

# Comparative Survival Outcomes of Uterine Papillary Serous Carcinoma, Clear Cell Carcinoma, Grade 3 Endometrioid Adenocarcinoma, and Carcinosarcoma of Endometrial Cancer in Rajavithi Hospital

Nisa Prueksaritanond MD\*,  
Wasu Chantape MD\*\*

\* Department of Obstetrics and Gynecology, Rajavithi Hospital, College of Medicine, Rangsit University, Bangkok, Thailand

\*\* Department of Obstetrics and Gynecology, Rajavithi Hospital, Bangkok, Thailand

---

**Background:** Uterine papillary serous carcinoma (UPSC), clear cell carcinoma (CC), grade 3 endometrioid adenocarcinoma (G3EC), and carcinosarcoma (CS) have been identified as high-grade endometrial cancers and account for the majority of uterine cancer deaths.

**Objective:** To compare survival outcomes of patients with UPSC, CC, G3EC and CS in Rajavithi Hospital.

**Material and Method:** A retrospective review was performed of all patients with FIGO stage I-IV endometrial cancer in Rajavithi Hospital between 1 January 2007 and 31 December 2012. Kaplan-Meier estimates were made of overall survival (OS) and progression-free survival (PFS), and log-rank tests were used to compare survival distributions between histological subtypes. Cox regression was used to estimate hazard ratios for histological subtypes, adjusted for other significant prognostic factors.

**Results:** One hundred sixty-three patients had confirmed diagnosis of high-grade endometrial cancer: 45 had UPSC, 30 had CC; 58 had G3EC; and 30 had CS. The median age distribution of the four groups of patients was approximately 60 years. The body mass index, underlying disease, and parity were similar in each group. All patients underwent a hysterectomy and surgical staging procedure. The 2-year progression-free survival was poorest in the CS cases (79.4%), followed by CC (87.2%), G3EC (92.2%), and UPSC cases (95.5%), and these figures were statistically significantly different among the groups ( $p = 0.015$ ). The 2-year overall survival was poorest in the CC cases (70.0%), followed by CS (76.7%), UPSC (86.7%), and G3EC (87.9%); however, there were no significant differences among the groups ( $p = 0.071$ ). In multivariate analysis for OS, advanced stage and suboptimal surgery were significantly associated with increased risk of death. For PFS, advanced stage and positive peritoneal cytology were significantly associated with increased risk of recurrence.

**Conclusion:** CS patients had a significantly lower rate of progression-free survival than other subtypes. These findings should be taken into account when considering counseling, primary treatment and appropriate adjuvant treatment in order to improve survival outcomes in these high-risk patients.

**Keywords:** Overall survival, Progression-free survival, Grade 3 endometrioid adenocarcinoma, Carcinosarcoma, Clear cell carcinoma, Uterine papillary serous carcinoma

**J Med Assoc Thai 2016; 99 (Suppl. 2): S75-S83**

**Full text. e-Journal:** <http://www.jmatonline.com>

---

Endometrial cancer (EC) is the sixth most common female cancer worldwide. Approximately 320,000 new cases are found each year and 76,000 women die annually from this disease<sup>(1)</sup>. Unlike most

cancers, the number of new cases has risen in recent years, with an increase of over 40% between 1993 and 2013<sup>(2)</sup>.

There are two different clinic-pathologic types of endometrial cancer, which differ in incidence, responsiveness to estrogen, and prognosis. Type I EC is estrogen-responsive and has a favorable prognosis, and this type arises in women with obesity, hyperlipidemia, and signs of hyperestrogenism<sup>(3)</sup>. Type II EC accounts for approximately 20% of endometrial cancers,

---

**Correspondence to:**

Prueksaritanond N, Department of Obstetrics and Gynecology, Rajavithi Hospital, 2 Phayathai Road, Rajathewi, Bangkok 10400, Thailand.

Phone: +66-2-3548165 ext. 3226, Fax: +66-2-3548084

E-mail: [nisa3054@gmail.com](mailto:nisa3054@gmail.com)

including grade 3 endometrioid adenocarcinomas (G3EC), tumors of non-endometrioid histology such as uterine papillary serous (UPSC), and clear cell (CC). These tumors are often high-grade, have a poor prognosis, and are not clearly associated with estrogen stimulation<sup>(3,4)</sup>. Although high-grade endometrial cancers are less common, accounting for approximately 25% of new cases, they are responsible for nearly 75% of EC deaths annually<sup>(5,6)</sup>. The similarities in the clinical behaviors of G3EC and type II cancers and the frequency of their coexistence have generated debate about whether G3EC should be classified as a type I or type II EC<sup>(7-11)</sup>. Regarding survival outcomes in patients with UPSC, CC, and G3EC, previous studies of comparisons between these histologic types have not always agreed. Some studies have shown that UPSC and CC are associated with an unfavorable prognosis compared with G3EC<sup>(5,7)</sup>; thus, UPSC and CC are classified as high-grade endometrial cancers. In contrast, a recent clinico-pathologic analysis revealed no difference in outcomes between UPSC and CC, and G3EC<sup>(8,9)</sup>.

Uterine carcinosarcomas (CS), also known as malignant mixed müllerian tumors (MMMT), have characteristics of both carcinomas and sarcomas. Several pathological clues have been found to support the idea that uterine carcinosarcomas can be categorized as types of metaplastic carcinoma, since they are monoclonal in origin<sup>(12,13)</sup>.

In 2009, the International Federation of Gynecology and Obstetrics (FIGO) staging system was revised and classified uterine carcinosarcoma separately from sarcoma, putting it into the category of carcinoma<sup>(14)</sup>. The current treatment guideline recommended is to treat uterine carcinosarcoma according to the guideline for high-grade endometrial cancer<sup>(15)</sup>. Some studies have reported that the prognosis for carcinosarcomas was poor when compared to other high-grade endometrial cancers<sup>(16-19)</sup>. On the other hand, another study showed similar rates of recurrence-free survival, disease-free survival, and overall survival between CS, G3EC, CC, and UPSC cases<sup>(20)</sup>; however, the data in that study were limited and are still controversial.

The primary objective of this study was to compare rates of overall survival (OS) and progression-free survival (PFS) of four histologic subtypes of high-grade endometrial cancers in patients who underwent a hysterectomy. The secondary objective was to evaluate prognostic factors of high-grade endometrial cancers in order to predict the survival outcomes of

these patients.

### **Material and Method**

The protocol of this research was reviewed and approved by the ethics committee of Rajavithi Hospital (No. 42/2557).

### **Patients**

After Institutional Review Board approval had been obtained, medical records were retrospectively reviewed to identify patients who underwent treatment for FIGO stage I-IV endometrial cancers at Rajavithi Hospital between 1 January 2007 and 31 December 2012. Patients were considered to be eligible if diagnosed as having G3EC, UPSC, CC, or CS. Patients who had synchronous cancer or mixed subtype were excluded. Histopathology was reviewed by a pathologist.

### **Primary treatment**

Staging was performed according to the revised 2009 FIGO surgical staging criteria. Adjuvant radiotherapy or/and adjuvant chemotherapy was used for cases with intermediate to high-risk factors depending on patient preference and physician's discretion. Radiotherapy was performed using vaginal brachytherapy alone (6 Gy in 2 fractions), full pelvic external beam radiation alone (50 Gy in 25 fractions), or a combination of the two. For histological type G3EC, CC and UPSC, chemotherapy was used consisting of a platinum-based regimen for six cycles. For histological type CS, chemotherapy consisted of a platinum-based regimen, or paclitaxel and ifosfamide for six cycles. None of the patients received chemotherapy or radiotherapy before surgery.

### **OS and PFS evaluation**

OS was measured from the date of surgery until last follow-up or death. The follow-up data were recorded from a patient's registration. If a patient were lost to follow-up, the registered date of death was recorded. PFS was defined as the period between initial treatment and the occurrence of pathologically confirmed relapse. If there was no biopsy confirmation, recurrence was clinically assumed when the imaging studies were highly suggestive of recurrence and tumor markers were elevated from the basal level.

### **Recurrence evaluation**

Local recurrence was defined as recurrence at the vagina or at the surrounding tissue of the vagina. Regional recurrence was defined as tumor recurrence

at the pelvic or para-aortic lymph nodes. Distant metastasis was defined as treatment failure at any other location apart from these areas.

For recurrences that were diagnosed by histological examinations, the test date was used as the failure date of the treatment. For recurrences that were diagnosed by imaging study, the failure date of the treatment was set as the date when the computed tomography (CT) was taken.

### Statistical analysis

The sample size of each group was 27 patients, calculated using the following formula<sup>(21)</sup>

$$n = \frac{\{Z_{\alpha/2}\sqrt{2\pi(1-\pi)} + Z_{\beta}\sqrt{\pi_1(1-\pi_1) + \pi_2(1-\pi_2)}\}^2}{(\pi_1 - \pi_2)^2}$$

$\pi_1 = 0.750$ ,  $\pi_2 = 0.380$ ,  $\alpha = 0.05$ , Power = 80%

$\pi_1 = 0.750$  is the number of 2-year overall survival of G3EC and  $\pi_2 = 0.380$  is the number of 2-year overall survival of CS from the study by Evan George et al<sup>(22)</sup>.

The withdrawal adjustment rate was 5%, and 28 patients were required per group. Frequency distributions between categorical variables among the groups were compared using the Chi-square test, and Fisher's exact test was used if the expected frequency was less than 5. The survival curves were calculated according to the Kaplan-Meier method, and the log-rank test was used to compare survival between groups of factors. The Cox proportional-hazards model was used for multivariable analyses, and G3EC was the reference histological subtype. Statistical analyses were performed with SPSS ver. 17.0 (SPSS Inc., Chicago,

IL, USA). A *p*-value of less than 0.050 was used to determine the statistical significance for all tests.

## Results

### General characteristics

One hundred and sixty-three patients had a diagnosis of high-grade endometrial cancer confirmed by pathologists: 58 had G3EC; 30 had CS; 30 had CC; and 45 had UPSC. The disagreement between the review and primary diagnoses were cases of mixed subtype such as endometrioid adenocarcinoma mixed serous carcinoma or clear cell, grade 2 endometrioid adenocarcinoma, sarcoma, endometrial stromal sarcoma, adenosarcoma, and metastatic endometrioid adenocarcinoma to the intestine.

Distributions of demographic and clinical characteristics are shown by histological subtype in Table 1. The age distribution of the patients varied from 30 to 77 years (median, 60 years). All patients in our study underwent a hysterectomy and surgical staging procedure. Type of surgery and surgical-pathological characteristics classified by histological type are shown in Table 2.

Of the patients with G3EC, CC, CS, and UPSC, 87.9, 86.7, 83.3, and 100%, respectively underwent lymphadenectomy (Table 2). Types of adjuvant therapy after primary surgery were as follows: patients with G3EC more often received postoperative radiotherapy (29.3%) and patients with CC more often received postoperative chemotherapy (46.7%). We found significant differences in trans-peritoneal spread among the four histological subtypes, including lympho-vascular space invasion, peritoneal cytology, omental

**Table 1.** Clinical characteristics features classify by histologic types

Characteristics	G3EC n = 58 n (%)	CS n = 30 n (%)	CC n = 30 n (%)	UPSC n = 45 n (%)	<i>p</i> -value
Age >50 years	49 (84.5)	26 (86.7)	26 (86.7)	41 (91.1)	0.874
Mean ± SD	58.74±9.40	59.10±7.05	61.60±8.50	60.69±9.46	
BMI (kg/m <sup>2</sup> )					0.444
Underweight (below 18.5)	4 (6.9)	3 (10.0)	1 (3.3)	2 (4.4)	
Normal weight (18.5-24.9)	31 (53.4)	13 (43.3)	14 (46.7)	21 (46.7)	
Overweight (25.0-29.9)	16 (27.6)	10 (33.3)	9 (30.0)	18 (40.0)	
Obese (30 and above)	7 (12.1)	4 (13.3)	6 (20.0)	4 (8.9)	
Other medical illnesses (DM, HT, DLP)	30 (51.7)	15 (50.0)	16 (53.3)	29 (64.4)	0.214
Nulliparous	22 (37.9)	7 (23.3)	7 (23.3)	8 (17.8)	0.118

G3EC = grade 3 endometrioid adenocarcinoma; CS = carcinosarcoma; CC = clear cell carcinoma; UPSC = uterine papillary serous adenocarcinoma; DM = diabetes mellitus; HT = hypertension; DLP = dyslipidemia

**Table 2.** Surgico-pathological findings and types of surgery classify by cell types

Characteristics	G3EC n = 58 n (%)	CS n = 30 n (%)	CC n = 30 n (%)	UPSC n = 45 n (%)	p-value
Lymphadenectomy	51 (87.9)	26 (86.7)	25 (83.3)	45 (100.0)	0.020*
Primary treatment					0.002*
Surgery alone	19 (32.8)	4 (13.3)	5 (16.7)	17 (37.8)	
Surgery+ adjuvant RT	17 (29.3)	4 (13.3)	1 (3.3)	5 (11.1)	
Surgery+ adjuvant CMT	10 (17.2)	11 (36.7)	14 (46.7)	15 (33.3)	
Surgery+ adjuvant combination	12 (20.7)	11 (36.7)	10 (33.3)	8 (17.8)	
Optimal surgery optimal	51 (87.9)	23 (76.7)	21 (70.0)	44 (97.8)	0.002*
Cervical involvement	13 (22.4)	8 (26.7)	13 (43.3)	9 (20.0)	0.119
Myometrium					
No myometrium involvement	3 (5.2)	4 (13.3)	0 (0.0)	9 (20.0)	0.001*
<1/2 MI	17 (29.3)	5 (16.7)	15 (50.0)	20 (44.4)	
>1/2 MI	38 (65.5)	21 (70.0)	15 (50.0)	16 (35.6)	
Tumor size $\geq 2$ cm	55 (94.8)	27 (90.0)	27 (90.0)	37 (82.2)	0.227
LVSI positive	26 (44.8)	16 (53.3)	18 (60.0)	14 (31.1)	0.012*
Peritoneal cytology positive	2 (3.4)	3 (10.0)	8 (26.7)	2 (4.4)	0.004*
Omental positive	2 (3.4)	5 (16.7)	4 (13.3)	0 (0.0)	0.006*
Pelvic lymph node positive	5 (8.6)	4 (13.3)	10 (33.3)	8 (17.8)	0.007*
Para-aortic lymph node	8 (13.8)	5 (16.7)	8 (26.7)	4 (8.9)	0.091
Extrauterine disease	27 (46.6)	18 (60.0)	20 (66.7)	14 (31.1)	0.011*
2009 FIGO staging					0.006*
Stage 1	31 (53.4)	12 (40.0)	9 (30.0)	31 (68.9)	
Stage 2	6 (10.3)	3 (10.0)	2 (6.7)	4 (8.9)	
Stage 3	17 (29.3)	9 (30.0)	12 (40.0)	10 (22.2)	
Stage 4	4 (6.9)	6 (20.0)	7 (23.3)	0 (0.0)	
Advanced stage	21 (36.2)	15 (50.0)	19 (63.3)	10 (22.2)	0.002*

G3EC = grade 3 endometrioid adenocarcinoma; CS = carcinosarcoma; CC = clear cell carcinoma; UPSC = uterine papillary serous adenocarcinoma; LND = lymph node dissection; LVSI = lympho-vascular invasion; RT = radiotherapy; CMT = chemotherapy; MI = myometrium involvement

<sup>a</sup>Number may not be added up the total number due to missing data

\* Significant at  $p < 0.05$

status and pelvic lymph node status. The CC group was most likely to spread to pelvic and para-aortic lymph nodes. Extra-uterine disease was significantly most frequent in CC followed by CS, G3EC, and UPSC, respectively (66.7%, 60.0%, 46.6%, 31.1%;  $p = 0.011$ ).

G3EC and UPSC were more often in stage I of 2009 FIGO surgical staging, while CC and CS were more commonly in stage III. Sixty-three percent of CC cases were advanced stage compared to 50.0% of CS, 36.2% of G3EC, and 22.2% of UPSC cases.

#### **Survival, recurrence pattern and prognostic variables**

The median follow-up duration was 37.5 months (range, 1.07-88.0 months). The median time to recurrence was 46.4, 36.8, 28.6, 24.1 months in G3EC, UPSC, CS, and CC, respectively. CS cases had the highest prevalence of recurrence (23.3%), followed by

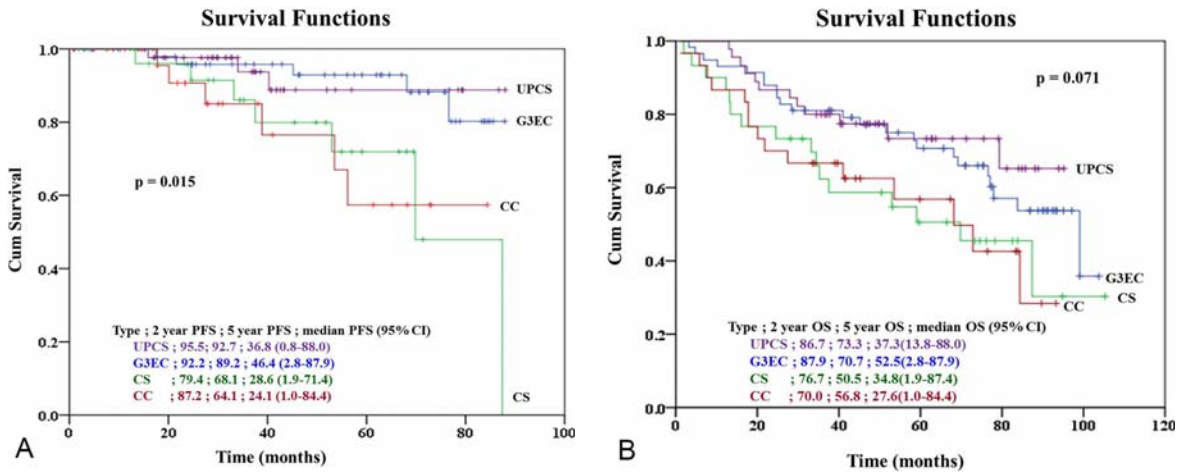
CC (20.0%), G3EC (8.6%), and UPSC (6.7%). All histological subtypes had more distant recurrence than loco-regional recurrence: G3EC 5/5 [100.0%]; CS 5/7 [71.4%]; UPSC 4/6 [66.6%]; and CC 2/3 [66.6%] ( $p = 0.301$ ) (Table 3). The 2-year progression-free survival was poorest in the CS cases (79.4%), followed by CC (87.2%), G3EC (92.2%), and UPSC (95.5%), and the differences were statistically significant among the groups ( $p = 0.015$ ).

The CS group had the highest prevalence of death (53.3%), followed by CC (50.0%), G3EC (39.7%), and UPSC (26.7%). The 2-year overall survival was poorest in the CC cases (70.0%), followed by CS (76.7%), UPSC (86.7%), and G3EC (87.9%); however, there were no significant differences among the groups ( $p = 0.071$ ) (Fig. 1). Kaplan-Meier survival curves for OS and PFS outcomes according to histological type are shown in

**Table 3.** Survival and pattern of recurrence

	G3EC n = 58 n (%)	CS n = 30 n (%)	CC n = 30 n (%)	UPSC n = 45 n (%)	p-value
Death	23 (39.7)	16 (53.3)	15 (50.0)	12 (26.7)	0.080
Recurrence	5 (8.6)	7 (23.3)	6 (20.0)	3 (6.7)	0.081
Local	0 (0.0)	2 (28.6)	2 (33.3)	1 (33.3)	0.525
Distant	5 (100.0)	5 (71.4)	4 (66.7)	2 (66.7)	

G3EC = grade 3 endometrioid adenocarcinoma; CS = carcinosarcoma; CC = clear cell carcinoma; UPSC = uterine papillary serous adenocarcinoma



**Fig. 1** Survival outcome according to the histologic type after adjusting for clinicopathologic factors. G3EC = grade 3 endometrioid carcinoma; CS = carcinosarcoma; CC = clear cell; UPSC = uterine papillary serous carcinoma. (A) Progression-free survival, (B) Overall survival.

Fig. 1.

Univariate and multivariate Cox regression models for PFS and OS are summarized in Table 4. In univariate analysis for PFS, CS cases had significantly poorer outcomes compared to G3EC cases (HR, 3.23; 95% CI, 1.02-10.21) ( $p=0.046$ ). In multivariate analysis for PFS, advanced stage and positive peritoneal cytology were significantly associated with increased risk of recurrence (adjusted HR, 5.27; 95% CI, 1.12-24.75) ( $p=0.035$ ), (adjusted HR, 2.73; 95% CI, 1.22-6.12) ( $p=0.014$ ). In multivariate analysis for OS, advanced stage and suboptimal surgery were significantly associated with increased risk of death. In both univariate and multivariate analysis for OS and PFS, we found that only advanced stage was significantly associated with poorer outcomes and histological subtype was not a significant prognostic factor.

### Discussion

UPSC, CC, G3EC and CS have been identified

as high-grade endometrial cancers and are responsible for the majority of uterine cancer deaths<sup>(5)</sup>. This study is one of a series that have compared survival outcomes and prognostic factors of patients with UPSC, CC, G3EC and CS. We found that the CS and CC groups had a worse overall rate of survival than the UPSC and G3EC groups. These findings are similar to those of Ashley SF et al<sup>(20)</sup> and George et al<sup>(22)</sup>, but different from those of the study by Soslow et al<sup>(8)</sup>. The explanation may be that in our study G3EC and UPSC were more often in stage 1 of FIGO surgical staging, while CC and CS were more commonly in stage 3. The present study also found that the G3EC group had better prognosis than the other groups, similar to the findings of some other research<sup>(7,23)</sup>. However, in our study, overall survival was not significantly different between the groups, and this is in keeping with the results of some other reports<sup>(8,20)</sup>.

We also found that the CS group had a worse prognosis than the other groups. The 2-years PFS of

**Table 4.** Univariate and multivariate analyses for progression-free survival and overall survival outcomes according to individual parameters

Parameter	Progression-free survival		Overall survival	
	HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value
Uni-variate analysis				
Histology				
G3EC	1		1	
CS	3.23 (1.02-10.21)	0.046*	1.73 (0.91-3.28)	0.094
CC	3.00 (0.91-9.88)	0.071	1.77 (0.92-3.40)	0.090
UPSC	0.79 (0.19-3.30)	0.743	0.82 (0.40-1.65)	0.568
Suboptimal Sx	3.39 (1.11-10.39)	0.033*	4.01 (2.29-7.04)	<0.001*
PW positive	8.86 (3.01-26.08)	<0.001*	2.82 (1.43-5.57)	0.003*
LVSI positive	4.43 (1.65-11.87)	0.003	2.05 (1.22-3.46)	0.007*
Stage (3-4)	4.31 (1.76-10.56)	0.001*	2.94 (1.80-4.80)	<0.001*
Multi-variate analysis				
Histology				
G3EC	1		1	
CS	2.29 (0.66-7.96)	0.191	1.69 (0.86-3.32)	0.125
CC	1.33 (0.33-5.30)	0.684	1.05 (0.50-2.18)	0.888
UPSC	0.71 (0.16-3.11)	0.653	0.85 (0.41-1.78)	0.680
Suboptimal Sx	0.96 (0.26-3.59)	0.955	2.45 (1.23-4.89)	0.010*
PW positive	4.92 (1.39-17.38)	0.013*	1.75 (0.84-3.65)	0.135
LVSI positive	0.46 (0.11-2.03)	0.312	1.79 (0.65-4.89)	0.253
Stage (3-4)	5.27 (1.12-24.75)	0.035*	2.73 (1.22-6.12)	0.014*

G3EC = grade 3 endometrioid adenocarcinoma; CS = carcinosarcoma; CC = clear cell carcinoma; UPSC = uterine papillary serous adenocarcinoma; HR = hazard ratio; Sx = surgery; PW = peritoneal washing; LVSI = lympho-vascular invasion

\* Significant at  $p < 0.05$

CS was 79.4%, followed by CC (87.2%), G3EC (92.9%), and UPSC (95.5%) ( $p = 0.015$ ). Similarly, several reports<sup>(16-19)</sup> found that uterine CS cases tended to show poor prognosis compared to the other high-grade endometrial carcinomas.

Previous studies<sup>(5,7,24)</sup> have shown that women with UPSC had progression-free and overall survival rates that were significantly worse than women with G3EC. In contrast, we found that G3EC groups had a progression-free survival rate which was significantly worse than the UPSC group (92.9% vs. 95.5%,  $p = 0.015$ ). The explanation may be that the G3EC cases had had much more suboptimal surgery and had more advanced stages than the UPSC cases (12.1% vs. 2.2%, and 36.2% vs. 22.2%).

Thomas et al<sup>(25)</sup> reported that 52% of patients with CC who presented with disease clinically confined to the uterus were found to have extra-uterine disease during comprehensive surgical staging. The present study confirmed this finding and found that the majority of the members of the CC group had an advanced stage

at the time of diagnosis and had a high incidence of extra-uterine disease as shown in Table 3.

Using univariate analysis for OS and PFS, CS histologic subtypes, suboptimal surgery, positive peritoneal cytology, presence of LVSI, and advanced stage (III-IV) appeared to determine the outcomes. Cox regression multivariate analysis for OS and PFS suggested that only advanced stage was of prognostic significance (Hazard ratio (95% CI) were 2.73 (1.22-6.12) ( $p = 0.014$ ) and 5.27 (1.12-24.75) ( $p = 0.035$ )), respectively. These findings are similar to those of Amant et al's study<sup>(26)</sup> which revealed that both stage III-IV disease and histological type (carcinosarcoma) were of prognostic significance for PFS in high-risk endometrial cancer patients.

To determine whether significant discrepancies resulted from the large number of pathologists involved, all cases in our study had their slides reviewed by a single pathologist. This study had some limitations: first, the number of patients was relatively small, which may have affected the results;

second, this was a retrospective study, and may have some recall bias; third, the difference between basic data, such as stage, may have affected the results of survival; and fourth, comprehensive surgical staging was performed in only 87.7% of cases, and occult disease could have been missed in those patients who did not undergo comprehensive surgical staging.

### Conclusion

CS patients had a significantly lower progression-free survival rate compared to other histological subtypes. These findings should be taken into account in considering patient counseling, primary treatment and appropriate adjuvant treatment in order to improve survival outcomes in these high-risk patients.

### What is already known on this topic ?

UPSC, CC, G3EC and CS have been identified as high-grade endometrial cancers and account for the majority of uterine cancer deaths. Some studies reported that the prognosis of carcinosarcomas was poor when compared to other high-grade endometrial cancers. On the other hand, another study showed similar recurrence-free survival, disease-free survival, and overall survival between CS, G3EC, CC, and UPSC cases. However, the data were limited and controversial until now.

### What this study adds ?

We observed that the CS patients had a significant lower progression-free survival compared to other histological subtypes. These findings should be considered in the counseling, primary treatment and appropriate adjuvant treatment in order to improved survival outcomes in these high-risk patients.

### Acknowledgement

The authors would like to thank Mr. Kitiphong Harncharoen for his statistical analysis and Rajavithi Hospital for funding this research.

### Potential conflicts of interest

None.

### References

1. International Agency for Research on Cancer. World cancer report 2014. Chapter 5.12. [Internet]. 2014 [cited 2015 Jan 15]. Available from: [http://en.wikipedia.org/wiki/Endometrial\\_cancer](http://en.wikipedia.org/wiki/Endometrial_cancer)
2. Galaal K, Al Moundhri M, Bryant A, Lopes AD, Lawrie TA. Adjuvant chemotherapy for advanced

endometrial cancer. *Cochrane Database Syst Rev* 2014; 5: CD010681.

3. Bokhman JV. Two pathogenetic types of endometrial carcinoma. *Gynecol Oncol* 1983; 15: 10-7.
4. Felix AS, Weissfeld JL, Stone RA, Bowser R, Chivukula M, Edwards RP, et al. Factors associated with Type I and Type II endometrial cancer. *Cancer Causes Control* 2010; 21: 1851-6.
5. Hamilton CA, Cheung MK, Osann K, Chen L, Teng NN, Longacre TA, et al. Uterine papillary serous and clear cell carcinomas predict for poorer survival compared to grade 3 endometrioid corpus cancers. *Br J Cancer* 2006; 94: 642-6.
6. Tavassoli FA, Devilee P. WHO classification of tumors: pathology and genetics. Tumors of the breast and female genital organs. Lyon, France: IARC Press; 2003.
7. Boruta DM, Gehrig PA, Groben PA, Bae-Jump V, Boggess JF, Fowler WC Jr, et al. Uterine serous and grade 3 endometrioid carcinomas: is there a survival difference? *Cancer* 2004; 101: 2214-21.
8. Soslow RA, Bissonnette JP, Wilton A, Ferguson SE, Alektiar KM, Duska LR, et al. Clinicopathologic analysis of 187 high-grade endometrial carcinomas of different histologic subtypes: similar outcomes belie distinctive biologic differences. *Am J Surg Pathol* 2007; 31: 979-87.
9. Voss MA, Ganesan R, Ludeman L, McCarthy K, Gornall R, Schaller G, et al. Should grade 3 endometrioid endometrial carcinoma be considered a type 2 cancer-a clinical and pathological evaluation. *Gynecol Oncol* 2012; 124: 15-20.
10. Alektiar KM, McKee A, Lin O, Venkatraman E, Zelefsky MJ, McKee B, et al. Is there a difference in outcome between stage I-II endometrial cancer of papillary serous/clear cell and endometrioid FIGO Grade 3 cancer? *Int J Radiat Oncol Biol Phys* 2002; 54: 79-85.
11. McMeekin DS, Filiaci VL, Thigpen JT, Gallion HH, Fleming GF, Rodgers WH. The relationship between histology and outcome in advanced and recurrent endometrial cancer patients participating in first-line chemotherapy trials: a Gynecologic Oncology Group study. *Gynecol Oncol* 2007; 106: 16-22.
12. McCluggage WG. Uterine carcinosarcomas (malignant mixed Mullerian tumors) are metaplastic carcinomas. *Int J Gynecol Cancer* 2002; 12: 687-90.
13. McCluggage WG. Malignant biphasic uterine tumours: carcinosarcomas or metaplastic

- carcinomas? *J Clin Pathol* 2002; 55: 321-5.
14. Pecorelli S, Zigliani L, Odicino F. Revised FIGO staging for carcinoma of the cervix. *Int J Gynaecol Obstet* 2009; 105: 107-8.
  15. Garcia-Martinez E, Egea Prefasi L, Garcia-Donas J, Escolar-Perez PP, Pastor F, Gonzalez-Martin A. Current management of uterine sarcomas. *Clin Transl Oncol* 2011; 13: 307-14.
  16. Callister M, Ramondetta LM, Jhingran A, Burke TW, Eifel PJ. Malignant mixed Mullerian tumors of the uterus: analysis of patterns of failure, prognostic factors, and treatment outcome. *Int J Radiat Oncol Biol Phys* 2004; 58: 786-96.
  17. Sampath S, Schultheiss TE, Ryu JK, Wong JY. The role of adjuvant radiation in uterine sarcomas. *Int J Radiat Oncol Biol Phys* 2010; 76: 728-34.
  18. Makker V, Abu-Rustum NR, Alektiar KM, Aghajanian CA, Zhou Q, Iasonos A, et al. A retrospective assessment of outcomes of chemotherapy-based versus radiation-only adjuvant treatment for completely resected stage I-IV uterine carcinosarcoma. *Gynecol Oncol* 2008; 111: 249-54.
  19. Vaidya AP, Horowitz NS, Oliva E, Halpern EF, Duska LR. Uterine malignant mixed mullerian tumors should not be included in studies of endometrial carcinoma. *Gynecol Oncol* 2006; 103: 684-7.
  20. Felix AS, Stone RA, Bowser R, Chivukula M, Edwards RP, Weissfeld JL, et al. Comparison of survival outcomes between patients with malignant mixed mullerian tumors and high-grade endometrioid, clear cell, and papillary serous endometrial cancers. *Int J Gynecol Cancer* 2011; 21: 877-84.
  21. Selvin S. *Statistical analysis of epidemiologic data*. 3<sup>rd</sup> ed. New York: Oxford University Press; 2004.
  22. George E, Lillemoe TJ, Twiggs LB, Perrone T. Malignant mixed mullerian tumor versus high-grade endometrial carcinoma and aggressive variants of endometrial carcinoma: a comparative analysis of survival. *Int J Gynecol Pathol* 1995; 14: 39-44.
  23. Kim HJ, Kim TJ, Lee YY, Choi CH, Lee JW, Bae DS, et al. A comparison of uterine papillary serous, clear cell carcinomas, and grade 3 endometrioid corpus cancers using 2009 FIGO staging system. *J Gynecol Oncol* 2013; 24: 120-7.
  24. Creasman WT, Kohler MF, Odicino F, Maisonneuve P, Boyle P. Prognosis of papillary serous, clear cell, and grade 3 stage I carcinoma of the endometrium. *Gynecol Oncol* 2004; 95: 593-6.
  25. Thomas M, Mariani A, Wright JD, Madarek EO, Powell MA, Mutch DG et al. Surgical management and adjuvant therapy for patients with uterine clear cell carcinoma: a multi-institutional review. *Gynecol Oncol* 2008; 108: 293-7.
  26. Amant F, Cadron I, Fuso L, Berteloot P, de Jonge E, Jacomen G, et al. Endometrial carcinosarcomas have a different prognosis and pattern of spread compared to high-risk epithelial endometrial cancer. *Gynecol Oncol* 2005; 98: 274-80.



---

การเปรียบเทียบอัตราการรอดชีวิตระหว่างมะเร็งเยื่อโพรงมดลูกได้แก่ ชนิดแพทิลลารีซีรีส์ เคลิเยร์เซลล์ เอนโดเมทริออยด์  
อดีโนคาร์สิโนมาในระดับสาม และคาร์สิโนซาร์โคมา ในโรงพยาบาลราชวิถี

นิตา พุกษะรัตนานนท์, วสุ จันทร์เทพย์

ภูมิหลัง: มะเร็งเยื่อโพรงมดลูกชนิดแพทิลลารีซีรีส์ เคลิเยร์เซลล์ เอนโดเมทริออยด์อดีโนคาร์สิโนมาในระดับสาม และคาร์สิโนซาร์โคมาจัดเป็นมะเร็ง  
เยื่อโพรงมดลูกที่มีความรุนแรงสูงและเป็นสาเหตุส่วนใหญ่ของการเสียชีวิตในผู้ป่วยมะเร็งเยื่อโพรงมดลูก

วัตถุประสงค์: เพื่อศึกษาเปรียบเทียบอัตราการรอดชีวิตระหว่างมะเร็งเยื่อโพรงมดลูกชนิดรุนแรง 4 ชนิดได้แก่ ชนิดแพทิลลารีซีรีส์, เคลิเยร์เซลล์,  
เอนโดเมทริออยด์อดีโนคาร์สิโนมาในระดับสามและคาร์สิโนซาร์โคมา ในโรงพยาบาลราชวิถี

วัสดุและวิธีการ: ทบทวนเวชระเบียนย้อนหลังของผู้ป่วยมะเร็งเยื่อโพรงมดลูกที่ได้รับการรักษาด้วยการผ่าตัดที่โรงพยาบาลราชวิถีตั้งแต่วันที่ 1 มกราคม  
พ.ศ. 2550 ถึง 31 ธันวาคม พ.ศ. 2555 ทำการวิเคราะห์ข้อมูลอัตราการรอดชีวิตโดยรวม อัตราการรอดชีวิตโดยปราศจากโรค และปัจจัยต่างๆ ที่มีผลต่อ  
อัตราการรอดชีวิต

ผลการศึกษา: ผู้ป่วยที่ได้รับการยืนยันจากการตรวจทางพยาธิวิทยาว่าเป็นมะเร็งเยื่อโพรงมดลูกชนิดรุนแรง มีจำนวน 163 ราย โดยแบ่งเป็นชนิด  
แพทิลลารีซีรีส์ 45 ราย ชนิดเคลิเยร์เซลล์ 30 ราย ชนิดเอนโดเมทริออยด์อดีโนคาร์สิโนมาในระดับสาม 58 ราย และชนิดคาร์สิโนซาร์โคมา 30 ราย  
ผู้ป่วยทั้ง 4 กลุ่ม มีอายุเฉลี่ยประมาณ 60 ปี มีดัชนีมวลกาย, โรคประจำตัว, จำนวนบุตรไม่แตกต่างกันทางสถิติ อัตราการรอดชีวิตโดยปราศจากโรคที่ 2  
ปี พบว่าในกลุ่มชนิดคาร์สิโนซาร์โคมาต่ำที่สุด (ร้อยละ 79.4) รองลงมา คือ ชนิดเคลิเยร์เซลล์ (ร้อยละ 87.2), ชนิดเอนโดเมทริออยด์ อดีโนคาร์สิโนมา  
ระดับสาม (ร้อยละ 92.2) และชนิดแพทิลลารีซีรีส์ (ร้อยละ 95.5) ซึ่งมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ( $p = 0.015$ ) ส่วนอัตราการรอดชีวิต  
โดยรวมที่ 2 ปี ในกลุ่มชนิดเคลิเยร์เซลล์มีค่าต่ำที่สุด (ร้อยละ 70.0) รองลงมาคือ ชนิดคาร์สิโนซาร์โคมา (ร้อยละ 76.7), ชนิดแพทิลลารีซีรีส์ (ร้อยละ  
86.7) และชนิดเอนโดเมทริออยด์อดีโนคาร์สิโนมาในระดับสาม (ร้อยละ 87.9) แต่ไม่มีความแตกต่างกันทางสถิติ ( $p = 0.071$ ) ปัจจัยที่มีผลต่ออัตรา  
การรอดชีวิตโดยรวมอย่างมีนัยสำคัญทางสถิติได้แก่ โรกระยะลุกลามและการหลงเหลือก้อนมะเร็งหลังผ่าตัด ส่วนตัวแปรที่มีผลต่ออัตราการรอดชีวิต  
โดยปราศจากโรครอย่างมีนัยสำคัญทางสถิติ ได้แก่ โรคในระยะลุกลามและการตรวจพบเซลล์มะเร็งในน้ำในเยื่อช่องท้อง

สรุป: ผู้ป่วยมะเร็งเยื่อโพรงมดลูกในกลุ่มชนิดคาร์สิโนซาร์โคมามีอัตราการรอดชีวิตโดยปราศจากโรคต่ำกว่าผู้ป่วยมะเร็งเยื่อโพรงมดลูกชนิดรุนแรงอื่น ๆ  
อย่างมีนัยสำคัญทางสถิติ การวิจัยนี้จึงมีประโยชน์ในการพิจารณาวางแผนการรักษาหลักและการรักษาเพิ่มเติม เพื่อให้ผู้ป่วยเหล่านี้มีอัตราการรอดชีวิตที่สูงขึ้น

---