Correlation of Clinicopathological and Prognostic Characteristics between Endometriosis-Associated and Primary Ovarian Cancer

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Research

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Abstract

Background: To establish the clinicopathological and prognostic correlations between endometriosis-associated and non-endometriosis-associated primary ovarian cancer, with a view to providing a reference guide for revision of diagnostic criteria for malignant transformation of endometriosis.

Methods: Retrospectively collected clinicopathological and follow-up data of 174 clear cell and endometrial ovarian cancer patients. Cases were divided into endometriosis-associated and non-endometriosis-associated primary ovarian cancer, and comparative analysis of the clinicopathological characteristics and prognosis conducted.

Results: Average age and proportion of menopausal patients in the endometriosis-associated ovarian cancer group were lower relative to the primary ovarian cancer group ($P < 0.05$). Other clinicopathological features examined, including body mass index, age at menopause, operation history, dysmenorrhea, complications, tumor size, tumor side, ascites, CA125, HE4, CA199, stage, differentiation, expression of ER, PR, P53, P16, Ki67, MMR, HNF-1 β and Napsin A were not significantly different between the groups ($P > 0.05$). Furthermore, rates of resistance to platinum chemotherapy, relapse, progression-free survival and overall survival were comparable between the two groups ($P > 0.05$).

Conclusion: Endometriosis-associated and primary ovarian cancers of the same pathological type are speculated to be homologous in terms of origin from malignant transformation of endometriosis. It may therefore be necessary to revise the diagnostic criteria for ovarian endometriosis malignancy.

1 Background

Endometriosis is a common disease in women of childbearing age, with an incidence of 15–20%[1]. Studies to date have shown that endometriosis has the same molecular biological and genetic background as ovarian cancer and presents a high risk factor for ovarian cancer development[2]. According to the current internationally recognized Sampson and Scott diagnostic criteria: first, there must be a clear example of endometriosis in association or close proximity to the cancer; secondly, no other primary tumour site must exist and the histology of the tumour must be consistent with an endometrial origin; thirdly, the endometriosis associated with cancers must show a morphologic progression from benign to malignant in a contiguous fashion[3–4], the malignant transformation rate of endometriosis is 0.5–1.0%[5]. However, due to the significant heterogeneity of endometriosis and atypical hyperplasia, high rates of missed pathological diagnosis, the actual incidence of malignant transformation of endometriosis may be higher[6–7], which presents a challenge in establishing accurate diagnostic criteria.

The major pathological types of endometriosis-associated ovarian cancer are endometrioid and clear cell cancers, accounting for 75–90% cases[8]. However, according to the diagnostic criteria of Sampson and Scott, only 50–70% ovarian clear cell and endometrioid carcinoma cases are diagnosed as endometriosis-associated ovarian cancer (EAOC). According to the theory of external origin of ovarian cancer, clear cell and endometrioid carcinoma types are closely related to endometriosis, potentially resulting from endometriosis-associated malignancy[9]. Our research is focused on the malignant transformation of endometriosis. Previous studies have demonstrated comparable abnormal expression of EAOC-related genes, such as mismatch repair gene

human mutL homolog 1(hLMH1) and runt-related transcription factor3(RUNX3), between EAOc and non-endometriosis-associated primary ovarian cancer(non-EAOc) groups[10–11], leading to the speculation that clear cell carcinoma and endometrioid carcinoma of the ovary may be all originate from malignant transformation of endometriosis. Since the pathological changes of endometriosis are heterogeneous, particularly after malignant transformation, tumor tissues grow vigorously and destroy the original tissues, and the histological basis of endometriosis remains unclear; pathological sampling has a number of limitations; cancer and endometriosis lesions are not obtained at the same time, and concurrent endometriosis is often overlooked, resulting in a low diagnostic rate of malignant transformation of endometriosis using the standards of Sampson and Scott. Further relevant clinical and basic research evidence is thus warranted to validate this theory.

2 Materials And Methods

(1) Research Objects

174 cases of ovarian clear cell carcinoma and ovarian endometrioid carcinoma were diagnosed and treated in China Medical University Cancer Hospital and Affiliated Shengjing Hospital from January 2008 to November 2018. According to the standards proposed by Sampson and Scott, patients were divided into EAOc group and non-EAOc group, including 74 patients in EAOc group and 100 patients in non-EAOc group. According to different pathological types, the endometriosis associated ovarian clear cell carcinoma (EOCC) group and the endometriosis associated ovarian endometrioid carcinoma (EOEC) group were further divided. The non-endometria-related primary ovarian cancer group was divided into two groups: clear cell carcinoma (OCC) and endometrioid carcinoma (OEC), including 39 EOCC cases, 35 EOEC cases, 35 OCC cases and 65 OECC cases. Samples were fully encoded to protect patient confidentiality.

Inclusion criteria: 1) Clear pathological diagnosis, limited to clear cell carcinoma and endometrioid carcinoma; 2) Complete case data; 3) Complete the initial treatment plan (surgery and chemotherapy). Exclusion criteria: 1) Other histological types of ovarian malignancies and ovarian borderline tumors of non-clear cell carcinoma and endometrioid carcinoma; 2) Patients with other primary malignant tumors. 3) Patients with metastatic ovarian cancer. The samples of the selected cases were rechecked by the same gynaecological pathologist to further confirm the diagnosis.

(2) Data Collection

Clinicopathological data of all patients were collected. The details are as follows:

Clinical data: age; Body Mass Index (BMI), history of menstrual, postmenopausal status, age of menopause, history of surgery, complications, results of related serum tumor markers (CA125, CA199, HE4).

Pathological data: tumor size, tumor side, ascites, FIGO stage, histological classification, immunohistochemical results (ER, PR, P53, P16, Ki67, MMR, HNF-1, Napsin A).

(3) Treatment

All the included patients received standard surgical treatment: patients in the early stage (FIGO I-II) received comprehensive staging surgery, and patients in the advanced stage (FIGO III-IV) received tumor cell reduction surgery. Postoperative chemotherapy regimens containing platinum were adopted according to international guidelines: paclitaxel and carboplatin (TC regimen), docetaxel and carboplatin (DC regimen), 6–8 cycles of chemotherapy, with an interval of 21 days.

(4) Follow-up

All cases were followed up to the end of recurrence, death or the end of follow-up, up to 31/3/2019, the follow-up time was 6-132 months, and the median time was 67 months. Reoperation to obtain histopathological evidence and/or imaging evidence of new developments and/or continued abnormal elevation of tumor markers is considered to tumor recurrence.

(5) Statistical methods

The data were analyzed by SPSS 25.0 software. Enumeration data are expressed in terms of rates, Measurement data are expressed as mean $\pm$ standard deviation ($\pm s$), T test was used for comparison between groups, The enumeration data were compared using the test and Fisher's exact test, survival analysis using Kalan - Meier survival curve and using Log - rank test to compare the difference, $P < 0.05$ was statistically significant.

3 Results

(1) General data analysis

In total, 174 cases of clear cell carcinoma and endometrioid carcinoma of the ovary were included, including 74 in the EAOc and 100 in the non-EAOc group. Analysis of epidemiological data revealed lower average age and proportion of menopause of patients in the EAOc group than the non-EAOc group ($P < 0.05$). No significant differences in BMI, dysmenorrhea history, menopausal age, surgical history, and complications were observed between the two groups (all $P > 0.05$), as shown in Table 1.

Table 1
Comparative analysis of the epidemiological data of EAOc and non-EAOc patients (n,x ± s)

Characteristics	EAOc	Non-EAOc	P
	74	100	
Age(year)	49.4 ± 7.7	54.0 ± 10.0	0.001
BMI	23.6 ± 3.3	23.5 ± 3.7	0.731
History of menstrual			0.064
Yes	29	26	
No	55	74	
Postmenopausal status			0.001
Yes	32	68	
No	42	32	
Age of menopause	49.1 ± 4.3	49.3 ± 3.9	0.815
History of surgery			0.115
Yes	19	16	
No	65	84	
Complications			0.683
Yes	31	45	
No	43	55	

Further intra-group and inter-group analyses of the same pathological types showed significantly lower average age of onset and proportion of menopause in the EOCC than OCC group ($P < 0.05$). We observed no marked differences in the remaining parameters between the groups ($P > 0.05$; Table 2).

Table 2
Intra-group and inter-group analyses of EAOc and non-EAOc patients (n,x ± s)

Characteristics	EOEC	EOCC	OEC	OCC	P
	35	39	65	35	
Age(year)	50.6 ± 8.4	48.2 ± 6.7	54.3 ± 10.7	53.3 ± 8.6	0.177 ^a /0.060 ^b / <0.01^c
BMI	23.9 ± 2.9	23.3 ± 3.6	23.7 ± 3.8	22.8 ± 3.1	0.430 ^a /0.782 ^b /0.570 ^c
History of menstrual					0.076 ^a /0.667 ^b /0.075 ^c
Yes	10	19	16	10	
No	25	20	49	25	
Postmenopausal status					0.178 ^a /0.199 ^b / <0.01^c
Yes	18	14	42	26	
No	17	25	23	9	
Age of menopause	48.8 ± 4.7	49.2 ± 3.8	49.9 ± 4.1	48.2 ± 3.2	0.802 ^a /0.408 ^b /0.363 ^c
History of surgery					0.599 ^a /0.106 ^b /0.810 ^c
Yes	8	11	7	9	
No	27	28	58	26	
Complications					0.528 ^a /0.916 ^b /0.892 ^c
Yes	16	15	29	14	
No	19	24	36	21	
a:EOEC vs. EOCC, b:EOEC vs. OEC, c:EOCC vs. OCC.					

(2) Analysis of clinical features

No significant differences were evident between the two groups in terms of tumor size, tumor side, ascites, CA125, HE4, and CA199 levels (all P > 0.05). The collective data are presented in Table 3.

Table 3
Comparative analysis of clinical features of EAOc and non-EAOc patients (n,x ± s)

Characteristics	EAOc	Non-EAOc	P
	74	100	
Ascites			0.666
Yes	39	56	
No	35	44	
Tumor size			0.769
≥ 10cm	45	63	
<10cm	29	37	
Tumor side			0.355
Unilateral	53	65	
Bilateral	21	35	
Biomaker			
CA125(U/ml)	448.9 ± 980.0	739.8 ± 1141.4	0.080
HE4(pmol/L)	203.4 ± 240.0	264.5 ± 217.5	0.620
CA199(U/ml)	194.0 ± 460.4	274.2 ± 546.7	0.465

Further intra-group and inter-group analyses disclosed significantly higher incidence of bilateral tumors in the EOEC than EOCC group (40.0% vs 17.9%, $P < 0.05$). Moreover, the HE4 level in the EOEC group was higher than that in the EOCC group to a significant extent (355.4 vs 89.4 pmol/L, $P < 0.05$). No significant differences were found in the remaining parameters (Table 4). tumor size, tumor side;Ascites;FIGO staging.Histological classification

(3)Pathological characteristics

Pathological characteristics were comparable between the two groups in terms of FIGO stage, differentiation degree, ER, PR, P53, P16, Ki67, MMR, hnf-1, and Napsin A-positive expression (all $P > 0.05$; Table 5, Fig. 1).

TABL 4 Intra-group and inter-group clinical features analyses of EAOc and non-EAOc patients (n×x±s×)

Characteristics	EOEC	EOCC	OEC	OCC	P
	35	39	65	35	
Ascites					0.469 ^a /0.295 ^b /0.209 ^c
Yes	20	19	44	12	
No	15	20	21	23	
Tumor size					0.892 ^a /0.881 ^b /0.363 ^c
≥10cm	21	24	38	25	
<10cm	14	15	27	10	
Tumor side					0.036^a /0.303 ^b /0.316 ^c
Unilateral	21	32	33	32	
Bilateral	14	7	32	3	
Biomaker					
CA125[U/ml]	618.0±1309.8	297.0±509.6	870.3±895.0	493.7±1479.0	0.161 ^a /0.255 ^b /0.437 ^c
HE4[pmol/L]	355.4±319.5	89.4±69.1	498.9±547.0	132.7±259.0	0.039^a /0.575 ^b /0.651 ^c
CA199[U/ml]	248.1±525.4	160.6±423.0	276.9±586.0	220.5±547.0	0.556 ^a /0.877 ^b /0.663 ^c

a:EOEC vs. EOCC, b:EOEC vs. OEC, c:EOCC vs. OCC.

Table 5
Comparative analysis of pathological characteristics of
EAOC and non-EAOC patients(n,%)

Characteristics	EAOC	Non-EAOC	P
	74	100	
FIGO stage			0.417
I/II	51	63	
III/IV	23	37	
Differentiation			0.932
Low	18	21	
Middle	34	52	
High	22	27	
Biomarker			
ER(+)	32	52	0.253
PR(+)	24	45	0.094
P53(+)	59	68	0.085
P16(+)	41	54	0.854
MMR(-)	19	37	0.114
Ki67(%)	30.0 ± 18.0	30.8 ± 18.94	0.767
Napsin A(+)	18	37	0.075
HNF-1β(+)	15	31	0.113

The rates of ER and PR positivity in the EOEC group were significantly higher than those in the EOCC group (71.4% vs. 17.9%, 60.0% vs. 7.7%; $P < 0.05$). Conversely, the rates of HNF-1 and Napsin A positivity in the EOCC group were significantly higher relative to the EOEC group (28.2% vs. 20.0%, 30.8% vs. 7.7%; $P < 0.05$). HNF-1 and Napsin A positive rates in the OCC group were significantly higher than those in the OEC group (74.2% vs. 16.9%, 80.0% vs. 4.6%; $P < 0.05$), as shown in Table 6.

Table 6
Intra-group and inter-group pathological characteristics of EAOC and non-EAOC patients(n,%)

Characteristics	EOEC	EOCC	OEC	OCC	P
	35	39	65	35	
FIGO stage					
I/II	21	30	37	26	0.116 ^a /0.767 ^b /0.792 ^c
III/IV	14	9	28	9	
Differentiation					
Low	11	7	18	3	0.177 ^a /0.695 ^b /0.239 ^c
Middle	17	17	40	12	
High	7	15	7	20	
Biomarker					
ER(+)	25	7	49	3	<0.01 ^a /0.667 ^b /0.311 ^c
PR(+)	21	3	40	5	<0.01 ^a /0.880 ^b /0.635 ^c
P53(+)	29	30	43	25	0.526 ^a /0.076 ^b /0.589 ^c
P16(+)	16	25	32	22	0.112 ^a /0.710 ^b /0.912 ^c
MMR(-)	8	11	22	15	0.072 ^a /0.548 ^b /0.291 ^c
Ki67(%)	29.1 ± 20	30.7 ± 14	29.6 ± 19	33.0 ± 16.5	0.718 ^a /0.907 ^b /0.564 ^c
Napsin A(+)	7	11	11	26	<0.01 ^a /0.459 ^b /0.230 ^c
HNF-1β(+)	3	12	3	28	<0.01 ^a /0.317 ^b /0.273 ^c
a:EOEC vs. EOCC, b:EOEC vs. OEC, c:EOCC vs. OCC.					

(4) Prognostic characteristics

Overall, 74 patients in the EAOC group were subjected to initial analyses, 64 of whom were followed up (follow-up rate of 86.5%). Rates of platinum therapy resistance, recurrence and mortality were determined as 6.25%, 39.1%, and 28.1%, respectively. Among the 100 patients in the non-EAOC group, 85 were followed up (85.0%). The platinum resistance rate was determined as 9.41%, recurrence rate as 54.1%, and mortality rate as 40.0%, which were not significantly different between the two groups (all $P > 0.05$; Table 7).

Table 7
Prognosis comparison between EAOc and non-EAOc patients(n)

Characteristics	EAOc	non-EAOc	P
	74	100	
Platinum resistance	4	8	0.483
Relapse	25	39	0.405
Death	19	34	0.193

Kaplan-Meier analysis and log-rank test showed that the average overall survival (OS) of the EAOc group was 91.6 months (95% CI: 76.9–106.5 months) while that of the non-EAOc group was 77.8 months (95% CI: 66.1–90.0 months), with no significant differences ($P = 0.068$, > 0.05). The median progression-free survival (PFS) of the EAOc group was 78.4 months (95% CI: 62.2–94.5 months), which was not significantly different from the non-EAOc group (64.0 months; 95% CI: 50.7–77.1 months) ($P = 0.216$, > 0.05), as shown in Fig. 2.

Intra-group and inter-group analyses of the same pathological types via Kaplan-Meier and log-rank tests showed that OS of the EOCC group was 90.8 months (95% CI, 69.9–111.8 months), EOEC group was 96.8 months (95% CI, 76.8–116.8 months), OCC group was 77.4 months (95% CI, 51.49–103.30 months), and OEC group was 81.10 months (95% CI, 68.0–94.2 months). We observed no significant differences in OS in EOCC vs. EOEC, EOCC vs. OCC, and EOEC vs. OEC groups ($P = 0.290$, 0.262 , 0.070 , all $P > 0.05$). PFS of patients in the EOCC group was 80.9 months (95% CI, 61.2–100.6 months), EOEC group was 82.3 months (95% CI 59.4–105.2 months), OCC group was 85.9 months (95% CI 68.4–108.3 months), and OEC group was 60.0 months (95% CI 45.50–74.6 months). We observed no significant differences in PFS in EOCC vs EOEC, EOCC vs OCC, and EOEC vs OEC groups ($P = 0.222$, 0.675 , 0.071 , all $P > 0.05$; Fig. 3).

4 Discussion

Several recent studies have shown that endometriosis patients have significantly increased risk of ovarian cancer[12]. As a precancerous lesion, endometriosis is closely related to ovarian clear cell and endometrioid carcinomas. The theory of external origin of ovarian cancer hypothesizes that both clear cell and endometrioid carcinoma of the ovary originate from malignant transformation of endometriosis, which poses a challenge to the current diagnostic criteria for malignant transformation of endometriosis. However, further clinical and basic research evidence is needed to substantiate this theory. In the current study, the two ovarian cancer types(ovarian clear cell carcinoma and ovarian endometrioid carcinoma) most closely associated with endometriosis were examined as a whole. According to the diagnostic criteria of Sampson and Scott, samples were divided into EAOc and non-EAOc groups, and clinicopathologic features and prognosis between the groups compared. Our results showed no significant differences between the groups, supporting the theory that both non-endometriosis-associated primary ovarian endometrial carcinoma and ovarian clear cell carcinoma potentially have the same origin as EAOc from endometriosis.

We retrospectively analyzed the clinical features of 174 patients from EAOc and non-EAOc groups. The average age and proportion of menopausal patients in the EAOc group was lower than the non-EAOc group ($P < 0.05$). The differences may be attributed to a potential drop in postmenopausal hormone levels, gradual

atrophic degradation of ectopic endometrium[13], limitations of pathological materials, and errors due to insufficient pathological evidence of endometriosis, but further experiments on larger sample sizes are required to confirm these findings. No significant differences were evident in BMI, dysmenorrhea history, surgical history, complications, ascites, tumor size and relevant serum tumor markers (CA125, HE4, CA199) between the two groups (all $P > 0.05$), consistent with earlier results. Our experiments support similar characteristics of endometriosis-associated and non-endometriosis-associated primary ovarian cancers. Furthermore, upon stratified analysis according to pathological type into EOCC and EOEC, OCC and OEC groups, relevant epidemiological and clinical characteristics, such as BMI, dysmenorrhea history, history of surgery, complications, ascites, tumor size and serum tumor marker (CA125, HE4, CA199) levels were not significantly different ($P > 0.05$). Our findings provide further evidence that primary ovarian endometrial carcinoma and clear cell carcinoma are associated with corresponding pathological types in endometriosis-associated ovarian cancer, with similar clinical features.

Histopathology evaluation is the gold standard of ovarian cancer diagnosis and classification. Immunohistochemical analysis revealed high expression of ER and PR in endometrioid carcinoma of ovary and low expression in clear cell carcinoma[14]. Compared with other epithelial ovarian cancer types, the characteristics of ovarian clear cell carcinoma included HNF-1 β increase, high expression of Napsin A and positive expression of P53[15]. MMR expression in ovarian endometrial carcinoma and clear cell carcinoma is abnormally higher than that in other subtypes of ovarian cancer[16]. The above molecules are therefore useful as biomarkers to distinguish epithelial ovarian cancer subtypes. Ki-67 is currently used as a positive nuclear proliferation marker and its expression reflects the biological behavior of tumor cells[17]. For analysis of differences, similarities and potential mechanisms of EAO and non-EAO, we compared the pathologies of the two groups. Our data showed no histological differences in terms of pathologic differentiation degree, ER, PR, P53, and P16, Ki67, MMR, HNF-1 β and Napsin A-positive expression ($P > 0.05$) between EAO and non-EAO groups. The majority of previous reports have focused on the malignant transformation of endometriosis and few studies have been conducted on the characteristics of different pathological types of endometrial carcinoma and clear cell carcinoma. However, there are a number of specific differences in clinicopathological characteristics between endometrioid and clear cell carcinoma types. Further grouping analysis revealed no significant differences in expression of relevant non-specific indicators, such as P53, P16, Ki67 and MMR, among the groups. The positive expression rates of ER and PR were markedly different between endometrioid carcinoma and clear cell carcinoma groups, but not from the primary ovarian carcinoma of the same pathologic type. Differentiation of endometriosis into two tissue types is reported to occur in a dual mode regulated by sex hormones [18–19]: (1) estrogen and progesterone receptor-positive endometriosis lesions undergo malignant transformation to form hormone-dependent endometrioid carcinoma after long-term stimulation without antagonistic estrogen and (2) atrophic ectopic endometrial lesions negative for estrogen and progesterone receptors are stimulated by oxidative stress for a long period of time, resulting in malignant transformation and formation of non-hormone-dependent clear cell carcinoma. The results of this study were consistent with earlier literature, validating that clear cell carcinoma is a non-hormone-dependent tumor. The positive expression rates for HNF-1 β and Napsin A were significantly higher in the clear cell carcinoma than endometrioid carcinoma group. Accordingly, we conclude that different histological types undergo distinct mechanisms for development of endometriosis-associated ovarian cancer, which will be the focus of follow-up investigations.

The majority of previous studies focused on comparing clinicopathological and prognostic differences between intrauterine endometriosis-associated ovarian cancers of a single pathologic type. However, sample sizes were usually small and the results obtained were inconsistent. Some findings suggest that ovarian endometrial carcinoma and ovarian clear cell carcinoma are early phases with better prognosis than the two pathological types of primary ovarian cancer[20–21], while other researchers have reported no obvious differences[22–23]. Here, we examined 174 cases of ovarian endometrial carcinoma and clear cell carcinoma, with a median follow-up period of 67 months. Our data showed that platinum resistance, recurrence and mortality rates between the EAO and non-EAO groups were not significantly different ($P > 0.05$). PFS and OS were comparable between the two groups ($P > 0.05$), supporting similar prognosis of EAO and non-EAO. In 2020, Marjolein Hermens [24] analyzed 32,419 patients with ovarian cancer and found synchronous endometriosis of ovarian cancer staging of early, higher survival and overall survival is longer, perhaps because of more frequent hospital visits of patients with endometriosis due to simultaneous treatment with endometriosis drugs, long-term state of inflammation caused by endometriosis, which activates immune function, in turn, leading to early detection and better prognosis, giving rise to the theory that ovarian cancer with endometriosis may have different pathophysiological features to other ovarian cancer types. Earlier studies have established a low early incidence of epithelial ovarian cancer. In this research, early incidence rates of EAO and non-EAO were 68.9% and 63.0%, respectively, which were significantly higher than the average early incidence of ovarian cancer (30.0%). Overall survival rates of the EAO and non-EAO groups were 71.9% and 60.0%, which were significantly higher than the average five-year survival rate of ovarian epithelial carcinoma (44%- 50%)[25]. Further indicates that ovarian clear cell carcinoma and endometrioid carcinoma are sources of malignant transformation of endometriosis, therefore can be detected early. But accelerated growth of tumor tissue destroys the tissue of origin because of malignant transformation, pathological materials can not remove cancer and ectopic foci lesions at the same time, consequently, a proportion of clear cell and endometrioid carcinomas of the ovary are not diagnosed as endometriosis-associated ovarian cancer.

In summary, no obvious clinicopathological differences between EAO and non-EAO were observed in this study, leading to the speculation that primary ovarian endometrial and clear cell carcinoma have the same origin with EAO. Our findings support the theory of dualism of ovarian cancer that endometrial carcinoma and clear cell carcinoma originate from progression of ovarian endometriosis. Therefore, it is worth exploring whether the stringent diagnostic criteria for malignant transformation of endometriosis require revision. However, the retrospective nature of this study is a limitation, and further large-scale, prospective multicenter clinical and molecular biology studies are required to verify the associations of malignant transformation of endometriosis with ovarian clear cell and endometrial carcinomas, which should aid in clarifying the biological mechanisms and developing individualized treatments for patients with endometriosis-associated ovarian cancer.

Abbreviations

EAO

endometriosis-associated ovarian cancer

non-EAO

non-endometriosis-associated primary ovarian cancer

EOCC
endometriosis associated ovarian clear cell carcinoma
EOEC
endometriosis associated ovarian endometrioid carcinoma
OCC
clear cell carcinoma
OEC
endometrioid carcinoma
BMI
Body Mass Index
OS
overall survival
PFS
progression-free survival

Declarations

Ethics approval and consent to participate: Samples were fully encoded to protect patient confidentiality. The study and its protocols were approved by the Research Ethics committees of Liaoning Cancer Hospital & Institute (2020G0322).

Consent for publication: Not applicable.

Availability of data and materials: Not applicable.

Competing interests: The authors declare that they have no conflict of interest.

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Authors' contributions: HW and CC carried out most parts of the experiment; YZ participated in the experiment; DW participated in the design of the study; HW, CC and PC performed the statistical analysis. All authors read and approved the final manuscript.

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Figures

Figure 1

The expression of ER,PR,P53,P16,Ki67,MMR,HNF-1 β ,Napsin A in tissue(SP 200X). 1.ER-positive;2.ER-negative;3.PR-positive;4.PR-negative; 5.P53-positive;6.P53-negative;7.P16-positive;8.P16-negative;9.Ki67-positive;10.Ki67-negative;11.MLH1-positive;12.MLH1-negative;13.MSH2-positive;14.MSH2-negative;15.MSH6-positive;16.MSH6-negative;17.PMS2-positive;18.PMS2-negative;19.HNF-1 β -positive;20.HNF-1 β -negative;21.Napsin A-positive;22.Napsin A-negative

Figure 2

The differences of OS and PFS between EAO and non-EAO patients.

Figure 3

OS and PFS differences of EOCC vs. EOEC EOCC vs. OCC EOEC vs. OEC.