ORIGINAL RESEARCH

Analysis of Clinical Characteristics and Prognostic Factors Related to EMs Correlation in Ovarian Cancer Patients

Qiaomei Zheng, MD; Shaozhan Chen, MM; Lihong Chen, BM; Jinhua Wang, MM

ABSTRACT

Objective • To investigate the clinical characteristics and prognostic factors in patients with endometriosis-associated ovarian cancer.

Methods • In this study, we retrospectively analyzed the medical records of 135 ovarian cancer patients admitted to our hospital from January 2016 to January 2018. Based on the presence of concomitant endometriosis (EMs), the patients were divided into two groups: the Endometriosis-Associated Ovarian Cancer (EAOC) group (n=64) and the non-EAOC (NEAOC) group (n=71). We compared the clinical characteristics of the two groups. Additionally, in the EAOC group, we followed up with patients for 5 years, categorized them into the survival group (n=40) and the deceased group (n=24) based on their prognosis, and conducted univariate and multivariate logistic regression analyses to identify influencing factors.

Results • In comparison to the NEAOC group, patients in the EAOC group exhibited higher rates of menopause occurrence, pathological stages I-II, vaginal bleeding, and history of cesarean section, with statistical significance ($P < .05$). They also had a lower incidence of dysmenorrhea, lymph node metastasis, and abdominal distension, as well as an earlier age of onset, all of which were statistically significant ($P < .05$). There were no statistically significant differences ($P > .05$) between the two groups in terms of parity, gravidity, tumor diameter, abdominal pain incidence, and body mass index. Based on prognosis, the patients were categorized into a survival group (n=40) and a deceased group (n=24). Comparison between the two groups showed statistically significant differences ($P < .05$) in terms of postoperative residue, epithelial-mesenchymal transition, and lymph node metastasis. In contrast, there were no statistically significant differences ($P > .05$) in terms of tumor laterality, histological type, tumor stage, differentiation degree, and vaginal bleeding. The variables with $P < .05$ were assigned as independent variables, with the prognosis of death as the dependent variable. Multivariate logistic regression analysis revealed that epithelial-mesenchymal transition and lymph node metastasis were independent risk factors for mortality in EAOC patients ($P < .05$).

Conclusion • Clinical characteristics of EAOC patients show significant differences, with epithelial-mesenchymal transition and lymph node metastasis being identified as independent adverse prognostic factors associated with poor outcomes in EAOC patients. However, this study has limitations such as a relatively small sample size, and further research is therefore necessary. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

Endometriosis (EMs) is a common gynecological disorder that affects 5-10% of women of reproductive age worldwide.[1] It is characterized by the growth of functional endometrial tissue outside the uterine cavity, which infiltrates and invades adjacent tissues.[2] Although EMs is a benign condition, it tends to undergo malignant transformation. With continuous research both domestically and internationally, the malignant transformation rate of EMs has been found to increase. Consequently, the concept of Endometriosis Associated Ovarian Cancer (EAOC) has been proposed.[3] EAOC refers to histologically confirmed ovarian cancers that are closely associated with EMs and may potentially originating from the

Table 1. Comparison of Clinical Characteristics Between the EAOC and NEAOC Groups

Variables		EAOC Group (n = 64)	NEAOC Group (n = 71)	χ^2/t value	*P* value
Menopausal Status (cases)	Postmenopausal	50 (78.13)	34 (47.89)	13.092[a]	.000
	Premenopausal	14 (21.87)	37 (52.11)		
Dysmenorrhea (cases)	Yea	23 (35.94)	8 (11.27)	11.580[a]	.000
	No	41 (64.06)	63 (88.73)		
Pathological Staging (cases)	Stages I-II	48 (75.00)	25 (35.21)	21.457[a]	.000
	Stages III-IV	16 (25.00)	46 (64.79)		
Lymph Node Metastasis (cases)	Metastasis	6 (9.38)	35 (49.30)	25.366[a]	.000
	No metastasis	58 (90.62)	36 (50.70)		
Gravidity (number of pregnancies)	0	4 (6.25)	6 (8.45)	0.343[a]	.558
	≥1	60 (93.75)	65 (91.55)		
Parity (number of live births)	0	7 (10.94)	8 (11.27)	0.003[a]	.951
	≥1	57 (89.06)	63 (88.73)		
Tumor Diameter (cm)		13.02±2.85	12.92±2.90	0.202[b]	.840
Abdominal Pain (cases)		15 (23.44)	22 (30.99)	0.963[a]	.326
Abdominal Distension (cases)		17 (26.56)	37 (52.11)	9.155[a]	.002
Vaginal Bleeding (cases)		10 (15.63)	2 (2.82)	6.817[a]	.009
Age of Onset (years)		47.95±7.15	53.30±8.30	3.991[b]	.000
BMI (kg/m^2)		21.79±1.21	22.01±1.17	1.073[b]	.285
History of Cesarean Section (cases)		16 (25.00)	4 (5.63)	10.003[a]	.001

[a]indicates χ^2
[b]indicates *t*

malignant transformation of endometriotic lesions.[4] The main pathological subtypes include Ovarian Clear Cell Carcinoma (OCCC) and Ovarian Endometrioid Carcinoma (OEC), both of which exhibit a higher mortality rate and poorer prognosis.[5] Therefore, analyzing the clinical characteristics (such as vaginal bleeding, dysmenorrhea, and other conditions) and prognostic factors of EAOC patients is of paramount importance. In view of this, the present study retrospectively analyzed the medical records of 135 ovarian cancer patients in our hospital (from January 2016 to January 2018) in order to explore the clinical characteristics and prognostic factors of EAOC patients and provide valuable insights for deeper investigations into the mechanisms underlying EAOC development, early diagnosis, and targeted treatments.

PATIENTS AND METHODS

General Information

We conducted a retrospective analysis of medical records for 135 ovarian cancer patients admitted to our hospital from January 2016 to January 2018. Patients were categorized into two groups based on the presence or absence of EMs: the Endometriosis Associated Ovarian Cancer (EAOC) group (n=64) and the non-EAOC (NEAOC) group (n=71), as determined by physicians. Furthermore, based on their prognosis, the patients were classified into a survival group (n=40) and a deceased group (n=24).

Inclusion criteria: Pathologically diagnosed with ovarian cancer; Primary malignant ovarian tumor; Surgically confirmed with or without EMs; Complete medical records; Informed consent obtained from patients to include their data in the study.

Exclusion criteria: Presence of other malignant tumors; Severe cardiovascular or organic diseases; Concurrent autoimmune diseases; Metastatic non-primary ovarian malignancies; History of preoperative adjuvant radiotherapy or chemotherapy; Pre-existing psychiatric disorders or history; Incomplete medical records.

Methods

We collected medical records of 135 patients, including information such as age of onset, body mass index (BMI), menopausal Status, dysmenorrhea, parity, gravidity, history of cesarean section, pathological Staging, lymph node involvement, tumor diameter, abdominal Pain, abdominal distension, and vaginal bleeding.

In the EAOC group, we conducted a 5-year follow-up where we recorded surgical and postoperative follow-up information. This included postoperative residue, tumor laterality, histological type, tumor stage, differentiation degree, presence of epithelial-mesenchymal transition, lymph node metastasis, and vaginal bleeding. We used univariate and multivariate logistic regression analysis to identify prognostic factors influencing the outcomes of EAOC.

Observation Indices

In this study, we compared the clinical characteristics of patients in the EAOC and NEAOC groups and conducted univariate and multivariate logistic regression analyses to identify prognostic factors.

Statistical Analysis

The data were uniformly entered into Statistic Package for Social Science (SPSS) 22.0 statistical software (IBM, Armonk, NY, USA) and presented as counts and percentages [n(%)] for qualitative data. Differences were compared using the χ^2 test. Quantitative data were presented as mean ± standard deviation (mean ± s). Data comparisons were performed using the *t* test, with $P < .05$ indicating significant differences.

RESULTS

Comparison of Clinical Characteristics Between the EAOC and NEAOC Groups

Compared to the NEAOC group, the EAOC group showed a higher incidence of menopause, pathological stages I-II, vaginal bleeding, and a higher proportion of a history of cesarean section. Conversely, they exhibited a lower incidence of dysmenorrhea, lymph node metastasis, and abdominal distension, as well as an earlier age of onset. These differences were statistically significant ($P < .05$). There were no statistically significant differences ($P > .05$) between the two groups in terms of parity, gravidity, tumor diameter, abdominal pain incidence, and body mass index. See in Table 1.

Univariate Analysis of Prognostic Factors for EAOC Patients

The patients were categorized into a survival group (n=40) and a deceased group (n=24) based on their prognosis. Comparison between the two groups showed statistically significant differences ($P < .05$) in terms of postoperative residue, presence of epithelial-mesenchymal transition, and lymph node metastasis. However, there were no statistically significant differences ($P > .05$) between the two groups in terms of tumor laterality, histological type, tumor stage, differentiation degree, and vaginal bleeding. See in Table 2.

Table 2. Univariate Analysis of Prognostic Factors for EAOC Patients

Variables		Survival Group (n = 40)	Deceased Group (n = 24)	χ^2 value	*P* value
Postoperative Residue (cm)	No or ≤1	35 (87.50)	10 (41.67)	15.095	.000
	>1	5 (12.50)	14 (58.33)		
Tumor Laterality (cases)	Unilateral	38 (95.00)	23 (95.83)	0.209	.646
	Bilateral	2 (5.00)	1 (4.17)		
Histological Type	OEC	25 (62.50)	14 (58.33)	0.109	.740
	OCCC	15 (37.50)	10 (41.67)		
Tumor Stage	I+II	30 (75.00)	18 (75.00)	0.000	1.000
	III+IV	10 (25.00)	6 (25.00)		
Differentiation Degree	poorly differentiated	29 (72.50)	17 (70.83)	0.020	.885
	moderately differentiated	7 (17.50)	5 (20.83)		
	well differentiated	4 (10.00)	2 (8.33)		
Epithelial-Mesenchymal Transition (EMT)	Yes	11 (27.50)	19 (79.17)	16.079	.000
	No	29 (72.50)	5 (20.83)		
Lymph Node Metastasis	Yes	13 (32.50)	20 (83.33)	15.519	.000
	No	27 (67.50)	4 (16.67)		
Vaginal Bleeding	Yes	32 (80.00)	20 (83.33)	0.000	1.000
	No	8 (20.00)	4 (16.67)		

Table 3. Assignment of Independent Variables

Independent Variables	Assignment
Postoperative Residue	"1" for "None or ≤1 cm" and "2" for ">1 cm"
Epithelial-Mesenchymal Transition (EMT)	"1" for "Yes" and "2" for "No"
Lymph Node Metastasis	"1" for "Yes" and "2" for "No"

Table 4. Multivariable Logistic Regression Analysis of Independent Prognostic Factors for EAOC Patients

Independent Variables	*β*	*SE*	*Wald*	*P* value	*OR*	95%*CI*
Postoperative Residue>1cm	0.450	0.485	0.911	>.050	0.641	0.252~1.559
Epithelial-Mesenchymal Transition (EMT)	0.982	0.416	5.550	<.050	2.712	1.185~6.090
Lymph Node Metastasis	0.540	0.243	4.692	<.050	1.719	1.062~2.833

Multivariable Logistic Regression Analysis of Independent Prognostic Factors for EAOC Patients

The variables with $P < .05$ were assigned as independent variables, with prognosis of death as the dependent variable. Multivariable logistic regression analysis revealed that epithelial-mesenchymal transition and lymph node metastasis were independent risk factors for mortality in EAOC patients ($P < .05$). See in Table 3 and Table 4.

DISCUSSION

The prevalence of EMs among women of reproductive age is approximately 5% to 10%. This condition is characterized by the growth of endometrial tissue outside the uterine cavity which may include areas such as the pelvic peritoneum and ovaries. Patients often experience symptoms such as pelvic Pain and irregular vaginal bleeding, which can adversely affect their physical health.[6] Despite being a benign disease, studies have reported that approximately 0.5% to 1% of EMs patients may progress to ovarian cancer, leading to increased mortality rates and posing a threat to patients' lives.[7]

The mechanisms underlying the development of EAOC include: (1) Due to the chronic inflammatory response associated with EMs, pathological features similar to those of tumors may appear before malignant transformation. Prolonged stimulation from chronic inflammation in EMs increases the risk of malignant transformation in ovarian epithelial cells. (2) Ectopic endometrial tissue, shedding and bleeding during the menstrual cycle, releases iron ions, which stimulate oxidative stress in tissue cells. This oxidative stress can damage cellular genetic material, making them more susceptible to malignancy.[7] (3) Both EMs and ovarian cancer exhibit hormone reactivity, with ovarian cells in EMs being more sensitive to hormonal stimulation. In recent years, the prevalence of EMs has shown an upward trend, prompting further research in the clinical domain. Consequently, there is increasing attention on the prevention and treatment of malignant transformation in EMs.

EMs carries inherent potential for malignant transformation. Clinical evidence has confirmed a close correlation between the occurrence of OCCC and OEC and the malignant transformation of EMs. However, compared to other types of ovarian tumors, these specific tumor types exhibit unique characteristics in their occurrence and clinical features, necessitating further exploration to guide clinical diagnosis and early treatment.[9] Our analysis revealed that, compared to patients in the NEAOC group, those in the EAOC group had a higher incidence of menopause, pathological stages I-II, vaginal bleeding, and a higher proportion of a history of cesarean section, with statistically significant differences ($P < .05$). There is speculation that EMs patients may have a higher risk of abnormal vaginal bleeding compared to patients with other types of ovarian tumors.[10,11] Additionally, cesarean section may stimulate the endometrium in situ to a certain extent, thereby promoting cellular oxidative stress, which could contribute to the onset of EMs. However, our study also revealed that, compared to patients in the NEAOC group, those in the EAOC group had a lower incidence of dysmenorrhea, lymph node metastasis, and abdominal distension, and an earlier age of onset, showing statistically significant differences ($P < .05$). The early onset of the disease may be attributed to more prominent clinical symptoms of EMs, enabling early disease detection.[12] However, the specific reasons for the lower incidence of dysmenorrhea, lymph node metastasis, and abdominal distension in the EAOC group have not been reported. It is evident that EAOC patients exhibit various differences in clinical characteristics, which play a crucial role in assisting with early clinical diagnosis of EAOC.

The present study identified, through univariate and multivariate analyses, epithelial-mesenchymal transition and lymph node metastasis as independent risk factors ($P < .05$) leading to mortality in EAOC patients. This research underscores the poorer prognosis of EAOC patients, which is closely linked to the processes of epithelial-mesenchymal transition and lymph node metastasis. However, some scholars argue that further long-term observation and validation are necessary to determine whether EAOC patients have a better prognosis.

In conclusion, this study revealed significant differences in clinical characteristics between EAOC patients and those

without concurrent EMs. Epithelial-mesenchymal transition and lymph node metastasis were identified as independent risk factors for the poorer prognosis of EAOC patients compared to ovarian cancer patients without EMs. This study provided valuable insights for a more in-depth understanding of the mechanisms underlying the development of EAOC, early diagnosis, and targeted treatment. However, this study has its limitations, including a relatively small sample size and a relatively short study and follow-up duration. Therefore, future research, including the expansion of the sample size and extension of the study and follow-up duration, is necessary to address these limitations and delve deeper into the subject.

ETHICAL COMPLIANCE

The ethics committee of Binhai Campus of the First Affiliated Hospital approved this study. Signed written informed consents were obtained from the patients and/or guardians.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

AUTHOR CONTRIBUTIONS

QZ, LC and JW designed the study and performed the experiments, QZ and SC collected the data, LC, JW and SC analyzed the data, QZ, LC and JW prepared the manuscript. All authors read and approved the final manuscript.

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