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Survival Rate of Endometrial Cancer Patients at Phramongkutklao Hospital

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ABSTRACT

Objective: To determine the five-year overall survival rate of patients with endometrial cancer after complete treatment at Phramongkutklao Hospital.

Materials and Method: This was a retrospective descriptive study. A total of 54 patients were enrolled, each with a histologically confirmed diagnosis of endometrial cancer and had received complete treatment from January 1, 2009 to December 31, 2010 at Phramongkutklao hospital. Overall survival was estimated according to the Kaplan-Meier method and a univariate analysis employed the Log-rank test to compare between groups.

Main outcome measure: The five-year overall survival rate of patients with endometrial cancer.

Results: The mean age of the 54 patients was 60 ± 10.6 years. All patients presented with the symptom of abnormal uterine bleeding. The majority of patients in this study had early stage disease (66.7%) and, histopathology cell types which were endometrioid carcinoma (90.6%). The majority of adjuvant therapies in advanced stage was chemotherapy plus radiotherapy (27.7%), and for early stage was radiotherapy alone (33.4%). The five-year overall survival rate of endometrial cancer was 80.1%, however this depended on the stage of cancer. In the early stage (FIGO stage I-II) it was 91.6% while in the advanced stage (FIGO stage III-IV) it was 50%. The statistically significant variables affecting overall survival included stage, tumor grade, cervical invasion, lymph nodes metastasis, positive peritoneal cytology and post operative residual tumor more than 2 cm.

Conclusion: The five-year overall survival rate of endometrial cancer was 80.1%. The FIGO stage and tumor grade were correlated with the overall survival rate of patients with endometrial cancer.

Keywords: survival rate, endometrial cancer, The 2009 FIGO staging

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Introduction

Endometrial cancer remains the most common form of gynecologic malignancy in developed countries, and the second most common in developing countries after cervical cancer. In the United States, the incidence rate of endometrial cancer was 12.9 per 100,000 women in 2010[1]. The American Cancer Society estimated 49,000 new cases of endometrial cancer and 4,000

deaths from endometrial cancer in 2013[2]. In Thailand, endometrial cancer is the third most common form of female genital cancer with an estimated incidence rate of 4.3 per 100,000 women[2].

The majority of woman with endometrial cancer have a postmenopausal status with an average age of 61 years at diagnosis[3]. The most common symptom is abnormal uterine bleeding[4]. The prognosis and survival outcomes of endometrial cancer are excellent for most patients diagnosed with early stage and low-grade disease. Overall survival of endometrial cancer was reported to be approximately 84% in the early stage and 30-70% in the advanced stage[5].

In 1988, the International Federation of Gynecology and Obstetrics (FIGO) recommended that surgical staging, instead of clinical staging, was to be the standard management of endometrial cancer. The 2009, FIGO staging procedure of endometrial cancer included total hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymphadenectomy[6]. Suboptimal surgical staging was defined if there was still a residual tumor more than 2 cm. Adjuvant treatment includes radiotherapy, chemotherapy, hormonal therapy and others which considers advanced stage and risk of recurrence amongst endometrial cancer patients[7].

Recently, the incidence rate of endometrial cancer has increased and is found in a greater proportion amongst younger women. The changes in the updated FIGO staging system reflect new data on prognosis and survival outcomes. This retrospective descriptive study aims to assess the five-year overall survival rate of patients with endometrial cancer at Phramongkutklao hospital.

Materials and Method

This is a retrospective descriptive study. All endometrial cancer patients that were enrolled had complete treatment from January 1, 2009 to December 31, 2010 at the Department of Obstetrics and Gynecology, Phramongkutklao Hospital, Thailand. The study protocol received ethics approval from the Institutional Review Board, Royal Thai Army Medical Department, Phramongkutklao Hospital.

The inclusion criteria for this study required patients with a histologically confirmed diagnosis of endometrial cancer who obtained surgical staging according to the 2009 FIGO staging system. Some patients underwent operations at Phramongkutklao Hospital while some had operations at other hospitals and were then referred to Phramongkutklao Hospital for further management and regular follow ups. Patients who had other forms of cancer or comorbid diseases that may affect the treatment planning or outcome were excluded from this experiment.

Data collected in this study includes characteristics of patients and symptoms, stage, histopathology, grade of tumor, cervical involvement, myometrial invasion, peritoneal cytology, lymphovascular invasion, lymph node metastasis, residual tumor, adjuvant therapy, disease status, recurrent type, the date of first diagnosis of endometrial cancer, the date of last visit and the date of death.

The analyzed prognostic variables include patient age, body mass index (BMI), stage, histopathology, grade of tumor, cervical involvement, myometrial invasion, peritoneal cytology, lymphovascular invasion, lymph node metastasis and residual tumor.

The progression free survival (PFS), overall survival (OS) and the five-year survival rates were determined. The definition of progression-free survival is the time between the start of treatment and the time of recurrent treatment. The overall survival rate is defined as the time between the date of diagnosis and the date of last visit or death from any causes[8].

The data was analyzed using STATA/MP12 statistical software. The demographic data was analyzed using descriptive statistics and summarized using numbers representing the percentage, mean, and median. Categorical variables were analyzed with the Chi-square test and Fisher's exact test to compare the outcomes between groups. OS and PFS were analyzed by the Kaplan-Meier method and compared between groups by the log-rank test in univariate analysis. A p-value less than 0.05 was considered statistically significant.

Results

From January 2009 to December 2010, a total of 59 patients with endometrial cancer were enrolled, from which 54 patients met the inclusion criteria. Five patients were excluded from the study due to them also being diagnosed with another cancer; two primary cancers, ovarian cancer, breast cancer or comorbid diseases such as chronic renal disease, immunodeficiency disease which may have an effect on the treatment outcome.

The characteristics of patients are shown in Table 1. The patients' ages ranged from 36 to 84 years, with a mean patient age of 60 ± 10.6 years and a mean BMI of 27.4 ± 5.9 kg/m^2. The BMI was ≥ 30 kg/m^2 in 11 patients. The majority of patients were homemakers (21 patients, 38.9%), married (39 patients, 72.2%), multiparous (41 patients, 75.9%) and postmenopausal status about 64.8% (35 patients). All presented symptoms of abnormal uterine bleeding (54 patients, 100%).

Table 1. The number of aflatoxin B1 detected cases and its effect on fetal birth weight and placental apoptotic indices in the two groups.

Characteristics	n = 54	(%)
Age (yrs)		
≤ 60	26	48.1
> 60	28	51.9
Mean ± SD	60 ± 10.6	
Median (Min - Max)	61 (36 - 84)	
BMI (kg/m2)		
≤ 60	26	48.1
> 60	28	51.9
Mean ± SD	27.4 ± 5.9	
Median (Min - Max)	27.1 (17.6 - 44.1)	
Occupation		
Business	4	7.4
Homemaker	21	38.9
Government employee	12	22.2
Private sector employee	17	31.5
Underlying disease*		
No	20	37.0
HT	30	55.6
DM	12	22.2
Other	6	11.1
Status		
Single	11	20.4
Married	39	72.2
Divorce	4	7.4
Parity		
Nulliparous	13	24.1
Multiparous	41	75.9

Table 1. The number of aflatoxin B1 detected cases and its effect on fetal birth weight and placental apoptotic indices in the two groups. (Cont.)

Characteristics	n = 54	(%)
Menopausal status		
Premenopause	19	35.2
Postmenopause	35	64.8
Residual tumor		
No	44	81.5
Yes	10	18.5
Histopathology		
Endometrioid	49	90.6
Papillary serous	1	1.9
Clear cell	1	1.9
Mixed	3	5.6
FIGO stage		
I	33	61.1
II	3	5.6
III	10	18.5
IV	8	14.8
Tumor grade		
I	18	33.3
II	26	48.2
III	10	18.5
Cervical invasion		
No	49	90.7
Yes	5	9.3
Myometrial invasion		
Inner half	23	42.6
Outer half	31	57.4
Peritoneal cytology		
Negative	48	88.9
Positive	6	11.1
Lymphovascular invasion		
No	47	87.0
Yes	7	13.0
Lymph node metastasis		
Negative	39	72.2
Positive	15	27.8

* Data had one or more underlying diseases per person

All patients had surgical staging, and 44 patients (81.5%) had no residual tumor from surgical staging. The majority of histopathology cell types were endometrioid carcinoma (90.6%). The patients

presented surgical staging according to the 2009 FIGO classification: 36 patients (66.7%) had early stage (FIGO stage I-II) and 18 patients (33.3%) had advanced stage (FIGO stage III-IV). Amongst patients with advanced stage, ten had residual tumors greater than 2 cm. The majority of tumors were grade I, about 33.3%, while no cervical and lymphovascular invasion occurred in 90.7% and 87.0%, respectively. Myometrial inner half invasion was documented among 42.6% and outer half among 57.4%. Patients with and without lymph node metastasis totaled 27.8% and 72.2%, respectively. Treatment and primary outcome of treatment are shown in Table 2. The majority of the disease statuses was complete clinical response (25 patients, 46.2%), followed by stable disease (13 patients, 24.1%), progressive disease (9 patients, 16.7%) and partial response (7 patients, 13.0%). A total of 13 patients (24.1%) developed recurrent disease, 6 patients (11.1%) had locoregional recurrence and 7 patients (13%) had distant recurrence. Forty-two patients (77.8%) were still alive. Twelve patients (22.2%) were deceased due to endometrial cancer related causes.

Table 2. Treatment and primary outcome of treatment.

Treatment/primary outcome of treatment	n = 54	(%)
Adjuvant therapy		
No	16	29.6
Yes	38	70.4
Chemotherapy		
No	34	63.0
Yes	20	37.0
Cisplatin-doxorubicin	4	7.4
Carboplatin-paclitaxel	5	9.3
Cisplatin-doxorubicin-paclitaxel	11	20.3
Disease status		
Complete clinical response	25	46.2
Partial response	7	13.0
Stable disease	13	24.1
Progressive disease	9	16.7
Recurrent		
No	41	75.9
Loco-regional	6	11.1
Distant	7	13.0
Cause of death		
Disease related	12	22.2
Not disease related	0	0
Alive	42	77.8

Postoperative adjuvant treatments discussed in multidisciplinary team meetings with a radiotherapist, gynecologic and oncologist are shown in Table 3. Thirty-eight patients (70.4%) received adjuvant therapy. The majority of adjuvant therapies in advance stage was chemotherapy plus radiotherapy (15 patients,

27.7%). Meanwhile, the majority of adjuvant therapies in early stage included radiotherapy alone (18 patients, 33.4%), followed by chemotherapy alone (5 patients, 9.3%). In this study, no patients received hormonal therapy.

Table 3. Adjuvant treatment according to stage of disease in endometrial cancer patients.

FIGO stage	Radiotherapy	Chemotherapy	Chemotherapy + radiotherapy	Other
Stage I				
IA	1	1	-	-
IB	9	4	-	-
Stage II	5	-	-	-
Stage III				
IIIA	-	-	1	-
IIIB	-	-	-	-
IIIC1	2	-	5	-
IIIC2	1	-	1	-
Stage IV				
IVA	-	-	-	-
IVB	-	-	8	-
Total (%)	18 (33.4)	5 (9.3)	15 (27.7)	-

Statistic significant ($p<0.05$)

Table 4. Survival of patients according various characteristic features.

Characteristics	n = 54	PFS (95%CI)	P	5-year OS (95%CI)	P
Age			0.718		0.117
≤ 60	26	81.8 (58.5-92.8)		69.2 (47.8-83.3)	
> 60	28	71.4 (50.9-84.6)		85.4 (65.7-94.3)	
BMI (kg/m^2)			0.973		N/A
< 30	43	76.9 (60.3-87.3)		72.1 (56.1-83.1)	
≥ 30	11	72.7 (37.1-90.3)		-	
FIGO stage			0.002		<0.001
Early	36	88.6 (72.4-95.6)		91.6 (76.1-97.2)	
Advanced	18	46.7 (21.2-68.8)		50 (25.9-70.1)	
Histopathology			0.146		0.207
Endometrioid	49	78.3 (63.4-87.7)		79.6 (65.4-88.5)	
Nonendometrioid	5	50 (5.8-84.5)		53.3 (6.8-86.3)	
Tumor grade			0.106		0.010
I	18	83.3 (56.8-94.3)		94.1 (65-99.2)	
II	26	79.2 (57-90.8)		76.9 (55.7-88.9)	
III	10	50 (15.2-77.5)		50 (18.4-75.3)	

Table 4. Survival of patients according various characteristic features. (Cont.)

Characteristics	n = 54	PFS (95%CI)	P	5-year OS (95%CI)	P
Cervical invasion			0.172		0.009
No	49	78.3 (63.4-87.7)		81.5 (67.4-89.9)	
Yes	5	50 (5.8-84.5)		40 (5.2-75.3)	
Myometrial invasion			0.653		0.410
Inner half	23	77.3 (53.7-89.9)		82 (58.8-92.8)	
Outer half	31	75 (54.6-87.2)		74.2 (55-86.2)	
Peritoneal cytology			0.016		0.001
Negative	48	80 (65.1-89.1)		83.2 (69.2-91.2)	
Positive	6	40 (5.2-75.3)		33.3 (4.6-67.6)	
Lymphovascular invasion			N/A		N/A
No	47	82.6 (68.2-90.9)		89.2 (76.0-95.4)	
Yes	7	0		0	
Lymph node metastasis			0.017		< 0.001
Negative	39	84.2 (68.2-92.6)		89.6 (74.6-96)	
Positive	15	50 (20.9-73.6)		46.7 (21.2-68.8)	
Residual tumor			0.173		< 0.001
No	44	79.1 (63.6-88.5)		86.2 (71.8-93.6)	
Yes	10	57.1 (17.2-83.7)		40 (12.3-67)	

PFS: progression free survival
OS: overall survival
N/A: not available
FIGO stage: early stage = FIGO stage I-II, advance stage = FIGO stage III-IV
Log-rank test
Significant (p<0.05)

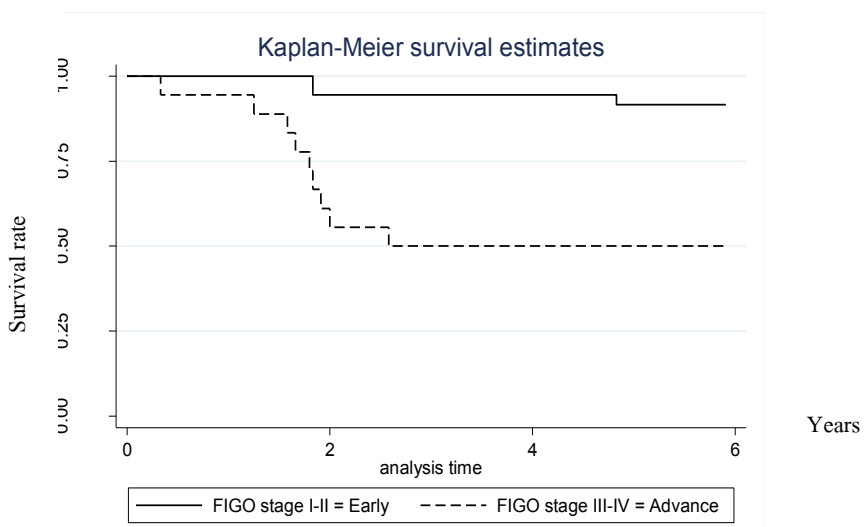

Fig. 1. Overall survival in endometrial cancer, according to stage

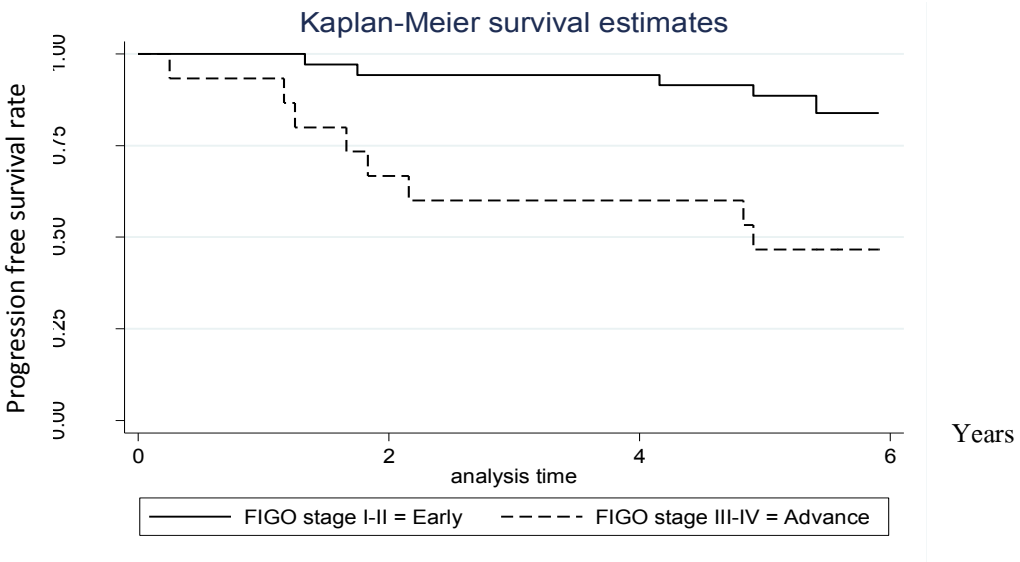

Fig. 1. Progression free survival in endometrial cancer, according to stage

The variable of prognostic factors affecting overall survival and progressive free survival are shown in Table 4. By univariate analysis, early stage disease, endometrioid histopathology, tumor grade I, no cervical invasion, no lymph node metastasis and no residual tumor were associated with significantly good overall survival.

The survival analyses were performed. The five-year overall survival rate of endometrial cancer was 80.1%, which depended on the stage. The survival rate was 91.6% in early stage (FIGO stage I-II) and 50% in advanced stage (FIGO stage III-IV). Fig. 1. shows the overall survival in this study was 91.6% in early stage and 50% in advanced stage and compared with early stage and advanced stage, early stage was associated with significantly improved overall survival ($p < 0.001$). Fig. 2. shows the progressive-free survival was 88.6% in early stage and 46.7% in advanced stage, while advanced stage was associated with a significantly higher risk of progression ($p=0.002$).

Discussion

The present study enrolled 54 patients with endometrial cancer receiving treatment in Phramongkutklao hospital. Some patients had comorbid diseases such as chronic renal disease, immunodeficiency disease, liver disease, or other cancers which may have an effect on treatment planning and treatment outcome. As shown in Table 1, death not related with disease was zero. The mean age of patients was 60 ± 10.6 years with the commonly presented symptom of postmenopausal bleeding similar to that reported by Sarikapan W[10], the peak incidence age of endometrial cancer patients in Thailand was 50-60 years. In our study the majority of patients were stage I, followed by stage III, IV and stage II similar to the study by Sarikapan W[10].

Recently, adjuvant therapy discussions on the role of using radiation amongst intermediate risk patients and chemotherapy amongst high risk patients is based on pathological feature (histopathology, tumor grade, lymphovascular invasion, myometrial invasion)[7]. Several randomized trials have demonstrated that adjuvant radiotherapy for patients in stage I or stage II reduces the local recurrence rate[8]. In our study, one patient in stage IA and nine patients in stage IB with high grade tumor (tumor grade III) received adjuvant radiotherapy. One patient in stage IA and four patients in stage IB with nonendometrioid carcinoma, such as papillary serous carcinoma and clear cell carcinoma, received adjuvant chemotherapy. The majority of subjects using adjuvant chemotherapy

plus radiotherapy (sandwich technique) were advanced stage patients (FIGO III-IV), and according to an article reviewed by Androutsopoulos G[11], the reported five-year overall survival rate in patients with advanced-stage who were treated with the sandwich technique was 79%[12]. Adjuvant chemotherapy is the mainstay of treatment for advanced stage endometrial cancer[11]. In patients with gross residual disease, adjuvant chemotherapy with paclitaxel and carboplatin is as effective as other regimens reported in literature and has less toxicity[13]. In our study, the most frequently used chemotherapy regimen was cisplatin-doxorubicin-paclitaxel (21%). Two patients in advanced stage with poor performance status received adjuvant radiotherapy alone.

Our study found the prognostic variables affecting good overall survival, depending on early stage, tumor grade, absence of cervical invasion, negative peritoneal cytology, and no lymph node metastasis similar to other studies[14-16].

We found the five-year overall survival rate was 91.6% in early stage and 50% in advanced stage, similar to the study by Shaeffer DT et al[5]. The overall survival rate of endometrial cancer was reported at 84% in early stage and 30-70% in advanced stage, in agreement with data reported by other authors[17, 18]. Altekruse et al[19], reported endometrial cancer had a good prognosis because most patients are diagnosed in the early stage. Siegel et al[20], reported the five-year overall survival rate in all stages of endometrial cancer patients was at 83-87%.

Wilson et al[21], reported the 5-year overall survival rate for endometrioid compared with non endometrioid was 92% vs. 33%. Nonendometrioid carcinoma has a lower incidence but a poorer prognosis than endometrioid carcinoma. Our study found the most common histopathology was endometrioid carcinoma (90.6%). This study revealed the histopathology did not significantly affect overall survival rate and progression-free survival, which may be explained by the small number of patients in this study, limiting the statistical power of the analysis.

The benefit of this study is that all these finding could be considered in appropriate endometrial cancer treatment, especially using adjuvant therapy with current data changing the discussion about the roles of radiation in intermediate risk patients and chemotherapy in high risk patients. Nevertheless, this study had several limitations that could affect the accuracy of the analysis of clinical outcomes. Firstly, the time available to collect data was short, which limited us to having to use a median survival time analysis. Secondly, the study enrolled a small number of endometrial cancer patients, limiting us to using a multivariate analysis. Thirdly, the potential of confounding factors may have been missed because of the study's retrospective nature. This study should encourage more future studies, especially about prognosis factors improving progression-free survival and overall survival rate.

Conclusion

The overall survival in this study was 80.1%. The FIGO stage and tumor grade was associated with overall survival of patients with endometrial cancer.

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อัตราการรอดชีวิตของผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกในโรงพยาบาลพระมงกุฎเกล้า

ศันสนีย์ พยันตา, สุทธิดา อินทรบุหรั่น

วัตถุประสงค์: *เพื่อศึกษาอัตราการรอดชีวิตรวมที่ 5 ปี ของผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกที่รักษา ในโรงพยาบาลพระมงกุฎเกล้า*

วิธีการศึกษา: *เป็นการศึกษาวิจัยเชิงพรรณนาแบบเก็บข้อมูลย้อนหลัง ในผู้ป่วยที่ได้รับวินิจฉัยเป็นมะเร็งเยื่อบุโพรงมดลูก จำนวน 54 ราย และได้รับการรักษาระหว่างวันที่ 1 มกราคม พ.ศ.2552 ถึงวันที่ 31 ธันวาคม พ.ศ.2553 ในโรงพยาบาลพระมงกุฎเกล้า ใช้สถิติ Kaplan-Meier method เพื่อวิเคราะห์อัตราการรอดชีวิตรวม และใช้ Log-rank test เพื่อเปรียบเทียบอัตราการรอดชีวิตระหว่างกลุ่มผู้ป่วย*

ผลการศึกษา: *ผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกมีอายุเฉลี่ย 60± 0.6 ปี อาการนำเป็นเลือดออกทางช่องคลอดทั้งหมด ส่วนใหญ่จัดอยู่ในกลุ่มผู้ป่วยระยะแรก คิดเป็นร้อยละ 66.7 ผลการตรวจจุลพยาธิวิทยาเป็นเอ็นโดเมตริออย คิดเป็นร้อยละ 90.6 การรักษาเสริมหลังผ่าตัดในกลุ่มผู้ป่วยระยะลุกลาม ส่วนใหญ่คือการให้ยาเคมีบำบัดร่วมกับการฉายรังสีรักษา คิดเป็นร้อยละ 27.7 และในกลุ่มผู้ป่วยระยะแรกส่วนใหญ่คือการฉายรังสีรักษาอย่างเดียว คิดเป็นร้อยละ 33.4 อัตราการรอดชีวิตรวมที่ 5 ปี ของผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกคิดเป็นร้อยละ 80.1 ซึ่งขึ้นกับระยะของโรค คิดเป็นร้อยละ 91.6 และร้อยละ 50 ในกลุ่มผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกระยะแรก (FIGO stage I-II) และระยะลุกลาม (FIGO stages III-IV) ตามลำดับ พบว่าปัจจัยที่มีผลต่ออัตราการรอดชีวิตของผู้ป่วยอย่างมีนัยสำคัญ ได้แก่ ระยะของโรค เกรดของมะเร็ง การลุกลามปากมดลูก การแพร่กระจายไปต่อมน้ำเหลือง การพบผลบวกของเซลล์จากน้ำในช่องท้อง และการผ่าตัดที่ยังมีก้อนมะเร็งเหลืออยู่ 2 เซนติเมตร*

สรุป: *อัตราการรอดชีวิตรวมที่ 5 ปี ของผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก คิดเป็นร้อยละ 80.1 ระยะของโรคและเกรดของมะเร็ง มีความสัมพันธ์กับอัตราการรอดชีวิตอย่างมีนัยสำคัญ ในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก*