RESEARCH COMMUNICATION

Endometrial Cancer in Thai Women aged 45 years or Younger

Jitti Hanprasertpong[1]*, Suchada Sakolprakraikij[1], Alan Geater[2]

Abstract

The aim of this retrospective study was to clarify the clinopathologic profile of endometrial cancers in women aged 45 years or younger. All patients with histopathologically confirmed endometrial cancer treated at Songklanagarind Hospital from 1996-2005 were included. Of the 51 identified, 40 (78.4%) were in stage I, 7 (13.7%) in stage II, and 4 (7.8%) in stage III. The age range was 25-45 years (median 41) with a body mass index ranging from 17.6-44.2 (median 27.2). Eighty one percent reported abnormal vaginal bleeding, and twenty four percent polycystic ovaries. Prevalences of diabetes mellitus, hypertension and thyroid disease were 17.7%, 15.7%, and 3.9%, respectively. Seven cases (13.7%) had synchronous ovarian cancer with endometriod adenocarcinoma as the most common histopathological form. Forty patients had well differentiated, 8 moderately differentiated and 2 poorly differentiated tumors. The 5-year disease-free survival (and 95% CI) and 5-year overall survival rates were 88.0% (75.1-94.4%) and 87.5% (74.1-94.2%), respectively. Univariate analysis revealed that patients who had a history of hypertension or lymph node metastasis had a poor prognosis. We conclude that the majority of women aged 45 years or younger with endometrial cancer were obese and the tumors were most commonly in an early stage and were well differentiated.

Key Words: Endometrial cancer - young age - risk factor - synchronous tumor - prognosis

Asian Pacific J Cancer Prev, **9**, 58-62

Introduction

Endometrial cancer is the most common gynecological malignancy in the Western countries. The mean age for adenocarcinoma of the corpus uteri is 61 years (Soliman et al., 2005). Although primarily a disease of postmenopausal patients, 8-14% of these cancers are found in patients before 45 years of age (Evans-Metcalf et al., 1998; Tran et al., 2000; Pellerin and Finan, 2005). Young patients with endometrial cancer tend to have history of estrogen related disorders, such as chronic anovulation, nulliparity, obesity, polycystic ovarian syndrome, and use of sequential oral contraception (Gitsch et al., 1995; Evans-Metcalf et al., 1998; Tran et al., 2000; Soliman et al., 2005; Pellerin and Finan, 2005; Ota et al., 2005). The tumors in these patients are often estrogen receptor positive, which is believed to be a good prognostic indicator (Duska et al., 2001). Moreover, some authors have reported synchronous ovarian neoplasms were more common in these patients (Gitsch et al., 1995; Evans-Metcalf et al., 1998; Soliman et al., 2005; Tran et al., 2000).

Many studies in Western countries suggest that endometrial cancer in young patients is often associated with early stage disease, good differentiation, and an excellent prognosis (Gallup and Stock, 1984; Quinn et al.,1985; Colafranceschi et al., 1989; Kim et al., 1997; Pellerin and Finan, 2005). However, there have been very few Asian epidemiological reports concerning the clinicopathologic studies of endometrial cancer in premenopausal women (Kaku et al., 1993; Ota et al., 2005).

In Asian countries, and Thailand in particularly, the incidence of endometrial cancer is still low. It is the third in frequency after cervical cancer and ovarian cancer. The estimated incidence rate of endometrial cancer in Thailand is 2.9 per 100,000 female population while that of cervical cancer is 19.5 per 100,000 female population (Sriplung et al., 2003). This finding may reflect the differences in the genetic or ethnic background and lifestyle between Western and Thai patients. Therefore, to clarify the clinopathologic profile of young Thai patients, we performed a retrospective study of patients aged 45 years or younger with endometrial cancer who underwent treatment at our hospital.

Materials and Methods

After obtaining approval from the Research Ethics Committee of the Faculty of Medicine, Prince of Songkla University, a retrospective review of patients who had been treated for endometrial cancer at Songklanagarind Hospital from January 1, 1996 to December 31, 2005 was conducted.

The hospital records were reviewed for age at diagnosis, presenting symptoms, body mass index [calculated as weight (kg)/height (m^2)], parity, medical

*[1]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, [2]Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Songkhla 90110, Thailand, *For correspondence: Email ; hjitti@medicine.psu.ac.th*

Table 1. Characteristics of the 51 Patients with Endometrial Cancer

Characteristic		No. of patients (%)
Age (yr)	≤40	22 (43.1)
	40≤45	29 (56.9)
Chief complaint	Abnormal bleeding	43 (81.1)
	Pelvic pain	4 (7.6)
	Pelvic mass	4 (7.6)
	Other	2 (3.7)
BMI (kg/m2)	≤20	6 (11.8)
	20-25	13 (25.5)
	25-30	15 (29.4)
	>30	17 (33.3)
Parity	0	30 (58.8)
	1	7 (13.7)
	2	5 (9.8)
	3	8 (15.7)
	4	1 (2.0)
Medical comorbidity	Diabetes mellitus	9 (17.7)
	Hypertension	8 (15.7)
	Thyroid disease	2 (3.9)
Polycystic ovaries	No	39 (76.5)
	Yes	12 (23.5)

Table 2. Histopathology of 51 Patients with Endometrial Cancer

Characteristic		No. of patients (%)
Stage	I	40 (78.4)
	II	7 (13.7)
	III	4 (7.8)
Histology	Endometrioid	50 (98.0)
	Adenoacanthoma	1 (2.0)
Grade	1	40 (78.4)
	2	8 (15.7)
	3	2 (3.9)
Peritoneal cytology	Negative for malignancy	41 (80.4)
	Positive for malignancy	3 (5.9)
	Not done	7 (13.7)
Omental involvement	No	9 (17.6)
	Yes	1 (2.0)
	Not done	41 (80.4)
Cervical involvement	No	45 (88.2)
	Yes	6 (11.8)
Depth myometrial invasion	None	13 (25.5)
	≤50%	32 (62.7)
	>50%	6 (11.8)
Ovarian metastasis	No	48 (94.1)
	Yes	3 (5.9)
Lymph node involvement	No	28 (54.9)
	Yes	2 (3.9)
	Not done	21 (41.2)

comorbidity (diabetes mellitus, hypertension, thyroid disease), polycystic ovaries, synchronous ovarian cancer, International Federation of Gynecology and Obstetrics (FIGO) staging, histology, tumor grade, peritoneal cytology, omental metastasis, cervical involvement, depth of myometrial invasion, ovarian involvement and lymph node involvement.

Polycystic ovaries were considered present when enlarged ovaries with multiple small cysts were observed by ultrasound or pathological examination of surgical specimens. The diagnosis of synchronous primary cancers of ovarian and endometrial cancer was considered if the tumors had dissimilar histologies. When the ovarian histology resembled that of the uterus, a diagnosis of synchronous or metastatic malignancy was made based on the criteria proposed by Ulbright and Roth (Ulbright and Roth, 1985) or Scully et al. (Scully et al., 1998).

The histologic determination followed the World Health Organization Committee classification, and endometrial cancer stages were assigned based on the surgical staging criteria set forth by FIGO 1988. Postoperative adjuvant therapies (radiation and/or chemotherapy) were administered in cases of documented extrauterine disease and in selected patients with early stage disease based on histopathologic findings.

Survival times were calculated from the date of beginning of treatment until the date of death or last follow up. Disease-free survival was calculated from the date that the patients received surgery to the date of appearance a new lesion. Survival profiles of the entire group and subgroups were examining using Kaplan–Meier method and compared using the log-rank test. All tests were 2-sided; a P value of less than 0.05 was considered statistically significant. Statistical analysis of the data was carried out using STATA version 7 (Stata Corporation, Texas USA).

Table 3. Clinical Characteristics of 7 Patients with Synchronous Endometrial and Ovarian Cancer

Case	Age	Nulliparous	Endometrial		Ovarian		Treatment		Follow-up
	(year)	(Y/N)	Stage and grade	Histology	Stage and grade	Histology	Surgery	Adjuvant	(month)
1	42	N	Ia1	E	Ic1	E	TAH + BSO	PAC + CBDCA	NED (34)
2	45	N	Ib1	E	Ic3	E	TAH + BSO +P + O + L	CDDP + CPM	NED (32)
3	44	N	Ib1	E	IIIc1	M	TAH + BSO + P + O + L	CDDP + CPM	DWD (7)
4	36	N	Ib2	E	Ic1	E	TAH + BSO + P + O + A	CDDP + CPM	NED (57)
5	36	N	Ib1	E	Ic	G	TAH + BSO + P + O + L	XRT	NED (103)
6	43	Y	Ib1	E	Ic1	E	TAH + BSO + P + O + L	CDDP + CPM	NED (55)
7	45	Y	Ib1	E	IIIa1	E	TAH + BSO + P + O	CDDP + CPM	NED (79)

Y = yes, N = no, E = endometrioid, M = mucinous, G = granulosa cell, TAH = total abdominal hysterectomy, BSO = bilateral salpingo-oophorectomy, P = peritoneal washing, O = omentectomy, L = Lymph node sampling or dissection, A = appendectomy, PAC = paclitaxel, CBDCA = carboplatin, CDDP = cisplatin, CPM = cyclophosphamide, XRT = radiation, NED = no evidence of disease, DWD = dead with disease

Table 4. Univariate Analysis of 51 Patients with Endometrial Cancer

Variable	Level	Overall survival		Recurrence-free survival	
		5-yr survival (95% CI)	P-value	5-yr survival (95% CI)	P-value
Obesity (BMI>25)	No	78.6 (52.5-91.4)	0.107	78.6 (52.5-91.4)	0.222
	Yes	92.8 (73.8-98.2)		93.7 (76.9-98.4)	
Nulliparity	No	80.1 (55.2-92.1)	0.558	80.4 (55.8-92.2)	0.284
	Yes	93.3 (75.9-98.3)		93.3 (75.9-98.3)	
History of DM	No	90.2 (75.9-96.2)	0.333	90.2 (75.9-96.2)	0.373
	Yes	76.2 (33.2-93.5)		77.8 (36.5-93.9)	
History of hypertension	No	92.9 (79.6-97.7)	0.008	92.9 (79.6-97.7)	0.005
	Yes	56.3 (14.7-84.2)		56.3 (14.7-84.2)	
History of Thyroid disease	No	87.0 (73.1-94.0)	0.599	87.5 (74.2-94.2)	0.607
	Yes	100.0		100.0	
Polycystic ovaries	No	83.8 (67.4-92.4)	0.167	84.2 (68.2-92.6)	0.114
	Yes	100.0		100.0	
Synchronous ovarian cancer	No	87.9 (73.2-94.8)	0.760	88.3 (74.2-95.0)	0.950
	Yes	85.7 (83.4-97.9)		85.7 (83.4-97.9)	
Stage	I	89.4 (74.1-95.9)	0.524	89.9 (75.4-96.1)	0.807
	II	83.3 (27.3-97.5)		83.3 (27.3-97.5)	
	III	75.0 (12.8-96.1)		75.0 (12.8-96.1)	
	IV	-		-	
Histology	Endometrioid	87.2 (73.6-94.1)	0.713	87.7 (74.7-94.3)	0.719
	Other	≤100.0		≤100.0	
Grade	1	89.7 (74.8-96.0)	0.528	89.7 (74.8-96.0)	0.589
	2	75.0 (31.5-93.1)		75.0 (31.5-93.1)	
	3	100.0		100.0	
Positive cytology	No	87.0 (71.5-94.4)	0.555	87.5 (72.4-94.6)	0.452
	Yes	100.0		100.0	
Omental metastasis	No	87.5 (38.7-98.1)	0.724	87.7 (72.9-94.7)	0.724
	Yes	100.0		100.0	
Cervical involvement	No	88.4 (74.1-95.0)	0.685	88.8 (75.2-95.2)	0.811
	Yes	80.0 (20.4-96.9)		80.0 (20.4-96.9)	
Myometrial invasion	None	82.1 (41.4-95.3)	0.125	93.9 (49.4-95.7)	0.256
	≤50%	93.8 (77.3-98.4)		93.8 (77.3-98.4)	
	>50%	62.5 (14.2-89.3)		62.5 (14.2-89.3)	
Ovarian metastasis	No	86.7 (72.5-93.8)	0.515	87.2 (73.7-94.0)	0.393
	Yes	100.0		100	
Lymph node metastasis	No	95.5 (71.9-99.4)	<0.00005	96.3 (76.5-99.5)	<0.00005
	Yes	0		0	

BMI = body mass index, DM = diabetes mellitus, *Log rank test

Results

Of the total of 288 patients, 51 (17.7%) were 45 years of age or younger at the time of diagnosis and had undergone surgery from 1996-2005. Their characteristics are summarized in Table 1. The age range was 25-45 years (median 41) with body mass index ranging from 17.6-44.2 (median 27.2). The most common presenting symptom was abnormal vaginal bleeding (81.1%). Thirty women were nulliparous, seven had one child, and fourteen had more than one child. Prevalences of diabetes mellitus, hypertension and thyroid disease were 17.7%, 15.7%, and 3.9%, respectively. Twenty four percent had polycystic ovaries.

Histopathology of the 51 patients is shown in Table 2. The distribution by International Federation of Gynecology and Obstetrics surgical stage I, II, III and IV was 78.4%, 13.7%, 7.8% and 0%, respectively. Endometriod adenocarcinoma was the most common histological form of endometrial cancer. Forty patients had well differentiated tumors (G1), 8 moderately differentiated tumors (G2) and 2 poorly differentiated tumors (G3). Thirty cases (58.8%) had undergone lymph node dissection or sampling, and only two of these patients (6.7%) had lymph node involvement.

In seven cases (13.7%) had synchronous ovarian cancer (Table 3). Five patients (71.4%) had concordant endometriod histology of the endometrium and ovary (endometriod/endometriod). One case (14.3%) had an endometriod tumor of the endometrium and a component of mucinous cystadenocarcinoma in the ovary (endometriod/mucinous). The remaining one patient (14.3%) had an endometriod tumor of the endometrium and a component of granulosa cell carcinoma in the ovary (endometriod/granulosa). At the time of writing 6 in 7 cases are alive and free of disease after complete treatment.

The 5-year disease-free survival (DFS) (and 95% CI) and 5-year overall survival (OS) were 88.0% (75.1-94.4%) and 87.5% (74.1-94.2%), respectively. In univariate analysis (Table 4), DFS and OS were found to be statistically significantly poorer in patients with a history of hypertension (P value = 0.005, 0.008, respectively) and in node-positive patients (P value <0.00005, <0.00005, respectively).

Table 5. Summary of Selected Studies of Endometrial Cancer in Women 45 years or Younger

Authors	No	Stage (%)		Histology (%)		Grade (%)		Myometrial invasion (%)		Synchronous	PCO
		I, II	III, IV	E	others	1-2	3	≤50%	>50%	ovarian cancer(%)	(%)
Gitsch et al., 1995	17	70.6	29.4	94.1	5.9	94.1	5.9	NS	NS	29.4	17.7
Evans-Metcalf et al., 1998	40	74.3	25.6	88	12	NS	NS	NS	NS	10	NS
Tran et al., 2000	41	71	29	NS	NS	78	22	76	24	7	7
Pellerin et al., 2005	38	86.8	13.2	89.5	10.5	79	21	NS	NS	NS	NS
Hanprasertpong et al. (present study)	51	92.2	7.8	98	2	96.1	3.9	88.2	11.8	13.7	23.5

PCO = polycystic ovaries, E = endometrioid, NS = not stated

Discussion

Despite the conservative treatment approach for young women with endometrial cancer being very appealing; it should be remembered that the data are available only from small series or case reports, with short follow up time. The basic treatment for these patients consists of a staging laparotomy with total abdominal hysterectomy and bilateral salpingo-oophorectomy (Yamazawa et al., 2007). In the present study, we report the clinicophathological characteristics of 51 surgical cases of endometrial cancer in women aged 45 years or younger. The proportion of young patients in our study was 17.7%. This proportion is higher than in previous studies in Austria and the United States, which reported that the proportion in the range 6.7-13.8% (Gitsch et al., 1995; Evans-Metcalf et al., 1998; Tran et al., 2000; Pellerin and Finan, 2005).

Many studies suggest that diagnosis of endometrial cancer in young women can be difficult and delayed. It usually presents as abnormal uterine bleeding at an age when dysfunctional bleeding is much more common (Evans-Metcalf et al., 1998; Pellerin and Finan, 2005). Our study confirmed that the most common presenting symptom was abnormal vaginal bleeding (81.1%). Previous studies have reported that obesity, nulliparity and infertility are strongly associated with the development of endometrial cancer in young women (Soliman et al., 2005; Schmeler et al., 2005; Pellerin and Finan, 2005). This theory is supported in our finding that 62.7% of the patients had a body mass index (BMI) more than 25 kg/m2. Among 38 endometrial cancer patients 45 years of age or younger reported by Pellerin et al., 13% were overweight [BMI (25-30)] and 71% obese [BMI>30] (Pellerin and Finan, 2005). We found that 58.8% of patients were nulliparous, which is similar to previous study (Pellerin and Finan, 2005). Conditions associated with infertility or nulliparity have also been linked to occurrence of endometrial cancer, in particular polycystic ovarian syndrome, and granulosa-theca cell ovarian tumor (Purdie and Green, 2001).

Polycystic ovarian syndrome (PCOS) has been reported to be associated with the development of endometrial cancer for many years (Dockerty and Jackson, 1957). The mechanism which is generally assumed to be responsible for any increased risk of endometrial carcinoma in women with PCOS relates to prolonged anovulation with consequent continued secretion of estrogen unopposed by progesterone (Hardiman et al., 2003). However, the diagnostic criteria used to define PCOS have varied, making it difficult to establish the relationship between PCOS and endometrial cancer risk (Soliman et al., 2005). Previous studies have reported that proportions of PCOS and polycystic ovaries ranging from 7.4-30% (Gallup and Stock, 1984; Soliman et al., 2005) and 7-17.7% (Gitsch et al., 1995; Tran et al., 2000), respectively. In our retrospective study we found 23.5% of patients had polycystic ovaries.

Diabetes mellitus and hypertension are frequently associated with endometrial cancer (Purdie and Green, 2001). In part this association may relate to obesity but there is evidence for a specific effect of hyperinsulinaemia (Hardiman et al., 2003). Medical comorbidity of young women in our study showed that proportions of diabetes mellitus, hypertension and thyroid disease were 17.7%, 15.7%, and 3.9%, respectively. This finding is in agreement with study in the Unites States which showed the proportion of diabetes mellitus in patients 45 years of age and younger was 20% (Evans-Metcalf et al., 1998).

In our study, about 90% of patients had early stage, 98% of patients had endometriod carcinoma and 78% of patients had well differentiated tumors. The present findings seem to be consistent with previous studies (Table 5), which found that endometrial cancer in women 45 years or younger is often associated with early stage disease, favorable histologic type, good differentiation, and good prognosis (Gitsch et al., 1995; Evans-Metcalf et al., 1998; Tran et al., 2000; Pellerin and Finan, 2005). Myometrial invasion is relatively uncommon in premenopausal women (Tran et al., 2000; Nakanishi et al., 2001) which are in accord with our finding of 88.2% of patients with myometrial invasion ≤50%. As mentioned in the literature review, the incidence of ovarian metastases in women with early stage endometrial cancer has been reported to be approximately 5% (Boronow et al., 1984; Creasman et al., 1987). The incidence of ovarian metastasis in our study is slightly higher than that in other reports. This rate of ovarian metastasis has provided the basis for the practice of removing both ovaries at the time of surgery in young patients.

Synchronous primary endometrial and ovarian cancers represent an uncommon event and are found in 10% of women with ovarian cancer and 5% of women with endometrial cancer (Zaino et al., 2001). Pathologic criteria to distinguish synchronous primary cancers from metastatic lesions were first proposed by Ulbright and Roth (Ulbright and Roth, 1985), and were modified by Scully et al. (Scully et al., 1998). In a previous large series

of patients, women with synchronous primary cancer of the endometrium and ovary were young, obese, nulliparous, and premenopausal (Soliman et al., 2004). In our study, we found that incidence of synchronous ovarian cancer in endometrial cancer patients 45 years of age and younger was 13.7%. This finding is in agreement with previous study which showed that the incidence varies from 7-29.4% (Gitsch et al., 1995; Evans-Metcalf et al., 1998; Tran et al., 2000).

In our study, the 5-year disease-free survival (DFS) (and 95% CI) and 5-year overall survival were 88.0% (75.1-94.4%) and 87.5% (74.1-94.2%), respectively. This finding is in agreement with most series which showed the outcome of endometrial cancer in young patients has been excellent (Tran et al., 2000; Pellerin and Finan, 2005; Ota et al., 2005). Univariate analysis revealed that patients who had history of hypertension or lymph node metastasis had poor prognosis.

However, our results must be cautiously interpreted because of the retrospective nature of our study and the limited patient numbers and specific only to those aged 45 years or younger. Further research should be done to investigate the clinopathologic difference between patients aged 45 years or younger and older women with endometrial carcinoma before the association between age and endometrial cancer is more clearly understood.

In conclusion, the proportion of patients with endometrial cancer who were 45 years of age or younger in our study was 17.7%. The majority of patients was obese and nulliparous, and the cancer was most commonly as an early stage and had a high degree of tumor differentiation. In addition, there was a high number of synchronous ovarian cancer and polycystic ovaries. Univariate analysis revealed that patients who had a history of hypertension or lymph node metastasis had a poor prognosis.

Acknowledgement

This study received a full grant from the Faculty of Medicine, Prince of Songkla University.

References

Soliman PT, Oh JC, Schmeler KM, et al (2005). Risk factors for young premenopausal women with endometrial cancer. *Obstet Gynecol*, **105**, 575-80.

Evans-Metcalf ER, Brooks SE, Reale FR, Baker SP (1998). Profile of women 45 years of age and younger with endometrial cancer. *Obstet Gynecol*, **91**, 349-54.

Tran BN, Connell PP, Waggoner S, Rotmensch J, Mundt AJ (2000). Characteristics and outcome of endometrial carcinoma patients age 45 years and younger. *Am J Clin Oncol*, **23**, 476-80.

Pellerin GP, Finan MA (2005). Endometrial cancer in women 45 years of age or younger: a clinicopathological analysis. *Am J Obstet Gynecol*, **193**, 1640-4.

Gitsch G, Hanzal E, Jensen D, Hacker NF (1995). Endometrial cancer in premenopausal women 45 years and younger. *Obstet Gynecol*, **85**, 504-8.

Ota T, Yoshida M, Kimura M, Kinoshita K (2005). Clinicopathologic study of uterine endometrial carcinoma in young women aged 40 years and younger. *Int J Gynecol Cancer*, **15**, 657-62.

Duska LR, Garrett A, Rueda BR, et al (2001). Endometrial cancer in women 40 years old or younger. *Gynecol Oncol*, **83**, 388-93.

Gallup DG, Stock RJ (1984). Adenocarcinoma of the endometrium in women 40 years of age or younger. *Obstet Gynecol*, **64**, 417-20.

Quinn MA, Kneale BJ, Fortune DW (1985). Endometrial carcinoma in premenopausal women: a clinicopathological study. *Gynecol Oncol*, **20**, 298-306.

Colafranceschi M, Taddei GL, Scarselli G, et al (1989). Clinico-pathological profile of endometrial carcinoma in young women (under 40 years of age). *Eur J Gynaecol Oncol*, **10**, 353-6.

Kim YB, Holschneider CH, Ghosh K, Nieberg RK, Montz FJ (1997). Progestin alone as primary treatment of endometrial carcinoma in premenopausal women. Report of seven cases and review of the literature. *Cancer*, **79**, 320-7.

Kaku T, Matsuo K, Tsukamoto N, et al (1993). Endometrial carcinoma in women aged 40 years or younger: a Japanese experience. *Int J Gynecol Cancer*, **3**, 147-53.

Sriplung H, Sontipong S, Martin N, et al (2003). Cancer in Thailand Vol. III, 1995-1997. Bangkok: National Cancer Institute.

Ulbright TM, Roth LM (1985). Metastatic and independent cancers of the endometrium and ovary: a clinicopathologic study of 34 cases. *Hum Pathol*, **16**, 28-34.

Scully RE, Young RH, Clement PB (1998). Tumors of the ovary, maldeveloped gonads, fallopian tube, and board ligament. Washington Armed Forces Institute of Pathology. Atlas of Tumor Pathology.

Yamazawa K, Hirai M, Fujito A, et al (2007). Fertility-preserving treatment with progestin, and pathological criteria to predict responses, in young women with endometrial cancer. *Hum Reprod*, **22**, 1953-8.

Purdie DM, Green AC (2001). Epidemiology of endometrial cancer. *Best Pract Res Clin Obstet Gynaecol*, **15**, 341-54.

Dockerty MB, Jackson RL (1957). The Stein-Leventhal syndrome: analysis of 43 cases with special reference to association with endometrial carcinoma. *Am J Obstet Gynecol*, **73**, 161-73.

Hardiman P, Pillay OC, Atiomo W (2003). Polycystic ovary syndrome and endometrial carcinoma. *Lancet*, **361**, 1810-2.

Nakanishi T, Ishikawa H, Suzuki Y, et al (2001). Association between menopausal state and prognosis of endometrial cancer. *Int J Gynecol Cancer*, **11**, 483-7.

Boronow RC, Morrow CP, Creasman WT, et al (1984). Surgical staging in endometrial cancer: clinical pathologic findings of prospective study. *Obstet Gynecol*, **63**, 825–32.

Creasman WT, Morrow PC, Bundy BN, et al (1987). Surgical pathologic spread patterns of endometrial cancer. *Cancer*; **60**: 2035-41.

Zaino R, Whitney C, Brady MF, et al (2001). Simultaneously detected endometrial and ovarian carcinomas--a prospective clinicopathologic study of 74 cases: a gynecologic oncology group study. *Gynecol Oncol*, **83**, 355-62.

Soliman PT, Slomovitz BM, Broaddus RR, et al (2004). Synchronous primary cancers of the endometrium and ovary: a single institution review of 84 cases. *Gynecol Oncol*, **94**, 456-62.