Preoperative serum CA125 level and age at diagnosis: An effective prognosis prediction tool for patients with early-stage endometrial cancer

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Abstract

Objective

To investigate the combined predictive value of the preoperative serum cancer antigen 125 (CA125) level and age at diagnosis among patients with early-stage endometrial cancer (EC) after initial treatment.

Methods

We retrospectively analyzed data from patients with early-stage EC from January 1999 to December 2015 in multiple institutions in China. All patients received primary hysterectomy ± bilateral salpingo-oophorectomy and adjuvant radiotherapy for pathology-confirmed stage I and II EC (FIGO 2009 staging). In total, 447 patients with complete data on preoperative serum CA125 levels were included. All patients were divided into low-risk, intermediate-risk, high-intermediate-risk and high-risk groups according to the ESMO-ESGO-ESTRO risk classification. Binary logistic regression was used to calculate the predictive probability of 5-year overall survival (OS) for each patient, and the receiver operating characteristic (ROC) curve was used to calculate the sensitivity and specificity of variables, as well as the combined predictive value of CA125 and age.

Results

The median follow-up time was 59 months (3–201 months). The 5-year OS and disease-free survival (DFS) rates were 94.4% and 89.1%, respectively. Multivariate analysis showed that the preoperative CA125 level and age at diagnosis were independent prognostic factors for 5-year OS. The best cutoff value for age at diagnosis was 61 years. The cutoff values of CA125 for patients aged ≤61 years and >61 years were 37.7 U/mL and 39.35 U/mL, respectively. Patients aged >61 years with CA125 > 39.35 U/mL and patients aged ≤61 years with CA125 > 37.7 U/mL were classified as the CA125-positive group; the remaining patients constituted the CA125-negative group. The area under the curve (AUC) for CA125 combined with age at diagnosis was 0.692, and the corresponding sensitivity and specificity were 68.2% and 68.2% ($P < 0.002$), respectively, which were significantly better than the corresponding values for CA125 or age alone.

Conclusions

Although preoperative CA125 had limited sensitivity in predicting the prognosis for early-stage EC after initial treatment, it remains a useful serum marker for risk assessment of early-stage EC. Combining CA125 with age may increase its predictive sensitivity.

Introduction

Endometrial cancer (EC) is the most common gynecological malignant tumor, and its incidence is increasing. Although most patients are diagnosed early and cured by hysterectomy, 15–20% of patients experience recurrence without locally advanced or metastatic disease [1]. Therefore, identifying adverse factors related to recurrence and metastasis from clinicopathological information for patients with early-stage EC and providing appropriate treatment is especially beneficial for improving overall survival (OS). Serum biomarkers are of great value for the early detection of primary and recurrent diseases, monitoring responses to adjuvant therapy, preoperative selection of high-risk patients, and more personalized treatment. Cancer antigen 125 (CA125) levels have been shown to be associated with a number of clinicopathological factors in EC. However, most of the current studies on CA125 in EC are focused on the prediction of advanced EC [2–5], and the literature on the predictive role of CA125 in early-stage EC is limited. This study aimed to analyze the predictive value of preoperative serum CA125 combined with clinicopathological factors in patients with early-stage EC after initial treatment.

Methods And Materials

1. Ethics Approval and Informed Consent

This retrospective study was approved by the Ethics Review Committee of Peking Union Medical College Hospital, Chinese Academy of Medical Sciences [Protocol number S-K139]. The clinical trial ID of the study is ChiCTR-PRC-17010712. Evaluation of all data met the requirements of the Helsinki Declaration.

2. Materials and Evaluation

After obtaining Institutional Review Board approval, we retrospectively reviewed the medical records in our multi-institutional EC database. A total of 1268 patients with early-stage EC treated at 13 grade A tertiary hospitals in China between January 1999 and December 2015 were included. Preoperative serum CA125 levels were recorded for 447 of the 1268 patients (Figure 1). All patients underwent primary hysterectomy±bilateral salpingo-oophorectomy, had confirmed FIGO2009 stage I or stage II EC and had a World Health Organization performance score between 0 and 2. All patients received postoperative adjuvant radiotherapy and were followed up for at least 3 months. Risk classification was carried out according to ESMO-ESGO-ESTRO risk classification. Treatment-related late toxicity was evaluated according to the Radiation Therapy Oncology Group (RTOG) criteria. The electrochemiluminescence method of Roche Cobas was used to detect CA125. The normal range of CA125 was ≤ 35 u/ml.

Figure 1 Flow chart of patient enrollment

3. Radiotherapy Modalities

All patients received postoperative pelvic external beam radiotherapy (EBRT)±vaginal brachytherapy (VBT) or VBT alone. The target volume of EBRT included the vaginal stump and upper 1/2 of the vagina, parauterine, presacral, obturator, internal and external iliac and common iliac lymphatic drainage areas. Conventional four-field “box” radiotherapy (CRT), three-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT) were used in external beam irradiation. VBT was performed by irradiating the vaginal stump and upper 1/2 of the vagina with single-channel or multichannel applicators, and two- and three-dimensional HDR brachytherapy plans were used for brachytherapy.

4. Follow-up

All patients had complete clinical, pathological, and follow-up information. Patients were assessed every 3-6 months for the first 2 years after radiotherapy, every 6-12 months during the following three years, and then annually. The prognostic factors analyzed included age at diagnosis, preoperative serum CA125 levels, surgical type, pathological type, grade, myometrial invasion (MI), lymphatic vascular space invasion (LVSI), lower uterine segmental invasion (LUSI), cervical stromal invasion (CSI), FIGO 2009 stage, ESMO-ESGO-ESTRO risk classification, time interval between surgery and radiotherapy, radiotherapy mode, and use of chemotherapy.

The primary endpoint was 5-year OS. The secondary endpoint was 5-year disease-free survival (DFS). The primary endpoint was defined as the time from the operation to death from any cause or the last follow-up. The secondary endpoint was defined as the time from the operation to disease recurrence or metastasis or the last follow-up. After the initial treatment, new lesions in the pelvic area were defined as local regional recurrence (including vaginal recurrence), and new lesions beyond the pelvic area were defined as distant metastasis.

5. Statistical Analysis Methods

The Kaplan-Meier method was used to calculate OS and DFS. Cox proportional hazard regression was used for multivariate analysis. Binary logistic regression was used to calculate the predictive probability of 5-year OS for each patient, and the ROC curve was used to calculate the sensitivity and specificity of the variables, as well as the combined predictive value of CA125 and age. All analyses were performed using IBM SPSS Statistics for Windows version 19.0, and $P < 0.05$ was considered statistically significant.

Results

1. Clinical characteristics

The median follow-up time was 59 months (3-201 months). Four hundred seven patients (91.1%) were staged as I (FIGO2009), and forty patients (8.9%) were staged as II. A total of 313 patients (70.0%) underwent completely staged surgery. Among the 447 patients, 51.7% (231 cases) had deep MI, and 64% (286 cases) had grade 2-3 MI. According to the ESMO-ESGO-ESTRO risk classification, there were 16.8% (75 cases) in the high-intermediate-risk group and 21.5% (96 cases) in the high-risk group. The median time interval between surgery and radiotherapy was 38 days (14-174 days), and the cutoff value of the time interval between surgery and radiotherapy for OS and DFS was 49.5 days. The median number of lymph node dissections was 18 (range 1-65). In patients receiving EBRT, 33.6% received CRT, 14.3% received 3DCRT, and 52.1% received IMRT. The dose range to EBRT was 40-50.4 Gy in 25-28 fractions. When VBT was used as a boost to EBRT, the dose to the vaginal mucosa was 8-25 Gy in 2-5 fractions. For postoperative VBT alone, the dose to the vaginal mucosa was 25-40 Gy in 5-8 fractions. Ninety-five patients (21.3%) underwent chemotherapy. The clinical characteristics and initial treatment of the patients are shown in Table 1.

2. Preoperative serum CA125 level and age at diagnosis

Serum CA125 levels were negatively correlated with age ($P=0.001$). The median preoperative serum CA125 level and age at diagnosis for 447 patients were 20.6 U/ml (1.9-863.2 U/ml) and 57 years (23-86 years), respectively. The best cutoff value of age at diagnosis was 61 years (AUC=0.654, sensitivity=54.5%, specificity=76.5%).

According to its cutoff value, age was divided into two groups: ≤ 61 years and > 61 years. For patients aged ≤ 61 years, the median CA125 value was 22.3 U/ml (1.9-863.2 U/ml), and the cutoff value was 37.7 U/ml (AUC 0.535, sensitivity =0.4, specificity =0.751). For patients aged > 61 years, the median CA125 value was 19.48 U/ml (3.36-337.5 U/ml), and the cutoff value was 39.35 U/ml (AUC 0.609, sensitivity =0.417, specificity =0.840). Patients aged >61 years with CA125 > 39.35 U/ml and patients aged ≤ 61 years with CA125 > 37.7 U/ml were classified as the CA125-positive group. In contrast, patients aged >61 years with CA125 < 39.35 U/ml and patients aged ≤ 61 years with CA125 < 37.7 U/ml were classified as the CA125-negative group. Finally, CA125 was statistically analyzed in the form of a positive group and a negative group.

3. Survival analysis

The 5-year OS and DFS rates were 94.4% and 89.1%, respectively. Among all 447 patients, 22 patients died, among whom 14 died of EC, 7 died of cardiovascular comorbidities and 1 died of secondary primary cancer. Of all 447 patients, 32 had recurrence or metastasis after initial treatment. In the first disease progression, 8 patients had local regional recurrence, 5 patients had both distant metastasis and local regional recurrence, and 19 patients had distant metastasis. The sites of metastasis included the peritoneum (peritoneal dissemination), lung, liver, bone, brain, adrenal gland and lymph node.

4. Analysis of prognostic factors

In the univariate analysis, preoperative serum CA125, surgical type and time interval between surgery and radiotherapy were significant for 5-year OS. Age, surgical type, LVSI and time interval between surgery and radiotherapy were significant for 5-year DFS. As shown in **Table 1**.

Table 1 Clinical characteristics of 447 patients and univariate analysis for OS and DFS

Variable		No.	P for OS	P for DFS
Age	≤61y	335 (74.9%)	0.001	0.002
	>61y	112 (25.1%)		
Preoperative serum CA125	Positive	341 (76.3%)	0.033	0.154
	Negative	106 (23.7%)		
Surgical type	Completely surgically staged	313 (70.0%)	0.036	0.095
	Incompletely surgically staged	134 (30.0%)		
Pathology	Endometrioid carcinoma	416 (93.1%)	0.673	0.614
	Non-endometrioid carcinoma	31 (6.9%)		
Grade ^a	Grade1	161 (36.0%)	0.314	0.321
	Grade2	187 (41.8%)		
	Grade3	99 (22.2%)		
MI	≥1/2	216 (48.3%)	0.306	0.374
	<1/2	231 (51.7%)		
LVSI	Positive	68 (15.2%)	0.300	0.008
	Negative	379 (84.8%)		
LUSI	Yes	171 (38.3%)	0.681	0.454
	No	276 (61.7%)		
CSI	Yes	39 (8.7%)	0.537	0.109
	No	408 (91.3%)		
FIGO2009stage	Ia	213 (47.7%)	0.495	0.252
	Ib	194 (43.4%)		
	II	40 (8.9%)		
ESMO-ESGO-ESTRO Risk classification	Low risk	136 (30.4%)	0.887	0.129
	Intermediate risk	140 (31.3%)		
	High-intermediate risk	75 (16.8%)		
	High risk	96 (21.5%)		
Time interval between S and R	≤49 days	314 (70.2%)	0.019	0.023
	>49 days	133 (29.8%)		
Radiotherapy mode	EBRT alone	20 (4.5%)	0.150	0.517
	VBT alone	295 (66.0%)		
	EBRT+VBT	132 (29.5%)		
Chemotherapy	Yes	95 (21.3%)	0.601	0.583
	No	352 (78.7%)		

^aEndometrioid cancers were designated as grade 1, 2, or 3. All poorly differentiated cancers, uterine papillary serous cancers, and clear cell cancers were designated as grade 3. LUSI=lower uterine segment invasion, LVSI=lymphatic vascular space invasion, EBRT= external beam radiotherapy, VBT=vaginal brachytherapy, MI=myometrial invasion, CSI=cervical stromal invasion. S=surgery, R=radiotherapy

The results of the multivariate analysis of all 447 patients for OS showed that older age and CA125 positivity were independent prognostic factors for OS (see Table 2). The nomogram is shown in Figure 2. In the multivariate analysis for DFS, age, complete surgical stage, LVSI

and time interval between surgery and radiotherapy were independent prognostic factors, while CA125 was not statistically significant in the univariate and multivariate analyses, as shown in Table 3.

Table 2 Results of the multivariate analysis of all 447 patients for OS

Variable	HR	P	95% CI	
			2.5%	97.5%
Age	4.33	0.0007	1.858	10.082
CA125	2.86	0.0162	1.215	6.732

OS=Overall survival, HR=hazard ratio, CI=confidence interval.

Age 0: ≤ 61 y, 1: > 61 y, CA125 0: negative, 1: positive.

Figure 2 Nomogram for 5y OS

Table 3 Results of the multivariate analysis of DFS in all 447 patients

Variable	HR	P	95% CI	
			2.5%	97.5%
Age	1.04	0.0117	1.010	1.078
Surgical type	0.48	0.0329	0.2449	0.942
LVSI	2.60	0.0065	1.3057	5.167
Interval	1.01	0.0200	1.002	1.021

We further analyzed the relationship between CA125 and clinical parameters. The clinical characteristics of each group are shown in **Table 5**. We found that there were more patients with deep MIs, with LUSI(+), with FIGO 2009 stage Ib and II, and receiving EBRT and chemotherapy ($P < 0.05$) in the CA125-positive group. The survival function is shown in Figure 3. There was a significant difference between the two groups. The 5-year OS of the patients in the CA125-positive group was 90.5%, and the 5-year OS of the patients in the CA125-negative group was 95.5% ($P = 0.033$).

The 5-year OS rates among patients aged ≤ 61 years and those aged > 61 years were 96.2% and 88.8%, respectively ($P = 0.001$). The survival function is shown in Figure 3.

Figure 3 Survival function of CA125(3-a) and age(3-b) alone and in combination(3-c) to predict 5-year OS

Finally, the relationship between CA125 combined with age and other clinical features was analyzed. The AUC of CA125 combined with age at diagnosis was 0.692 (sensitivity=68.2%, specificity=68.2%, $P < 0.002$), which was significantly better than the predictive value of CA125 or age alone, as shown in Table 4.

Table 4 Value of CA125 and age alone or in combination in predicting OS in early-stage EC

	AUC	Sensitivity (%)	Specificity (%)	P-value
CA125 combined with age	0.692	0.682	0.682	0.002
CA125 alone	0.590	0.409	0.772	0.152
Age alone	0.654	0.545	0.765	0.015

Therefore, patients were divided into 4 groups according to age and CA125: age ≤ 61 years and CA125 < 37.7 U/ml; age ≤ 61 years and CA125 > 37.7 U/ml; age > 61 years and CA125 < 39.35 U/ml; and age > 61 years and CA125 > 39.35 . In the analysis of the clinicopathological factors of these four groups of patients, the proportion of complete surgical staging and stage Ia decreased gradually, and that of MI increased gradually (see **Table 5**). The 5-year OS rates of the four groups were 96.9%, 93.6%, 91.4% and 75.6%, respectively ($P = 0.000$) (see Figure 3).

Table 5 The baseline characteristics of the 447 patients with EC stratified by CA125 and age

Characteristic		CA125groups		P	Age and CA125 combined groups				P
		Negative	Positive		1	2	3	4	
		341(%)	106(%)		250(%)	85(%)	91(%)	21(%)	
Age	≤61y	250(73.5%)	85(80.2%)	0.161	/	/	/	/	/
	>61y	91(26.7%)	21(19.8%)		/	/	/	/	
Endometrioid carcinoma		318(93.3%)	98(92.5%)	0.827	234(93.6%)	79(92.9%)	84(92.3%)	19(90.5)	0.938
Surgical type	Completely surgically staged	242(71.0%)	71(67.0%)	0.467	186(74.4%)	61(71.8%)	56(61.5%)	10(47.6%)	0.014
Grade	G1	124(36.4%)	37(34.9%)	0.963	93(37.2%)	30(35.3%)	31(34.1%)	7(33.3%)	0.997
	G2	142(41.6%)	45(42.5%)		104(41.6%)	36(42.4%)	38(41.8%)	9(42.9%)	
	G3	75(22.0%)	24(22.6%)		53(21.2%)	19(22.4%)	22(24.2%)	5(23.8%)	
MI	≥1/2	156(45.7%)	60(56.6%)	0.049	100(40.0%)	45(52.9%)	56(61.5%)	15(71.4%)	0.000
	<1/2	185(54.3%)	46(43.4%)		150(60.0%)	40(47.1%)	35(38.5%)	6(28.6%)	
LVSI	Positive	47(13.8%)	21(19.8%)	0.163	34(13.6%)	16(18.8%)	13(14.3%)	5(23.8%)	0.453
	Negative	294(86.2%)	85(80.2%)		216(86.4%)	69(81.2%)	78(85.7%)	16(76.2%)	
LUSI	Yes	121(35.5%)	50(47.2%)	0.039	94(37.6%)	45(52.9%)	27(29.7%)	5(23.8%)	0.006
	No	220(64.5%)	56(52.8%)		156(62.4%)	40(47.1%)	64(70.3%)	16(76.2%)	
CSI	Yes	26(7.6%)	13(12.3%)	0.167	20(8%)	13(15.3%)	6(6.6%)	0(0%)	0.063
	No	315(92.4%)	93(87.7%)		230(92.0%)	72(84.7%)	85(93.4%)	21(100%)	
FIGO 2009 stage	Ia	172(50.4%)	41(38.7%)	0.048	139(55.6%)	36(42.4%)	33(36.3%)	5(23.8%)	0.000
	Ib	143(41.9%)	51(48.1%)		91(36.4%)	36(42.4%)	52(57.1%)	15(71.4%)	
	II	26(7.6%)	14(13.2%)		20(8.0%)	13(15.3%)	6(6.6%)	1(4.8%)	
ESMO-ESGO-ESTROrisk classification	Low risk	108(31.7%)	28(26.4%)	0.367	88(35.2%)	24(28.2%)	20(22.0%)	4(19.0%)	0.088
	Intermediaterisk	109(32.0%)	31(29.2%)		71(28.4%)	21(24.7%)	38(41.8%)	10(47.6%)	
	High-intermediaterisk	57(16.7%)	18(17.0%)		42(16.8%)	16(18.8%)	15(16.5%)	2(9.5%)	
	High risk	67(19.6%)	29(27.4%)		49(19.6%)	24(28.2%)	18(19.8%)	5(23.8%)	
Radiotherapy mode	VRT alone	238(69.8%)	57(53.8%)	0.003	178(71.2%)	43(50.6%)	60(65.9%)	14(66.7%)	0.007
	EBRT±VBT	103(30.2%)	49(46.2%)		72(28.8%)	42(49.4%)	31(34.1%)	7(33.3%)	
Chemotherapy	Yes	65(19.1%)	30(28.3%)	0.049	48(19.2%)	25(29.4%)	17(18.7%)	5(23.8%)	0.217
	No	276(80.9%)	76(71.7%)		202(80.8%)	60(70.6%)	74(81.3%)	16(76.2%)	
Time interval between S and R	≤49 days	244(71.6%)	70(66.0%)	0.277	180(72%)	56(65.9%)	64(70.3%)	14(66.7%)	0.736
	>49 days	97(28.4%)	36(34%)		70(28%)	29(34.1%)	27(29.7%)	7(33.3%)	
Overall mortality	Yes	13(3.8%)	9(8.5%)	0.069	6(2.4%)	4(4.7%)	7(7.7%)	5(23.8%)	0.000
	No	328(96.2%)	97(91.5%)		244(97.6%)	81(95.3%)	84(92.3%)	16(76.2%)	

1= age≤61 years and CA125<37.7, 2= age≤61 years and CA125>37.7, 3=age>61 years and CA125<39.35, and 4=age>61 years and CA125>39.35.LUSI=lower uterine segment invasion, LVSI=lymphatic vascular space invasion, EBRT= external beam radiotherapy, VBT=vaginal brachytherapy, MI=myometrial invasion, CSI=cervical stromal invasion. S=surgery, R=radiotherapy

Discussion

At present, the commonly used clinicopathological risk stratification system does not include all used factors[6, 7]. According to the results of previous studies, preoperative tumor markers such as CA125 and age are prognostic factors for EC[8, 9]. In this study, the multivariate analysis of the 5-year OS of all patients with early-stage EC showed that none of the clinicopathological factors, except preoperative serum CA125 and age at diagnosis, had an independent prognostic advantage for OS. Therefore, for patients with early-stage EC, preoperative CA125 detection may help us distinguish between high- and low-risk groups earlier.

CA125 is a glycoprotein expressed in mesenchymal cells of the adult pleura, pericardium, and peritoneum, as well as cells derived from embryonic Mullerian tubes, namely, the oviduct, endometrium, and endometrial cells of the cervix. In premenopausal women, its level can be elevated due to a variety of physiological states and benign diseases, including inflammation, endometriosis, and menstruation, among others[10]. In EC, CA-125 levels have been shown to be associated with several clinicopathological factors[2–4, 8, 11–19] to predict LVSI, MI, lymph node metastasis, adnexal involvement, distant metastasis, OS, and DFS. There are different cutoff values for different age groups and for predicting different endpoints[2, 13, 15, 18]. Therefore, CA125 is considered to be a valuable prognostic marker in EC patients.

However, most of the current studies on CA125 in EC are focused on finding ways to predict of advanced EC, such as distinguishing cases of extrauterine spread of EC from those with localized disease or monitoring advanced and recurrent cases[2–5, 11–15, 17, 18]. Only two studies have reported the independent predictive value of CA125 for OS, LRFS and DFS after adjuvant therapy for early-stage EC[19, 20]. However, they were single-center retrospective studies with a small number of cases.

The purpose of this study was to evaluate the predictive value of CA125 for the prognosis of early-stage EC after surgery and adjuvant therapy. Due to the influence of age on CA125, the cutoff values of CA125 were different for different ages in this study. In the results, the CA125-positive group had a higher proportion of MI and LUSI, resulting in a higher proportion of patients with stage Ib and II disease, as well as a higher proportion of patients receiving EBRT and chemotherapy. OS was also significantly different between the two groups. Therefore, CA125 has its own value in the prognosis of early-stage EC. However, its AUC was only 0.590 (sensitivity=0.409, specificity=0.772). Therefore, the predictive value of CA125 alone is limited.

Age is another important clinical factor for EC. Our previous results showed that age was an important independent prognostic factor for early-stage EC and that the disease-related mortality of patients increased gradually with increasing age[9]. In this study, age was also shown to be an independent prognostic factor for early-stage EC. However, its AUC, sensitivity and specificity for EC were only 0.654, 0.545 and 0.765, respectively.

Therefore, CA125 or age alone is of limited efficacy in predicting early-stage EC. When CA125 combined with age predicted the OS of early-stage EC, the AUC and sensitivity were significantly improved. In the previous literature, CA125 combined with a variety of clinicopathological factors was also suggested to increase the accuracy of clinical diagnosis, such as MRI[21], Mesothelin[22] and HE4. At present, HE4 and CA125 are clinically approved tumor markers for the diagnosis and prognosis of EC. Among them, HE4 is considered to be more correlated with the prognostic factors of EC[5, 23–26]. Its sensitivity to predict the survival of EC patients is better than that of CA125 (0.71 vs.0.35), with no significant difference in specificity between the two markers. However, in the subgroup analysis, the sensitivity of HE4 in Asian patients (0.53) was significantly lower than that in Caucasian patients (0.86). Therefore, the role of HE4 needs further clinical investigation in Asian populations. In this study, OS was significantly different among the CA125-combined age groups with older age, and the CA125-positive group had a worse prognosis. According to the current results, simple and easily obtained indicators can be used to distinguish the high-risk group of patients faster, which is quite helpful for decision-making in terms of the clinical treatment plan.

In addition, why did CA125 not show any statistical significance for DFS in this study? In most previous studies, CA125 elevation was associated with extrauterine invasion. However, in stage I-II EC, there is no extrauterine spread, such as lymph node metastasis or adnexal involvement. Therefore, CA125 did not show significance for DFS in these patients with early-stage EC in this study. However, the increase in CA125 indicates that there is a potential risk of tumor progression, such as MI and LUSI. Age plus CA125 as an overall indicator showed greater significance for OS. Therefore, for older patients with CA125 positivity, a more active treatment approach should be considered as the clinical treatment strategy, if possible.

This study is the only multicenter study to evaluate the prognostic value of preoperative serum CA125 for early-stage EC after initial treatment thus far. This study provides new and powerful evidence for the application of CA125 in early-stage EC. However, its limitation is that it is a retrospective study, which leads to the lack of some clinical information. In addition, due to the limitation of enrollment time, there is no molecular typing in the current data. Only patients with data on CA125 were included, which may result in selection bias.

Conclusion

Although preoperative CA125 has limited sensitivity in predicting the prognosis of early-stage EC after initial treatment, it remains a useful serum marker for the risk assessment of early-stage EC. Combining CA125 with age increases its predictive sensitivity. Thus, this study provides new and powerful evidence for the application of CA125 in early-stage EC.

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Ethics Review Committee of Peking Union Medical College Hospital, Chinese Academy of Medical Sciences [Protocol number S-K139]. The clinical trial ID of the study is ChiCTR-PRC-17010712. Evaluation of all data met the requirements of the Helsinki Declaration.

Consent for publication

The Authors declare that the paper is being submitted for consideration for publication in Radiation Oncology, that the content has not been published or submitted for publication elsewhere.

Availability of data and material

The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

Shuai Sun: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing. Lijuan Zou: Data curation, Validation. Tiejun Wang: Data curation, Validation. Zi Liu: Data curation, Validation. Jianli He: Data curation, Validation. Xiaoge Sun: Data curation, Validation. Wei Zhong: Data curation, Validation. Fengju Zhao: Data curation, Validation. Xiaomei Li: Data curation, Validation. Sha Li: Data curation, Validation. Hong Zhu: Data curation, Validation. Zhanshu Ma: Data curation, Validation. Wenhui Wang: Data curation, Investigation, Resources. Meng Jin: Data curation, Investigation, Resources. Fuquan Zhang: Conceptualization; Data curation; Funding acquisition; Project administration; Resources; Validation; Writing - review & editing. Xiaorong Hou: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing - review & editing. Lichun Wei: Conceptualization; Data curation; Funding acquisition; Project administration; Resources; Validation; Writing - review & editing. Ke Hu: Conceptualization; Data curation; Funding acquisition; Project administration; Resources; Validation; Writing - review & editing.

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no

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Figures

Figure 1
Flow chart of patient enrollment

Figure 2
Nomogram for 5y OS

A

C

B

Figure 3

Survival function of CA125(3-a) and age(3-b) alone and in combination(3-c) to predict 5-year OS