient solely had a CT scan, and for all the remaining patients, both ultrasound and CT scan were used to confirm the diagnosis. Two of the patients who developed a symptomatic lymphocele were on anticoagulants when the surgery was carried out (acetylsalicylic acid 80 milligrams). One patient developed a deep venous thrombosis as a direct result of a lymphocele, without the need for invasive intervention, and was classified as a grade 2 symptomatic lymphocele. All other patients with symptomatic lymphoceles (*n* = 36) were considered a grade 3 adverse event.

All patients with grade 3 symptomatic and infected lymphoceles (*n* = 36) were readmitted to the hospital. Median length of readmission hospitalization was 8 days [interquartile range 6–11]. The exact length of readmission was irretrievable for 2 patients. In 8 patients, treatment consisted solely of intravenous antibiotics. In 28 patients, drainage of the lymphocele, in addition to antibiotics, was required. One patient solely underwent drainage of the lymphocele and did not receive antibiotics. Micro-organisms found in drained fluids of 14 patients differed, and both vaginal, intestine, and skin bacteria were found. Most common micro-organisms were *Staphylococcus aureus* (*n* = 3), *Streptococcus agalactiae* (*n* = 2), *Streptococcus lugdunensis* (*n* = 2), *Pepto-streptococcus anaerobius* (*n* = 2) and *Streptococcus anginosus* (*n* = 2).

Table 1

Baseline characteristics of entire cohort				
Variable	Study population (n = 387)	Cervix (n = 258)	Endometrial (n = 129)	p-value
Age, yrs (median)	48 [36–65]	39 [33–49]	69 [60–73]	p < .001
BMI, kg/m ² (median)	24.61 [21.97–28.26]	23.76 [21.30–26.53]	26.93 [23.53–30.67]	p < .001
Smoking, n (%)				p < .001
Never	242 (62.5%)	143 (55.4%)	99 (76.7%)	
Stopped	69 (17.8%)	54 (20.9%)	15 (11.6%)	
Currently	76 (19.6%)	61 (23.6%)	15 (11.6%)	
Prior abdominal surgery, n (%)	138 (35.7%)	79 (30.6%)	59 (45.7%)	p = .003
Hypertension, n (%)	70 (18.1%)	23 (8.9%)	47 (36.4%)	p < .001
ASA classification, n (%) (n = 377)				p < .001
ASA 1	197 (50.9%)	179 (69.4%)	18 (14%)	
ASA 2	153 (39.5%)	69 (26.4%)	84 (65.1%)	
ASA 3	27 (7%)	6 (2.3%)	21 (16.3%)	
Pelvic lymph nodes dissected (n = 385)	20 [15–27]	22 [18–29]	15 [11.5–20.0]	p < .001
Paraortic lymph node dissection performed, n (%)	111 (28.7%)	0 (0%)	111 (86%)	N/A
Metastatic lymph nodes, n (%)	43 (11.1%)	31 (12%)	12 (9.3%)	p = .423
Adjuvant therapy, n (%)	174 (45%)	67 (30%)	107 (82.9%)	p < .001
Adjuvant pelvic radiotherapy, n (%)	88 (22.7%)	67 (30%)	21 (16.3%)	p < .001
Symptomatic lymphocele, n (%)	37 (9.6%)	27 (10.5%)	10 (7.8%)	p = .392
Grade 2	1 (0.3%)	1 (0.4%)	0 (0%)	
Grade 3	36 (9.3%)	26 (10.1%)	10 (7.8%)	

Two patients developed multiple symptomatic lymphoceles simultaneously. Three patients developed symptomatic lymphoceles at another location during follow-up. One patient had a recurrent symptomatic lymphocele and was repeatedly treated with intravenous antibiotics because the localization was difficult to drain ([Supplementary Table S3](#)).

Risk Analysis

The results of the univariate analysis are presented in [Table 2](#). Only smoking was significantly associated with the

risk of developing a symptomatic lymphocele (OR 2.47, 95% CI 1.19–5.11, p = .015). Other parameters, such as age, BMI, ASA classification, prior abdominal surgery, type of cancer (i.e., cervical or endometrial), operation time, PAOLND, metastatic lymph nodes, and external beam radiation therapy, showed no significant association with the development of a symptomatic lymphocele. Based on previous literature, a multivariate analysis was performed containing smoking, number of pelvic lymph nodes removed, and PAOLND: only smoking appeared to be a significant factor (OR 2.42 95% CI 1.16–5.07, p = .019) ([Table 2](#)).

Table 2

Risk factors for developing symptomatic lymphocele				
Variable	No symptomatic lymphocele (n = 350)	Symptomatic lymphocele (n = 37)	Univariate logistic regression OR (95% CI), p-value	
Age, yrs (median)	49 [36–66]	47 [38–56.5]	0.99 (0.97–1.01)	p = .249
BMI, kg/m ² (median)	24.58 [22.05–28.22]	24.62 [21.48–31.18]	1.02 (0.96–1.09)	p = .465
ASA classification, n (%) (n = 377)				
ASA 1	175 (51.3%)	22 (61.1%)	Reference	
ASA 2	141 (41.3%)	12 (33.3%)	0.68 (0.32–1.42)	p = .300
ASA 3	25 (7.3%)	2 (5.6%)	0.64 (0.14–2.87)	p = .557
Currently smoking, n (%)	63 (18%)	13 (35.1%)	2.47 (1.19–5.11)	p = .015
Hypertension, n (%)	65 (18.6%)	5 (13.5%)	0.69 (0.26–1.83)	p = .450
Prior abdominal surgery, n (%)	120 (34.3%)	18 (48.6%)	1.82 (0.92–3.59)	p = .086
Type of cancer (endometrial), n (%)	119 (34%)	10 (27%)	1.39 (0.65–2.97)	p = .394
Operation time, minutes (median)	260 [211–303]	251 [202–282]	1.00 (0.99–1.00)	p = .444
Pelvic lymph nodes dissected, n (median)	20 [15–26.25]	19 [15–27.5]	1.00 (0.97–1.04)	p = .891
Paraortic lymph node dissection, n (%)	102 (29.1%)	9 (24.3%)	0.78 (0.36–1.71)	p = .539
Metastatic lymph nodes, n (%)	39 (11.1%)	4 (10.8%)	0.97 (0.33–2.87)	p = .951
External radiotherapy, n (%)	80 (22.9%)	8 (21.6%)	0.93 (0.41–2.12)	p = .865
				2.42 (1.16–5.07), p = .019
				1.00 (0.96–1.04), p = .949
				0.88 (0.38–2.09), p = .778

Table 3

Risk factors symptomatic lymphocele CC

Variable	No symptomatic lymphocele (n = 231)	Symptomatic lymphocele (n = 27)	Univariate logistic regression OR (95% CI), p-value	Multivariate logistic regression *Based on significant in univariate analysis OR (95% CI), p-value
Age, yrs (median)	39 [33–48]	45 [35–50]	1.01 (0.98–1.04), p = .662	
BMI, kg/m ² (median)	23.53 [21.30–26.35]	24.97 [21.26–31.51]	1.09 (1.00–1.17), p = .040	1.09 (1.00–1.18), p = .045
ASA classification, n (%) (n = 254)	n = 227	n = 27		
ASA 1	161 (70.9%)	18 (66.7%)	Reference	
ASA 2	61 (26.9%)	8 (29.6%)	1.17 (0.49–2.84), p = .723	
ASA 3	5 (2.2%)	1 (3.7%)	1.79 (0.20–16.17), p = .605	
Currently smoking, n (%)	50 (21.6%)	11 (40.7%)	2.49 (1.09–5.70), p = .031	2.42 (1.03–5.70), p = .042
Hypertension	20 (8.7%)	3 (11.1%)	1.32 (0.37–4.77), p = .673	
Prior abdominal surgery, n (%)	65 (28.1%)	14 (51.9%)	2.75 (1.23–6.17), p = .014	2.44 (1.07–5.57), p = .033
Operation time, minutes (median)	272 [230–327]	266 [205–301]	1.00 (0.99–1.00), p = .220	
Pelvic lymph nodes dissected, n (median)	23 [18–29]	22 [18–28]	0.99 (0.95–1.03), p = .597	
Metastatic lymph nodes, n (%)	27 (11.7%)	4 (14.8%)	1.31 (0.42–4.09), p = .637	
External radiotherapy, n (%)	60 (26%)	7 (25.9%)	1.00 (0.40–2.48), p = .996	

When performing univariate analysis in the cervical cancer subgroup exclusively, BMI (OR 1.09 95% CI 1.00–1.17, p = .040), prior abdominal surgery (OR 2.75, 95% CI 1.23–6.17, p = .014) and smoking (OR 2.42, 95% CI 1.03–5.70, p = .031) proved to be a risk factor for the development of a symptomatic lymphocele and these factors remained significant in multivariate analysis. (Table 3) The prior abdominal surgeries in the cervical cancer group were highly diverse: this group included laparotomic surgeries, laparoscopic surgeries, and cesarean sections. When performing univariate analysis in the endometrial cancer subgroup exclusively, age (OR 0.90, 95% CI 0.83–0.97, p = .006) and

ASA classification (reference ASA 1, OR 0.18, 95% CI 0.04–0.78, p = .023) proved to be significant risk factors for the development of a symptomatic lymphocele, with only age as significant factor in multivariate analysis. (Table 4).

Discussion

In this retrospective cohort study of 387 patients who underwent robot-assisted laparoscopic PLND for cervical and endometrial cancer, the incidence of symptomatic lymphocele was 9.6% (n = 37). Smoking (p = .015) was identified as a risk factor for the entire cohort. Furthermore, in

Table 4

Risk factors symptomatic lymphocele EC

Variable	No symptomatic lymphocele (n = 119)	Symptomatic lymphocele (n = 10)	Univariate logistic regression OR (95% CI), p-value	Multivariate logistic regression *Based on significant in univariate analysis OR (95% CI), p-value
Age, yrs (median)	69 [62–74]	59 [57–64]	0.90 (0.83–0.97), p = .006	0.90 (0.82–0.99), p = .025
BMI, kg/m ² (median)	26.99 [23.88–30.48]	23.46 [21.97–30.85]	0.94 (0.83–1.07), p = .373	
ASA classification, n (%) (n = 123)	N = 114	N = 9		
ASA 1	14 (12.3%)	4 (44.4%)	Reference	
ASA 2	80 (70.2%)	4 (44.4%)	0.18 (0.04–0.78), p = .023	0.26 (0.06–1.23), p = .089
ASA 3	20 (17.5%)	1 (11.1%)	0.18 (0.02–1.74), p = .137	0.46 (0.04–5.40), p = .537
Currently smoking, n (%)	13 (10.9%)	2 (20.0%)	2.04 (0.39–10.65), p = .398	
Hypertension	45 (37.8%)	2 (20.0%)	0.41 (0.08–2.02), p = .274	
Prior abdominal surgery, n (%)	55 (46.2%)	4 (40.0%)	0.78 (0.21–2.90), p = .705	
Operation time, minutes (median)	231 [197–270]	233 [191–264]	1.00 (0.99–1.01), p = .701	
Pelvic lymph nodes dissected, n (median)	15 [11–20]	15 [12–17]	1.03 (0.93–1.14), p = .544	
Paraortic lymph node dissection, n (%)	102 (85.7%)	9 (90.0%)	1.50 (0.18–12.61), p = .709	
Metastatic lymph nodes, n (%)	12 (10.1%)	0 (0.0%)	NA	
External radiotherapy, n (%)	20 (16.8%)	1 (10.0%)	0.55 (0.07–4.59), p = .581	

addition to smoking, higher BMI and prior abdominal surgery were shown to be significant risk factors for the cervical cancer subgroup. For the endometrial cancer subgroup, only younger age were shown to be a significant risk factor in multivariate analysis.

The incidence of symptomatic lymphocele after robot-assisted PLND in patients with cervical and endometrial cancer is only reported in a limited number of studies. The study by Ko et al [11] describes symptomatic lymphoceles after robot-assisted laparoscopic PLND for early-stage cervical cancer and early-stage high or high-intermediate risk endometrial cancer, reporting a 6% incidence within a small retrospective cohort of 16 patients. Corrado et al [12] reported an incidence of 3.4% ($n = 3$) in a cohort of 86 stage IB1 cervical cancer patients who underwent robot-assisted PLND. Persson et al [10] study included 80 patients who underwent robot-assisted PLND as part of their treatment for early-stage cervical cancer ($n = 64$) or FIGO stage II endometrial cancer ($n = 16$). Follow-up included a routine vaginal ultrasonography, and 6 patients (8%) developed a lymphocele within 3 months postoperatively, though it was not specified if these were symptomatic. In other types of cancers in which robot-assisted PLND is frequently performed, such as prostate cancer, symptomatic lymphocele incidence varies from 2.5% to 7.9% [15,16].

The incidence of symptomatic lymphocele in the current study (9.6%) is higher compared to the available evidence in robot-assisted surgery and to the pooled incidence of symptomatic lymphoceles as recently reported in our meta-analysis. Click or tap here to enter text [6,7,9,15–18]. A possible explanation for the higher incidence of symptomatic lymphoceles in our cohort compared to the laparotomic and laparoscopic approaches is that robot-assisted surgery may facilitate more extensive removal of lymphoid tissue due to improved visualization [19]. Also, the relatively longer operation time could be a possible determining factor, although it appeared to be no significant risk factor in our analysis. Colpotomy is one of the last steps of the procedure completing the hysterectomy; at this moment, the serum concentration of the prophylactic antibiotics administered before surgery is expected to be at a low level and could fail to prevent vaginal flora colonizing the abdominal cavity. This theory could be supported by the lower incidence of symptomatic lymphoceles (3.4%) seen in the small study of Corrado et al [12] ($n = 86$) in which operation time was about 50 minutes shorter than our results. Due to the high incidence reported in this study, a second dose of antibiotics is now administered at a later point during surgery in our center. Another explanation for the higher incidence could be that this is the first study analyzing over 350 patients undergoing robot-assisted PLND, where available literature in this field mainly describes small cohorts with a maximum of 86 patients. Ideally, we need standardized registration, definitions, and population-based data to determine the true incidence of this complication following PLND.

Most data on risk factors are based on small patient populations, and therefore, generalizability is limited. In recent meta-analysis, decreased number of lymph nodes dissected ($n < 21$) and additional PAOLND were found to be risk factors for developing lymphoceles through meta-regression. However, these analyses require more clarity and could be analyzed on a patient level. In this study, we could not confirm the risk factors described in literature, such as number of lymph nodes dissected, additional PAOLND, presence of lymph node metastasis, and adjuvant radiotherapy [5,6,9,20]. This could be explained by our focus on symptomatic lymphoceles. Furthermore, reported risk factors are based on relatively small cohorts. Although larger studies to validate the risk factors for symptomatic lymphoceles are needed, our results suggest preventive measures, such as quitting smoking or losing weight, could help reduce the risk of developing a symptomatic lymphocele. Other preventive measures, such as the use of fibrin application or synthetic glues, nonperitonization, and omitting an intra-abdominal drain postoperatively, are not confirmed in literature and have been studied in small groups of patients [21–25]. Change of prophylactic antibiotics protocols, for example, a repeated antibiotics dose just before colpotomy, is another possible preventive option that should be explored in further studies.

Additionally, the less invasive SLN procedure could replace the need for PLND and has already been shown to be a safe substitute regarding survival outcomes in low-risk endometrial cancer. In these patients, SLN mapping is demonstrated to independently decrease the risk of lymphocele formation compared to full PLND in multiple studies, including a randomized control trial [26–30]. In cervical cancer and high-risk endometrial cancer, an SLN-only protocol is not yet unanimously accepted as the standard of care, as prospective and randomized controlled trials have not yet provided final results on its safety [31–33].

An important limitation of our study is that the 2 subgroups differ significantly, which made us decide to do a sub-analysis with inherently smaller numbers of patients. Because both subgroups underwent robot-assisted PLND, and there was no significant difference in the incidence of lymphocele between the 2 subgroups, it was considered feasible to conduct an analysis on the combined cohort to identify overall risk factors for lymphocele development. Other limitations of this study are its retrospective design, considering that the records at the time were not designed to be used for analysis, resulting in inadequate data on confounding factors and exposure data. Furthermore, the single-center nature of the study reduces its external validity.

Conclusion

In this retrospective cohort study on symptomatic lymphoceles after robot-assisted laparoscopic PLND in cervical and endometrial cancer, we found an incidence of 9.6% symptomatic lymphoceles. For the entire cohort, smoking

proved to be a significant risk factor for developing symptomatic lymphoceles. However, the 2 subgroups differed significantly from each other. For the cervical cancer subgroup, higher BMI, prior abdominal surgery, and smoking were shown to be a significant risk factor. For the endometrial cancer subgroup, younger age was showed to be a significant risk factor. Further research is warranted to identify other risk factors and explore strategies, such as the SLN procedure or risk-reducing measures, to prevent the development of symptomatic lymphoceles.

References

- Colombo N, Preti E, Landoni F, et al. Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2013;24(Suppl. 6):vi33–vi38.
- Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. *Int J Gynecol Cancer*. 2021;31:12–39.
- Zikan M, Fischerova D, Pinkavova I, et al. A prospective study examining the incidence of asymptomatic and symptomatic lymphoceles following lymphadenectomy in patients with gynecological cancer. *Gynecol Oncol*. 2015;137:291–298.
- United States Department of Health and Human Services, National Institutes of Health, National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE); 2017. Version 5 https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf.
- Weinberger V, Cibula D, Zikan M. Lymphocele: prevalence and management in gynecological malignancies. *Expert Rev Anticancer Ther*. 2014;14:307–317.
- Kim HY, Kim JW, Kim SH, Kim YT, Kim JH. An analysis of the risk factors and management of lymphocele after pelvic lymphadenectomy in patients with gynecologic malignancies. *Cancer Res Treat*. 2004;36:377–383.
- Ghezzi F, Uccella S, Cromi A, et al. Lymphoceles, lymphorrhea, and lymphedema after laparoscopic and open endometrial cancer staging. *Ann Surg Oncol*. 2012;19:259–267.
- Gezer Ş, Pulur A, Yücesoy İ. Application of thrombin gel matrix for the prevention of lymphocele in patients with endometrial cancer: a prospective randomized trial. *J Gynecol Obstet Hum Reprod*. 2021;50:101994.
- Jansen A, de Jong A, Hoogendam JP, et al. Lymphocele following lymph node dissection in cervical and endometrial cancer: a systematic review and meta-analysis. *Gynecol Oncol*. 2023;170:273–281.
- Persson J, Reynisson P, Borgfeldt C, Kannisto P, Lindahl B, Bossmar T. Robot assisted laparoscopic radical hysterectomy and pelvic lymphadenectomy with short and long term morbidity data. *Gynecol Oncol*. 2009;113:185–190.
- Ko EM, Muto MG, Berkowitz RS, Feltmate CM. Robotic versus open radical hysterectomy: a comparative study at a single institution. *Gynecol Oncol*. 2008;111:425–430.
- Corrado G, Vizza E, Legge F, et al. Comparison of different surgical approaches for stage IB1 cervical cancer patients: a multi-institution study and a review of the literature. *Int J Gynecol Cancer*. 2018;28:1020–1028.
- Hoogendam JP, Verheijen RHM, Wegner I, Zweemer RP. Oncological outcome and long-term complications in robot-assisted radical surgery for early stage cervical cancer: an observational cohort study. *BJOG*. 2014;121:1538–1545.
- Falconer H. The impact of surgical learning curve on survival—reopening the door for minimally invasive surgery in the management of cervical cancer? *BJOG*. 2021;128:572.
- Orvieto MA, Coelho RF, Chauhan S, Palmer KJ, Rocco B, Patel VR. Incidence of lymphoceles after robot-assisted pelvic lymph node dissection. *BJUI*. 2011;108:1185–1190.
- Keskin MS, Argun ÖB, Öbek C, et al. The incidence and sequela of lymphocele formation after robot-assisted extended pelvic lymph node dissection. *BJU Int*. 2016;118:127–131.
- Song SY, Park M, Kang BH, et al. Distribution of lymphocele following lymphadenectomy in patients with gynecological malignancies. *Obstet Gynecol Sci*. 2020;63:700–708.
- Ma X, Wang Y, Fan A, et al. Risk factors, microbiology and management of infected lymphocyst after lymphadenectomy for gynecologic malignancies. *Arch Gynecol Obstet*. 2018;298:1195–1203.
- Moon AS, Garofalo J, Koirala P, Vu MT, Chuang L. Robotic surgery in gynecology. *Surg Clin North Am*. 2020;100:445–460.
- Lu Y, Chen J, Wei R, et al. Application of robotic surgery and traditional laparoscopic surgery in lymph node dissection for gynecological cancer: a meta-analysis. *Oncol Lett*. 2023;25:175.
- Franchi M, Trimpos JB, Zanaboni F, et al. Randomised trial of drains versus no drains following radical hysterectomy and pelvic lymph node dissection: a European Organisation for Research and Treatment of Cancer–Gynaecological Cancer Group (EORTC–GCG) study in 234 patients. *Eur J Cancer*. 2007;43:1265–1268.
- JSurgOncol*. 1998;68:149–152.
- Gasparri ML, Ruscito I, Bolla D, Benedetti Panici P, Mueller MD, Papadia A. The efficacy of fibrin sealant patches in reducing the incidence of lymphatic morbidity after radical lymphadenectomy: a meta-analysis. *Int J Gynecol Cancer*. 2017;27:1283–1292.
- Charoenkwan K, Kietpeerakool C. Retroperitoneal drainage versus no drainage after pelvic lymphadenectomy for the prevention of lymphocyst formation in patients with gynaecological malignancies. *Cochrane Database Syst Rev*. 2014;CD007387.
- Bifulco G, Giampaolino P, Morra I, et al. Synthetic cyanoacrylic glue in the prevention of post-operative lymphocele after pelvic lymphadenectomy in patients with uterine malignancies: a prospective, single-blind, preliminary study. *Gynecol Oncol*. 2014;134:556–560.
- Diniz TP, Drizlionoks E, Faloppa CC, et al. Impact of sentinel node mapping in decreasing the risk of lymphocele in endometrial cancer. *Ann Surg Oncol*. 2021;28:3293–3299.
- Geppert B, Lönnerfors C, Bollino M, Persson J. Sentinel lymph node biopsy in endometrial cancer—feasibility, safety and lymphatic complications. *Gynecol Oncol*. 2018;148:491–498.
- Hagen B, Valla M, Aune G, et al. Indocyanine green fluorescence imaging of lymph nodes during robotic-assisted laparoscopic operation for endometrial cancer. A prospective validation study using a sentinel lymph node surgical algorithm. *Gynecol Oncol*. 2016;143:479–483.
- Plante M, Touhami O, Trinh XB, et al. Sentinel node mapping with indocyanine green and endoscopic near-infrared fluorescence imaging in endometrial cancer. A pilot study and review of the literature. *Gynecol Oncol*. 2015;137:443–447.
- Martinelli F, Ditto A, Bogani G, et al. Sentinel lymph node mapping in endometrial cancer: performance of hysteroscopic injection of tracers. *Int J Gynecol Cancer*. 2020;30:332–338.
- Persson J, Salehi S, Bollino M, Lönnerfors C, Falconer H, Geppert B. Pelvic Sentinel lymph node detection in High-Risk Endometrial Cancer (SHREC-trial)—the final step towards a paradigm shift in surgical staging. *Eur J Cancer*. 2019;116:77–85.
- Lennox GK, Covens A. Can sentinel lymph node biopsy replace pelvic lymphadenectomy for early cervical cancer? *Gynecol Oncol*. 2017;144:16–20.
- Mathevet P, Lécure F, Uzan C, et al. Sentinel lymph node biopsy and morbidity outcomes in early cervical cancer: results of a multicentre randomised trial (SENTICOL-2). *Eur J Cancer*. 2021;148:307–315.

Supplementary Table 1

Baseline cervical cancer

n=258

FIGO 2009

Missing

1 0.4%

IA1

7 2.7%

IA2

6 2.3%

IB1

235 91.1%

IIA

9 3.5%

Clinical FIGO 2018

Missing

1 0.4%

IA1

31 12.0%

IA2

36 14.0%

IB1

98 38.0%

IB2

82 31.8%

IB3

1 0.4%

IIA1

9 3.5%

Histology

Squamous cell carcinoma

165 64.0%

Adenocarcinoma

76 29.5%

Adenosquamous

11 4.3%

Other

6 2.3%

Grade

Missing

6 2.3%

1 I

56 21.7%

2 II

120 46.5%

3 III

76 29.5%

Type of procedure

Robot PLND+/SN + RHT

172 66.7%

Robot PLND+/SN + RVT

40 15.5%

Robot PLND+/SN

24 9.3%

Other procedure with robot (including PLND)

22 8.5%

SN mapping success

No SN mapping performed

22 8.5%

Detection failure

5 1.9%

Unilateral detection

31 12.0%

Bilateral detection

200 77.5%

Overall lymph node status

Tumor negative

221 85.7%

Tumor positive

37 14.3%

Presence of LVSI

109

42.2%

Parametrium invasion

10

3.9%

Adjuvant therapy

67

26.0%

Follow-up duration since intake (months), median (range)

56 (3-171)

Supplementary Table 2

Baseline endometrial cancer	
Variable	Study population (n = 129)
Surgical procedure, n (%)	
Hysterectomy	120 (93%)
BSO	117 (90.7%)
PAOLND	111 (86%)
Omentectomy	82 (63.6%)
Peritoneum biopsy	66 (51.1%)
Postoperative FIGO stage, n (%)	
IA	61 (47.3%)
IB	31 (24%)
II	16 (12.4%)
IIIA	3 (2.3%)
IIIB	3 (2.3%)
IIIC1	6 (4.7%)
IIIC2	3 (2.3%)
IVA	2 (1.6%)
IVB	3 (2.3%)
Postoperative grade, n (%)	
I	6 (4.7%)
II	5 (3.9%)
III	92 (71.3%)
Not applicable	26 (20.2%)
Histology of endometrial cancer, n (%)	
Endometrioid carcinoma	54 (41.9%)
Serous cell carcinoma	33 (25.6%)
Clear cell carcinoma	9 (7%)
Undifferentiated carcinoma	3 (2.3%)
Uterine carcinosarcoma	18 (14%)
Other	12 (9.3%)
Adjuvant therapy, n (%)	
Vaginal brachytherapy	75 (58.1%)
External radiotherapy (EBRT)	21 (16.3%)
Chemotherapy	6 (4.7%)
Other	5 (3.9%)
None	22 (17.1%)
Follow-up, months (median)	24 [12-51]

Supplementary Table 3

Symptomatic lymphoceles	
Variable	Symptomatic lymphocele (n = 37)
Grade, n (%)	
Grade 2	1 (2.7%)
Grade 3	36 (97.3%)
Time till occurrence in days (median)	59 [17-112]
Length of readmission hospitalization in days (median) (n = 35)	8 [6-11]
Interventions performed, n (%)	
Intravenous antibiotics	36 (97.3%)
Drainage	29 (78.4%)
Recurrent symptomatic lymphocele, n (%)	1 (2.7%)