Original Article
Prognostic indicators in patients with early stage endometrioid adenocarcinoma: a retrospective case-control study of 523 patients

Shien Zou, Hong Sun, Lingling Fan, Xirong Xiao, Lili Gong, Jin Zhu, Xing Chen

Department of Gynecology, Obstetrics and Gynecology Hospital of Fudan University, Shanghai 200011, China

Abstract: Objective: Endometrioid adenocarcinoma is a common malignant tumor of the female reproductive system. The factors of poor prognosis after surgery are still ambiguous. This study aimed to identify the risk factors for poor prognosis in postoperative patients with early stage endometrioid adenocarcinoma. Method: This was a retrospective case-control study of 523 patients who were treated at the Obstetrics and Gynecology Hospital of Fudan University. Patients were grouped into the favorable and unfavorable prognosis groups based on clinical outcomes. Charts and pathology reports were examined to extract prognostic factors. Results: In univariate analyses, there were significant differences in age, vimentin expression, estrogen receptor (ER) expression, and radiation therapy between the two groups. Two multivariate logistic models were used to examine the prognostic factors. In the first model (including age, vimentin, ER, and radiation therapy), positive vimentin expression was a protective factor (odds ratio (OR)=0.199, 95% confidence interval (95% CI): 0.054-0.734, P=0.015), while radiation therapy was a risk factor (OR=3.182, 95% CI: 1.080-9.376, P=0.036). In the second model (including age, surgical methods, differentiation degree, vimentin, ER, and progesterone receptor), positive vimentin (OR=0.173, 95% CI: 0.044-0.677, P=0.012) was a protective factor and radiation therapy (OR=3.302, 95% CI: 1.087-10.032, P=0.035) was a risk factor. Conclusion: Vimentin and ER expression could be possible factors of favorable prognosis in patients with early stage endometrioid adenocarcinoma, while radiation therapy could be a possible risk factor.

Keywords: Endometrioid cancer, prognostic indicators, vimentin, estrogen receptors

Introduction

Endometrioid adenocarcinoma is a common malignant tumor of the female reproductive system, representing about 7% of all cancers in women [1]. In the United Stated, there were about 42,000 new cases of endometrioid adenocarcinoma and 7780 deaths in 2009 [2]. Although the incidence of endometrioid adenocarcinoma is lower in developing countries, the mortality is higher [3]. Indeed, in Asian developing countries, the 2009 incidence was about 62,000, the mortality was 21,000, and the 5-year survival rate was 67%, compared with an incidence of 136,000, a mortality of 29,000, and a 5-year survival of 82% in developed countries [3].

Surgery is the main treatment for endometrioid adenocarcinoma. As most patients are diagnosed at early stages, a complete curative resection is often possible [4-6], but in case of treatment failure, patients will need radiation therapy and chemotherapy [5-7]. Radiation therapy is known to decrease the local recurrence rate by only 5% [8]. Moreover, the use of radiation therapy and chemotherapy for improving the prognosis of endometrioid adenocarcinoma is still controversial [9-11]. Some studies tried to identify risk factors for recurrence and have shown that depth of tumor invasion, vessel invasion, and expression of estrogen receptors (ER) and progesterone receptor (PR) were prognostic factor [12-14]. Indeed, Zhang et al. [12] have shown that age, PR, and depth of tumor invasion were independent risk factors for 5-year survival [12].

A comprehensive understanding of risk factors is still lacking, particularly the inclusion of radi-

ation therapy, chemotherapy, other treatments, and pathological characteristics as risk factors in predictive models. In addition, vimentin is expressed in most cases of endometrioid adenocarcinoma [15, 16], and most previous studies did not examine this marker. Therefore, the aim of the present large-scale retrospective case-control study was to identify and analyze the factors involved in the prognosis of early stage endometrioid adenocarcinoma.

Materials and methods

Patients and study design

This was a retrospective study of patients with endometrioid adenocarcinoma who underwent surgery between January 2009 and December 2011 at the Obstetrics and Gynecology Hospital of Fudan University. Eligibility criteria were: 1) confirmed diagnosis of stage I or II endometrioid adenocarcinoma; 2) underwent surgery; and 3) without any other cancer based on imagery and pathological examinations. Patients were excluded if they were lost to follow-up since no clinical outcome data was available. Patients were grouped into the favorable and unfavorable prognosis groups. Favorable prognosis was defined as no recurrence, no metastasis, and no death at the last visit available in the medical record system. Follow-up was censored on December 31st, 2013.

The present study was approved by the ethical committee of the Fudan University. The need for individual consent was waived by the committee because of the retrospective nature of the study.

Data collection

The Obstetrics and Gynecology Hospital of Fudan University has electronic charts. Age, height, and weight are recorded immediately at admission. Blood pressure and blood glucose are measured after an overnight fast. All surgical parameters and the presence of ascites were retrieved from the surgical recording. Differentiation degree, invasion, and the presence of lymphatic metastasis were retrieved from the pathology reports. The differentiation degree and stage of the tumor were scored according to the 2009 FIGO guidelines [17]. Immunohistochemistry examination was performed to detect cytokeratin (CK) 7, vimentin, cytokeratin AE1/AE3 (AE1/AE3), epithelial me-

mbrane antigen (EMA), CD10, ER, PR, P53, and/or Ki-67.

Follow-up

All patients underwent periodical follow-up every 3 months for the first 2 years and then every 6 months for years 3 and 4. They were asked to carry out periodical self-examination for suspicious lumps in breasts, chest-wall, and armpit, and to consult a doctor in case of suspicion. Each visit included a physical examination and breast and pelvic ultrasound. Patients were recommended to undergo mammography each year. Further computed tomography or magnetic resonance imaging was carried out in cases of suspected lesions.

Statistical analysis

Normally distributed continuous variables were presented as mean ± standard deviation and analyzed using the Student's t test. Non-normally distributed continuous variables were presented as median (range) and analyzed using the Mann-Whitney test. Categorical variables were presented as frequencies and analyzed using the chi-square test. Variables that were significantly different between the two groups in univariate analyses were included in a multivariate logistic regression model. A second model included the variables from model 1 and variables that were considered as clinically significant. All analyses were performed using SPSS 12.0 (SPSS Inc., Chicago, IL, USA). Two-sided *P*-values <0.05 were considered significant.

Results

Characteristics of the patients

A total of 523 patients were included (**Table 1**): 485 (92.7%) with stage I cancer and 38 (7.2%) with stage II. The median follow-up was 39 months. The favorable prognosis group included 505 patients and the unfavorable prognosis group included 18 patients. There was no significant difference in BMI, height, weight, follow-up time, prevalence of high blood glucose and diabetes mellitus, differentiation degree, tumor stage, invasion depth, tumor position, and number of pelvic and para-aortic lymph nodes and metastasis (all P>0.05). Patients in the unfavorable prognosis group were slightly older than patients in the favorable prognosis

Table 1. Characteristics of the patients according to prognosis

Parameters	Total (n=523)		Favorable prognosis		Unfavorable prognosis		P
	Value	N	Value	N	Value	N	
Age (years)	54 (30, 80)	523	54 (30, 80)	505	56.5 (43, 78)	18	0.031
BMI (kg/m^2)	24.35 (15.24, 41.02)	507	24.39 (15.24, 41.02)	489	23.63 (20.20, 29.73)	18	0.680
Height (cm)	160 (140, 172)	508	160 (140, 172)	490	160 (145, 172)	18	0.892
Weight (kg)	62 (36, 105)	522	62 (36, 105)	504	61.5 (52, 79)	18	0.761
Follow-up (months)	39 (21, 58)	509	39 (21, 58)	491	42.5 (23, 57)	18	0.726
High blood pressure	160 (30.65%)	522	154 (30.56%)	504	6 (33.33%)	18	0.802
Diabetes	46 (8.8%)	523	46 (9.11%)	505	0	18	0.359
Differentiation degree							
High	393 (77.36%)	508	381 (77.76%)	490	12 (66.67%)	18	0.374
Moderate	75 (14.76%)		71 (14.49%)		4 (22.22%)		
Low	40 (7.87%)		38 (7.76%)		2 (22.22%)		
Stage							
I	485 (92.73%)	523	468 (92.67%)	505	17 (94.44%)	18	1.000
II	38 (7.27%)		37 (7.33%)		1 (5.56%)		
Depth of muscle invasion							
Only inner membrane	101 (19.35%)	522	100 (19.84%)	504	1 (5.56%)	18	0.353
Superficial	349 (66.86%)		335 (66.47%)		14 (77.78%)		
Deep	72 (13.79%)		69 (13.69%)		3 (16.67%)		
Invasive vessels	54 (10.38%)	520	52 (10.36%)	502	2 (11.11%)	18	1.000
Cervix Invasion							
None	445 (85.00%)	523	429 (84.95%)	505	16 (88.89%)	18	1.000
Mucous layer	41 (7.84%)		40 (7.92%)		1 (5.56%)		
Mesenchyma	37 (7.7%)		36 (7.13%)		1 (5.56%)		
Pelvic Lymph nodes	20 (1, 44)	225	20 (1, 44)	217	17.5 (7, 27)	8	0.406
Pelvic lymphatic metastasis	1 (0.44%)	227	1 (0.46%)	219	0		1.000
Distant metastasis	0	523	0	505	0	18	---
Para aortic lymph nodes	3 (0, 10)	51	3 (0, 10)	50	4	1	0.731
Para aortic lymph node metastasis	0	51	0	50	0	1	---
Mirror/abdomen opening	64.50%/32.50%	523	67.72%/32.28%	505	61.11%/38.89%	18	0.556
Pelvic lymph node dissection (%)	225 (43.02%)	523	217 (42.97%)	505	8 (44.44%)	18	0.901
Ascites or abdominal fluid	0	283	0	272	0	11	---
Para aortic lymph node dissection (%)							
None	466 (89.10%)	523	450 (89.11%)	505	16 (88.89%)	18	1.000
Biopsy	27 (5.16%)		26 (5.15%)		1 (5.56%)		
Dissection	30 (5.74%)		29 (5.74%)		1 (5.56%)		
Chemotherapy	86 (16.48%)	522	80 (15.87%)	504	6 (33.33%)	18	0.101
Radiation therapy	80 (15.47%)	517	73 (14.63%)	499	7 (38.89%)	18	0.014

BMI: body mass index.

group (median, 56.5 (43-78) vs. 54.0 (30-80), P=0.031). More patients received radiation therapy in the unfavorable prognosis group (38.9% vs. 14.6%, P=0.014) (**Table 1**). No patient had ascites.

Immunohistochemistry

There were no differences between the two groups for CK7, AE1/AE3, EMA, ER, PR, P53, and Ki-67. Vimentin expression was lower in

the unfavorable group (P=0.009) while ER expression was higher (P=0.014) (**Table 2**).

Multivariate analyses

Since age, radiation therapy, ER, and vimentin were significantly different between the two groups in univariate analyses, they were included in a first multivariate logistic model. Results showed that positive vimentin expression was a protective factor (odds ratio (OR)=0.199, 95%

Table 2. Univariate analyses of immunohistochemistry markers with unfavorable prognosis (recurrence, metastasis, or death) of endometrioid carcinoma

Parameters	Total (n=523)		Favorable prognosis		Unfavorable prognosis		P
	Value	N	Value	N	Value	N	
CK7							
Negative	9 (2.24%)	401	9 (2.32%)	388	0	13	1.000
Positive	392 (97.76%)		379 (97.68%)		13 (100%)		
Vimentin							
Negative	25 (5.27%)	474	21 (4.60%)	457	4 (23.53%)	17	0.009
Positive	449 (94.73%)		436 (95.40%)		13 (76.47%)		
AE1/AE3							
Negative	3 (4.05%)	74	3 (4.29%)	70	0	4	1.000
Positive	71 (95.95%)		67 (95.71%)		4 (100%)		
EMA							
Negative	9 (4.25%)	212	9 (4.41%)	204	0	8	1.000
Positive	203 (95.75%)		195 (95.59%)		8 (100%)		
CD10							
Negative	190 (97.94%)		186 (97.89%)		4 (100%)		1.000
Positive	4 (2.06%)	194	4 (2.11%)	190	0	4	
ER							
Negative	30 (6.34%)	473	26 (5.70%)	456	4 (23.53%)	17	0.014
Positive	443 (93.66%)		430 (94.30%)		13 (76.47%)		
PR							
Negative	26 (5.50%)	473	23 (5.04%)	456	3 (17.65%)	17	0.060
Positive	447 (94.50%)		433 (94.96%)		14 (82.35%)		
P53							
Negative	368 (77.64%)	474	354 (77.46%)	457	14 (82.35%)	17	0.858
Positive	106 (22.36%)		103 (22.54%)		3 (17.65%)		
Ki-67 (median (range))	0.4 (0, 0.95)	474	0.4 (0, 0.95)	457	0.2 (0, 0.85)		0.299

CK: cytokeratin; AE1/AE3: cytokeratin AE1/AE3; EMA: epithelial membrane antigen; ER: estrogen receptors; PR: progesterone receptor.

confidence interval (95% CI): 0.054-0.734, P= 0.015), while radiation therapy was a risk factor (OR=3.182, 95% CI: 1.080-9.376, P=0.036) (**Table 3**).

To find out whether other relevant clinical factors could influence the association between age, radiation therapy, and vimentin and unfavorable prognosis, a second model was run and included clinically significant variables. In this second model, positive vimentin expression was protective factor (OR=0.173, 95% CI: 0.044-0.677, P=0.012), while radiation therapy was a risk factor (OR=3.302, 95% CI: 1.087-10.032, P=0.035) (**Table 4**).

Discussion

The factors of poor prognosis of endometrioid adenocarcinoma are still ambiguous. Therefore, the present study aimed to identify the risk factors for poor prognosis in patients with stage I or II endometrioid adenocarcinoma. Stages I and II were selected because they are the most commonly encountered in the clinical practice (about 86% vs. 14% for stages III and IV) [18, 19], and surgery is more likely to be performed on these patients. Results showed that in univariate analyses, there were significant differences in age, vimentin expression, ER expression, and radiation therapy between the two groups. Two multivariate logistic models were used to examine the prognostic factors. In the two models, positive vimentin expression was a protective factor, while radiation therapy was a risk factor.

A previous study by Zhang et al. [12] has shown that age and lymphovascular invasion were independent risk factors for local recurrence

Table 3. First multivariate logistic model (including significant variables in univariate analyses) of unfavorable prognosis (recurrence, metastasis, or death) as the dependent variable

Parameter	Value	β	Odds ratio	95% CI	P
Age		0.048	1.049	0.994-1.107	0.084
Vimentin	Negative		Reference		
	Positive	-1.614	0.199	0.054-0.734	0.015
ER	Negative		Reference		
	Positive	-0.859	0.423	0.113-1.593	0.204
Radiation therapy	Negative		Reference		
	Positive	1.157	3.182	1.080-9.376	0.036

CI: confidence interval.

Table 4. Second multivariate logistic model (including clinically significant variables)

Parameters	Value	β	Odds ratio	95% CI	P
Age		0.049	1.051	0.994-1.111	0.080
Surgical methods	Endoscopy		Reference		
	Laparotomy	0.304	1.355	0.479-3.834	0.567
Differentiation degree					
	High		Reference		
	Moderate	0.006	1.006	0.284-3.570	0.993
	Low	-0.440	0.644	0.101-4.107	0.641
Vimentin	Negative		Reference		
	Positive	-1.752	0.173	0.044-0.677	0.012
ER	Negative		Reference		
	Positive	-1.503	0.222	0.036-1.368	0.105
PR	Negative		Reference		
	Positive	-1.503	0.222	0.036-1.368	0.105
Radiation therapy	Negative		Reference		
	Positive	1.194	3.302	1.087-10.032	0.035

CI: confidence interval; ER: estrogen receptors; PR: progesterone receptor.

Hu et al. [20] have shown that low ERα and ERβ expression was associated with unfavorable prognosis of endometrioid adenocarcinoma. Other studies revealed that expression of ERα was a favorable prognosis marker [21, 22]. Similar results were observed in metastatic endometrioid adenocarcinoma [23]. A study revealed that the lack of ER expression in endometrioid adenocarcinoma was associated with epithelial-mesenchymal transition (EMT) and PI3K alteration, which are factors of poor prognosis [24]. In addition, endometrioid cancers that express ER are the most sensitive to endocrine therapy, which may be used to treat both primary and recurrent endometrioid cancer [25]. Accordingly, the present study showed that ER expression was a marker of good prognosis in endometrioid adenocarcinoma.

while PR positivity and muscle invasion were independent risk factors for distant recurrence. Weinberg et al. [13] have also shown that lymphovascular invasion was associated with increased recurrence rates and decreased survival. In the present study, age was associated with prognosis, but not lymphovascular invasion, muscle invasion, or PR positivity. These discrepancies may be due to the study population, to the selection criteria, and to the study objective. Indeed, Zhang et al. [12] focused on independent risk factors for local and distant recurrence while the present study focused on risk factors for unfavorable prognosis. Furthermore, all patients in the present study were without distant metastasis. Moreover, we included vimentin positivity in the multivariate analyses.

Reid-Nicholson et al. [15] have characterized the expression of ER, PR, and vimentin in endometrioid adenocarcinoma at different stages; they found that vimentin was most widely expressed, while ER and PR were not expressed in some types of endometrioid adenocarcinoma [15]. Therefore, vimentin could be a good and consistent factor for the prognosis of endometrioid adenocarcinoma. A previous study by Coppola et al. [26] has shown that vimentin expression was a marker of favorable prognosis. In the present study, vimentin expression at ++ and +++ was a protective factor after endometrioid adenocarcinoma, but not expression at ++++, which could be due to the small sample size in the unfavorable prognosis group. A recent review suggested that vimentin is involved in EMT and could be used as a thera-

peutic target against endometrioid cancer [27], but the exact role of vimentin in EMT and cancer treatment still need to be defined [27]. Indeed, vimentin seems to be a marker of poor prognosis in colorectal and breast cancers [28, 29].

Radiation therapy is usually used to improve the prognosis in some cases of endometrioid adenocarcinoma with factors of poor prognosis [9-11]. In the present study, radiation therapy was associated with worst outcomes. This may be because radiation therapy is used in patients who already have a poor prognosis, and because the sample size was small in this subgroup of patients.

The present study is not without limitations. Indeed, despite the fact that the study sample was large, there were only a few patients in the unfavorable prognosis group and in the radiation therapy subgroup, which could affect the results. In addition, the follow-up was relatively short. Prospective studies could be designed for better data sampling and standard operation of treatment decisions.

In conclusion, vimentin and ER expression could be possible protective factors for favorable prognosis in postoperative patients with early stage endometrioid adenocarcinoma.

Disclosure of conflict of interest

None.

Address correspondence to: Hong Sun, Department of Gynecology, Obstetrics and Gynecology Hospital of Fudan University, Shanghai 200011, China. Tel: +86-21-3318 9900; Fax: +86-21-5512 2025; E-mail: hongsun57@hotmail.com

References

[1] Greenlee RT, Murray T, Bolden S and Wingo PA. Cancer statistics, 2000. CA Cancer J Clin 2000; 50: 7-33.

[2] Jemal A, Siegel R, Ward E, Hao Y, Xu J and Thun MJ. Cancer statistics, 2009. CA Cancer J Clin 2009; 59: 225-249.

[3] Tangjitgamol S, Anderson BO, See HT, Lertbutsayanukul C, Sirisabya N, Manchana T, Ilancheran A, Lee KM, Lim SE, Chia YN, Domingo E, Kim YT, Lai CH, Dali AZ, Supakapongkul W, Wilailak S, Tay EH, Kavanagh J; Asian Oncology Summit. Management of endometrial cancer in asia: consensus statement from the asian oncology summit 2009. Lancet Oncol 2009; 10: 1119-1127.

[4] Giede C, Le T, Power P, Le T, Bentley J, Farrell S, Fortier MP, Giede C, Kupets R, Plante M, Power P, Renaud MC, Schepansky A, Senikas V, Kwon J, Préfontaine M, Germain I, Pearcey R, D'Souza D, Senterman M, Hoskins P; SOGC-GOC-SCC Policy and Practice Guideline Committee. The role of surgery in endometrial cancer. J Obstet Gynaecol Can 2013; 35: 370-374.

[5] Colombo N, Preti E, Landoni F, Carinelli S, Colombo A, Marini C, Sessa C; ESMO Guidelines Working Group. Endometrial cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013; 24 Suppl 6: vi33-38.

[6] American College of Obstetricians and Gynecologists. ACOG practice bulletin, clinical management guidelines for obstetrician-gynecologists, number 65, august 2005: management of endometrial cancer. Obstet Gynecol 2005; 106: 413-425.

[7] Kupets R, Le T, Le T, Bentley J, Farrell S, Fortier MP, Giede C, Kupets R, Plante M, Power P, Renaud MC, Schepansky A, Senikas V, Kwon J, Préfontaine M, Germain I, Pearcey R, D'Souza D, Senterman M, Hoskins P; SOGC-GOC-SCC Policy and Practice Guidelines Committee. The role of adjuvant therapy in endometrial cancer. J Obstet Gynaecol Can 2013; 35: 375-379.

[8] Ibarrola Vidaurre M, Muruzabal Torquemada JC, Aguirre Gorospe A, Segura Ortega V, Tarrio Fernandez O and Lapena Calavia S. [Survival by surgical approach in patients with endometrial adenocarcinoma treated in Navarra in the 2001-2009]. An Sist Sanit Navar 2015; 38: 61-69.

[9] Plataniotis G, Castiglione M; ESMO Guidelines Working Group. Endometrial cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010; 21 Suppl 5: v41-45.

[10] Zhang Y and Wang J. Controversies in the management of endometrial carcinoma. Obstet Gynecol Int 2010; 2010: 862908.

[11] Mehasseb MK and Latimer JA. Controversies in the management of endometrial carcinoma: an update. Obstet Gynecol Int 2012; 2012: 676032.

[12] Zhang GY, Wu LY, Li B, Huang MN, Zhang R and Li XG. Retrospective analysis of prognostic variables and clinical outcomes in surgically staged intermediate risk endometrial carcinoma. Eur J Obstet Gynecol Reprod Biol 2013; 169: 309-316.

[13] Weinberg LE, Kunos CA and Zanotti KM. Lymphovascular space invasion (LVSI) is an isolated poor prognostic factor for recurrence and survival among women with intermediate- to

high-risk early-stage endometrioid endometrial cancer. Int J Gynecol Cancer 2013; 23: 1438-1445.

[14] Brown AK, Gillis S, Deuel C, Angel C, Glantz C and Dubeshter B. Abnormal cervical cytology: a risk factor for endometrial cancer recurrence. Int J Gynecol Cancer 2005; 15: 517-522.

[15] Reid-Nicholson M, Iyengar P, Hummer AJ, Linkov I, Asher M and Soslow RA. Immunophenotypic diversity of endometrial adenocarcinomas: implications for differential diagnosis. Mod Pathol 2006; 19: 1091-1100.

[16] Desouki MM, Kallas SJ, Khabele D, Crispens MA, Hameed O and Fadare O. Differential vimentin expression in ovarian and uterine corpus endometrioid adenocarcinomas: diagnostic utility in distinguishing double primaries from metastatic tumors. Int J Gynecol Pathol 2014; 33: 274-281.

[17] Kim HS and Song YS. International federation of gynecology and obstetrics (FIGO) staging system revised: what should be considered critically for gynecologic cancer? J Gynecol Oncol 2009; 20: 135-136.

[18] Lyratzopoulos G, Abel GA, Brown CH, Rous BA, Vernon SA, Roland M and Greenberg DC. Socio-demographic inequalities in stage of cancer diagnosis: evidence from patients with female breast, lung, colon, rectal, prostate, renal, bladder, melanoma, ovarian and endometrial cancer. Ann Oncol 2013; 24: 843-850.

[19] Lee NK, Cheung MK, Shin JY, Husain A, Teng NN, Berek JS, Kapp DS, Osann K and Chan JK. Prognostic factors for uterine cancer in reproductive-aged women. Obstet Gynecol 2007; 109: 655-662.

[20] Hu K, Zhong G and He F. Expression of estrogen receptors ERalpha and ERbeta in endometrial hyperplasia and adenocarcinoma. Int J Gynecol Cancer 2005; 15: 537-541.

[21] Jongen V, Briet J, de Jong R, ten Hoor K, Boezen M, van der Zee A, Nijman H and Hollema H. Expression of estrogen receptor-alpha and -beta and progesterone receptor-A and -B in a large cohort of patients with endometrioid endometrial cancer. Gynecol Oncol 2009; 112: 537-542.

[22] Shabani N, Kuhn C, Kunze S, Schulze S, Mayr D, Dian D, Gingelmaier A, Schindlbeck C, Willgeroth F, Sommer H, Jeschke U, Friese K and Mylonas I. Prognostic significance of oestrogen receptor alpha (ERalpha) and beta (ERbeta), progesterone receptor A (PR-A) and B (PR-B) in endometrial carcinomas. Eur J Cancer 2007; 43: 2434-2444.

[23] Singh M, Zaino RJ, Filiaci VJ and Leslie KK. Relationship of estrogen and progesterone receptors to clinical outcome in metastatic endometrial carcinoma: a gynecologic oncology group study. Gynecol Oncol 2007; 106: 325-333.

[24] Wik E, Raeder MB, Krakstad C, Trovik J, Birkeland E, Hoivik EA, Mjos S, Werner HM, Mannelqvist M, Stefansson IM, Oyan AM, Kalland KH, Akslen LA and Salvesen HB. Lack of estrogen receptor-alpha is associated with epithelial-mesenchymal transition and PI3K alterations in endometrial carcinoma. Clin Cancer Res 2013; 19: 1094-1105.

[25] Carlson MJ, Thiel KW and Leslie KK. Past, present, and future of hormonal therapy in recurrent endometrial cancer. Int J Womens Health 2014; 6: 429-435.

[26] Coppola D, Fu L, Nicosia SV, Kounelis S and Jones M. Prognostic significance of p53, bcl-2, vimentin, and S100 protein-positive langerhans cells in endometrial carcinoma. Hum Pathol 1998; 29: 455-462.

[27] Satelli A and Li S. Vimentin in cancer and its potential as a molecular target for cancer therapy. Cell Mol Life Sci 2011; 68: 3033-3046.

[28] Toiyama Y, Yasuda H, Saigusa S, Tanaka K, Inoue Y, Goel A and Kusunoki M. Increased expression of slug and vimentin as novel predictive biomarkers for lymph node metastasis and poor prognosis in colorectal cancer. Carcinogenesis 2013; 34: 2548-2557.

[29] Yamashita N, Tokunaga E, Kitao H, Hisamatsu Y, Taketani K, Akiyoshi S, Okada S, Aishima S, Morita M and Maehara Y. Vimentin as a poor prognostic factor for triple-negative breast cancer. J Cancer Res Clin Oncol 2013; 139: 739-746.