Risk Factors of Pelvic Lymph Node Metastasis in Cervical Adenocarcinoma following Radical Hysterectomy and Pelvic Lymphadenectomy

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Background: *Lymph node metastasis is the most important prognostic factor in cervical cancer patients. However, most of the available knowledge about risk factors of pelvic nodal metastasis in cervical cancer has come from studies in which the majority of patients had the squamous cell carcinoma (SCC) subtype.*
Objective: *To determine the risk factors of pelvic lymph node metastasis in early-stage cervical adenocarcinoma (AC) patients following radical hysterectomy and bilateral pelvic lymphadenectomy.*
Material and Method: *Retrospective reviews were carried out of the medical charts and pathologic slides of 251 patients with cervical AC stage IB1-IIA who underwent radical hysterectomy and bilateral pelvic lymphadenectomy at Rajavithi Hospital from January 1, 2000 to December 31, 2011. The risk factors of pelvic lymph node metastasis were analyzed by multiple logistic regression.*
Results: *Of the 251 patients, pelvic node metastasis in stage IB1-IIA cervical AC was detected in 29 patients (11.6%). Multivariable analysis revealed that clinical stage IB2-IIA (adjusted OR 3.4, 95%CI 1.2-9.7), tumor size more than 2 cm (adjusted OR 3.5, 95%CI 1.1-11.8), and positive lymphovascular invasion (LVSI) (adjusted OR 55.5, 95%CI 7.2-427.6) were significantly associated with pelvic nodal metastasis. Early-stage cervical AC patients with no risk factor, one risk factor other than LVSI, LVSI factor alone, two risk factors, and three risk factors were identified as having pelvic nodal metastasis in 0%, 2.3%, 9.1%, 29.1% and 58.8% of cases respectively.*
Conclusion: *Clinical stage IB2-IIA, tumor size of more than 2 cm, and positive LVSI were significant risk factors for pelvic nodal metastasis in early-stage cervical AC patients. Those with no risk factors were not found to have pelvic nodal metastasis and might be candidates for less radical surgery, whereas patients with the presence of LVSI and/or 2 other risk factors were found to be at high risk of pelvic node metastasis and might benefit from extensive lymphadenectomy and adjuvant therapy.*

Keywords: *Cervical adenocarcinoma, Pelvic lymph node metastasis, Risk factors*

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Carcinoma of the uterine cervix is one of the most common cancers in women worldwide, including Thailand. It mostly consists of two cell types: squamous cell carcinoma (SCC) and adenocarcinoma (AC). During recent decades, the relative proportion of AC to SC in the total cervical incidences has increased from approximately 12.4% versus 87.6% to 24.0% versus 76.0% respectively[1].

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Lymph node metastasis is an important prognostic factor in women with carcinoma of the uterine cervix. Those with zero, one, and more than one lymph node metastasis have 87, 84, and 61% 5-year disease-free survival ($p = 0.0001$) respectively[2]. Risk factors for lymph node metastasis are important in the planning of treatment. Cervical cancer patients with positive nodal metastasis and AC histology experience significantly worse survival rates relative to their SCC histology counterparts. However, most knowledge about cervical cancer comes from studies in which the majority of the patients had SCC, with AC comprising on average only 10% of cases[3].

Since the incidence of AC has increased, this

study was undertaken to assess risk factors associated with pelvic lymph node metastasis in patients with cervical AC stage IB1-IIA following radical hysterectomy and bilateral pelvic lymphadenectomy.

Material and Method

After the study had been approved by the Institutional Review Board (IRB) of Rajavithi Hospital (No. 55056), medical records were retrospectively reviewed of stage IB1-IIA cervical cancer patients who had been histologically diagnosed with AC following radical hysterectomy and pelvic lymphadenectomy at Rajavithi Hospital between January 1, 2000 and December 31, 2011. Patients were excluded if they were non-AC type or had a history of pre-operative radiotherapy and/or chemotherapy. Information from the medical records of eligible women was recorded including their age at diagnosis, parity, weight, height, underlying diseases, tumor staging, duration from diagnosis to treatment, surgical procedures, estimated blood loss, and complications. Tumor staging was defined at the time of clinical examination by gynecologic oncologists according to the 1995 International Federation of Gynecology and Obstetrics (FIGO) clinical staging. All pathologic materials were reviewed by two of the authors (M. Yanaranop and S. Nakrangsee) blinded to previous pathologic diagnoses, and histologic variables were confirmed. Depth of stromal invasion was measured from the base of the surface epithelium to the deepest malignant cells. Lymphovascular space invasion (LVSI) was considered to be present only if viable tumor cells were demonstrated inside an endothelium-lined space within an area of cervical stroma. Uterine corpus invasion was defined histologically as a tumor extending over the histologic internal os and invading the endometrium and/or myometrium of the uterine corpus.

Sample size calculation was based on the formula for a one-sample comparison of proportion using 2-tail alpha equal 0.05 and acceptable error at 0.04. The prevalence of nodal metastasis in cervical adenocarcinoma was taken at 10% in accordance with the present study by Balega et al[4]. The sample size arrived at was at least 216 subjects, and 270 patients were therefore required taking into account an expected 20% drop out.

Statistical analysis of the data was performed using SPSS version 11.5 software for Windows (Chicago, IL). Comparison between categorical variables was calculated by Chi-square test and Fisher's exact test. Multivariable analysis by logistic regression was evaluated for the significant risk factors of pelvic node metastasis. The results of logistic regression were presented as odds ratio (OR) and 95% confidence interval (CI), A *p*-value of <0.05 was considered statistically significant.

Results

During the present study period, a total of 269 patients were identified with FIGO stage IB1-IIA cervical cancer histologically diagnosed as AC following primary radical hysterectomy and bilateral pelvic lymphadenectomy. Ten patients histologically diagnosed with adenosquamous carcinoma and eight with undifferentiated carcinoma were excluded. Ultimately, 251 patients were included in the present study.

The clinical and pathologic characteristics of all patients are summarized in Table 1 and 2 respectively. The mean age of patients at diagnosis was 46.6 years (standard deviation $\pm$8.8 years) and the median parity was 2 (range 0-10). The mean weight, height and body mass index (BMI) were 60.2 kg, 154.2 cm and 25.3 kg/m^2 respectively. According to FIGO clinical staging 1995, 216 patients (86.0%) were in stage IB1, 21 patients (8.4%) in stage IB2 and 14 patients (5.6%) in stage IIA. The median duration from diagnosis to treatment was 67 days (range 7-270 days). All patients had undergone radical hysterectomy and pelvic lymphadenectomy, whereas para-aortic lymphadenectomy was performed in only 12 patients.

Pathologically, the histologic subtypes were classified as endocervical 214 patients (85.3%), endometrioid 18 patients (7.2%) and others 19 patients (7.6%). The histologic grading was evaluated as: well, moderately and poorly differentiated in 185 patients (73.7%), 49 patients (19.5%) and 17 patients (6.8%) respectively. The median tumor size and depth of stromal invasion were 2 cm (range 0.1-6 cm) and 6 mm (range 1-24 mm) respectively. Levels of cervical stromal invasion were classified as inner third 117 patients (46.6%), middle third 57 patients (22.7%) and outer third 77 patients (30.7%). Presence of LVSI was found in 84 patients (33.5%) while tumor invasion of parametrium and uterine corpus was identified in 12 patients (4.8%), and positive surgical margin was demonstrated in 11 patients (4.4%). Of the 159 patients who underwent oophorectomy, only one was found to have ovarian metastasis. The median number of pelvic lymph nodes evaluated pathologically per patient was 18 (range 4-46 nodes). Twenty nine of the 251 patients (11.6%) were reported as having pelvic lymph node metastasis.

Table 1. Clinical characteristics of cervical adenocarcinoma patients who underwent radical hysterectomy and pelvic node dissection (n = 251)

Clinical variables	n (%)
Age (years), mean ± SD	46.6±8.8
Parity, median (range)	2 (0-10)
Weight (kg), mean ± SD	60.2±11.1
Height (cm), mean ± SD	154.2±6.4
BMI (kg/m^2), mean ± SD	25.3±4.6
Underlying diseases	
Diabetes	28 (11.2)
Hypertension	11 (4.4)
HIV infection	2 (0.8)
Other	15 (6.0)
FIGO clinical staging	
IB1	216 (86.0)
IB2	21 (8.4)
IIA	14 (5.6)
Duration from diagnosis to treatment (days), median (range)	67 (7-270)
Surgical procedure performed	
RHPL	239 (95.2)
RHPL with PAL	12 (4.8)
Estimated blood loss (ml), median (range)	700 (100-2,600)
Complications	
Massive blood loss	23 (9.2)
Urinary bladder injury	4 (1.6)
Vascular injury	2 (0.8)

SD = Standard deviation; BMI = Body mass index; FIGO = International Federation of Gynecology and Obstetrics; RHPL = Radical hysterectomy with pelvic lymphadenectomy; PAL = Para-aortic lymphadenectomy

The median number of positive pelvic nodes among those was 2 (range 1-7 nodes). The median number of para-aortic lymph nodes evaluated pathologically per patient was 1 (range 1-6 nodes). Two of 12 patients (16.7%) were reported as having para-aortic lymph node metastasis and positive in one node similarly. All patients with para-aortic node metastasis also had pelvic node metastasis.

To determine possible risk factors of pelvic node metastasis, the authors compared various clinicopathologic characteristics between 2 groups of patients: those with and without pelvic node metastasis, as shown in Table 3. Pelvic node metastasis was found more commonly in patients who had clinical stage IB2-IIA (crude OR 6.1, 95% CI 2.6-14.4), tumor size larger than 2 cm (crude OR 10.3, 95% CI 3.5-30.5), depth of invasion more than 5 mm (crude OR 12.8, 95% CI 3.0-55.0), middle or outer third of cervical stromal invasion (crude OR 14.5, 95% CI 3.4-62.5), presence of LVSI (crude OR 85, 95% CI 11.3-639.5), positive surgical margin (crude OR 7.5, 95% CI 2.1-26.4), parametrial invasion (crude OR 13.8, 95% CI 4.0-47.2), vaginal invasion (crude OR 6.4, 95% CI 1.2-1.7), or uterine corpus invasion (crude OR 4.9, 95% CI 1.1-2.8). However, age of patients at diagnosis, duration from diagnosis to treatment and histologic grading were not significantly different between the two groups.

Multiple logistic regression analysis was used to identify independent risk factors associated with pelvic node metastasis, as shown in Table 4. The only risk factors found were stage IB2-IIA, tumor size more than 2 cm and presence of LVSI, with adjusted OR of 3.4 (95% CI 1.2-9.7), 3.5 (95% CI 1.1-11.8) and 55.5 (95% CI 7.2-427.6) respectively.

Table 5 exhibits the relationship between independent risk factors and pelvic node metastasis. None of the early-stage cervical AC patients who had none of the risk factors were found to have pelvic node metastasis, whereas patients with one risk factor other than LVSI, LVSI alone, two risk factors and three risk factors were identified as having pelvic node metastasis in 2.3%, 9.1%, 29.1% and 58.8% of cases respectively.

Table 2. Pathologic characteristics of cervical adenocarcinoma patients who underwent radical hysterectomy and pelvic node dissection (n = 251)

Pathologic variables	n (%)
Histologic type	
Endocervical	214 (85.3)
Intestinal	6 (2.4)
Villoglandular	7 (2.8)
Minimal deviating	1 (0.4)
Endometrioid	18 (7.2)
Clear cell	2 (0.8)
Signet ring cell	3 (1.2)
Histologic grade	
Well differentiated	185 (73.7)
Moderately differentiated	49 (19.5)
Poorly differentiated	17 (6.8)
Tumor size (cm), median (range)	2 (0.1-6)
Depth of invasion (mm), median (range)	6 (1-24)
Cervical stromal invasion	
Inner third	117 (46.6)
Middle third	57 (22.7)
Outer third	77 (30.7)
Positive LVSI	84 (33.5)
Positive surgical margin	11 (4.4)
Positive parametrial invasion	12 (4.8)
Positive uterine corpus invasion	12 (4.8)
Ovarian metastasis	1 (0.6)
Number of examined pelvic nodes, median (range)	18 (4-46)
Pelvic node metastasis	29 (11.6)
Number of positive pelvic nodes, median (range)	2 (1-7)
Number of examined para-aortic nodes, median (range)	1 (1-6)
Para-aortic node metastasis	2 (16.7)
Number of positive para-aortic nodes	1

LVSI = Lymphovascular space invasion

Discussion

AC histology is known to be an independent prognostic factor for poorer survival outcomes in cervical cancer patients. Although several studies have found that the prognosis for patients with AC is poorer than those with SCC[5-7], the Gynecologic Oncology Group has reported that histologic type has no significant effect on survival in clinical stage IB disease[8,9]. Some studies have found that the presence of lymph node metastasis worsens the prognosis of cervical AC compared with SCC; however, no difference was found between the prognosis of patients with both AC and SCC without lymph node metastasis[10,11]. Lymph node metastasis is the most important prognostic factor to survival in cervical cancer patients. However, studies of these factors extract most data from cervical cancer patients with SCC. Some studies of the AC type can be found, but these factors cannot be evaluated by logistic regression analysis due to their small sample sizes. Covering a 12-year period, this research retrospectively reviewed larger amounts of cervical cancer patients with AC and had a sufficient number of patients with pelvic node metastasis for analysis.

The incidence of pelvic node metastasis was 11.6% which was comparable to the prior studies of Balega et al (10.2%)[4] and Hernandes et al (14%)[12]; however, some studies have documented higher rates of pelvic node metastasis (22-32%)[13-15], and this discrepancy may result from the fact that cases of stage IIB of cervical cancer were included in these studies.

In SCC of the uterine cervix, it has been accepted that tumor size, depth of stromal invasion, histologic grading and presence of LVSI are the risk

Table 3. Bivariate analysis of risk factors of pelvic node metastasis of cervical adenocarcinoma

Variables, n (%)	Total n	PLN metastasis (n = 29)			
		%	Crude OR	95%CI	*p*-value
Age					
≤45 years	134	12.7	1.0		
>45 years	117	10.3	0.8	0.4-1.7	0.548
Duration from diagnosis to treatment					
≤60 days	112	11.6	1.0		
>60 days	139	11.5	1.0	0.5-2.2	0.981
FIGO clinical staging					
IB1	216	7.9	1.0		
IB2-IIA	35	34.3	6.1	2.6-14.4	<0.001*
Histologic grading					
Well differentiated	185	9.7	1.0		
Moderately/poorly differentiated	66	16.7	1.9	0.8-4.2	0.130
Tumor size					
≤2 cm	142	2.8	1.0		
>2 cm	109	22.9	10.3	3.5-30.5	<0.001*
Depth of invasion					
≤5 mm	111	1.8	1.0		
>5 mm	140	19.3	13.0	3.0-56.0	<0.001*
Level of cervical stromal invasion					
Inner third	117	1.7	1.0		
Middle/outer third	134	20.1	14.5	3.4-62.5	<0.001*
LVSI					
Negative	168	0.6	1.0		
Positive	83	33.7	85.0	11.3-639.5	<0.001*
Margin status					
Negative	240	10.0	1.0		
Positive	11	45.5	7.5	2.1-26.4	<0.001*
Parametrial invasion					
Negative	239	9.2	1.0		
Positive	12	58.3	13.8	4.0-47.2	<0.001*
Vaginal invasion					
Negative	239	10.0	1.0		
Positive	12	41.7	6.4	1.9-21.7	0.001*
Uterine corpus invasion					
Negative	227	9.3	1.0		
Positive	24	33.3	4.9	1.9-12.8	<0.001*

PLN = Pelvic lymph node; OR = Odds ratio; CI = Confidence interval; FIGO = International Federation of Gynecology and Obstetrics; LVSI = Lymphovasular space invasion
* Significant at $p<0.05$

factors of pelvic node metastasis[16]. However, the risk factors of pelvic node metastasis in AC of the uterine cervix are not obviously apparent. In the present study, it was evident that clinical stage IB2-IIA, tumor size of more than 2 cm and presence of LVSI were the significant predictive factors for pelvic node metastasis. In 1985, Berek et al[17] established, in a series of 51 cervical AC patients with stage I-II, that tumor size, histologic grading and depth of stromal invasion were correlated with pelvic node metastasis. Kaspar et al[18], whose study was of 36 patients with stage I cervical AC, proposed that tumor volume of more than 500 mm^3 was a better predictor of pelvic node metastasis than depth of stromal invasion alone, but the series of Balega et al[4] reported that depth of stromal invasion of more than 5 mm was the main risk factor of pelvic node

Table 4. Multivariable analysis of risk factors of pelvic node metastasis of cervical adenocarcinoma

Variables			Adjusted OR	95% CI	*p*-value
Stage IB_2-IIA	1.2	0.5	3.4	1.2-9.7	0.023*
Size >2 cm	1.3	0.6	3.5	1.1-11.8	0.039*
Positive LVSI	4.0	1.0	55.5	7.2-427.6	<0.001*

SE = Standard error; OR = Odds ratio; CI = confidence interval; LVSI = Lymphovasular invasion
*Significant at $p<0.05$

Table 5. Relationships between significant risk factors and pelvic node metastasis of cervical adenocarcinoma

Risk factors	Pelvic node metastasis (%)
No risk factor	0/113 (0.0)
1 risk factor (stage IB_2-IIA or size >2 cm)	1/44 (2.3)
1 risk factor (LVSI)	2/22 (9.1)
2 risk factors (stage IB2-IIA and size >2 cm, stage IB2-IIA and LVSI, size >2 cm and LVSI)	16/55 (29.1)
3 risk factors (stage IB2-IIA, size >2 cm and LVSI)	10/17 (58.8)

metastasis in 84 patients with cervical AC stage IA1-IB1. However, these prior reports studied small sample sizes, and have not been analyzed by multivariate analysis.

Clinical staging is a consistent prognostic factor for survival in all cervical cancers. In addition, the incidence of pelvic node metastasis in cervical cancer increases in stage IB2-IIA when compared with stage IB1as demonstrated by Fuller et al[19], Lee et al[20] and Li et al[21]. On the other hand, a study by Creasman et al[22] was unable to demonstrate a difference in pelvic lymph node metastasis among cervical carcinoma patients in stage IB and IIA.

Size of tumor lesion is also a significant risk factor for nodal metastasis and a prognostic factor for recurrence. Maleemonkol et al[23] reported that tumor size was the only factor that significantly predicted pelvic lymph node metastasis in early-stage cervical carcinoma patients. Lymph node metastasis was found in 4.8% of patients with tumor size of 3 cm or less compared to 18.9% of those who had tumor size of greater than 3 cm.

LVSI has been shown to be one of the independent risk factors for pelvic node metastases[16]. Roman et al[24] examined the influence of quantity of LVSI on the risk of pelvic node metastasis in early-stage cervical carcinoma patients and found that LVSI was associated significantly with lymph node metastasis; these findings were similar to those of the study by Milam et al[25].

Associations between three independent risk factors and pelvic node metastasis in the present study revealed that in early-stage cervical AC patients with none of the risk factors, pelvic node metastasis was not identified; however, patients with presence of LVSI and/or two other risk factors were established as a high-risk group of pelvic node metastasis. Although the adjusted OR for LVSI was obviously higher than that of other risk factors, the width of 95% CI indicated the low power of this study; nonetheless, LVSI was the strongest risk factor of pelvic node metastasis. The ability to preoperatively predict the risk of lymph node metastasis in early-stage cervical AC patients could prove very helpful in terms of patient counseling and treatment planning. Women with zero, or just one risk factor of lymph node metastasis other than positive LVSI, might be suitable candidates for less radical surgery or conservative surgery including radical trachelectomy. Women with presence of LVSI and/or 2 other risk factors might require more involved lymph node evaluation to determine potential adjuvant treatment. Patients who are scheduled to undergo conservative surgery for early-stage cervical AC but with positive LVSI on the preoperative specimen might also benefit from extraperitoneal lymphadenectomy to confirm a negative nodal status.

The limitation of the present study is that it is a retrospective descriptive one. By its nature, this type

of research renders its results more susceptible to bias especially on preoperative treatment detail; moreover, the power test might not be sufficient for logistic regression analysis. However, taking into consideration the large number of cervical AC patients in this study along with the extensive histopathologic review and interpretation, the data obtained will be valuable as a basic description of the behavior of early-stage cervical AC.

In summary, the significant risk factors of pelvic node metastasis in early-stage cervical AC were clinical stage IB2-IIA, tumor size more than 2 cm, and presence of LVSI. Pelvic node metastasis was not identified in early-stage cervical AC patients who had none of the risk factors, and these patients might be candidates for less radical surgery, whereas those with presence of LVSI and/or 2 other risk factors were at a high risk of pelvic node metastasis and might benefit from extensive lymphadenectomy and adjuvant therapy.

What is already known on this topic?

Lymph node metastasis is the most important prognostic factor to survival in cervical cancer patients and knowledge of its risk factors are important in the planning of treatment. Studies of these factors have extracted most data from cervical cancer patients with squamous cell carcinoma, and although some studies of the adenocarcinoma type exist, these factors cannot be evaluated by logistic regression analysis due to their small sample sizes. Over a 12-year period, this research retrospectively reviewed larger amounts of cervical cancer patients with adenocarcinoma and had a sufficient number of patients with node metastasis for analysis.

What this study adds?

Knowledge of risk factors of lymph node metastasis in cervical cancer patients is mostly based on studies of squamous cell carcinoma type. This study explored the adenocarcinoma type whose incidence has increased in recent decades.

Potential conflict of interest

None.

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ปัจจัยเสี่ยงของการแพร่กระจายไปต่อมน้ำเหลืองอุ้งเชิงกรานของมะเร็งปากมดลูกชนิด adenocarcinoma ที่ผ่านการผ่าตัดมดลูกแบบถอนรากถอนโคนและเลาะต่อมน้ำเหลืองในอุ้งเชิงกราน

มรุต ญาณารณพ, ณัฐพร สถาพรธีระ, ศรัญยู นาครังษี

วัตถุประสงค์: เพื่อประเมินปัจจัยเสี่ยงของการแพร่กระจายไปยังต่อมน้ำเหลืองอุ้งเชิงกรานในผู้ป่วยมะเร็งปากมดลูกชนิด adenocarcinoma ระยะต้นที่ผ่านการผ่าตัดมดลูกแบบถอนรากถอนโคนและเลาะต่อมน้ำเหลืองในอุ้งเชิงกรานสองข้าง

วัสดุและวิธีการ: ทบทวนเวชระเบียนและสไลด์ชิ้นเนื้อพยาธิวิทยาของผู้ป่วยจำนวน 251 รายที่เป็นมะเร็งปากมดลูก ชนิด adenocarcinoma ระยะ IB1-IIA ที่เข้ารับการผ่าตัดมดลูกแบบถอนรากถอนโคนและเลาะต่อมน้ำเหลืองในอุ้งเชิงกรานที่โรงพยาบาลราชวิถี ตั้งแต่วันที่ 1 มกราคม พ.ศ. 2543 ถึง 31 ธันวาคม พ.ศ. 2554 ปัจจัยเสี่ยงของการแพร่กระจายไปยังต่อมน้ำเหลืองอุ้งเชิงกรานได้รับการวิเคราะห์โดยวิธีการถดถอยพหุโลจิสติกส์

ผลการศึกษา: จากผู้ป่วย 251 ราย พบการแพร่กระจายไปยังต่อมน้ำเหลืองอุ้งเชิงกรานในมะเร็งปากมดลูกชนิด adenocarcinoma ระยะ IB1-IIA 29 ราย (ร้อยละ 11.6) การวิเคราะห์พหุตัวแปรพบว่าระยะโรคทางคลินิก IB2-IIA (adjusted OR 3.4, 95%CI 1.2-9.7), ขนาดเนื้องอกมากกว่า 2 ซม. (adjusted OR 3.5, 95%CI 1.1-11.8) และการลุกลามหลอดเลือดหลอดน้ำเหลือง (adjusted OR 55.5, 95%CI 7.2-427.6) มีความสัมพันธ์กับการแพร่กระจายไปต่อมน้ำเหลืองอุ้งเชิงกรานอย่างมีนัยสำคัญ ผู้ป่วยมะเร็งปากมดลูกชนิด adenocarcinoma ระยะต้นที่ไม่มีปัจจัยเสี่ยง, มีหนึ่งปัจจัยเสี่ยงที่ไม่ใช่การลุกลามหลอดเลือดหลอดน้ำเหลือง, มีเพียงปัจจัยการลุกลามหลอดเลือด หลอดน้ำเหลือง, มีสองและสามปัจจัยเสี่ยงพบการกระจายไปต่อมน้ำเหลืองอุ้งเชิงกรานร้อยละ 0, 2.3, 9.1, 29.1 และ 58.8 ตามลำดับ

สรุป: มะเร็งระยะ IB2-IIA, ขนาดเนื้องอกมากกว่า 2 ซม. และการกระจายเข้าทางเดินน้ำเหลืองและเลือดเป็นปัจจัยเสี่ยงที่มีนัยสำคัญต่อการกระจายไปต่อมน้ำเหลืองอุ้งเชิงกรานในผู้ป่วยมะเร็งปากมดลูกชนิด adenocarcinoma ระยะต้นผู้ที่ไม่มีทั้งสามปัจจัยเสี่ยงไม่พบการกระจายไปต่อมน้ำเหลืองอุ้งเชิงกรานและอาจจะเหมาะสำหรับการผ่าตัดที่รุนแรงน้อยกว่า ในขณะที่ผู้ที่มีการลุกลามหลอดเลือดหลอดน้ำเหลืองและ/หรือสองปัจจัยเสี่ยงอื่นๆ มีความเสี่ยงสูงสำหรับการกระจายไปต่อมน้ำเหลืองอุ้งเชิงกรานและอาจจะได้รับประโยชน์จากการเลาะต่อมน้ำเหลืองและการรักษาเสริม