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Original Article

Premenopausal early-stage endometrial carcinoma patients with low CA-125 levels and low tumor grade may undergo ovary-saving surgery

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Objective: The purpose of this study was to determine the possible predicting factors of coexisting adnexal malignancies, and to evaluate the safety of ovary-saving surgery for early-stage endometrial carcinoma in premenopausal patients.
Methods: A retrospective review of 107 patients with endometrial carcinoma who underwent surgical treatment at our institution was conducted. All patients were younger than 50 years of age and premenopausal status. Statistical analysis was performed.
Results: Of the 107 patients, 78 patients had stage I to II disease and both preoperative CA-125 levels were measured and tumor grades evaluated. On multivariate analysis, preoperative CA-125 levels (p=0.018) and preoperative tumor grade (p=0.029) were independent predicting factors of adnexal diseases. The risk of coexisting ovarian malignancy was 1.8% in patients with preoperative CA-125 levels less than or equal to 34.5 U/ml and preoperative tumor grade 1 or 2. The risk increases to 20% for low CA-125 and grade 3, 13.3% for high CA-125 and grade 1 or 2, and 100% for high CA-125 and grade 3. Between patients who underwent unilateral salpingo-oophorectomy and those who underwent bilateral salpingo-oophorectomy, there was no statistically significant difference in terms of BMI, preoperative CA-125 levels, FIGO stage, histology, tumor grade, lymphadenectomy, and adjuvant treatment.
Conclusion: Ovary-saving surgery for premenopausal, early-stage endometrial cancer patients may be considered as a treatment option in those with low preoperative CA-125 and low tumor grade.

Key Words: Premenopausal women, Endometrial carcinoma, Ovary-saving surgery

INTRODUCTION

Endometrial cancer mostly affects postmenopausal women. Approximately 75% of endometrial cancers occur after the age of 50 years, and 5-30% before the age of 50 years.[1] Standard surgical treatment of endometrial carcinoma is total hysterectomy, bilateral salpingo-oophorectomy (BSO), peritoneal washings for cytology, and selective pelvic and para-aortic lymphadenectomy.[2] Removal of the adnexa is important for determining the extent of disease and eliminating the potential risk of adnexal disease. However, a surgeon may hesitate to perform BSO for a premenopausal woman diagnosed with early-stage endometrial cancer. Many women with early-stage endometrial carcinoma wish to preserve ovary and maintain their endocrine function. Considering whether it is possible to preserve ovary without compromising survival, it is essential to identify possible adnexal diseases for the successful ovary-saving surgery.

Several reports have estimated that the incidence of coexisting ovarian malignancy (primary or metastatic) is 5-29% of patients with endometrial carcinoma.[3-5] The prognosis of primary or metastatic ovarian cancers is quite different. Some investigators reported that synchronous early-stage ovarian cancers coexisting with endometrial cancers showed a favorable prognosis.[6-8] One prospective study demonstrated that the 5-year and 10-year survival rate was 85.9% and 80.3%, respectively, in women with dual primary carcinomas of the endometrium and ovary, with gross disease confined to the pelvis.[6] On the other hand, others reported that the prognosis for women with ovarian metastasis was relatively poor.[9-12] Two retrospective studies for large numbers of cases revealed the 5-year disease-free survival rate with a range of 37.1 to 72.2%.[11,12]

Although a recent report from M.D. Anderson Cancer

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Center showed a high rate of synchronous primary ovarian cancers,[13] some studies have focused on the preservation of ovarian function in young, premenopausal women with endometrial carcinoma.[4,5] There have been few studies comparing prognosis in patients undergoing USO (unilateral salpingo-oophorectomy) with BSO, and evaluating the predictors of coexisting adnexal diseases preoperatively.

The purpose of this study was to determine if premenopausal women with endometrial carcinoma could be candidates for ovarian preservation. We have also identified preoperative clinic-pathological factors of predicting adnexal diseases. The minor objective of this study was to evaluate which cut-off value of preoperative CA-125 level as a prognostic factor is optimal in premenopausal women with endometrial carcinoma, and to estimate the effect of unilateral adnexectomy on premenopausal patients with early-stage endometrial carcinoma.

MATERIALS AND METHODS

Between January 2002 and December 2007, we identified all patients from the hospital database who were treated by primary surgery for endometrial carcinoma at Ajou University Hospital, after obtaining Institutional Review Board approval. Patients were excluded if they were in postmenopausal status or older than 50 years of age. A total of 107 patients were eligible for these criteria and finally included. In this study population, 10 patients who have already been reported in a recent study by the KGOG[14] were included. The diagnosis of endometrial carcinoma was made by office endometrial biopsy in 98 (91.6%) patients. Preoperative serum CA-125 measurements and preoperative magnetic resonance (MR) imaging were done in most patients (82.2% and 77.6%, respectively). The medical records were reviewed retrospectively for various clinico-pathological factors such as patient age, parity, body mass index (BMI), personal history of diabetes and hypertension, preoperative CA-125 levels, type of primary surgery, preoperative histology and tumor grade, preoperative MR findings, FIGO stage, histology, grade, tumor size, depth of myometrial invasion, cervical extension, adnexal involvement, lymph-vascular space invasion, lymph node metastasis, adjuvant therapy, duration of follow-up, and development of disease recurrence. Endometrial carcinoma was staged according to the FIGO surgical staging system.

All patients underwent total hysterectomy (abdominal or laparoscopic) and unilateral (USO) or bilateral salpingo-oophorectomy (BSO). Of the 107 patients, 85 (79.4%) patients had complete surgical staging procedures, including peritoneal washings and pelvic/para-aortic lymphadenectomy. Omentectomy and peritonectomy was performed for two patients with intra-abdominal and peritoneal spread. Adjuvant treatment was proposed for 26 (24.3%) patients with high-risk factors, such as advanced stage, high tumor grade or unfavorable histology.

A gynecologic pathologist reviewed all surgical specimens, and differentiated ovarian metastasis from synchronous primary cancers according to previously defined criteria:[15] 1) Synchronous primary ovarian cancer, characterized by superficial or no myometrial invasion, low grade endometrial and ovarian tumors, low stage endometrial and ovarian tumors, different grades between endometrial and ovarian sites, or different tumor histologies; 2) Ovarian metastasis, characterized by deep myometrial invasion, small ovary, bilateral ovarian involvement, vascular invasion, high grade tumors, and the pattern of extra-pelvic tumor spread.

Statistical analysis was performed using SPSS ver. 12.0 (SPSS Inc, Chicago, IL, USA). Clinical and pathologic factors were compared between two groups with Pearson's χ^2 test or Fisher's exact test for categorical data, and the Student *t* test and Mann-Whitney *U* statistic for continuous data according to normality. Multivariate analysis was performed using logistic regression to assess the impact of various factors on coexisting ovarian malignancy, and non-significant factors were removed in a stepwise fashion. Goodness-of-fit of the logistic model was confirmed by the Hosmer-Lemeshow test. A sig-

Table 1. Clinico-pathological characteristics of patients

Number of patients	107
Mean age, yr (range)	45 (27-50)
Mean parity (range)	2 (0-5)
Mean BMI, kg/m^2 (range)	24.6 (16.0-40.0)
Mean preoperative CA-125, U/ml (range)	21.5 (5.0-404.8)
Adnexectomy	
Unilateral salpingoophorectomy	38
Bilateral salpingoophorectomy	69
Lymphadenectomy	
Pelvic	36
Pelvic and para-aortic	71
Histology, no. (%)	
Endometrioid	98 (91.6)
Non-endometrioid	9 (8.4)
Papillary serous carcinoma	1
Mixed	4
Carcinosarcoma	4
Tumor grade, no. (%)	
I	83 (77.6)
II	13 (12.1)
III	8 (7.5)
NA	3 (2.8)
FIGO stage, no. (%)	
Stage I	84 (78.5)
Stage II	7 (6.5)
Stage III	14 (13.1)
Stage IV	2 (1.9)
Coexisting adnexal disease, no. (%)	9 (8.4)
Ovarian metastasis	6 (5.6)
Primary ovarian cancer	4 (3.7)
Lymph node metastasis, no. (%)	
Pelvic	8 (7.5)
Para-aortic	4 (3.7)
Follow-up, months (range)	36.1 (11-72)

BMI: body mass index, NA: not available, FIGO: federation of international gynecologic oncology.

nificant level of 0.05 was used for all tests.

RESULTS

Table 1 shows the clinico-pathological characteristics of the 107 patients. Mean preoperative CA-125 level was 21.5 U/ml (range, 5.0 to 404.8 U/ml). There was one case with discrepancy between the pre- and post operative tumor grade. Eighty-four patients had FIGO stage I disease, 7 had stage II, 14 had stage III, and 2 had stage IV disease. Nine (8.4%) patients had coexisting adnexal diseases; six had metastatic ovarian carcinomas; three had primary ovarian carcinomas and one had both of them at the time of diagnosis.

Table 2 demonstrates the results of univariate and multivariate analysis for various preoperative clinico-pathological factors of predicting coexisting ovarian diseases. High preoperative CA-125 levels (>34.5 U/ml) and grade 3 tumors correlated significantly with coexisting ovarian diseases (p=0.001 and p=0.038, respectively). A multivariate analysis using logistic regression revealed that preoperative CA-125 levels (odds ratio OR, 25.0; 95% confidence interval CI, 1.7 to 363.4; p=0.018) and preoperative tumor grade (OR, 23.9; 95% CI, 1.4 to 411.9; p=0.029) were significant predictors of coexisting ovarian malignancies.

Fig. 1 shows the ROC curve to determine the best cut-off point for predicting adnexal diseases. The best cut-off point was determined to be 34.5 U/ml, and the sensitivity and specificity was 85.7 and 80.2%, respectively (area under curve, 0.935; 95% CI, 0.871 to 0.999; p<0.001).

To evaluate the clinical significance of ovary-preserving surgery in premenopausal women with endometrial carcinomas, we identified a total of 82 patients who had stage I to II disease. We classified them into two groups - patients who underwent USO and those who underwent BSO and compared the two groups. Patients who underwent USO had younger age and low parity than those who underwent BSO (p<0.001 and p=0.029, respectively). There was no statistically significant difference in terms of BMI, preoperative CA-125 levels, FIGO stage, histology, tumor grade, lymphadenectomy, and adjuvant treatment. The mean duration of follow-up for all patients was 36.1 months (range, 11 to 72 months, 34.4 for USO and 36.9 for BSO). Two patients experienced disease recurrence. The first patient underwent total abdominal hysterectomy (TAH), USO,

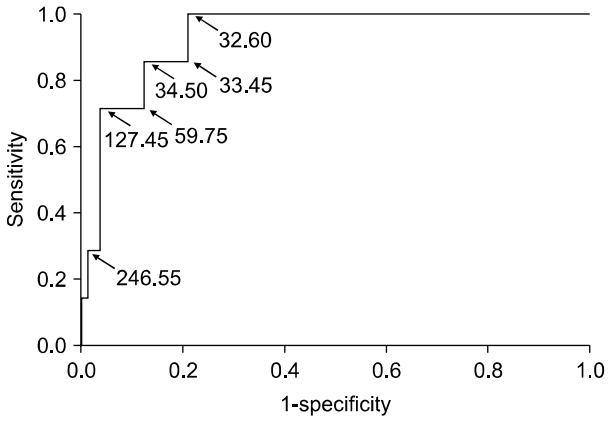

Fig. 1. ROC curve of preoperative CA-125 level for coexisting adnexal disease (AUC, 0.935; SE, 0.033; p<0.001; 95% CI, 0.871-0.999).

Table 2. Univariate and multivariate analysis of the association between coexisting adnexal disease and preoperative clinico-pathologic factors

Variable	Univariate			Multivariate				
	Adnexal involvement, no. (%)	OR (95% CI)	p-value	B	SE	Wald	OR (95% CI)	p-value
Preoperative CA-125			0.001					0.018
34.5 U/ml	1/66 (1.5)							
>34.5 U/ml	6/22 (27.3)	24.4 (2.7-217.0)		3.22	1.37	5.56	25.0 (1.7-363.4)	
Preoperative histology			0.241					0.086
Endometrioid	4/90 (4.4)							
Non-endometrioid	1/5 (20.0)	5.4 (1.5-59.8)		3.17	1.85	2.95	23.9 (0.6-892.1)	
Preoperative grade			0.038					0.029
Grade 1 or 2	3/79 (3.8)							
Grade 3	2/6 (33.3)	12.7 (1.6-98.6)		3.17	1.45	4.77	23.9 (1.4-411.9)	
MRI - Tumor size			0.072					0.585
≤2 cm	1/46 (2.2)							
>2 cm	7/57 (12.3)	6.3 (0.7-53.2)		-			-	
MRI - Myometrial invasion			0.586					
<1/2	5/72 (6.9)							
≥1/2	1/11 (9.1)	1.3 (0.1-12.7)						
MRI - Cervical invasion			0.999					
No	5/68 (7.4)							
Yes	1/15 (6.7)	0.9 (0.1-8.3)						

MRI: magnetic resonance imaging.

and pelvic/para-aortic lymphadenectomy for endometrioid adenocarcinoma, grade 1 on preoperative endometrial biopsy. On postoperative pathology, she had FIGO stage IB, carcinosarcoma. She received postoperative chemoradiation, but experienced recurrence in the pelvis 27 months after completion of adjuvant therapy. She was alive without disease after chemotherapy. The second patient had endometrioid adenocarcinoma, grade 3 on preoperative biopsy, and underwent TAH, BSO and pelvic/para-aortic lymphadenectomy. Final pathology showed FIGO stage IIB disease with the same histology and grade. She experienced recurrence in the brain 10 months after receiving postoperative chemoradiation. She died of disease during palliation chemotherapy. Due to the relatively small numbers of recurrences/deaths, progression-free and overall survival could not be analyzed (Table 3).

Table 3. Comparison of unilateral and bilateral adnexectomy for patients with FIGO stage I-II endometrial carcinoma

	Unilateral adnexectomy (N=29)	Bilateral adnexectomy (N=53)	p-value
Age (yr)	38.01±4.9	45.9±4.2	<0.001
Parity	1.3±1.0	1.9±0.9	0.029
BMI (kg/m^2)	24.7±3.1	25.2±4.1	0.529
CA-125 (U/ml)	23.7±16.7	33.0±42.3	0.317
Hypertension	2 (6.9)	9 (17.0)	0.313
Diabetes	1 (3.4)	3 (5.7)	0.999
FIGO stage			0.173
IA	15 (51.7)	17 (32.1)	
IB	8 (27.6)	28 (52.8)	
IC	2 (6.9)	5 (9.4)	
IIA	2 (6.9)	1 (1.9)	
IIB	2 (6.9)	2 (3.8)	
Histology			0.651
Endometrioid	28 (96.6)	49 (92.5)	
Non-endometrioid	1 (3.4)	4 (7.5)	
Grade			0.433
1	27 (93.1)	44 (84.6)	
2	2 (6.9)	6 (11.5)	
3	0	2 (3.8)	
Lymphadenenctomy			0.430
No	7 (24.1)	7 (13.2)	
Pelvic only	3 (10.3)	5 (9.4)	
Pelvic and para-aortic	19 (65.5)	41 (77.4)	
Adjuvant treatment	3 (10.3)	7 (13.2)	0.999
Disease recurrence	1 (3.4)	1 (1.9)	0.999

Four patients with synchronous primary ovarian cancers had endometrioid histology of the endometrium, and grossly enlarged ovarian masses at the time of surgery, except for one patient. On the postoperative pathologic reports, 2 patients showed papillary serous adenocarcinoma of the ovary, one showed endometrioid histology of the ovary, and the remaining one showed poorly differentiated granulosa cell tumor of the ovary. All patients with coexisting ovarian diseases had been suspected to have adnexal involvement preoperatively or intraoperatively, and underwent BSO (Table 4).

Fig. 2 shows the algorithm demonstrating the occurrence of coexisting adnexal disease in the cohorts of 78 patients with clinical stage I to II disease, and both preoperative CA-125 levels were measured and tumor grades evaluated. The risk of coexisting ovarian malignancy was 1.8% (1/57) in patients with preoperative CA-125 level less than or equal to 34.5 U/ml and preoperative tumor grade 1 or 2. The risk increases to 20% for low CA-125 and grade 3, 13.3% for high CA-125 and grade 1 or 2, and 100% for high CA-125 and grade 3.

DISCUSSION

Ovarian preservation for premenopausal women with endo-

Table 4. Details of 9 patients with coexisting adnexal disease

Patient	Age	Site	Histology (ovarian)	Lymph node metastasis	Intraoperative extrauterine disease	Endometrial stage and grade (ovarian stage) ovarian)	Major intraoperative findings
M1	49	LO	P	+	+	IVb3	LO, 6×5×4 cm, omental seeding
M2	52	LO	E	-	+	IIIa2	LO, 4×3×3 cm
M3	33	RO	E	-	+	IIIa1	RO, 10×6×4 cm with pedunculated nodules
M4	39	RO	E	+	+	IVb3	Peritoneal, omental, sigmoidal, cul-de-sac seeding
M5	47	BO	C	-	+	IIIa2	Peritoneal and omental seeding
S1	43	RO	E (P)	-	-	Ia1 (Ia)	RO, 4×3×2 cm, cystic
S2	45	LO	E (P)	-	+	IIIc3 (IIc)	LO, 5×4×4 cm, semicystic
S3*	46	RO	E (E)	-	+	IIIa1 (Ic)	RO, 9×8×5 cm, cancerous
S4	48	RO	E (G)	-	-	Ib1 (Ia)	NS

M1-M5: patients with extrauterine metastasis, S1-S4: patients with synchronous ovarian malignancy, E: endometrioid, P: papillary serous, C: carcinosarcoma, G: granulosa cell, RO: right ovary, LO: left ovary, BO: both ovary, NS: not significant.
*The patient S3 has both ovarian metastasis of uterine endometrial carcinoma and synchronous ovarian malignancy in final pathology.

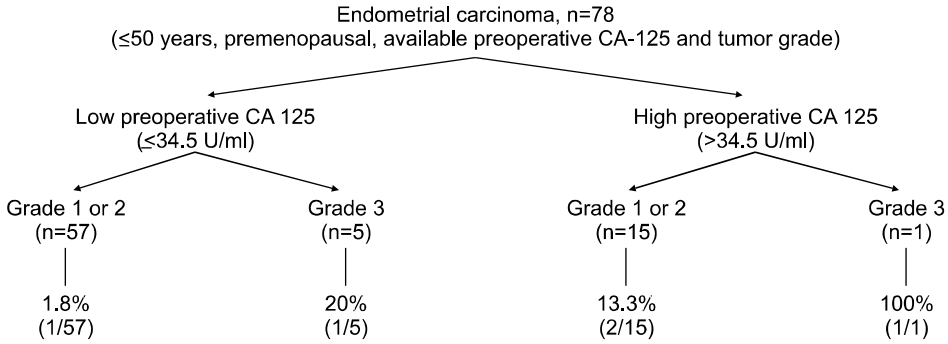

Fig. 2. Coexisting adnexal disease for the cohorts of 78 premenopausal women less than 50 years of age with endometrial carcinoma and who have available data of preoperative CA-125 and tumor grade.

metrial carcinoma has provoked a great deal of controversy. The first objective of this study was to estimate the occurrence of coexisting ovarian malignancy in premenopausal endometrial cancer patients. We found that 8.4% of premenopausal endometrial cancer patients under the age of 50 years had coexisting ovarian malignancy; synchronous primary ovarian cancer, 3.7% and ovarian metastasis, 5.6%. Previous studies have shown similar incidence to ours, with a range of 5 to 29%,[3-5] and this relatively high rate of adnexal involvement has not allowed premenopausal patients to undergo ovary-saving surgery.

We hypothesized that the preoperative prediction of potential adnexal involvement might be possible and that USO be performed safely in selected conditions, which have a low risk of adnexal disease. The second objective of this study was to determine various clinico-pathological factors in determining the need for BSO in premenopausal patients with endometrial carcinoma. On our univariate analysis, high preoperative CA-125 level ($p=0.001$) and preoperative tumor grade 3 ($p=0.038$) were significant preoperative factors predictive of adnexal involvement. Multivariate analysis showed that preoperative CA-125 levels and tumor grade were significant predictors of coexisting adnexal diseases. Serum CA-125 has become widely accepted as a useful marker for preoperative and postoperative evaluation in patients with endometrial carcinoma. In 1984, Niloff et al.[16] first described that serum CA-125 levels were elevated in patients with advanced or recurrent endometrial cancer. Other several reports revealed that the elevations of preoperative CA-125 were associated with advanced-stage disease and presence of extra-uterine disease.[17-20] Sood et al.[21] reviewed 210 women with endometrial carcinoma, and proposed that higher CA-125 levels (>35 U/ml) were associated with higher stage and grade, lymph node metastasis, and decreased survival. They also demonstrated that elevated CA-125 was the strongest predictor of extra-uterine disease. Koper et al.[22] showed that higher CA-125 levels significantly correlated with the adnexal involvement in patients with endometrial cancer.

The third objective of this study was to evaluate which cut-off value of preoperative CA-125 level is optimal in premenopausal women with endometrial carcinoma. Although many investigators regarded the CA-125 level of 35 U/ml as a cut-off level in endometrial carcinoma, some studies in early the 1990s reported that CA-125 levels lesser than 35 U/ml had prognostic significance in endometrial cancer.[23,24] Alagoz et al.[25] demonstrated that 95% of patients who had been free of disease after surgery for endometrial cancer had CA-125 levels less than 20 U/ml, and suggested that an optimal cut-off level in early detection of disease recurrence could be 20 U/ml. Other reports suggested that a CA-125 level of 20 U/ml is clinically useful for management of patients with endometrial cancer.[21,26,27] However, these results were derived from the studies of postmenopausal patients, and it is considered that the cut-off level of CA-125 greater than 20 U/ml be more appropriate in young, premenopausal patients. As shown in the ROC curve, the best cut-off point for predicting adnexal disease was 34.5 U/ml with good sensitivity and specificity.

The fourth objective of this study was to estimate the effect of unilateral adnexectomy on premenopausal patients with early-stage endometrial carcinoma. In our study, we compared the clinico-pathological outcomes of premenopausal women with early-stage endometrial carcinoma who underwent USO and BSO. We observed that there was no significant difference in disease recurrence between two groups. Although significant increases of age and parity were found in patients undergoing BSO, there were no significant differences in FIGO stage, postoperative histology and tumor grade, lymphadenectomy, adjuvant treatment, and the duration of follow-up. These results seem to indicate the possibility of ovary-saving surgery in endometrial cancer patients.

We wished to estimate whether adnexal involvement was predicted by preoperative CA-125 levels and tumor grade identified from our multivariate analysis. The occurrence of coexisting adnexal disease was in 1.8% (1/57) of patients with low preoperative CA-125 level and low-grade tumor. Because the patients had been expected to have ovarian malignancy preoperatively and undergone BSO, the actual risk of those who had low CA-125 and grade seemed to be negligible. Recently, some investigators suggested that ovarian preservation in young women with endometrial carcinoma could be feasible through careful preoperative and intraoperative assessment.[4,5,28,29] However, they demonstrated intraoperative

and postoperative factors but did not demonstrate which preoperative factors contributed to the prediction of coexisting ovarian malignancy, except the age of patients.

There are some limitations of our analysis that should be considered. First, all patients did not have preoperative assessments including endometrial biopsy, CA-125 measurements, or MR imaging, and comprehensive surgical staging. Second, the mean follow-up of 36.1 months is relatively short. Third, the small number of cases may be an obstacle to interpret our results appropriately. This is supported by the fact that in the multivariate analysis, the confidence interval of the variables is wide.

In conclusion, ovary-saving surgery seems to be a feasible procedure for premenopausal women with early-stage endometrial cancer, without worsening the prognosis. Based on the data presented in this report, we would carefully suggest the ovarian preservation in endometrial cancer patients with low preoperative CA-125 and low-grade tumors. Thorough intraoperative assessment in these patients should also be performed to identify and remove the potential risk of adnexal involvement.

REFERENCES

1. Schmeler KM, Soliman PT, Sun CC, Slomovitz BM, Gershenson DM, Lu KH. Endometrial cancer in young, normal-weight women. Gynecol Oncol 2005; 99: 388-92.
2. Homesley HD. Management of endometrial cancer. Am J Obstet Gynecol 1996; 174: 529-34.
3. Soliman PT, Slomovitz BM, Broaddus RR, Sun CC, Oh JC, Eifel PJ, et al. Synchronous primary cancers of the endometrium and ovary: a single institution review of 84 cases. Gynecol Oncol 2004; 94: 456-62.
4. Walsh C, Holschneider C, Hoang Y, Tieu K, Karlan B, Cass I. Coexisting ovarian malignancy in young women with endometrial cancer. Obstet Gynecol 2005; 106: 693-9.
5. Lee TS, Jung JY, Kim JW, Park NH, Song YS, Kang SB, et al. Feasibility of ovarian preservation in patients with early stage endometrial carcinoma. Gynecol Oncol 2007; 104: 52-7.
6. Zaino R, Whitney C, Brady MF, DeGeest K, Burger RA, Buller RE. Simultaneously detected endometrial and ovarian carcinomas: a prospective clinicopathologic study of 74 cases. A gynecologic oncology group study. Gynecol Oncol 2001; 83: 355-62.
7. Sheu BC, Lin HH, Chen CK, Chao KH, Shun CT, Huang SC. Synchronous primary carcinomas of the endometrium and ovary. Int J Gynaecol Obstet 1995; 51: 141-6.
8. Falkenberry SS, Steinhoff MM, Gordinier M, Rappoport S, Gajewski W, Granai CO. Synchronous endometrioid tumors of the ovary and endometrium: a clinicopathologic study of 22 cases. J Reprod Med 1996; 41: 713-8.
9. DiSaia PJ, Creasman WT, Boronow RC, Blessing JA. Risk factors and recurrent patterns in Stage I endometrial cancer. Am J Obstet Gynecol 1985; 151: 1009-15.
10. Morrow CP, Bundy BN, Kurman RJ, Creasman WT, Heller P, Homesley HD, et al. Relationship between surgical-pathological risk factors and outcome in clinical stage I and II carcinoma of the endometrium: a Gynecologic Oncology Group study. Gynecol Oncol 1991; 40: 55-65.
11. Takeshima N, Hirai Y, Yano K, Tanaka N, Yamauchi K, Hasumi K. Ovarian metastasis in endometrial carcinoma. Gynecol Oncol 1998; 70: 183-7.
12. Connell PP, Rotmensch J, Waggoner S, Mundt AJ. The significance of adnexal involvement in endometrial carcinoma. Gynecol Oncol 1999; 74: 74-9.
13. Soliman PT, Oh JC, Schmeler KM, Sun CC, Slomovitz BM, Gershenson DM, et al. Risk factors for young premenopausal women with endometrial cancer. Obstet Gynecol 2005; 105: 575-80.
14. Lee TS, Kim JW, Kim TJ, Cho CH, Ryu SY, Ryu HS, et al. Ovarian preservation during the surgical treatment of early stage endometrial cancer: a nation-wide study conducted by the Korean Gynecologic Oncololgy Group. Gynecol Oncol 2009; 115: 26-31.
15. Ulbright TM, Roth LM. Metastatic and independent cancers of the endometrium and ovary: a clinicopathologic study of 34 cases. Hum Pathol 1985; 16: 28-34.
16. Niloff JM, Klug TL, Schaetzl E, Zurawski VR Jr, Knapp RC, Bast RC Jr. Elevation of serum CA125 in carcinomas of the fallopian tube, endometrium, and endocervix. Am J Obstet Gynecol 1984; 148: 1057-8.
17. Duk JM, Aalders JG, Fleuren GJ, de Bruijn HW. CA-125: a useful marker in endometrial carcinoma. Am J Obstet Gynecol 1986; 155: 1097-102.
18. Rose PG, Sommers RM, Reale FR, Hunter RE, Fournier L, Nelson BE. Serial serum CA-125 measurements for evaluation of recurrence in patients with endometrial carcinoma. Obstet Gynecol 1994; 84: 12-6.
19. Patsner B, Mann WJ, Cohen H, Loesch M. Predictive value of preoperative serum CA-125 levels in clinically localized and advanced endometrial carcinoma. Am J Obstet Gynecol 1988; 158: 399-402.
20. Fanning J, Piver MS. Serial CA-125 levels during chemotherapy for metastatic or recurrent endometrial cancer. Obstet Gynecol 1991; 77: 278-80.
21. Sood AK, Buller RE, Burger RA, Dawson JD, Sorosky JI, Berman M. Value of preoperative CA-125 level in the management of uterine cancer and prediction of clinical outcome. Obstet Gynecol 1997; 90: 441-7.
22. Koper NP, Massuger LF, Thomas CM, Kiemeney LA, Verbeek AL. Serum CA-125 measurements to identify patients with endometrial cancer who require lymphadenectomy. Anticancer Res 1998; 18: 1897-902.
23. Granberg S, Wikland M, Friberg LG. Tumor marker CA-125 level and ovarian volume at different cycle day periods and in postmenopause. Int J Gynaecol Obstet 1990; 33: 149-52.
24. Zurawski VR Jr, Sjovall K, Schoenfeld DA, Broderick SF, Hall P, Bast RC Jr, et al. Prospective evaluation of serum CA-125 levels in a normal population, phase I: the specificities of single and serial determinations in testing for ovarian cancer. Gynecol Oncol 1990; 36: 299-305.
25. Alagoz T, Buller RE, Berman M, Anderson B, Manetta A, DiSaia P. What is a normal CA125 level? Gynecol Oncol 1994; 53: 93-7.
26. Kurihara T, Mizunuma H, Obara M, Andoh K, Ibuki Y, Nishimura T. Determination of a normal level of serum CA125 in postmenopausal women as a tool for preoperative evaluation and postoperative surveillance of endometrial carcinoma. Gynecol Oncol 1998; 69: 192-6.
27. Dotters DJ. Preoperative CA-125 in endometrial cancer: is it useful? Am J Obstet Gynecol 2000; 182: 1328-34.
28. Wright JD, Buck AM, Shah M, Burke WM, Schiff PB, Herzog TJ. Safety of ovarian preservation in premenopausal women with endometrial cancer. J Clin Oncol 2009; 27: 1214-9.
29. Richter CE, Qian B, Martel M, Yu H, Azodi M, Rutherford TJ, et al. Ovarian preservation and staging in reproductive-age endometrial cancer patients. Gynecol Oncol 2009; 114: 99-104.