RESEARCH COMMUNICATION

Clinicopathological Features Including Hormonal Receptor Expression and Survival in Young Endometrial Cancer Patients: A Case Control Study

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Abstract

Objective: To compare clinicopathological features, including hormonal receptor expression and survival, in young Thai endometrial carcinoma (EMC) patients with older patients. Methods: Young EMC patients aged ≤45 years, treated in the institution from 1992 to 2008, were identified as cases. Controls included EMC patients aged >45 years who had an operation on the nearest dates to the cases. Clinicopathological data and survival of the cases and controls were compared. Results: Mean ages of 41 cases and 123 controls were 40.4 ± 3.7 years and 58.4 ± 8.3 years, respectively. Cases were significantly different from controls in terms of having more nulliparity (58% vs 25%), less medical illness (57% vs 79%), more low-grade tumors (49% vs 14%), more positive estrogen (78% vs 56%) and progesterone (97% vs 61%) receptors expression, and fewer nodal metastases (3% vs 21%). Adjuvant therapy was administered in 29% of the cases and 46% of the controls. From a median follow up of 51 months, cases had significantly fewer progression events and recurrence (5% vs 19%), cancer-related deaths (2% vs 16%), and all deaths (5% vs 23%), with significantly longer 5-year disease-free (97.2% vs 79.6%, p=0.023), cancer-specific (97.1% vs 83.2%, p=0.020), and overall survival (93.1% vs 78.8% p=0.005) than controls as determined by univariate analysis. Survival of cases and controls were not significantly different after adjusting for other prognostic factors. Conclusion: Young Thai EMC patients had more favorable clinicopathological features with significantly longer survival than older patients as determined by univariate analysis.

Keywords: Young endometrial cancer - clinicopathological features - hormonal receptor expression - survival

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Introduction

According to recent World Health Organization data, the incidence of endometrial cancer (EMC) varies in different parts of the world (Ferlay et al., 2010). It is the most common female genital tract malignancy in the more developed regions, with an estimated incidence of 12.9 per 100,000 women. In the less developed regions where cervical cancer is more common, EMC has an estimated incidence of 5.9 per 100,000 women in general and 4.3 per 100,000 women in Thailand in particular.

Although the median age at the diagnosis of EMC is 63 years with the peak incidence reported between 55 and 64 years, a certain number of patients develop EMC at a younger age (Altekruse et al., 2010). Despite the fact that age references for a young EMC patient varies widely from <40 to <50 years, some different characteristic features were commonly observed in these patients in comparison to those in older age groups. For example, younger EMC patients appear to have a higher association with an imbalance of hormonal milieu, e.g., obesity or chronic anovulation (Evans-Metcalf et al., 1998; Soliman et al., 2005; Navarria et al., 2009) or genetic or familial risk (Lu et al., 2007), and a higher incidence of synchronous ovarian cancer (Gitsch et al., 1995; Evans-Metcalf et al., 1998). However, inconsistent findings with regard to certain clinicopathological features were observed in previous reports. Although most studies described more favorable characteristic features with respect to EMC in younger patients as compared to older ones, e.g., low grade tumor, early stage disease, and lesser extent of cancer involvement (Gitsch et al., 1995; Evans-Metcalf et al., 1998; Tran et al., 2000; Navarria et al., 2009; Richter et al., 2009), others found similar distribution of stage (Evans-Metcalf et al., 1998) or more advanced stage and lymph node (LN) metastasis in younger age groups (Gitsch et al., 1995; Ben-Arie et al., 2004). Another area of disagreement is the survival of younger EMC patients when compared

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to the older age groups. Some investigators observed similar survival outcomes (Evans-Metcalf et al., 1998) while others found better prognosis with longer survival rates in younger patients (Persson et al., 1984; Rosenberg et al., 1989).

Most reports of EMC in young patients are derived from Western countries with only a handful of reports originating from Asia (Kaku et al., 1993; Ota et al., 2005; Hanprasertpong et al., 2008; Manchana et al., 2008). Two studies from Thailand reported favorable clinical features and outcomes in young EMC patients (Hanprasertpong et al., 2008; Manchana et al., 2008); however, one of these studies did not demonstrate any significant difference between the younger and older age groups (Manchana et al., 2008). In this study, we aim to evaluate the prevalence and clinicopathological features, including survival outcomes, of EMC patients aged ≤45 years in comparison with older age groups. Immunohistochemical expression of estrogen receptor (ER), progesterone receptor (PR), and Her2/*neu* in the two groups were also compared.

Materials and Methods

An approval from the institutional Ethics Committee for Research Involving Human Subjects was obtained before the study was conducted. The archives of the Department of Anatomical Pathology and the Gynecologic Oncology Unit, Department of Obstetrics and Gynecology were searched for EMC patients who were treated in the institution between January 1992 and December 2008. Patients aged ≤45 years were identified as cases while patients aged >45 years who were operated on the nearest date to each identified case were selected as controls. The ratio between case and control subjects was 1:3. The other inclusion criteria were the patients who were operated in the institutions or had been operated elsewhere and were referred for further management, had available medical records, including pathological reports. Exclusion criteria included patients with endometrial sarcomas other than carcinosarcoma and those who had fertility sparing treatment.

The following clinicopathological data were collected from in- and out-patient charts and pathological reports: age; presenting symptom; other prior or current co-morbidities, including other cancers; type of primary surgery; stage of disease; histopathology and grade of tumors; presence of lymph-vascular invasion; depth of myometrial invasion; peritoneal cytology; cervical invasion or any extrauterine involvement; immunohistochemical expression of ER, PR, and Her2/*neu*; adjuvant therapy; and outcome after treatment. A diagnosis of co-incidental ovarian cancer was categorized as metastasis or synchronous tumor based on the primary pathological report. Staging was assigned according to the International Federation of Gynecology and Obstetrics (FIGO) 1988 criteria (FIGO News, 1989). Complete surgical staging was defined when hysterectomy and salpingo-oophorectomy was performed together with lymph node sampling, with or without omentectomy. ER, PR, and Her2/*neu* expression were obtained from the data set of our previous study (Srijaipracharoen et al., 2010).

Progression-free survival (PFS), overall survival (OS), and cancer-specific survival were determined. PFS was defined as an interval from the end date of treatment to the time of recurrence or progression of disease. For the patient who was lost to follow up, PFS data were right censored at the time of the last evaluation or contact when the patient was known to be progression free. OS and cancer-specific survival were defined as the time from the date of diagnosis to the date of all deaths from any cause and EMC-related death, respectively. For patients who were still alive at the time of the study, survival data were right censored at the date of the last follow-up visit.

Data were analyzed using SPSS statistical software, version 11.5 (SPSS Inc., Chicago, IL). Descriptive statistics were used to analyze demographic data, which were summarized as number and percentage or median and range. OS and PFS were analyzed by the Kaplan-Meier method and were compared between the groups with the log rank test. Cox regression was used for multivariate analysis to determine independent prognostic factor(s). P values of <0.05 were considered statistically significant.

Results

During the study period, 41 young EMC patients were identified as cases (15.7% out of 261 EMC patients with available data) while 123 patients aged > 45 were selected as controls. Mean age of cases and controls were 40.4 ± 3.7 years (range, 30-45 years) and 58.4 ± 8.3 years (range, 46-84 years), respectively. The clinical characteristic features

Table 1. Clinical Characteristic Features

Characteristic features	Cases n (%)	Controls n (%)	p value
Parity (N=105)			0.004
Nulliparous (n=34)	14 (58.3)	20 (24.7)	
Parous (n=71)	10 (41.7)	61 (75.3)	
Other illness (N=128)			0.036
No (n=33)	12 (42.9)	21 (21.0)	
Yes [a] (n=85)	16 (57.1)	79 (79.0)	
Symptoms (N=142)			0.739
Abnormal bleeding (n=66)	16 (47.1)	50 (46.3)	
Pelvic mass (n=18)	6 (17.6)	12 (11.1)	
Combined mass / bleeding (n=57)	12 (35.3)	45 (41.7)	
Abnormal Pap smear (n=1)	0	1 (0.9)	
Synchronous/metachronous cancers (N=164)			0.765[b]
No	36 (87.8)	109 (88.6)	
Yes	5 (12.2)	14 (11.4)	
Breast cancer	0	6 (4.9)	
Ovarian cancer	5 (12.2) [c]	2 (1.6)	
Colonic cancer	0	2 (1.6)	
Pre-invasive cervical cancer	0	2 (1.6)	
Vulvar cancer	0	1 (0.8)	
Appendiceal carcinoid tumor	0	1 (0.8)	

[a]Other illnesses included one or more of the following: diabetes mellitus, dyslipidemia, hypertension, ischemic heart diseases, obesity, past history or current thyroid diseases, history of other cancers; [b]p value comparing presence of synchronous or metachronous cancer between cases and controls; [c]All five cases of synchronous ovarian cancer had pelvic masses as the presenting symptom

Table 2. Type of Surgery and Surgico-Pathological Findings of Endometrial Cancer Patients (N=164)

Surgico-pathological features	Case n (%)	Control n (%)	p value
Type of surgery (N=164)			
Complete surgical staging [a] (n=158)	40 (97.6)	118 (95.9)	0.537
Incomplete surgical staging (n=4)	1 (2.4)	3 (2.4)	
Post radiation surgery (n=2)	0	2 (0.8)	
Histopathology (N=164)			
Endometrioid carcinoma, pure or mixed [b] (n=153)	41 (100.0)	112 (91.1)	0.067
Others histopathology [c] (n=11)	0	11 (8.9)	
Grade (N=164)			
I (n=37)	20 (48.8)	17 (13.8)	< 0.001
II-III (n=127)	21 (51.2)	106 (86.2)	
Lymph node status			
Positive pelvic nodes (n=21/155)	1 (2.5)	20 (17.4)	0.036
Positive para-aortic nodes (n=10/127)	0	10 (100.0)	0.062
Positive lymph node (n=25/157)	1 (2.5)	24 (20.5)	0.015
Positive cervical involvement (n=40/164)	8 (19.5)	32 (26.0)	0.529
Presence of lymph-vascular space invasion (n=33/164)	6 (14.6)	27 (22.0)	0.431
Myometrial invasion (N=164)			
Endometrium only (n=14)	5 (12.2)	9 (7.3)	0.003 [d]
Inner half (n=93)	30 (73.2)	63 (51.2)	
Outer half (n=57)	6 (14.6)	51 (41.5)	
Positive peritoneal cytology (n=3/132)	0	3 (2.9)	1.000
Staging (N=162)			
Stage I-II (n=128)	37 (90.2)	91 (75.2)	0.069
Stage III-IV (n=34)	4 (9.8)	30 (24.8)	
Immunohistochemical study of hormonal receptors (N=129)			
Positive ER expression (n=80)	28 (77.8)	52 (55.9)	0.036
Positive PR expression (n=92)	35 (97.2)	57 (61.3)	<0.001
Positive Her2/neu expression (n=6)	3 (8.3)	3 (3.2)	0.348

[a]Complete surgical staging referred to hysterectomy plus salpingoophorectomy and lymph node sampling ± omentecotmy; [b]Other mixed components in endometrioid CA: squamous (n=17), serous (n=3), clear or muicnous or neuroendocrine (n=3); [c]Other histopathology: carcinocsarcoma (n=3), clear cell carcinoma (n=3), serous carcinoma or villoglandular carcinoma (n=5); [d]p value comparing endometrial and inner half of myometrial invasion versus outer half of invasion

of the cases and controls are shown in Table 1. Cases were more frequently nulliparous and had lesser medical morbidity. Abnormal uterine bleeding was the most common presenting symptom in both cases and controls. Pelvic mass accompanying abnormal uterine bleeding or pelvic mass alone was also found to be similar in both groups: 52.9% cases (n=18) and 52.8% controls (n=57). Eight cases and one control, who presented with masses, were revealed to have had EMC intra- or postoperatively. Pelvic masses were found to be synchronous ovarian cancer in five cases and two controls; metastatic ovarian tumors in two controls; and leiomyoma, adenomyosis, or benign ovarian cyst in the remaining subjects. These conditions constituted 5.5% of co-existing ovarian tumors—as synchronous ovarian tumors in 12.2% of the cases and 1.6% of the controls and as metastatic ovarian tumors in 1.6% of the controls. Metachronous cancers of other sites were found only in the controls.

Except two patients in the control group, one aged 64 years with gross parametrial involvement and the other aged 56 years with poor performance status who had preoperative radiation treatment, all other 162 patients had primary surgical treatment. The surgery was complete surgical staging in 40 cases (97.6%) and 118 controls (95.9%). Among those who had lymph node resection, 33 cases (82.5%) and 86 controls (72.9%) had both pelvic and para-aortic node resection while the remaining had either pelvic or para-aortic nodal surgery.

We studied the association between age (cases vs controls) and various clinico-pathological features (Table 2). Cases appeared to have had a higher association with many favorable surgico-pathological characteristic features as compared to controls. However, the associations were significant only for grade, lymph node status, depth of myometrial invasion, and ER and PR expression. Although early stage disease and endometrioid histology were more commonly found in cases than controls (90.2% vs 75.2% for stage and 100.0% vs 91.1% for histology), these did not reach statistical significance (p=0.069 for stage and 0.067 for histology). Of note, endometrial tissue (areas not involved by cancer) of cases and controls had different pathological features: complex endometrial hyperplasia (with or without atypia) in 70% of cases and 21.9% of controls, functional endometrium (30% vs 18.8%), or atrophic change (0% vs 59.4%) (p=0.008).

After primary surgery, 12 cases (29.3%) and 57 controls (46.3%) had adjuvant therapy (p=0.083). Nine patients from the control group had progressive disease: four stage III patients had adjuvant hormonal or radiation therapy after surgery while the other five stage III or IV patients had no adjuvant treatment. From a median follow-up of 64.3 months (range, 4.4-212.3 months) for cases and 45.2 months (range, 0.4-185.9 months) for controls, two cases (4.9%) and 14 controls (11.4%) experienced recurrences while the remaining 39 cases and 109 controls had no new EMC-related events (p=0.043). At the time of

Table 3. Adjuvant Treatment and Outcomes of Endometrial Carcinoma Patients

Characteristic features	Case n (%)	Control n (%)	P value
Adjuvant treatment (N=69)	12 (29.3)	57 (46.3)	0.083
External radiation therapy (n=9)	0	9 (7.3)	
Brachytherapy (n=9)	4 (9.8)	5 (4.1)	
External radiation and brachytherapy (n=42)	5 (12.2)	37 (30.1)	
Radiation plus chemotherapy (n=2)	0	2 (1.6)	
Chemotherapy (n=3)	2 (4.9)	1 (0.8)	
Hormonal therapy (n=4)	1 (2.4)	3 (2.4)	
Outcomes after primary treatment (N=164)			0.060 [a]
No new events relevant to endometrial cancer (n=139)	39 (95.1)	100 (81.3)	
Progressive diseases (n=9)	0	9 (7.3)	
Recurrences (n=16)	2 (4.9)	14 (11.4)	
Local recurrence	0	3 (2.4)	
Distant metastasis	2 (4.9)	10 (8.1)	
Local and distant recurrences	0	1 (0.8)	
Status (N=164)			0.010[b]
Alive (n=134)	39 (95.1)	95 (77.2)	
Dead of endometrial cancer (n=21)	1 (2.4)	20 (16.3)	
Dead of other causes (n=9)	1 (2.4)	8 (6.2)	

[a]Compared between new events (progressive diseases and recurrences) and no new events of cases and control; [b]Compared between alive and dead (dead of both endometrial cancer and other causes) of cases and control

Table 4. Survival of Patients According to Age (Case And Control) and Other Characteristic Features (N=164)

Characteristic features	n	5-year DFS (95% CI)	P value	5-year OS (95% CI)	P value	5-year CA specific survival (95% CI)	P value
Age							
Young (≤45 years)	41	97.2 (91.8-100.0)		93.1 (83.7-100.0)		97.1 (91.6-100.0)	
Older (> 45 years)	123	79.6 (71.9-87.3)	0.023	78.8 (71.1-86.4)	0.005	83.2 (76.2-90.2)	0.020
Stage							
Early	128	97.3 (94.3-100.0)		92.0 (86.6-97.4)		97.0 (93.5-100.0)	
Advance	34	32.0 (12.6-51.5)	<0.001	48.6 (31.2-65.9)	<0.001	48.6 (31.2-65.9)	<0.001
Histopathology							
Endometrioid	153	87.1 (81.4-92.8)		86.0 (80.0-92.0)		89.9 (84.8-95.0)	
Others	11	45.5 (16.0-74.9)	<0.001	22.7 (0-57.5)	<0.001	45.5 (16.0-74.9)	<0.001
Grade							
I	37	100.0		94.7 (84.7-100.0)		100.0	
II-III	127	79.5 (72.0-87.0)	0.004	78.5 (71.0-86.1)	0.006	82.8 (75.8-89.8)	0.009
Immunohistochmeical expression (N=129)							
ER expression							
Negative	49	72.1 (59.0-85.2)		66.4 (52.2-80.6)		74.7 (61.2-88.1)	
Positive	80	91.0 (83.9-98.1)	0.004	92.1 (85.1-99.0)	<0.001	94.5 (89.2-99.8)	0.006
PR expression							
Negative	37	71.4 (56.1-86.6)		67.9 (52.0-83.8)		76.5 (61.9-91.0)	
Positive	92	88.8 (81.7-96.0)	0.013	88.0 (80.4-95.6)	0.017	91.4 (85.2-97.6)	0..044
Her2/ neu expression							
Negative	123	85.8 (79.1-92.4)		83.9 (76.7-91.2)		89.4 (83.6-95.1)	
Positive	6	44.4 (0.9-88.0)	0.014	44.4 (0.9-88.0)	0.029	44.4 (0.9-88.0)	<0.002

this report, 39 (95.1%) cases and 95 (77.2%) controls were alive without any evidence of disease (p=0.005). Amongst the two (4.9%) cases and 28 (22.8%) controls who were dead, the cause of death in one case and 20 controls was EMC while other medical illnesses were responsible for the death of the remaining cases and eight controls. The only case who died of EMC had declined adjuvant treatment for stage III disease; she then experienced a recurrence at 3 months and was dead 11 months after primary surgery. Data for adjuvant treatment and outcomes of EMC patients are shown in Table 3.

Table 4 shows the association of age and other clinicopathological features with survival. Results of univariate analyses suggest that patients with younger age (cases), early stage disease, endometrioid histopathology, grade I tumor, positive ER or PR, and negative Her2/*neu* expression had significantly longer survivals than older patients (controls) and other comparative groups. After adjustments for other prognostic factors using multivariate analyses, age was not found to be a significant prognostic factor while stage; histopathology; and expression of ER, PR, and Her2/*neu* were significant predictors for survivals.

Discussion

In Western countries, the prevalence of EMC in young women varies from 3% to 18% using age <40 or <45 years (Evans-Metcalf et al., 1998; Ben-Arie et al., 2004; Navarria et al., 2009) and up to 35% using age <60 years to define "young" (Aziz et al., 1996). We used the age <45

years criterion and observed 15.7% prevalence of EMC in young adults as compared to 10% (Manchana et al., 2008) and 18% (Hanprasertpong et al., 2008) prevalence reported in other institutions in Thailand. Our young EMC patients had a median age of 41 years, which was similar to that reported in other studies, including 35 (Chen et al., 1998), 37 (Manchana et al., 2008), 39 (Navarria et al., 2009), and 41 years (Soliman et al., 2005; Hanprasertpong et al., 2008; Richte et al., 2009).

Our findings were consistent with those of other studies in young EMC patients, which also reported abnormal uterine bleeding as the most common symptom (Evans-Metcalf et al., 1998; Navarria et al., 2009; Richter et al., 2009). In addition, previous studies also noted that the abnormal uterine bleeding in young women was frequently misinterpreted as dysfunctional bleeding, which could lead to a delay in diagnosis (Chen et al., 1998; Evans-Metcalf et al., 1998; Ben-Arie et al., 2004; Pellerin et al., 2005). Another study found that 9% of young patients diagnosed with EMC underwent surgery because of a presumed benign disease (Navarria et al., 2009). Our study demonstrated that the dominating pelvic masses, especially in younger women, attracted more attention from the physicians as compared to a minor symptom of bleeding because eight of our cases and only one control had EMC as an incidental finding from a preoperative diagnosis of myoma or ovarian masses.

Some predisposing factors commonly reported in young EMC patients in studies from the West as well as in the two studies from Thailand included nulliparity (Soliman et al., 2005; Hanprasertpong et al., 2008; Manchana et al., 2008; Navarria et al., 2009), obesity (Soliman et al., 2005; Hanprasertpong et al., 2008; Manchana et al., 2008), chronic anovulation or infertility (Soliman et al., 2005), polycystic ovary syndrome (Evans-Metcalf et al., 1998; Uharcek et al., 2008), and other medical illnesses such as diabetes and hypertension (Evans-Metcalf et al., 1998; Soliman et al., 2005; Hanprasertpong et al., 2008). Some authors even reported that these risk factors could be demonstrated in approximately 20%-50% of young EMC patients (Chen et al., 1998; Evans-Metcalf et al., 1998; Hanprasertpong et al., 2008). We also found that our cases were more nulliparous and had lesser prevalence of medical illnesses than the control group. Unfortunately, data regarding the other associated features such as body mass index or chronic anovulation were not available in our study.

Some authors studied various etiologic risk factors for EMC in young patients as fractions of exposure and occurrence (Parslov et al., 2000). Statistically significant odds ratios for EMC in young women included 2.1 for positive family history, 0.2-0.3 for parity ≥2, and 0.2 for 1 to 5 years use of oral contraceptives (Parslov et al., 2000). The familial risk, which includes Lynch syndrome, is a well recognized risk factor especially in Western countries and has been reported in 5%-9% of young EMC patients (Berends et al., 1999; Lu et al., 2007; Richter et al., 2009). Limited by being a retrospective study, we could obtain only the history of other cancers in an individual but not the familial history of cancers. Among metachronous cancers, which were identified only in the control group, inadequate data were available to indicate whether the events were sporadic or familial. This limitation was also reported in another study wherein some clinical features, especially familial history, were frequently missing (Navarria et al., 2009).

Synchronous ovarian tumor is another important feature in young EMC patients and were reported in 4%-25% of young patients (Metcalf et al., 1998; Soliman et al., 2005; Walsh et al., 2005; Evans-Navarria et al., 2009; Richter et al., 2009), including in the reports from Thailand, which found 7% (Manchana et al., 2008) and 14% (Hanprasertpong et al., 2008) of patients with this event. These figures are higher than the 2%-5% prevalence observed in older patients (Evans-Metcalf et al., 1998; Manchana et al., 2008; Navarria et al., 2009). We observed similar findings with previous studies wherein synchronous tumor was more commonly found in younger patients as compared to the older ones (12.2% vs 1.6%, respectively). This feature should be regarded as a precaution during a surgical approach in young EMC patients taking into account ovarian preservation or surgical techniques for ovarian cancer including additional sampling of peritoneal tissue.

Most studies found low-risk features in young EMC patients, e.g., low grade tumor (Rosenberg et al., 1989; Chen et al., 1998; Evans-Metcalf et al., 1998; Tran et al., 2000; Uharcek et al., 2008), endometrioid histology (Walsh et al., 2005), early stage disease (Rosenberg et al., 1989; Chen et al., 1998; Evans-Metcalf et al., 1998; Uharcek et al., 2008; Navarria et al., 2009; Richter et al., 2009), and less myometrial invasion (Rosenberg et al., 1989; Tran et al., 2000; Uharcek et al., 2008). However, others have found no difference in these prognostic factors between younger and older patients in terms of grade (Tran et al., 2000; Navarria et al., 2009), histopathology (Evans-Metcalf et al., 1998; Tran et al., 2000; Navarria et al., 2009), or stage (Tran et al., 2000). These inconsistent findings were also observed in the two previous studies from Thailand (Hanprasertpong et al., 2008; Manchana et al., 2008). One study reported good prognostic features, including low grade tumor, endometriod carcinoma, early stage, and ≤50% myometrial invasion in EMC patients aged ≤45 years (Hanprasertpong et al., 2008), while the other study did not demonstrate any clinicopathological differences between EMC patients aged <40 years and older patients (Manchana et al., 2008). Our cases or young EMC patients appeared to have an association with favorable surgico-pathological characteristics in comparison with controls. The associations were statistically significant for grade, lymph node status, depth of myometrial invasion, and ER and PR expression but not for stage and histology. These favorable findings may help select patients who can be exempted from a complete surgical staging, including nodal resection, or select those who may respond to hormonal therapy. It is noteworthy that there were few studies reporting more frequent high-risk features in young EMC patients (Gitsch et al., 1995; Ben-Arie et al., 2004). However, the sample sizes in these studies were too small to merit a strong counter-argument.

For survival outcomes, we studied cancer-specific survival in addition to PFS and OS because we realized

the impact of medical illnesses on EMC patients (which are more common in the older age groups). Our study clearly demonstrated that younger age was a significantly favorable prognostic factor, with longer survival of cases as compared to controls. The previous studies from Thailand also reported excellent prognosis of EMC in younger patients with 5-year survival rates of 87% to 92% (Hanprasertpong et al., 2008; Manchana et al., 2008). In studies comparing survival of younger patients with older ones, conflicting data were reported. Some investigators found longer survival rates in younger patients as compared to older ones (Persson et al., 1984; Rosenberg et al., 1989; Uharcek et al., 2008) while others could not identify any significant survival difference between these age groups (Kaku et al., 1993; Tran et al., 2000; Manchana et al., 2008; Navarria et al., 2009). Few investigators additionally demonstrated that age was an independent favorable prognostic factor (Persson et al., 1984; Rosenberg et al., 1989). We could not demonstrate that age was an independent factor for survival after adjusting for other prognostic factors. Longer survival of young EMC patients may result from other favorable characteristic features such as positive hormonal receptors or negative Her2/neu expression, early stage, and endometrioid histology.

In conclusions, Young Thai EMC patients had more favorable clinicopathologic features, including higher expression of hormonal receptors. Although significantly longer survival of young EMC patients was observed by univariable analysis, this could not be confirmed by multivariable analysis. These findings might help the physician to counsel young endometrial cancer patients in terms of prognosis and tailor their treatment accordingly.

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