



Prognostic significance of pretreatment serum carcinoembryonic antigen (CEA) level in epithelial ovarian cancer

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Introduction:

CEA is superfamily of glycoproteins found on cell membranes, plays role in cell recognition and adhesion. Tumor cells may produce this protein more and altered in posttranscriptional regulation. CEA is also critical to the metastatic dissemination of colon cancer cells. Pretreatment CEA value has been evidenced as an independent factor for disease prognosis in breast cancer, colorectal cancer, gastric cancer and non-small cell lung cancer. Currently, CEA is less investigated as the prognostic significance in epithelial ovarian cancer and is more controversial. It was only reported in differentiating metastatic tumors from primary ovarian cancer, the diagnosis and prognosis in mucinous histology. The aim of the study was to evaluate the prognostic significance of pretreatment serum CEA level in epithelial ovarian cancer.

Materials and methods:

This retrospective cohort study was carried out in 326 epithelial ovarian cancer patients at Kaohsiung Chang Gung Memorial hospital between 2008-2016. All patients had histopathological confirmed diagnosis and pretreatment measurements of serum CA125 and CEA value. Data acquired from medical records including: age, FIGO stage, Histology type, tumor size and debulking status. Statistical analysis: The difference between proportions was evaluated by chi-square test. Univariate survival curves for progression-free survival (PFS) and overall survival (OS) were estimated using Kaplan–Meier method. Multivariate Cox regression analysis was used to compare independent prognostic factors for PFS and OS. SPSS (version 20) was used for all statistical analyses.

Results:

Clinical characteristics of patients with respect to pretreatment CEA level was different in histology type and CA-125 level (table 1). Our analysis showed the elevated pretreatment serum CEA value (cutoff 5 ng/ml) is an independent prognostic factor in epithelial ovarian cancer. (figure 1&2). The results of univariate and multivariate analysis were presented in table 2.& 3

Discussion:

Our analysis showed the elevated pretreatment serum CEA value (cutoff 5 ng/ml) is an independent prognostic factor in epithelial ovarian cancer. These patients has lower PFS and OS compared with patients with normal CEA value. The prognostic value of CEA had been investigated by some studies with controversial result. In Danish ‘MALOVA’ ovarian cancer study, the protein expression level of CEA is an independent prognostic factor in ovarian cancer. Besides, a higher proportion of mucinous tumors were CEA positive compared with other histological types. Recent data from Beijing revealed prognostic significance of preoperative serum CEA in primary mucinous ovarian carcinoma in univariate analysis but not in multivariate analysis. Though past studies revealed more specific role of elevated CEA value in mucinous type ovarian cancer, our data showed similar distribution of elevated CEA value in serous, endometrioid and mucinous ovarian cancer. This distribution may be discussed in further larger study size. Detecting serum value of CEA was more convenient in clinical practice compared with CEA value in tissue. CEA may carry prognostic information and this result may indicate that patients showing elevated value of pretreatment CEA could be included in high-risk group for recurrence. Currently, this study included extended and comprehensive database of relationship between epithelial ovarian cancer and serum CEA.

Conclusion:

Our study included all epithelial ovarian cancer patients with subgroup analysis and the detection of serum CEA value provided the convenience in clinical practice. Elevated pretreatment serum CEA value is an independent prognostic factor in epithelial ovarian cancer in both univariate and multivariate analysis.

Table 1. Clinical characteristics of patients with respect to pretreatment CEA concentration (ng/ml)

	CEA<5 (n=279)	CEA ≥ 5 (n=47)	P value
Age, Median, yr (25 th -75 th)	53 (45-60)	58 (53-71)	
FIGO stage			0.839
Early (I, II)	138 (49.5)	24 (51.1)	
Late (III, IV)	141 (50.5)	23 (48.9)	
Histology			0.002
Serous	106 (38.0)	9 (19.1)	
Mucinous	32 (11.5)	11 (23.4)	
Clear cell	54 (19.4)	3 (6.4)	
Endometrioid	49 (17.6)	13 (27.7)	
Other	38 (13.6)	11 (23.4)	
Tumor size (cm)			0.022
< 10	157 (56.3)	18 (38.3)	
≥ 10	122 (43.7)	29 (61.7)	
Surgical debulking			0.902
Optimal	211 (84.1)	39 (84.8)	
Suboptimal	40 (15.9)	7 (15.2)	
Preoperative CA 125 level (U/ml)			0.029
< 35	46 (16.5)	2 (4.3)	
≥ 35	233 (83.5)	45 (95.7)	

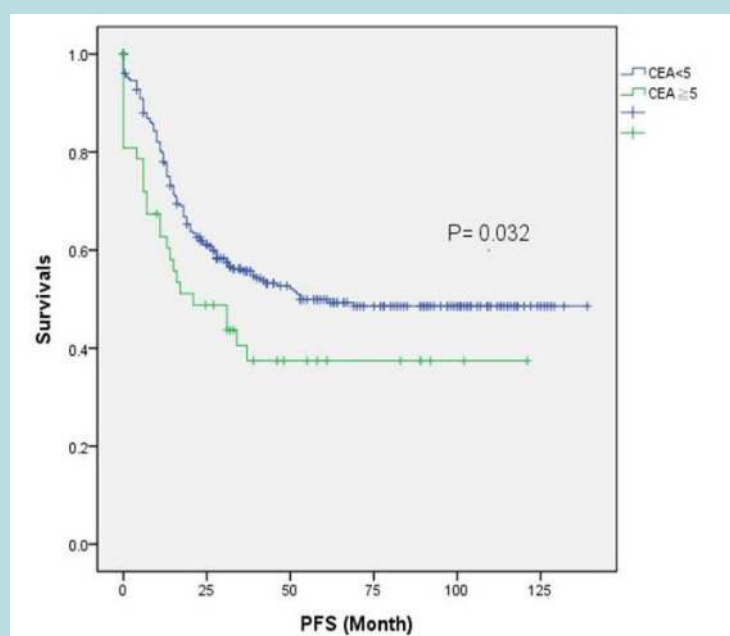


Fig. 1. Progression-free survival (PFS) curves of epithelial ovarian cancer patients relative to pretreatment CEA levels (ng/ml).

Table 2.

Variable	Univariate analysis			
	PFS		OS	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (yr)				
< 50	1.559 (1.110-2.190)	0.01	1.638 (1.071-2.504)	0.023
≥ 50				
Stage				
Early (I, II)	5.776 (3.940-8.470)	<0.001	4.088 (2.620-6.379)	<0.001
Late (III, IV)				
Histology				
Serous	-	<0.001	-	0.002
Mucinous	0.409 (0.227-0.737)	0.003	0.622 (0.314-1.234)	0.174
Clear cell	0.558 (0.352-0.882)	0.013	0.739 (0.424-1.290)	0.288
Endometrioid	0.235 (0.131-0.424)	<0.001	0.316 (0.155-0.645)	0.002
Other	1.115 (0.735-1.694)	0.608	1.387 (0.848-2.288)	0.201
Size (cm)				
< 10	0.594 (0.429-0.824)	0.002	0.897 (0.609-1.320)	0.581
≥ 10				
CEA (pre-op)				
< 5	1.562 (1.032-2.366)	0.035	2.492 (1.587-3.913)	<0.001
≥ 5				
CA125 (pre-op)				
< 35	4.429 (2.173-9.025)	0.001	7.505 (2.379-23.672)	0.001
≥ 35				
Debulking				
Optimal	3.895 (2.683-5.655)	<0.001	3.621 (2.299-5.705)	<0.001
Suboptimal				

Table 3.

Variable	Multivariate analysis			
	PFS		OS	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (yr)				
< 50	0.811 (0.561-1.173)	0.267	0.857 (0.533-1.380)	0.527
≥ 50				
Stage				
Early (I, II)	5.155 (3.167-8.391)	<0.001	3.675 (2.057-6.565)	<0.001
Late (III, IV)				
Histology				
Serous	-	0.004	-	0.023
Mucinous	1.881 (0.894-3.956)	0.096	-	0.224
Clear cell	2.06 (1.190-3.565)	0.01	-	-
Endometrioid	0.626 (0.328-1.193)	0.154	0.721 (0.330-1.578)	0.413
Other	-	-	-	-
Size (cm)				
< 10	0.802 (0.544-1.183)	0.266	-	-
≥ 10				
CEA (pre-op)				
< 5	2.115 (1.337-3.345)	0.001	3.082 (1.856-5.118)	0.001
≥ 5				
CA125 (pre-op)				
< 35	2.602 (1.236-5.480)	0.012	4.719 (1.455-15.301)	0.010
≥ 35				
Debulking				
Optimal	1.933 (1.275-2.930)	0.002	2.205 (1.313-3.702)	0.003
Suboptimal				

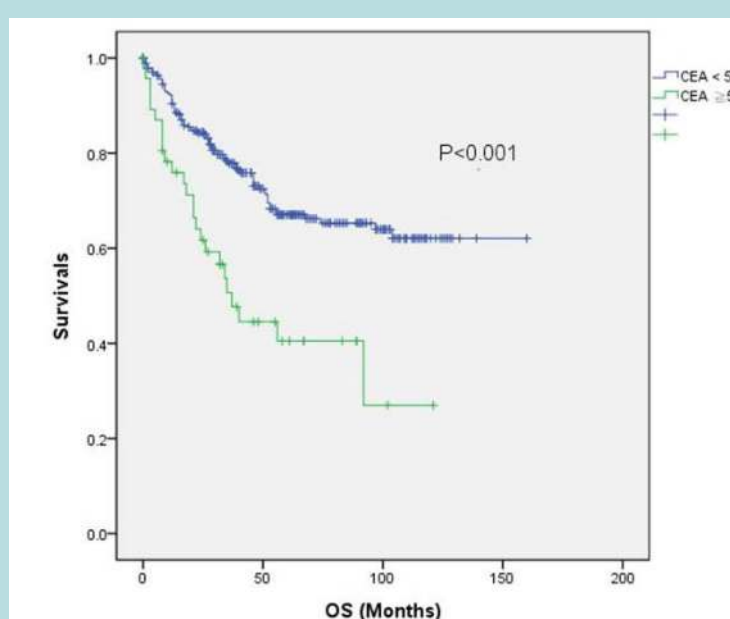


Fig. 2. Overall survival (OS) curves of epithelial ovarian cancer patients relative to pretreatment CEA levels (ng/ml).