Hong Kong J Gynaecol Obstet Midwifery 2020;20(1):32-8 | https://doi.org/10.12809/hkjgom.20.1.04

Incidence and risk factors for pelvic lymph node metastasis in early-stage endometrial cancer: a retrospective study

Tony SC LING, MBBS, MRCOG
Hoi-Fong HUI, MBBS, MRCOG, FHKAM(O&G)
Department of Obstetrics and Gynaecology, Tuen Mun Hospital, Hong Kong

Objective: We aimed to determine the incidence and risk factors of pelvic lymph node metastasis in patients with presumably early-stage endometrial cancer in a hospital in Hong Kong.
Methods: We retrospectively reviewed medical records of patients with endometrial cancer confined to the uterus who underwent total hysterectomy with bilateral salpingo-oophorectomy, with or without pelvic lymphadenectomy at Tuen Mun Hospital between 1 January 2011 and 31 December 2015. Patients with gross uterine serosa involvement, extrauterine disease, synchronised ovarian cancers, or sarcomatous tumour (adenosarcoma and endometrial stromal sarcoma) were excluded. Pelvic lymph node metastasis is defined as the presence of metastasis in the excised lymph nodes or within 12 months if pelvic lymphadenectomy was not performed.
Results: Of 268 patients (mean age, 54.8 years), 249 (92.8%) had endometrioid or mucinous adenocarcinoma, 14 (5.3%) had serous or clear cell carcinoma, and 5 (1.9%) had carcinosarcoma. Overall, 33 (12.5%) patients had high-grade pathology. 179 (66.8%) patients underwent pelvic lymphadenectomy with a mean of 25.2 (range, 7-85) pelvic lymph nodes removed; 16 of them had pelvic lymph node metastasis. Among the remaining 89 patients with no pelvic lymphadenectomy, 14 had selective lymph node sampling and 2 of them had pelvic lymph node metastasis. The incidence of pelvic lymph node metastasis in our cohort was 6.7% (n=18). In univariate logistic regression, large tumour size, deep myometrial invasion, cervical stromal invasion, and lymphovascular space invasion were significant risk factors of pelvic lymph node metastasis. In multivariate logistic regression, only large tumour size (adjusted OR=9.18, 95% CI=1.12-75.48, p=0.039) and cervical stromal invasion (adjusted OR=5.14, 95% CI=1.72-15.3, p=0.003) were significant independent risk factors.
Conclusion: Large tumour with maximal tumour diameter >2 cm and cervical stromal invasion are independent risk factor for pelvic lymph node metastasis in patients with early-stage endometrial cancer. Pelvic lymphadenectomy may not be necessary in patients with small tumour and absence of cervical involvement, especially when there is no evidence of high-grade pathology or deep myometrial invasion.

Keywords: Endometrial neoplasms; Lymph node excision

Introduction

Endometrial cancer is the most common gynaecological malignancy in high-income regions including Hong Kong.[1,2] The cumulative risk of endometrial cancer up to the age of 75 years was estimated to be 1.6% in high-income regions (1.75% in Hong Kong) and 0.7% in low-income regions.[2,3] The increased risk is attributed to the increased rate of obesity in high-income regions[4]. Total hysterectomy with bilateral salpingo-oophorectomy remains the gold standard treatment for most patients with early-stage endometrial cancer confined to the uterus.

The International Federation of Gynecology and Obstetrics (FIGO) has recommended surgical staging since 1988[5]. The pelvic lymph nodes are the most common site of extrauterine spread of endometrial cancer and metastasis is often clinically occult[6]. Pelvic lymph node metastasis is associated with worse outcome in terms of both disease-free and overall survival[7]. Pelvic lymphadenectomy was therefore proposed as a staging procedure (by providing prognostic information and stratifying patients for adjuvant therapy) and a potentially therapeutic procedure (by removing metastasis). However, it is associated with significant morbidity such as lymphoedema and lymphocysts in 11% to 38% of cases[8-10]. Prospective randomised studies and meta-analysis failed to demonstrate survival benefit of pelvic lymphadenectomy[11-13], as did a recent population-based registry study in Germany[14]. Hence, there is an international trend to reserve pelvic lymphadenectomy for patients with high risk of pelvic lymph node metastasis[5,15].

Correspondence to: Dr Tony SC LING
Email: lsc721@ha.org.hk

Risk factors for pelvic lymph node metastasis include large tumour size (maximal tumour diameter >2 cm), high-grade histology (FIGO grade 3 endometrioid adenocarcinoma and non-endometrioid carcinoma), deep myometrial invasion, cervical stromal invasion, and lymphovascular space invasion[16-20]. There is no international or local consensus on treatment[21,22], although validated protocols have been proposed by institutions such as the Mayo Clinic.

This study aimed to determine the incidence and risk factors of pelvic lymph node metastasis in patients with early-stage endometrial cancer in a hospital in Hong Kong so as to develop a protocol for stratifying patients to undergo lymphadenectomy.

Materials and Methods

The study was approved by the New Territories West Cluster Research Ethics Committee (reference number: NTWC/REC/18095). We retrospectively reviewed medical records of patients with endometrial cancer confined to the uterus who underwent total hysterectomy with bilateral salpingo-oophorectomy, with or without pelvic lymphadenectomy, by either laparotomy or laparoscopy, without neoadjuvant treatment in the Department of Obstetrics and Gynaecology, Tuen Mun Hospital between 1 January 2011 and 31 December 2015. Patients with gross uterine serosa involvement, extrauterine disease, synchronised ovarian cancers, or sarcomatous tumour (adenosarcoma and endometrial stromal sarcoma) were excluded.

All operations were performed by two consultant gynaecologists or under their supervision. Preoperative computed tomography or magnetic resonance imaging (MRI) were not routinely performed. Pelvic lymphadenectomy was routinely performed unless in very low risk cases (tumour was grossly limited to endometrium and <2 cm in maximal diameter, and preoperative biopsy did not yield high-grade pathology (ie, FIGO grade 3 endometrioid adenocarcinoma, serous carcinoma, clear cell carcinoma, and carcinosarcoma) or when the operation was limited by patient factors such as old age, obesity, previous pelvic irradiation, and medical comorbidities. Pelvic lymphadenectomy involved dissection and removal of all lymph node–bearing tissues along the iliac vessels (from the deep circumflex vein to common iliac bifurcation) and in the obturator fossa (anterior to the obturator nerve), between the genitofemoral nerve and iliopsoas muscle laterally and obliterated umbilical artery medially. If pelvic lymphadenectomy was not performed, pelvic lymph node regions were routinely explored and any suspicious lymph nodes were sampled, as were any suspicious para-aortic lymph nodes. Postoperatively, patients were referred to the department of clinical oncology for assessment; adjuvant treatment was given if indicated. Patients were followed up for any recurrence or metastasis every 3 to 4 months in the first 3 years, every 6 months in the fourth and fifth year, and annually from the sixth to the tenth year.

Data collected included age at surgery, menopausal state, parity, body mass index, comorbidities (hypertension, diabetes mellitus, hyperlipidaemia, polycystic ovarian syndrome), hereditary nonpolyposis colorectal cancer gene mutation carrier status, history of other malignancies or pelvic irradiation, and histopathological variables of the endometrial tumour (maximal tumour dimension, tumour type and grade, depth of myometrial invasion, any cervical stromal invasion, and any lymphovascular space invasion).

FIGO grade 1 and 2 endometrioid adenocarcinoma and mucinous adenocarcinoma are considered low-grade pathology[23,24], whereas FIGO grade 3 endometrioid adenocarcinoma, serous carcinoma, clear cell carcinoma, and carcinosarcoma were considered high-grade pathology. Pelvic lymph node metastasis is defined as the presence of metastasis in the excised lymph nodes or within 12 months if pelvic lymphadenectomy was not performed.

Statistical analyses were performed using SPSS (Windows version 22; IBM Corp, Armonk [NY], US). Patients with or without pelvic lymph node metastasis were compared using two-tailed *t*-test for continuous variables and Fisher's exact test or Pearson Chi-squared test for categorical variables. A p value of <0.05 was considered statistically significant. Univariate and multivariate binary logistic regression models were used to identify risk factors for pelvic lymph node metastasis.

Results

Of 268 patients with a mean age of 54.8±9.7 years, 249 (92.8%) had endometrioid or mucinous adenocarcinoma, 14 (5.3%) had serous or clear cell carcinoma, and 5 (1.9%) had carcinosarcoma (Table 1). Overall, 33 (12.5%) patients had high-grade pathology.

179 (66.8%) patients underwent pelvic lymphadenectomy with a mean of 25.2±10.9 (range, 7-85) pelvic lymph nodes removed; 16 of them had pelvic lymph node metastasis. Among the remaining 89 patients with no pelvic lymphadenectomy, 14 had selective lymph node sampling and 2 of them had pelvic lymph node metastasis.

Table 1. Patients with or without pelvic lymph node metastasis in terms of clinical characteristics and pathological variables

Parameter	Overall (n=268)*	Pelvic lymph node metastasis		p Value
		No (n=250)*	Yes (n=18)*	
Age, y	54.8±9.7	54.9±9.7	53.1±9.9	0.553
Parity	1.87±1.50	1.85±1.43	2.11±2.32	0.474
Body mass index, kg/m^2	26.6±5.3	26.6±5.2	26.4±5.6	0.900
Menopaused	143 (53.4)	134 (53.6)	9 (50)	0.810
Diabetes mellitus	60 (22.4)	56 (22.4)	4 (22.2)	1.000
Hypertension	110 (41.0)	106 (42.4)	4 (22.2)	0.135
Hyperlipidaemia	8 (17.9)	45 (18.0)	3 (16.7)	1.000
Polycystic ovary syndrome	6 (2.2)	6 (2.4)	0	1.000
Hereditary nonpolyposis colorectal cancer gene mutation carrier	3 (1.1)	3 (1.2)	0	1.000
Previous pelvic irradiation	4 (1.5)	3 (1.2)	1 (5.6)	0.244
Previous malignancy, overall	26 (9.7)	24 (9.6)	2 (11.1)	0.689
Previous breast cancer on tamoxifen	12 (4.5)	12 (4.8)	0	1.000
Previous malignancy, colon	4 (1.5)	3 (1.2)	1 (5.6)	0.244
Tumour types and grades (according to International Federation of Gynecology and Obstetrics)				0.140
Endometrioid or mucinous grade 1	154 (58.6)	148 (60.4)	6 (33.3)	
Endometrioid grade 2	76 (28.9)	67 (27.3)	9 (50.0)	
Endometrioid grade 3	14 (5.3)	13 (5.3)	1 (5.6)	
Serous or clear cell carcinoma or carcinosarcoma	19 (7.2)	17 (6.9)	2 (11.1)	
Maximal tumour diameter >2 cm	142 (53.0)	125 (50)	17 (94.4)	<0.001
Myometrial invasion ≥50%	69 (25.7)	59 (23.6)	10 (55.6)	0.009
Cervical stromal invasion	31 (11.6)	22 (8.8)	9 (50.0)	<0.001
Lymphovascular space invasion	40 (15.0)	34 (13.7)	6 (33.3)	0.037
Microscopic uterine serosal involvement	4 (1.5)	3 (1.2)	1 (5.6)	0.244
Microscopic adnexal involvement	5 (1.9)	4 (1.6)	1 (5.6)	0.296
Para-aortic lymph node involvement	1 (0.04)	0 (0.0)	1 (5.6)	0.067
Pelvic lymphadenectomy done	179 (66.8)	163 (65.2)	16 (88.9)	0.04
No. of pelvic lymph nodes removed	25.2±10.9	25.5±11.1	22.3±9.1	0.264

* Data are presented as mean±standard deviation or No. (%) of patients

The incidence of pelvic lymph node metastasis in our cohort was 6.7% (n=18). None of the patient without pelvic lymphadenectomy had pelvic lymph node recurrence both in the immediate 12 months and in the entire review period.

Compared with patients without pelvic lymph node metastasis, patients with pelvic lymph node metastasis were more likely to have large tumour size (maximal tumour diameter >2 cm) [94.4% vs 50%, p<0.001], deep myometrial invasion (≥50% myometrial thickness) [55.6% vs 23.6%, p=0.009], cervical stromal invasion (50.0% vs 8.8%, p<0.001), and lymphovascular space invasion (33.3% vs 13.7%, p=0.037) [Table 1]. More (but not significantly) patients with pelvic lymph node metastasis had high-grade pathology (16.7% vs 12.2%, p=0.481).

In univariate logistic regression, high-grade pathology had increased odds of pelvic lymph node

metastasis but not significantly (odds ratio [OR]=1.43, 95% confidence interval [CI]=0.39-5.24, p=0.586). Large tumour size, deep myometrial invasion, cervical stromal invasion, and lymphovascular space invasion were significant risk factors of pelvic lymph node metastasis (Table 2). In multivariate logistic regression, only large tumour size (adjusted OR=9.18, 95% CI=1.12-75.48, p=0.039) and cervical stromal invasion (adjusted OR=5.14, 95% CI=1.72-15.3, p=0.003) were significant independent risk factors.

Discussions

In 1987, the Gynecologic Oncology Group established the role of surgical staging and popularised lymphadenectomy in the treatment of endometrial cancer. In that seminal large-scale prospective study, the incidence of pelvic lymph node metastasis was 9% for all women with presumably early-stage endometrial cancer, 18% for those with high-grade pathology, 25% for those with deep one-third myometrial invasion, and 34% for those with high-grade pathology with deep one-third myometrial

Table 2. Incidence of pelvic lymph node metastasis by different pathological variables and predictors of lymph node metastasis

Variables	No. (%) of patients with pelvic lymph node metastasis	Univariate logistic regression		Multivariate logistic regression	
		Odds ratio (95% confidence interval)	p Value	Adjusted odds ratio (95% confidence interval)	p Value
Tumour types and grades (according to International Federation of Gynecology and Obstetrics)					
Grade 1 & 2	15 (6.5)	Reference			
Grade 3, serous or clear cell carcinoma, or carcinosarcoma	3 (9.1)	1.43 (0.39-5.24)	0.586	-	-
Maximal tumour diameter					
≤2 cm	1 (0.8)	Reference			
>2 cm	17 (12)	17 (2.23-129.69)	0.006	9.18 (1.12-75.48)	0.039
Depth of myometrial invasion					
<50%	8 (4)	Reference			
≥50%	10 (14.5)	4.05 (1.53-10.72)	0.005	1.52 (0.51-4.55)	0.457
Cervical stromal invasion					
Negative	9 (3.8)	Reference			
Positive	9 (29)	10.36 (3.73-28.81)	<0.001	5.14 (1.72-15.3)	0.003
Lymphovascular space invasion					
Negative	12 (5.3)	Reference			
Positive	6 (15)	3.15 (1.11-8.95)	0.031	1.31 (0.42-4.12)	0.646

Table 3. Comparison of the current study and a population-based study by Vargas et al.22 in terms of incidence of pelvic lymph node metastasis by tumour grade and depth of myometrial invasion

Depth of myometrial invasion	No. (%) of patients			
	Low-grade pathology		High-grade pathology	
	Current study	Vargas et al.	Current study	Vargas et al.
<50%	6/176 (4.6)	250/11771 (2.12)	0/16 (0.0)	147/2591 (5.6)
≥50%	7/54 (13.0)	411/3576 (11.5)	3/17 (17.6)	229/1391 (16.5)

invasion[6]. In our study, however, the incidence of pelvic lymph metastasis was 6.7% for the entire cohort, 9.1% for those with high-grade pathology, 14.5% for those with deep myometrial invasion, and 17.6% for those with high-grade pathology and deep myometrial invasion. The true incidence of pelvic lymph node metastasis could be underestimated because of the retrospective design of our study. Patients with undiagnosed occult pelvic lymph node metastasis may have undergone adjuvant radiotherapy and did not present as clinical disease. Nonetheless, in a population-based study of the United States Surveillance, Epidemiology, and End Results registry involving 19 329 women with surgically staged endometrial cancer diagnosed between 1988 and 2010[22], the incidences of pelvic lymph node metastasis were consistent with those in our cohort (Table 3).

In our study, tumour size >2 cm was independent risk factor for pelvic lymph node metastasis. Only one patient with tumour size ≤2 cm had pelvic lymph node metastasis. In a cohort of 91 patients with early-stage endometrial cancer, tumour size was independently associated with lymph node metastasis[25]. In a retrospective study involving 328 patients with low-grade endometrial cancer confined to the uterus who underwent surgery with or without pelvic lymphadenectomy and followed up for a median of 88 months, no patient with tumour diameter ≤2 cm and myometrial invasion <50% had positive lymph nodes or died of disease, and thus pelvic lymphadenectomy was deemed unnecessary[16].

Although the validity of the Mayo criteria was confirmed[18,21], assessment of the depth of myometrial invasion by intraoperative frozen section is not available in many institutions. In our unit, intraoperative gross evaluation was used instead. In a meta-analysis of 35 studies, intraoperative frozen section is superior to intraoperative gross evaluation in both sensitivity (85% vs 71%, p=0.0008) and specificity (97% vs 91%, p=0.0021) in determining deep myometrial invasion[26]. Thus, traditionally we performed pelvic lymphadenectomy if intraoperative gross evaluation suggested any degree of myometrial invasion or when tumour size >2 cm. With the introduction of Enhancing Radiological Investigation Services through Collaboration with the Private Sector project (Radi Collaboration) of the Hospital Authority, we have routinely referred patients with endometrial cancer for preoperative MRI of pelvis in the private sector since 2016. A meta-analysis of nine studies showed that MRI had a pooled sensitivity and specificity of both 86% in detecting deep myometrial invasion[27], which is comparable to intraoperative frozen section. There is no study comparing intraoperative frozen section with MRI yet.

In the Gynecologic Oncology Group study, high-grade pathology is a risk factor for pelvic lymph node metastasis[6]. However, in our study such correlation was not significant. This may be because our cohort had fewer patients with high-grade pathology (12.5%), compared with 20.6% in the registry study by Vargas et al.[22] and 25% in the Gynecologic Oncology Group study[6]. Our study is insufficient to disprove the correlation between high-grade pathology and pelvic lymph node metastasis because of its retrospective nature and absence of pathological re-review of specimens, and large-scale prospective study or population-based registry study is needed to confirm this observation.

Lymphovascular space invasion and cervical involvement have been reported to be independent risk factors for pelvic lymph node metastasis[17,19]. In our study, only cervical stromal invasion was an independent risk factor for pelvic lymph node metastasis. This is of importance as lymphovascular space invasion can only be assessed postoperatively. For patients with suspected cervical stromal invasion, the current paradigm is to perform total extrafascial 'simple' hysterectomy (rather than radical hysterectomy) because of a lack of survival benefits[28,29]. Pelvic lymphadenectomy remains an important staging procedure for patients with suspected cervical stromal invasion, and adjuvant radiotherapy should be considered especially when pelvic lymphadenectomy is not performed.

The main limitation of this study is its retrospective design, which cannot confirm correlations. A low rate of high-grade pathology is insufficient to disprove its correlation with pelvic lymph node metastasis. Para-aortic lymph node metastasis, late lymph node recurrence, and long-term survival data were not analysed, as were preoperative CA-125 level and MRI tumour volume index, which have been identified as independent risk factors for pelvic lymph node metastasis[30,31].

The incidence of endometrial cancer in Hong Kong has increased to 1050 new cases in 2016 from 570 new cases in 2006[2], but local data on pelvic lymph node metastasis are scarce. Pelvic lymphadenectomy is currently not indicated for small endometrial tumour, unless there is evidence suggestive of cervical involvement, deep myometrial invasion, or high-grade pathology.

Conclusion

Large tumour with maximal tumour diameter >2 cm and cervical stromal invasion are independent risk factor for pelvic lymph node metastasis in patients with early-stage endometrial cancer. Pelvic lymphadenectomy may not be necessary in patients with small tumour and absence of cervical involvement, especially when there is no evidence of high-grade pathology or deep myometrial invasion.

Acknowledgements

Dr Yin-Fong KWOK and Dr Man-Chi CHAN of the Department of Obstetrics and Gynaecology, Tuen Mun Hospital contributed to the design of the study. Dr Edmond Pui-Hang CHOI of the School of Nursing, Li Ka Shing Faculty of Medicine, The University of Hong Kong contributed to the statistical analysis.

Declaration

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The authors have no conflict of interest to disclose.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424. Crossref
2. Hong Kong Cancer Registry, Hospital Authority. Overview of Hong Kong Cancer Statistics of 2016. Available at: http://www3.ha.org.hk/cancereg/pdf/overview/Summary%20of%20CanStat%202016.pdf Updated: October 2018. Assessed 24 May 2019.
3. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015;65:87-108. Crossref
4. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: A systematic review and meta-analysis of prospective observational studies. Lancet 2008;371:569-78. Crossref
5. Amant F, Mirza MR, Koskas M, Creutzberg CL. Cancer of the corpus uteri. Int J Gynaecol Obstet 2018;143(Suppl 2):37-50. Crossref
6. Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB. Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study. Cancer 1987;60(8 Suppl):2035. Crossref
7. Morrow CP, Bundy BN, Kurman RJ, et al. Relationship between surgical-pathological risk factors and outcome in clinical stage I and II carcinoma of the endometrium: a Gynecologic Oncology Group study. Gynecol Oncol 1991;40:55-65. Crossref
8. Nunns D, Williamson K, Swaney L, Davy M. The morbidity of surgery and adjuvant radiotherapy in the management of endometrial carcinoma. Int J Gynecol Cancer 2000;10:233-8. Crossref
9. Todo Y, Yamamoto R, Minobe S, et al. Risk factors for postoperative lower-extremity lymphedema in endometrial cancer survivors who had treatment including lymphadenectomy. Gynecol Oncol 2010;119:60. Crossref
10. Yost KJ, Cheville AL, Al-Hilli MM, et al. Lymphedema after surgery for endometrial cancer: prevalence, risk factors, and quality of life. Obstet Gynecol 2014;124:307-15. Crossref
11. Benedetti Panici P, Basile S, Maneschi F, et al. Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. J Natl Cancer Inst 2008;100:1707. Crossref
12. ASTEC study group; Kitchener H, Swart AM, et al. Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. Lancet 2009;373:125. Crossref
13. Frost JA, Webster KE, Bryant A, Morrison J. Lymphadenectomy for the management of endometrial cancer. Cochrane Database Syst Rev 2017;10:CD007585. Crossref
14. Pölcher M, Rottmann M, Brugger S, et al. Lymph node dissection in endometrial cancer and clinical outcome: a population-based study in 5546 patients. Gynecol Oncol 2019. Crossref
15. Colombo N, Creutzberg C, Amant F, et al. ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: Diagnosis, treatment and follow-up. Ann Oncol 2016;27:16-41. Crossref
16. Mariani A, Webb MJ, Keeney GL, Haddock MG, Calori G, Podratz KC. Low-risk corpus cancer: is lymphadenectomy or radiotherapy necessary? Am J Obstet Gynecol 2000;182:1506. Crossref
17. Akbayir O, Corbacioglu A, Goksedef BP, et al. The novel criteria for predicting pelvic lymph node metastasis in endometrioid adenocarcinoma of endometrium. Gynecol Oncol 2012;125:400-3. Crossref
18. Milam MR, Java J, Walker JL, Metzinger DS, Parker LP, Coleman RL. Nodal metastasis risk in endometrioid endometrial cancer. Obstet Gynecol 2012;119:286-92. Crossref
19. Solmaz U, Mat E, Dereli M, et al. Lymphovascular space invasion and cervical stromal invasion are independent risk factors for nodal metastasis in endometrioid endometrial cancer. Aust N Z J Obstet Gynaecol 2015;55:81-6. Crossref
20. Al Hilli MM, Podratz KC, Dowdy SC, et al. Preoperative biopsy and intraoperative tumor diameter predict lymph node dissemination in endometrial cancer. Gynecol Oncol 2013;128:294-9. Crossref

21. Mariani A, Dowdy SC, Cliby WA, et al. Prospective assessment of lymphatic dissemination in endometrial cancer: a paradigm shift in surgical staging. Gynecol Oncol 2008;109:11. Crossref
22. Vargas R, Rauh-Hain JA, Clemmer J, et al. Tumor size, depth of invasion, and histologic grade as prognostic factors of lymph node involvement in endometrial cancer: a SEER analysis. Gynecol Oncol 2014;133:216-20. Crossref
23. Melhem MF, Tobon H. Mucinous adenocarcinoma of the endometrium: a clinico-pathological review of 18 cases. Int J Gynecol Pathol 1987;6:347-55. Crossref
24. Soslow RA, Tornos C, Park KJ, et al. Endometrial carcinoma diagnosis: use of FIGO grading and genomic subcategories in clinical practice: Recommendations of the International Society of Gynecological Pathologists. Int J Gynecol Pathol 2019;38(Suppl 1):S64-S74. Crossref
25. Schink JC, Lurain JR, Wallemark CB, Chmiel JS. Tumor size in endometrial cancer: a prognostic factor for lymph node metastasis. Obstet Gynecol 1987;70:216-9. Crossref
26. Alcazar JL, Dominguez-Piriz J, Juez L, Caparros M, Jurado M. Intraoperative gross examination and intraoperative frozen section in patients with endometrial cancer for detecting deep myometrial invasion: a systematic review and meta-analysis. Int J Gynecol Cancer 2016;26:407-15. Crossref
27. Andreano A, Rechichi G, Rebora P, Sironi S, Valsecchi MG, Galimberti S. MR diffusion imaging for preoperative staging of myometrial invasion in patients with endometrial cancer: a systematic review and meta-analysis. Eur Radiol 2014;24:1327-38. Crossref
28. Phelippeau J, Koskas M. Impact of radical hysterectomy on survival in patients with Stage 2 Type1 endometrial carcinoma: a matched cohort study. Ann Surg Oncol 2016;23:4361-7. Crossref
29. Takano M, Ochi H, Takei Y, et al. Surgery for endometrial cancers with suspected cervical involvement: Is radical hysterectomy needed (a GOTIC study)? Br J Cancer 2013;109:1760-5. Crossref
30. Todo Y, Okamoto K, Hayashi M, et al. A validation study of a scoring system to estimate the risk of lymph node metastasis for patients with endometrial carcinoma for tailoring the indication of lymphadenectomy. Gynecol Oncol 2007;104:623-8. Crossref
31. Kang S, Kang WD, Chung HH, et al. Preoperative identification of a low-risk group for lymph node metastasis in endometrial cancer: a Korean gynecologic oncology group study. J Clin Oncol 2012;30:1329-34. Crossref