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Original Article

Serum biomarkers and clinicopathologic postoperative prognostic factors for in endometrial cancer patients

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Abstract: Objective: To explore the factors influencing the prognosis of endometrial cancer (EC) patients and assess their quality of life. Methods: A retrospective study was conducted involving 190 patients with EC who underwent surgical treatment in the Department of Obstetrics and Gynecology at Beijing Chao-Yang Hospital Affiliated to Capital Medical University between January 2008 and December 2018. Clinical and pathologic data were collected, and all patients received appropriate follow-up. Univariate analysis and Cox proportional hazards regression models were used to identify the factors related to EC prognosis and independent predictors of outcome. Additionally, the predictive performance of the serum biomarkers carcinoembryonic antigen (CEA), cancer antigen 125 (CA125), and CA199 for patient prognosis were evaluated. Results: All 190 EC patients had complete clinical, pathologic, and follow-up data. The median survival time was 88.95 months, with a 5-year survival rate of 94.4%. Univariate analysis showed that older age, postmenopausal status, higher FIGO stage, deeper myometrial invasion, poorer tissue differentiation, lymph node metastasis, and receipt of postoperative chemotherapy and combined radiotherapy were significantly associated with worse prognosis ($P<0.05$). The sensitivities of CEA, CA125, and CA199 for predicting adverse prognosis were 86.7%, 97.6%, and 82.4%, respectively; specificities were 72.0%, 68.0%, and 80.0%, respectively. The areas under the receiver operating characteristic curves (AUCs) were 0.681, 0.867, and 0.853, respectively. Conclusion: Postoperative prognosis in patients with endometrial cancer is influenced by multiple clinical and pathological factors. Serological markers CEA, CA125, and CA199 demonstrated favorable predictive value.

Keywords: Endometrial cancer, surgery, prognosis, survival treatment, influencing factors

Introduction

Endometrial cancer (EC) is one of the most common malignancies of the female reproductive system and has garnered attention due to its rising incidence [1, 2]. According to data from global cancer statistics, the incidence of EC has shown a marked upward trend over the past few decades, particularly in developed countries [3]. This increase is closely associated with changes in lifestyle factors among women, notably the growing prevalence of obesity, diabetes, and other chronic metabolic disorders. These conditions not only adversely affect overall health but are also recognized as risk factors for the development of EC [4].

Currently, histopathologic biopsy remains the gold standard for the diagnosis of EC. Surgical resection remains the preferred method, with the ultimate goal of removing both primary and metastatic lesions. Previous studies have confirmed that early diagnosis and timely treatment are critical for improving prognosis. In contrast, patients diagnosed at advanced stages or with high-risk pathologic features often have a poorer prognosis and typically require multimodal treatment strategies to extend survival [5, 6]. With recent advances in clinical research and the implementation of standardized diagnostic and therapeutic protocols, the overall prognosis of EC patients has significantly improved. Accurate prognostic assessment and appropriate treatment are essential for guiding individualized treatment decisions and prolonging patient survival. Furthermore, due to geographic variability in incidence and clinical characteristics, it is important to investigate region-specific epidemiological and prognostic patterns. In this study, we retrospectively ana-

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lyzed the clinical data of EC patients who underwent their first surgical treatment at our center, aiming to identify prognostic factors influencing postoperative outcome and provide theoretical data for improving patient prognosis.

Patients and methods

General information

A retrospective analysis was conducted on the clinical and pathologic data of EC patients who underwent surgical treatment in the Department of Obstetrics and Gynecology at Beijing Chao-Yang Hospital Affiliated to Capital Medical University between January 2008 and December 2018. This study has been reviewed and approved by the Beijing Chao-Yang Hospital Affiliated to Capital Medical University's ethics committee.

Inclusion criteria

Patients were eligible for inclusion if they met all of the following criteria: 1. Preoperative evaluation suggested the presence of endometrial lesions, and postoperative histopathologic examination confirmed a diagnosis of endometrial cancer; 2. Age between 18 and 80 years; 3. Availability of complete medical records, including current and past medical history, preoperative laboratory findings and imaging data; 4. No prior history of gynecologic diseases.

Exclusion criteria

1. Patients were excluded based on the following conditions: Presence of concurrent malignancies in other organs (e.g., digestive or hematologic cancers) detected preoperatively; 2. Pregnancy or lactation; 3. Secondary involvement of the endometrium by other metastatic malignancies; 4. Dysfunction of major organs, such as heart or renal failure; 5. Presence of mental illness or speech impairments that interfere with communication; 6. Incomplete clinical data.

Data collection

Clinical data were obtained by reviewing the electronic medical records, including baseline demographic information, results of preoperative blood tests, and CT scan images. Serum levels of carcinoembryonic antigen (CEA), cancer antigen 125 (CA125), and CA199 were measured. Peripheral venous blood samples (3-5 mL) were collected in the morning after an overnight fast upon hospital admission. Fasting is crucial to minimize variability and enhance the reliability of biochemical measurements, as most biomarkers exhibit greater stability in the morning. Collected samples were centrifuged at 3000 r/min for 20 minutes to separate the serum, which was subsequently stored under appropriate conditions for further analysis. Biomarker concentrations were measured using electrochemiluminescence or enzyme-linked immunosorbent assay (ELISA), with all test kits purchased from Roche (Shanghai, China). Procedures were strictly conducted according to the manufacturer's instructions.

All enrolled patients were followed up through landline phones, mobile phone contacts, and outpatient visits. The follow-up period ended on December 31, 2021. The primary endpoint was patient mortality, and overall survival (OS) was recorded. The relationship between baseline data, pathologic staging, and patient prognosis was analyzed.

Data processing

Statistical analysis was performed using SPSS 26.0 software. Continuous data were expressed as mean ± standard error of the mean (SEM), and the comparison between two groups used the t test. The categorical data were expressed as rates (percentages). The Kaplan-Meier method was employed to generate survival curves, and the log-rank test was used for univariate analysis to assess the impact of baseline factors on the prognosis of EC patients. Multivariate analysis of prognosis was conducted using the Cox proportional hazards regression model. The predictive value of preoperative serum levels of CEA, CA125 and CA199 for patient prognosis was evaluated using receiver operating characteristic (ROC) curve analysis. A p-value of <0.05 was considered significant.

Results

Baseline characteristics of patients

A total of 194 patients were enrolled during the study period. During the follow-up period, 4 patients were lost to follow-up, resulting in a

Table 1. General data of patients

Classification	Frequency (n)	Percentage (%)
Age (years)		
≤40	40	21.06
40-60	115	60.52
≥60	35	18.42
BMI		
≤24	69	36.32
24-27.9	81	42.63
≥28	40	21.05
Hypertension		
Yes	98	51.57
No	92	48.43
Diabetes		
Yes	42	22.11
No	148	77.89
Menopausal Status		
Pre-menopausal	95	50.00
Post-menopausal	95	50.00
FIGO Stage		
I/II	103	54.21
III/IV	87	45.79
Myometrial Invasion Depth		
Shallow/Deep	115	60.53
Full-thickness	75	39.47
Histological Grade		
Grade I	88	46.32
Grade II	102	53.68
Histological Differentiation		
Low/Intermediate	117	61.56
High	73	38.44
Lymph Node Metastasis		
Yes	77	59.47
No	113	40.53
Surgical Approach		
Open surgery	76	40.00
Laparoscopy	114	60.00
Postoperative Adjuvant Therapy		
None	93	48.95
Chemotherapy	33	17.37
Radiotherapy	54	28.42
Chemotherapy + Radiotherapy	10	5.26

BMI: Body mass index; FIGO: International Federation of Gynecology and Obstetrics.

loss rate of 2.06%. After excluding these cases, 190 patients were included in the final analysis. Their general information is shown in **Table 1**.

Prognostic analysis of endometrial cancer patients

Among the 190 patients analyzed, 25 deaths were recorded during the follow-up period. The median follow-up duration was 87.5 months, with the longest follow-up reaching 168 months. The 3-year survival rate was 95.1%, and the 5-year survival rate was 94.4%. The Kaplan-Meier survival curve is shown in **Figure 1**.

Univariate analysis of endometrial cancer patients

Univariate analysis using the Log-rank test revealed that older age, postmenopausal status, advanced FIGO surgical stage, deep myometrial invasion, poor tissue differentiation, presence of lymph node metastasis, and receipt of postoperative chemotherapy or combined radiotherapy were all associated with lower survival rate (all $P<0.001$). In contrast, younger age, premenopausal status, early FIGO stage, superficial myometrial invasion, well-differentiated tumors, absence of lymph node metastasis, and no adjuvant treatment were associated with better survival outcome. Detailed results are shown in **Figures 2** and **3**.

Multivariate analysis of prognostic imaging factors in endometrial cancer patients

To identify independent prognostic factors for survival in EC patients, a univariate analysis was performed. Variables that were statistically significant in the univariate analysis - including advanced age, postmenopausal status, advanced FIGO surgical stage, deep myometrial invasion, poor tissue differentiation, lymph node metastasis, and receipt of postoperative chemotherapy or combined radiotherapy - were included as covariates. Variable selection was conducted using the forward Wald method. The final Cox regression model identified three independent predictors of poor prognosis: older age, presence of

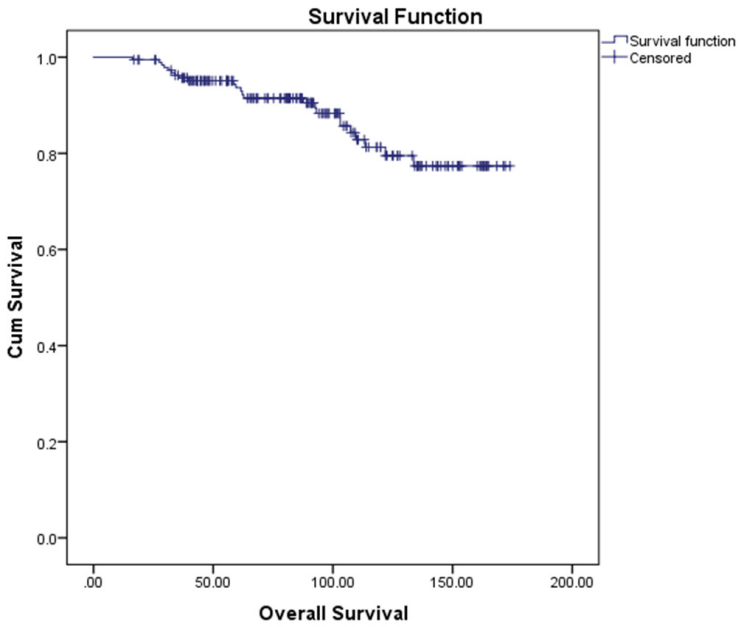

Figure 1. Survival analysis of patients with endometrial cancer.

lymph node metastasis, and receipt of postoperative chemotherapy with combined radiotherapy (**Table 2**). These results indicated that these factors have a significant adverse efrect on long-term survival in EC patients.

Comparison of serum CEA, CA125, and CA199 levels between survivors and non-survivors

Among the 25 patients who died during follow-up, peripheral blood levels of CEA, CA125, and CA199 were higher compared to those in the surviving cohort (**Table 3**).

Prognostic value of serum CEA, CA125, and CA199 levels in endometrial cancer patients

The results of this study showed that thresholds of CEA at 55.11 U/mL, CA125 at 48.84 U/mL, and CA199 at 68 U/mL indicated a poor prognosis (**Table 4** and **Figure 4**).

Discussion

The clinical manifestations of EC typically include postmenopausal vaginal bleeding, menstrual irregularities in premenopausal women, and abnormal vaginal discharge. These symptoms are often apparent and prompt medical attention, allowing for early diagnosis and timely intervention in the majority of patients, which contributes to improved prognosis [7-9]. In recent years, advancements in clinical research, enhanced diagnostic and therapeutic techniques, and increased awareness of gynecologic malignancies have collectively led to further improvement in the overall outcomes of EC patients [10]. Currently, the prognosis of EC is primarily determined by pathologic data, including histologic subtype, tumor grade, and FIGO stage. According to the 2015 report by the International Federation of Gynecology and Obstetrics (FIGO), high-risk prognostic factors for EC include poorly differentiated tumors (grade G3), myometrial infiltration (>112), lymphovascular space invasion, non-endometrioid histology, and cervical stromal involvement [11, 12]. Therefore, systematic evaluation of prognostic factors in surgically treated EC patients is of considerable clinical importance.

Recent studies have confirmed that both preoperative baseline data and intraoperative pathological findings can serve as reliable predictors of prognosis in EC patients [13-15]. Consistent with these findings, this study identified several factors significantly associated with poor outcomes, including older age, postmenopausal status, higher FIGO stage, deeper myometrial invasion, poor tissue differentiation, lymph node metastasis, and the receipt of postoperative chemotherapy or combined radiotherapy. The main mechanisms through which these factors influence prognosis are multifaceted. Older patients, for instance, are more likely to present with multiple comorbidities such as hypertension, diabetes, and heart disease. These comorbidities not only affect the overall health status of the patient but also compromise their resilience, potentially increasing the risks during the treatment process [16]. For example, patients with cardiovascular diseases may face heightened anesthesia risks during surgery, while those with diabetes may experience delayed wound healing, which can affect the recovery process. A higher FIGO surgical stage usually indicates more advanced disease progression, possibly involving adja-

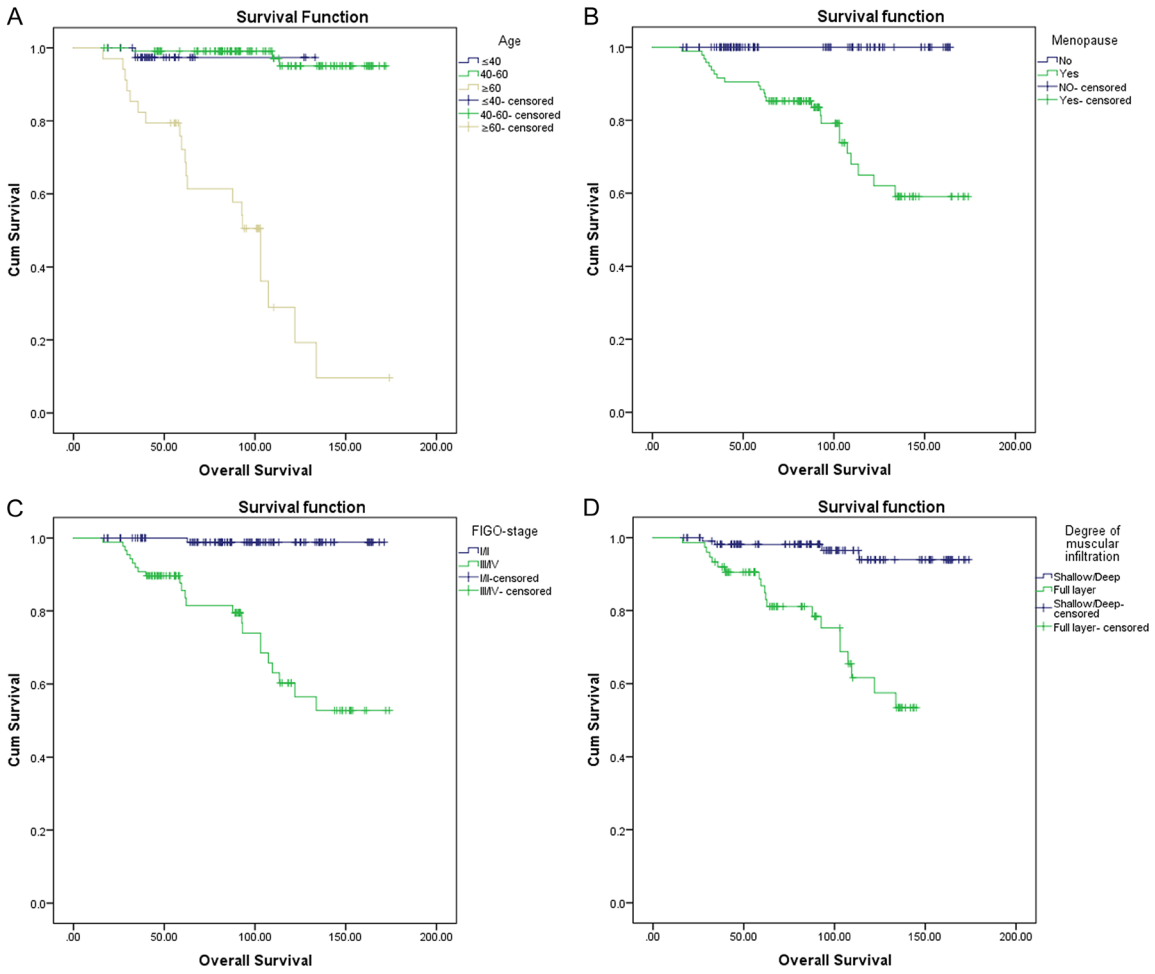

Figure 2. Analysis chart of prognostic factors for patients with endometrial cancer. A: Prognostic outcomes based on age; B: Comparative analysis of prognosis in premenopausal and postmenopausal patients; C: Prognostic analysis according to different FIGO surgical stages; D: Prognostic comparison based on the depth of myometrial invasion in endometrial cancer patients.

cent tissues, organs, or even distant metastases. Patients at this stage often require multimodal treatment strategies and face significantly increased risks of recurrence and mortality. In contrast, early-stage diagnosis and intervention are associated with favorable prognosis, whereas late-stage detection correlates with higher recurrence rates and reduced survival [17]. Therefore, FIGO staging serves as a critical determinant in both therapeutic decision-making and prognostic evaluation.

Similarly, the depth of myometrial invasion is a well-established indicator of tumor aggressiveness. Extensive invasion into the myometrium not only reflects enhanced tumor invasiveness but is also closely related to poor prognosis. Studies have shown that patients with deep myometrial infiltration generally have lower survival rates compared to those with superficial invasion. Tissue differentiation is another key indicator for assessing tumor prognosis. Poorly differentiated tumors exhibit marked cellular atypia and diminished resemblance to normal endometrial tissue, which are typically associated with increased malignant potential. In contrast, well-differentiated tumors tend to resemble normal cells in function and are generally associated with better prognosis. Lymph node metastasis represents a crucial indicator of tumor dissemination. As a primary conduit for metastatic spread, the lymphatic system facilitates tumor cell metastasis. The detection of tumor cells in regional lymph nodes is indicative of advanced disease and is consistently associated with unfavorable prognosis. Adju-

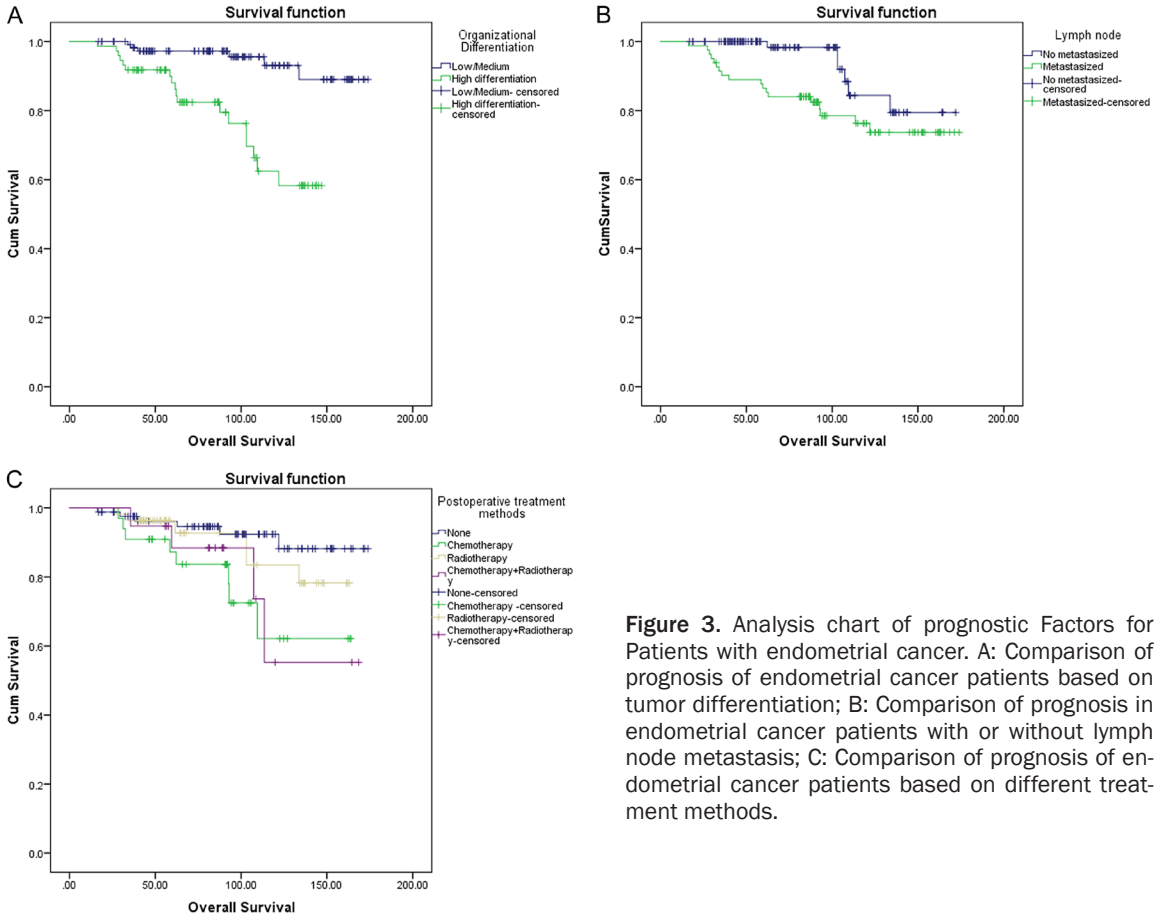

Figure 3. Analysis chart of prognostic Factors for Patients with endometrial cancer. A: Comparison of prognosis of endometrial cancer patients based on tumor differentiation; B: Comparison of prognosis in endometrial cancer patients with or without lymph node metastasis; C: Comparison of prognosis of endometrial cancer patients based on different treatment methods.

Table 2. Cox proportional hazards regression analysis of prognostic factors in endometrial cancer patients

Variable	B	S.E.	P	OR	95% CI
Age	1.182	1.395	0.018	3.260	1.101-4.248
Lymph Node Metastasis	1.438	0.663	0.030	4.212	1.148-15.460
Postoperative Chemotherapy and Combined Radiotherapy	1.350	0.801	0.042	3.857	1.052-14.144

Table 3. Comparison of serum CEA, CA125, and CA199 levels between survivors and non-survivors

Group	CEA (U/mL)	CA125 (U/mL)	CA199 (U/mL)
Survivor Group (n=25)	41.69±2.66	38.65±1.13	39.56±15.40
Deceased Group (n=165)	59.12±2.31	51.87±1.48	82.56±14.32
t	34.45	42.77	7.383
P	<0.001	<0.001	<0.001

CEA: Carcinoembryonic Antigen; CA125: Cancer Antigen 125; CA199: Carbohydrate antigen199.

vant chemotherapy and radiotherapy are traditional treatments aimed at inhibiting tumor cell growth and spread, thereby improving the patient's survival rate. Therefore, the need for such therapies often indicates more severe disease, and worse prognosis, as evidenced by previous studies [18-22].

In addition, the prognostic factors in EC are not isolated variables; rather, they frequently coex-

Table 4. Diagnostic efficacy of serum CEA, CA125, and CA199 levels in predicting mortality in patients with endometrial carcinoma

Detection Indicator	Sensitivity	Specificity	AUC (95% CI)
CEA	86.70%	72.00%	0.861 (0.559-0.904)
CA125	97.60%	68.00%	0.867 (0.754-0.979)
CA199	82.40%	80.00%	0.853 (0.753-0.953)

CEA: Carcinoembryonic Antigen; CA125: Cancer Antigen 125; CA199: Carbohydrate antigen199.

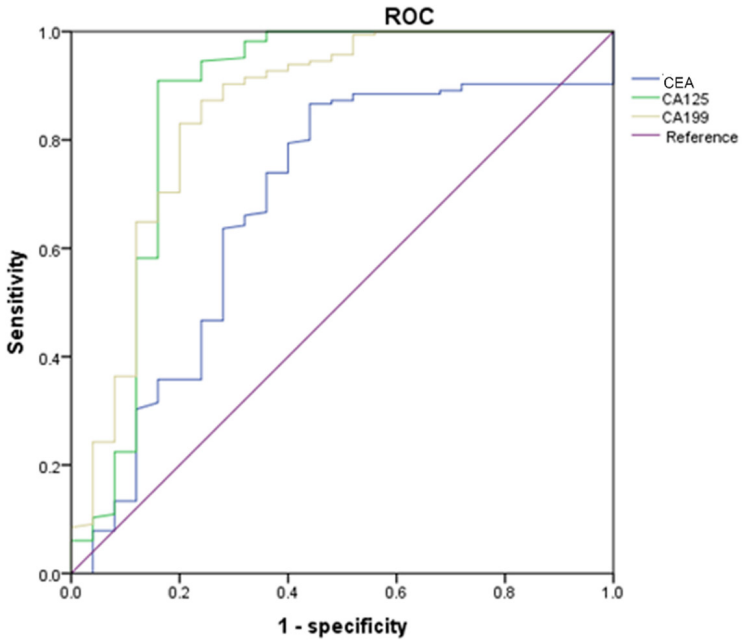

Figure 4. Predictive efficacy of different serum markers. CEA: Carcinoembryonic Antigen; CA125: Cancer Antigen 125; CA199: Carbohydrate antigen199.

ist and interact, collectively influencing patient outcomes. Identifying independent prognostic factors is therefore essential for advancing both standardized treatment protocols and personalized therapeutic strategies. While traditional clinicopathological parameters are strongly associated with prognosis, our findings indicate that patients with similar histological subtypes, FIGO stages, and treatment regimens may still exhibit markedly different clinical outcomes. Notably, some patients diagnosed at an early stage experience recurrence and metastasis, whereas certain late-stage patients achieve unexpectedly favorable survival. This discrepancy highlights the limitations of relying solely on histopathological classification to predict tumor behavior and underscores the substantial biological heterogeneity inherent in EC. Consequently, there remains an urgent need for more objective and robust classification systems capable of accurately reflecting tumor aggressiveness and guiding individualized prognosis and treatment.

Tumor markers are biomolecules produced by either tumor cells or the tumor microenvironment, which can be detected in blood, urine, or other body fluids. Their presence is closely related to the initiation and progression of cancer, providing important diagnostic information for clinicians [23]. In this study, we retrospectively analyzed the clinical data and serum markers of EC patients to explore the diagnostic and prognostic significance of CEA, CA125, and CA199 levels in EC. Previous studies have shown that peripheral serum levels of CEA, CA125, and CA199 are significantly elevated in patients who succumb to EC compared to survivors [24]. The underlying mechanisms are as follows: Carcinoembryonic Antigen (CEA) is a glycoprotein produced during normal embryonic development, typically present at very low levels in adults. However, when certain types of cancers - particularly malignant tumors such as colorectal cancer, breast cancer, and lung cancer - develop, CEA levels rise significantly. As a result, the medical community regards it as an important tumor marker, widely used in cancer screening, diagnosis, prognosis evaluation, and treatment monitoring, among other applications. CA125, one of the most widely recognized tumor markers in female reproductive cancers, was originally discovered for the detection of ovarian cancer. While CA125 is most commonly used for the early detection and monitoring of ovarian cancer, it also serves a critical role in the diagnosis of EC. Elevated levels of CA125 are usually observed in EC patients, making it an important indicator for assessing disease status. CA199, another significant tumor marker,

is often correlated with tumor burden, pathologic type, and disease staging. Studies have found that CA199 may be elevated in some patients with EC, providing additional diagnostic value and supporting findings from previous research [24-26]. The results of this study further confirm that the clinical use of these serological indicators provides reliable prognostic predictions for EC patients.

However, several limitations exist in this study, including its relatively small sample size and single-center design. Additionally, the variation in disease severity among patients and the nested case structure warrant further validation of these findings through multi-center, large-scale studies. Furthermore, this study did not evaluate the diagnostic efficacy of the three markers in conjunction for EC, since the individual diagnostic performance of each marker was found to be superior. Therefore, exploring the combined predictive potential of these markers would be a worthy way to extend the findings of this study.

In conclusion, the prognosis of EC patients is closely related to baseline clinical data, and to peripheral serum levels of CEA, CA125, and CA199 are significant prognostic indicators of EC, making them worthy of clinical use.

Disclosure of conflict of interest

None.

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