
GYNECOLOGY

Prognostic Factors and Survival Rates in Early-stage Cervical Cancer Patients Treated with Radical Hysterectomy and Pelvic Lymphadenectomy

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ABSTRACT

Objectives: To evaluate prognostic factors and survival rates in early-stage cervical cancer patients who had been treated with radical hysterectomy and pelvic lymphadenectomy (RHPL).

Materials and Methods: Medical records and pathologic findings of 177 cervical cancer patients who had International Federation of Gynecology and Obstetrics (FIGO) stage IA2-IIA and underwent RHPL at Buddhachinaraj Phitsanulok Hospital from January 2005 to December 2016 were retrospectively reviewed. Clinicopathologic variables and treatment data were collected.

Results: Among 177 patients, mean age was 49.9 ± 11.0 years. The median follow-up time was 42 months. Twenty-five patients had a recurrence and 7 patients died from disease. A five-year disease free survival (DFS) rate and a 5-year cancer-specific survival (CSS) rate were 89% and 96.6%, respectively. The independent prognostic factors for DFS were increasing age and pelvic lymph node metastasis (hazard ratio [HR] 1.06; 95%CI 1.02-1.10, and HR 4.63; 95%CI 1.21-17.64, respectively). No significant differences in FIGO stage, histology, positive surgical margin, parametrial involvement, pelvic lymph node metastasis, deep stromal invasion, lymph vascular space invasion, and tumor size were identified as independent prognostic factors for CSS. However, adenocarcinoma (AC) patients with parametrial involvement, pelvic lymph node metastasis, and postoperative treatment followed by concurrent chemoradiotherapy (CCRT) had a significantly worse survival outcome than those with squamous cell carcinoma (SCC) (HR 11.87; 95%CI 1.46-46.20, HR 7.00; 95%CI 1.55-31.66, and HR 7.20; 95%CI 1.57-32.85, respectively).

Conclusion: Early-stage cervical cancer patients who underwent RHPL showed good survival rates. The independent prognostic factors for DFS were increasing age and pelvic lymph node metastasis whereas no prognostic factors for CSS were found. Furthermore, parametrial involvement, pelvic lymph node metastasis, and postoperative treatment followed by CCRT were likely to be predictors for poorer survival outcomes in AC than those in SCC.

Keywords: cervical cancer, prognostic factor, survival, radical hysterectomy

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ปัจจัยพยากรณ์โรคและอัตราการรอดชีวิตของผู้ป่วยมะเร็งปากมดลูกระยะแรกที่รักษาโดยการตัดมดลูกออกแบบถอนรากถอนโคนร่วมกับการเลาะต่อมน้ำเหลืองในอุ้งเชิงกราน

พลอยไพลิน ธนาภินันท์, บุญชัย นาคอริยกุล, พรสวรรค์ วาสินนท์

บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาปัจจัยพยากรณ์โรค และอัตราการรอดชีวิตในผู้ป่วยมะเร็งปากมดลูกระยะแรก ที่รักษาโดยการตัดมดลูกออกแบบถอนรากถอนโคน และเลาะต่อมน้ำเหลืองในอุ้งเชิงกราน

วัสดุและวิธีการ: การศึกษาย้อนหลังโดยการทบทวนเวชระเบียนของผู้ป่วยมะเร็งปากมดลูกระยะ IA2-IIA ที่รักษาโดยการตัดมดลูกออกแบบถอนรากถอนโคน จำนวน 177 คน ในโรงพยาบาลพุทธชินราช พิษณุโลก ในช่วงระยะเวลาตั้งแต่ มกราคม พ.ศ.2548 ถึง ธันวาคม พ.ศ.2559 โดยเก็บข้อมูลทางคลินิก ผลพยาธิวิทยา และการรักษา

ผลการศึกษา: ในผู้ป่วยมะเร็งปากมดลูกจำนวน 177 คน มีค่าอายุเฉลี่ยเท่ากับ 49.9 ± 11.0 ปี ค่ามัธยฐานของช่วงเวลาในการติดตามการรักษาเท่ากับ 42 เดือน มีผู้ป่วยจำนวน 25 คน เกิดการกลับเป็นซ้ำของโรค และ 7 คน เสียชีวิตจากมะเร็งปากมดลูก อัตราการกลับเป็นซ้ำของโรคและอัตราการรอดชีวิตที่ 5 ปี เท่ากับร้อยละ 89 และ 96.6 ตามลำดับ ปัจจัยพยากรณ์โรคที่มีผลต่อการกลับเป็นซ้ำของโรค คือ อายุที่เพิ่มขึ้น และการแพร่กระจายของมะเร็งไปที่ต่อมน้ำเหลืองในอุ้งเชิงกราน นอกจากนี้ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติของระยะโรค ชนิดพยาธิวิทยา การตรวจพบรอยโรคที่ขอบของชิ้นเนื้อ การลุกลามพารามิเทรียม การแพร่กระจายของมะเร็งไปที่ต่อมน้ำเหลืองในอุ้งเชิงกราน การลุกลามสตรีมาชั้นลึก การลุกลามหลอดเลือดหรือหลอดน้ำเหลือง และขนาดของก้อนมะเร็งใหญ่กว่า 4 เซนติเมตร ที่เป็นปัจจัยพยากรณ์โรคที่มีผลต่ออัตราการรอดชีวิต อย่างไรก็ตาม พบว่าพยาธิวิทยาชนิด adenocarcinoma (AC) ที่มีการลุกลามพารามิเทรียม การแพร่กระจายของมะเร็งไปที่ต่อมน้ำเหลืองในอุ้งเชิงกราน และการรักษาหลังผ่าตัดโดยการให้เคมีบำบัดและฉายแสงร่วมด้วย มีพยากรณ์โรคของการรอดชีวิตต่ำกว่าชนิด squamous cell carcinoma (SCC) อย่างมีนัยสำคัญทางสถิติ

สรุป: ผู้ป่วยมะเร็งปากมดลูกระยะแรกที่รักษาโดยการตัดมดลูกออกแบบถอนรากถอนโคน และเลาะต่อมน้ำเหลืองในอุ้งเชิงกรานมีอัตราการรอดชีวิตที่สูง ปัจจัยพยากรณ์โรคสำคัญต่อการกลับเป็นซ้ำของโรคคือ อายุที่เพิ่มขึ้นและการแพร่กระจายของมะเร็งไปที่ต่อมน้ำเหลืองในอุ้งเชิงกราน แต่ไม่พบปัจจัยพยากรณ์โรคที่มีผลต่ออัตราการรอดชีวิต นอกจากนี้การลุกลามพารามิเทรียม การแพร่กระจายของมะเร็งไปที่ต่อมน้ำเหลืองในอุ้งเชิงกราน และการรักษาหลังผ่าตัดโดยการให้เคมีบำบัด และฉายแสงเป็นปัจจัยที่ทำให้อัตราการรอดชีวิตในชนิด AC แย่กว่าเมื่อเปรียบเทียบกับชนิด SCC

คำสำคัญ: มะเร็งปากมดลูก, ปัจจัยพยากรณ์โรค, อัตราการรอดชีวิต, การตัดมดลูกออกแบบถอนรากถอนโคน

Introduction

Cervical cancer is the fourth most common female cancers worldwide. In 2012, there were approximately 527,624 new cases of cervical cancer and 265,672 additional cases that resulted in death⁽¹⁻³⁾. Moreover, it is the second most common cancer and the leading cause of death among women in Thailand⁽⁴⁾. Currently surgery is considered to be the gold standard treatment for early-stage cervical cancer patients, especially radical hysterectomy and pelvic lymphadenectomy (RHPL)^(5,6). The prognosis in early-stage cervical cancer is relatively reliable. A five-year survival rate of those patients is estimated to be 80-90%⁽⁷⁾. However, the survival rate after being treated with RHPL depends on several factors. Some studies have found that histology, tumor size, parametrial involvement, lymph vascular space invasion, pelvic lymph node metastasis, or even number of lymph node metastasis had a significant effect on the survival rate in early-stage cervical cancer patients⁽⁸⁻¹¹⁾. Nevertheless, the assessment of independent prognostic factors that are helpful to predict survival and recurrence of disease is still needed.

The aim of this study was to evaluate prognostic factors and survival rates in early-stage cervical cancer patients who had been treated with RHPL.

Materials and Methods

A retrospective study was conducted at Department of Obstetrics and Gynecology, Buddhachinaraj Phitsanulok Hospital and approved by the Ethics Committee of Buddhachinaraj Phitsanulok Hospital. Seven hundred and thirty medical records of cervical cancer patients from January 1, 2005 to December 31, 2016 were retrospectively reviewed. The cervical cancer patients who had the International Federation of Gynecology and Obstetrics (FIGO) stage IA2-IIA and underwent RHPL reached the inclusion criteria for the study⁽¹²⁾. Twenty-one patients were excluded from the study due to incomplete medical records or limited data. Five of those patients had adenosquamous carcinoma subtype and 1 patient had neuroendocrine. Additionally, patients who received neoadjuvant chemotherapy were also excluded from the study. Thus, 177 patients who met the inclusion criteria were enrolled in this study (Fig. 1). The estimation of participants in this study was calculated by WG Cochran formula and the results of the study by Lee YY, et al⁽¹⁰⁾, for the current study based on 95% confidence level and 80% power of test. The finite population correction for proportions formula was used to calculate the final cohort of participants, thus the adequate number of patients needed in this study was 230.

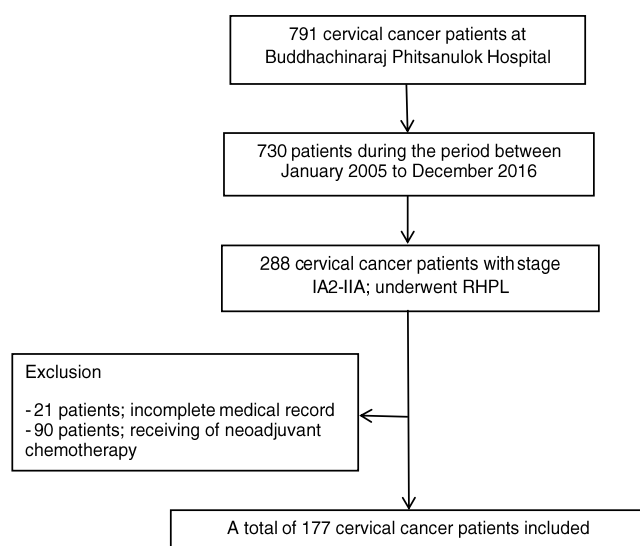


Fig. 1. Criteria Inclusion Flow Chart.

The clinical data including age, parity, body mass index (BMI), menstrual status, FIGO stage of cervical cancer, histology, presenting symptoms, tumor characteristics, surgical treatments, date of surgery, date of diagnosis of recurrence, and date of death from disease (if present) was collected. Tumor characteristics were classified as exophytic, infiltrative, ulcerative, and microscopic. Exophytic lesion was defined as a tumor that grew outward from an epithelial surface, while infiltrative lesion was the invasion of cancer cells into the underlying matrix of cervical tissue. Ulcerative lesion meant the carcinoma that invaded or destroyed cervical tissue causing indented lesion or ulcer. Patients who had any invisible lesions before undergoing RHPL were classified as microscopic. Surgical treatments were allocated as surgery alone, surgery followed by concurrent chemoradiotherapy (CCRT) or surgery followed by radiotherapy (RT).

The pathologic data consisted of surgical margins, parametrial involvement, pelvic lymph node metastasis, deep stromal invasion (DSI), lymph vascular space invasion (LVSI), and tumor size. DSI was defined as carcinoma invasion into the middle or deep third of total cervical stromal thickness, and LVSI as tumor invasion into the endothelium of vascular or lymphatic vessels. The measurement of tumor dimension was performed and reported by pathologists for accurate measurements, which were then divided into 2 groups: tumor size less than or equal to 4 centimeters (cm), and tumor size greater than 4 cm. The diagnosis of recurrence was confirmed with tissue biopsy or radio diagnostic tools such as chest x-ray, computerized tomography (CT) of the whole abdomen and/or a bone scan. Disease free survival (DFS) was defined as a period between initial operation and the recurrence of the disease. Meanwhile, cancer-specific survival (CSS) was declared as the time from initial operation to the time of death caused by cervical cancer; or for living patients, to the date of last follow up.

Statistical analysis was performed by using SPSS software version 22.0. The continuous data was demonstrated as mean and standard deviation (SD).

For categorical variables, percentages were used. CSS and DFS curves were undertaken the Kaplan-Meier method with log-rank test. The possible factors that could affect the recurrence of disease and survival rate including age, FIGO stage, treatments, histology, surgical margins, parametrial involvement, pelvic node metastasis, DSI, LVSI, and tumor size were analyzed in the univariate analysis, the multivariate analysis and the stratified survival analysis by using the Cox proportional hazards model. Any statistically significant data had a p value < 0.05.

Results

A total of 177 patients were enrolled in this study, mean age was 49.9 ± 11.0 years and mean BMI was 24.4 ± 4.1 kg/m². There were 5 patients in stage IA2, 157 patients in stage IB1-IB2, and 15 patients in stage IIA1-IIA2. Most patients 83.1% were in FIGO stage IA2-IB1 and the remaining 16.9% were in stage IB2-IIA (Table 1). There were only 2 histological subtypes identified, 125 patients were in the squamous cell carcinoma (SCC) group and 52 in the adenocarcinoma (AC) group. Other subtypes were not available due to limited data. The median follow-up time was 42 months (range 1-143 months). Twenty-five patients had a recurrence and 7 patients died from the disease. The five-year DFS rate and CSS rate were 89% and 96.6%, respectively. The pathologic findings were comprised of the surgical margins, parametrial involvement, pelvic lymph node metastasis, DSI, LVSI, and tumor size.

After using univariate analysis (Table 2), a prognostic factor that significantly impacted on DFS was increasing age (HR 1.05; 95%CI 1.01-1.08). Meanwhile, the significant prognostic factors for CSS were postoperative treatment with CCRT, and pelvic lymph node metastasis (HR 6.04; 95%CI 1.34-27.21, and HR 6.25; 95%CI 1.39-28.06, respectively).

Table 3 shows the multivariate analysis of DFS and CSS. The independent prognostic factors for DFS were increasing age and pelvic lymph node metastasis (HR, 1.06; 95% CI, 1.02-1.10, HR, 4.63; 95% CI, 1.21-17.64, respectively) whereas no significant results were found in the CSS.

Table 1. Clinicopathologic variables.

Characteristic	N = 177
Age (years), mean (SD)	49.9 (11.0)
Parity (%)	
0-1	39 (22.0)
2-3	121 (68.4)
≥ 4	17 (9.6)
BMI (kg/m ²), mean (SD)	24.4 (4.1)
Menstruation (%)	
Premenopause	91 (51.4)
Postmenopause	86 (48.6)
FIGO stage (%)	
IA2-IB1	147 (83.1)
IB2-IIA	30 (16.9)
Histological subtypes (%)	
SCC	125 (70.6)
AC	52 (29.4)
Other subtypes	NA
Presenting symptoms (%)	
Check up	72 (40.7)
Vaginal bleeding	86 (48.6)
Pelvic pain	7 (3.9)
Abnormal discharge	12 (6.8)
Tumor characteristics (%)	
Exophytic	57 (32.2)
Infiltrative	37 (20.9)
Ulcerative	31 (17.5)
Microscopic	52 (29.4)
Treatment (%)	
Surgery alone	132 (74.6)
Surgery + CCRT	39 (22.0)
Surgery + RT	6 (3.4)
Positive surgical margin (%)	18 (10.2)
Parametrial involvement (%)	17 (9.6)
Pelvic lymph node metastasis (%)	35 (19.8)
Positive DSI (%)	118 (66.6)
Positive LVSI (%)	39 (22.0)
Tumor size (cm) (%)	
≤ 4	155 (87.6)
> 4	22 (12.4)

BMI, body mass index; FIGO, the International Federation of Gynecology and Obstetrics; SCC, squamous cell carcinoma; AC, adenocarcinoma; CCRT, concurrent chemoradiotherapy; RT, radiotherapy; SD, standard deviation; DSI, deep stromal invasion; LVSI, lymph vascular space invasion; NA, not available.

Table 2. Univariate analysis for disease free survival and cancer-specific survival.

Variables ^c	DFS		CSS	
	HR (95% CI)	p value	HR (95% CI)	p value
Age	1.05 (1.01-1.08)	0.004*	0.94 (0.87-1.02)	0.161
FIGO stage				
IA2-IB1	1		1	
IB2-IIA	1.41 (0.56-3.35)	0.463	3.16 (0.70-14.22)	0.133
Treatment				
Surgery alone	1		1	
Surgery + CCRT	1.35 (0.54-3.40)	0.515	6.04 (1.34-27.21)	0.019*
Surgery + RT	NA	NA	NA	NA
Histological subtypes				
SCC	1		1	
Positive	1.68 (0.57-4.92)	0.337	1.41 (0.17-11.77)	0.747
AC	1.12 (0.48-2.60)	0.785	3.20 (0.71-14.31)	0.128
Surgical margin				
Negative	1		1	
Parametrial involvement				
Negative	1		1	
Positive	2.29 (0.78-6.69)	0.130	4.64 (0.89-24.07)	0.067
Pelvic lymph node metastasis				
Negative	1		1	
Positive	2.28 (0.98-5.28)	0.055	6.25 (1.39-28.06)	0.017*
Deep stromal invasion				
Negative	1		1	
Positive	1.05 (0.46-2.38)	0.907	0.78 (0.17-3.51)	0.753
Lymph vascular space invasion				
Negative	1		1	
Positive	0.70 (0.24-2.04)	0.518	2.77 (0.62-12.37)	0.182
Tumor size (cm)				
≤ 4	1		1	
> 4	1.33 (0.39-4.45)	0.645	4.00 (0.76-20.95)	0.101

DFS, disease free survival; CSS, cancer-specific survival; FIGO, the International Federation of Gynecology and Obstetrics; SCC, squamous cell carcinoma; AC, adenocarcinoma; CCRT, concurrent chemoradiotherapy; RT, radiotherapy; HR, hazard ratio; CI, confidence interval; NA, not available.

*Significance at $p < 0.05$

Table 3. Multivariate analysis for disease free survival and cancer-specific survival.

Variables	DFS		CSS	
	HR (95% CI)	p value	HR (95% CI)	p value
Age	1.06 (1.02-1.10)	0.004*	0.94 (0.86-1.03)	0.230
FIGO stage				
IA2-IB1	1		1	
IB2-IIA	1.89 (0.66-5.38)	0.230	0.96 (0.10-8.47)	0.971
Treatment				
Surgery alone	1		1	
Surgery + CCRT	0.19 (0.02-1.42)	0.106	5.46 (0.14-20.72)	0.355
Surgery + RT	NA	NA	NA	NA
Histological subtypes				
SCC	1		1	
AC	1.33 (0.53-3.31)	0.533	5.21 (0.77-35.07)	0.089
Surgical margin				
Negative	1		1	
Positive	2.05 (0.34-12.23)	0.430	0.71 (0.02-21.43)	0.847
Parametrial involvement				
Negative	1		1	
Positive	1.38 (0.23-8.07)	0.715	6.37 (0.32-12.75)	0.225
Pelvic lymph node metastasis				
Negative	1		1	
Positive	4.63 (1.21-17.64)	0.025*	2.11 (0.16-26.92)	0.563
Deep stromal invasion				
Negative	1		1	
Positive	1.06 (0.41-2.70)	0.895	0.31 (0.02-3.65)	0.356
Lymph vascular space invasion				
Negative	1		1	
Positive	0.79 (0.24-2.63)	0.709	1.66 (0.19-13.95)	0.640
Tumor size (cm)				
≤ 4	1		1	
> 4	1.06 (0.18-5.97)	0.945	0.55 (0.03-9.08)	0.683

DFS, disease free survival; CSS, cancer-specific survival; FIGO, the International Federation of Gynecology and Obstetrics; SCC, squamous cell carcinoma; AC, adenocarcinoma; HR, hazard ratio; CI, confidence interval; NA, not available.

*Significance at $p < 0.05$

Fig. 2 demonstrates the correlation between DFS and pelvic lymph node metastasis. There were no significant differences in FIGO stage, histology, positive surgical margin, parametrial involvement, pelvic lymph node metastasis, DSI, LVSI, or tumor size that were identified as independent prognostic factors for CSS. However, the stratified survival analysis calculated the

survival outcome between SCC and AC (Table 4), where AC patients with parametrial involvement, pelvic lymph node metastasis, or postoperative treatment followed by CCRT had a significantly worse survival outcome than those with SCC (HR, 11.87; 95% CI, 1.46-46.20, HR, 7.00; 95% CI, 1.55-31.66, HR, 7.20; 95% CI, 1.57-32.85, respectively).

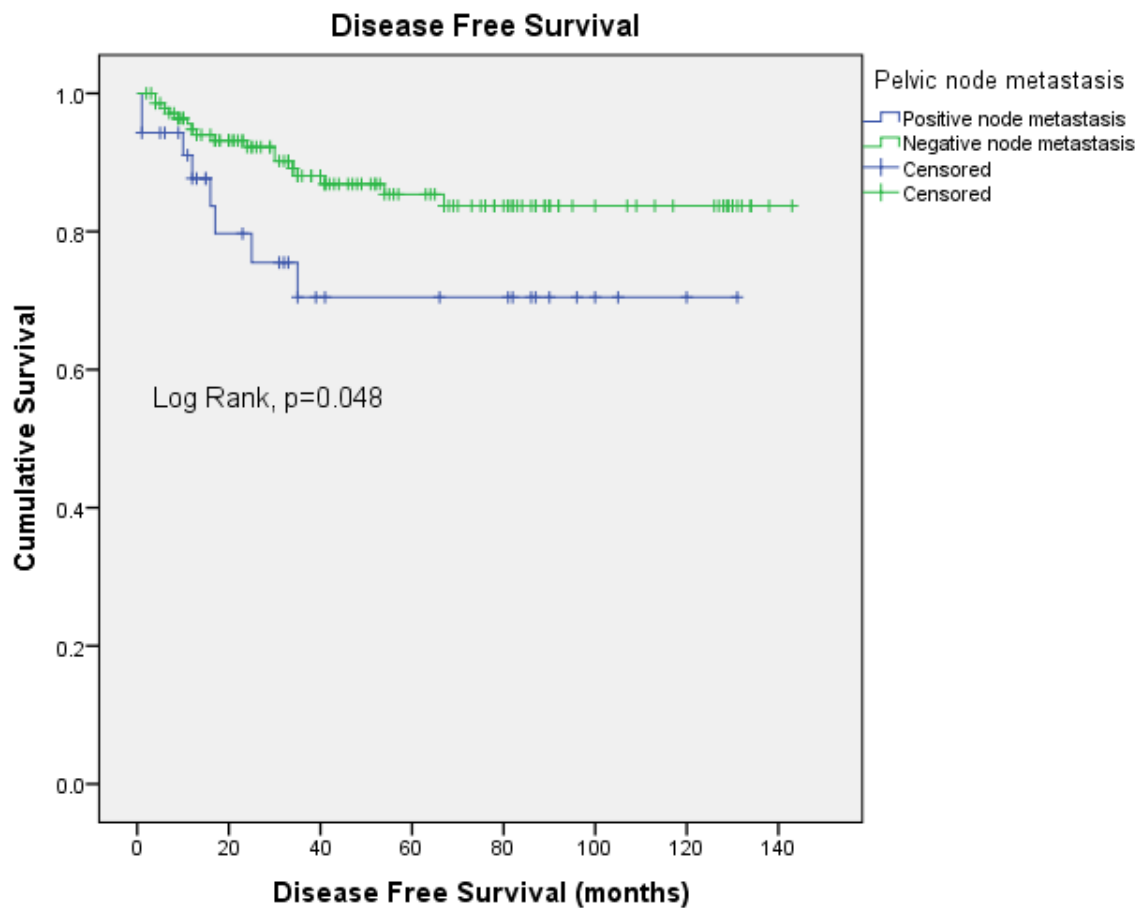


Fig. 2. Disease free survival based on pelvic node metastasis after radical hysterectomy and pelvic lymphadenectomy.

Table 4. Stratified survival analysis for cancer-specific survival.

Variables	SCC (n = 125)		AC (n = 52)		HR (95% CI)	p value
	n	Event (%)	n	Event (%)		
Overall	125	3 (2.4)	52	4 (7.6)		
Age	125	3 (2.4)	52	4 (7.6)	0.94 (0.87-1.02)	0.179
FIGO stage						
IA2-IB1	104	1 (1.0)	43	3 (6.9)	1	
IB2-IIA	21	2 (9.5)	9	1 (11.1)	3.38 (0.75-15.21)	0.112
Treatment						
Surgery alone	88	1 (1.1)	44	2 (4.5)	1	
Surgery + CCRT	31	2 (6.4)	8	2 (25.0)	7.20 (1.57-32.85)	0.011*
Surgery + RT	6	0 (0.0)	0	0 (0.0)	NA	NA
Surgical margin						
Negative	109	3 (2.7)	50	3 (6.0)	1	
Positive	16	0 (0.0)	2	1 (50.0)	2.10 (0.23-18.81)	0.506
Parametrial involvement						
Negative	109	2 (1.8)	51	3 (5.8)	1	
Positive	16	1 (6.2)	1	1 (100.0)	11.87 (1.46-46.20)	0.020*
Pelvic node metastasis						
Negative	97	1 (1.0)	45	3 (6.6)	1	
Positive	28	2 (7.1)	7	1 (14.3)	7.00 (1.55-31.66)	0.011*
Deep stromal invasion						
Negative	37	1 (2.7)	22	2 (9.1)	1	
Positive	88	2 (2.3)	30	2 (6.6)	1.09 (0.22-5.25)	0.910
LVSI						
Negative	93	2 (2.1)	45	2 (4.4)	1	
Positive	32	1 (3.1)	7	2 (28.6)	3.65 (0.78-16.88)	0.098
Tumor size (cm)						
≤ 4	107	1 (1.0)	48	4 (8.3)	1	
> 4	18	2 (11.1)	4	0 (0.0)	4.59 (0.86-24.31)	0.073

FIGO, the International Federation of Gynecology and Obstetrics; SCC, squamous cell carcinoma; AC, adenocarcinoma; LVSI, lymph vascular space invasion; HR, hazard ratio; CI, confidence interval; NA, not available.

*Significance at $p < 0.05$

Discussion

According to the most recent statistical data for survival rates, there has been a good survival rate in early-stage cervical cancer. Similar results were found in this study; a 5-year DFS rate and a 5-year CSS rate

of 89% and 96.6% respectively. Likewise, other studies revealed the 5-year survival rates in patients who underwent RHPL were more than 90%^(13,14). One research was conducted on surgical outcomes and prognostic factors in early-stage cervical cancer during

the past 12 years; its 5-year DFS rate was 84%, which concurred with the result found in this study⁽¹⁵⁾.

From the univariate analysis, increasing age was found to be the only significant factor that impacted DFS. It showed that an increasing age every 1 year significantly increased the risk of recurrence for 1.05 times. One study discovered that age was a significant prognostic factor for both DFS and CSS⁽¹⁶⁾. However, after adjusting confounding values by using the multivariate analysis, increasing age and pelvic node metastasis were independent prognostic factors in this study. Likewise, some studies supported that pelvic node metastasis was independent prognostic factor for DFS^(15,17,18).

In the previous studies, there have been many significant prognostic factors that affected the CSS such as tumor stage, tumor size larger than 4 cm, pelvic node metastasis, number of positive pelvic node, and histological subtype^(11,17,19,20). Compared to this study, postoperative treatment followed by CCRT and pelvic node metastasis were the significant factors that correlated to CSS after using the univariate analysis. The patients whose pathological findings had a positive surgical margin, parametrial involvement, or pelvic lymph node metastasis required treatment with CCRT as the Hospital's protocol. It was found that patients in the postoperative treatment followed by CCRT group had a significantly poorer survival rate, by 6 times, compared to that of the patients who underwent surgery alone. Data was unable to be interpreted for the postoperative treatment followed by RT group due to the small number of patients.

With regards to the National Comprehensive Cancer Network guidelines⁽²¹⁾, if the cervical cancer patients had a negative LVSI, a positive 1/3 middle or deep stromal invasion, and a tumor size equal to or greater than 4 cm; an adjuvant pelvic radiation was also necessary. Sixty-six percent of the participants in this study had DSI, but mostly negative LVSI in any tumor sizes which did not meet the criteria for pelvic radiation after RHPL, possibly leading to a lower number of patients in the RT group. Nevertheless, no statistically significant prognostic factors for CSS were found in the

multivariate analysis. The reason for varying results from previous studies may be reflected by the variance of patient demographic data, number of participants, type of treatment and follow-up time.

Despite no independent prognostic factors for CSS were found, the secondary outcome in this study after using the stratified survival analysis showed that the patients with the histology of AC had a significantly worse survival rate than those with SCC if there was parametrial involvement, pelvic node metastasis, and postoperative treatment followed by CCRT. Several studies supported that AC was one of the independent prognostic factors that impacted CSS^(10,22). In contrast, histology did not have any influences on CSS in some studies, comparable to the findings^(13,23,24). Few studies discussed the prognostic factors in AC patients who had been treated with RHPL, and the results showed that pelvic lymph node metastasis or parametrial involvement were significant prognostic factors to predict survival outcome in AC^(23,25).

The strengths of this study were the collection of data that originated from a single institution that was able to treat patients with cervical cancer. Moreover, all of pathologic findings were performed and reported by experienced pathologists at the Hospital, providing precise measurements. However, the study design was retrospective and involved a long period of data collection as a result, bias could have occurred and results were interpreted cautiously. The consequence from a long period of data was that some important information had not been available at the time of collection. Other limitations were the inadequate number of patients and the low number of participants for postoperative treatment followed by RT, where the statistical analysis was unable to draw a conclusive result, which may have affected the result of survival rates. A future study may involve one with a prospective design and larger number of patients.

Conclusion

Early-stage cervical cancer patients who had been treated with RHPL showed good survival rates. The independent prognostic factors for DFS were

increasing age and pelvic lymph node metastasis. In contrast, no independent prognostic factors for CSS were identified after using the multivariate analysis. It was found that parametrial involvement, pelvic lymph node metastasis, and postoperative treatment followed by CCRT were likely to be predictors for a worse survival outcome in AC than in SCC. Furthermore, this study may be a useful database with reference to cervical cancer at the Hospital, and/or used for counseling cervical cancer patients in relations to prognosis and further management.

Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Bruni L, Barrionuevo-Rosas L, Albero G, Serrano B, Mena M, Gomez D, et al. ICO Information centre on HPV and cancer (HPV Information Centre). Human papillomavirus and related diseases in the world summary report 2017:8-41.
2. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 2015;136:E359-86.
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.
4. Imsamran W, Chaiwerawattana A, Wiangnon S, Pongnikorn D, Suwanrungrung K, Sangrajrang S, et al. National Cancer Institute Thailand. *Cancer in Thailand: Vol. VIII, 2010-2012*. 2015;8:5-12.
5. Brucker SY, Ulrich UA. Surgical Treatment of Early-Stage Cervical Cancer. *Oncol Res Treat* 2016;39:508-14.
6. American Cancer Society. Treating cervical cancer 2016:3-9.
7. American Cancer Society. Cervical cancer early detection, diagnosis, and staging 2016:13-5.
8. Ayhan A, Al RA, Baykal C, Demirtas E, Ayhan A, Yuce K. Prognostic factors in FIGO stage IB cervical cancer without lymph node metastasis and the role of adjuvant radiotherapy after radical hysterectomy. *Int J Gynecol Cancer* 2004;14:286-92.
9. Kasamatsu T, Onda T, Sawada M, Kato T, Ikeda S. Radical hysterectomy for FIGO stage IIB cervical cancer: clinicopathological characteristics and prognostic evaluation. *Gynecol Oncol* 2009;114:69-74.
10. Lee YY, Choi CH, Kim TJ, Lee JW, Kim BG, Lee JH, et al. A comparison of pure adenocarcinoma and squamous cell carcinoma of the cervix after radical hysterectomy in stage IB-IIA. *Gynecol Oncol* 2011;120:439-43.
11. Park JW, Bae JW. Prognostic significance of positive lymph node number in early cervical cancer. *Mol Clin Oncol* 2016;4:1052-6.
12. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. *Int J Gynaecol Obstet* 2009;105:103-4.
13. Rudtanasudjatun K, Charoenkwan K, Khunamornpong S, Siriaunkgul S. Impact of histology on prognosis of patients with early-stage cervical cancer treated with radical surgery. *Int J Gynaecol Obstet* 2011;115:183-7.
14. Ruengkachorn I, Therasakvichya S, Warnnissorn M, Leelaphatanadit C, Sangkarat S, Srisombat J. Pathologic Risk Factors and Oncologic Outcomes in Early-stage Cervical Cancer Patients Treated by Radical Hysterectomy and Pelvic Lymphadenectomy at a Thai University Hospital: A 7 year Retrospective Review. *Asian Pac J Cancer Prev* 2015;16:5951-6.
15. Tantitamit T, Hamontri S. Surgical Outcomes and Prognostic Factors in Cervical Cancer: A 12 year, Single-Center Experience. *Asian Pac J Cancer Biol* 2017;2:67-72.
16. Singh P, Tripcony L, Nicklin J. Analysis of prognostic variables, development of predictive models, and stratification of risk groups in surgically treated FIGO early-stage (IA-IIA) carcinoma cervix. *Int J Gynecol Cancer* 2012;22:115-22.
17. Nakanishi T, Ishikawa H, Suzuki Y, Inoue T, Nakamura S, Kuzuya K. A comparison of prognoses of pathologic stage Ib adenocarcinoma and squamous cell carcinoma of the uterine cervix. *Gynecol Oncol* 2000;79:289-93.
18. Grisaru DA, Covens A, Franssen E, Chapman W, Shaw P, Colgan T, et al. Histopathologic score predicts recurrence free survival after radical surgery in patients with stage IA2-IB1-2 cervical carcinoma. *Cancer* 2003;97:1904-8.
19. Horn LC, Fischer U, Raptis G, Bilek K, Hentschel B. Tumor size is of prognostic value in surgically treated FIGO stage II cervical cancer. *Gynecol Oncol* 2007;107:310-5.
20. Horn LC, Bilek K, Fischer U, Eichenkel J, Hentschel B. A cut-off value of 2 cm in tumor size is of prognostic value in surgically treated FIGO stage IB cervical cancer. *Gynecol Oncol* 2014;134:42-6.
21. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology cervical cancer 2016:11-34.
22. Mabuchi S, Okazawa M, Matsuo K, Kawano M, Suzuki O, Miyatake T, et al. Impact of histological subtype on survival of patients with surgically-treated stage IA2-

- IIB cervical cancer: adenocarcinoma versus squamous cell carcinoma. *Gynecol Oncol* 2012;127:114-20.
23. Kasamatsu T, Onda T, Sawada M, Kato T, Ikeda S, Sasajima Y, et al. Radical hysterectomy for FIGO stage I-IIb adenocarcinoma of the uterine cervix. *Br J Cancer* 2009;100:1400-5.
24. Winer I, Alvarado-Cabrero I, Hassan O, Ahmed QF, Alesh B, Bandyopadhyay S, et al. The prognostic significance of histologic type in early stage cervical cancer - A multi-institutional study. *Gynecol Oncol* 2015;137:474-8.
25. Kodama J, Seki N, Masahiro S, Kusumoto T, Nakamura K, Hongo A, et al. Prognostic factors in stage IB-IIb cervical adenocarcinoma patients treated with radical hysterectomy and pelvic lymphadenectomy. *J Surg Oncol* 2010;101:413-7.