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RESEARCH REPORT

# Prognostic value of preoperative serum tumor markers in gastric cancer

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#### **Abstract**

**AIM:** To evaluate the prognostic value of preoperative carcinoembryonic antigen (CEA), carbohydrate antigen (CA)19-9, and CA50 in patients undergoing D2 resection.

METHODS: We evaluated 363 patients with gastric cancer who underwent gastrectomy at our hospital from January 2006 to December 2009. Blood samples were obtained from each patient within 1 wk before surgery. The cut-off values for serum CEA, CA19-9, and CA50 were 5 ng/mL, 37 U/mL, and 20 U/mL, respectively. The correlation between preoperative tumor marker levels and prognosis was studied by means of univariate and multivariate analyses.

**RESULTS:** The preoperative serum positive rates of CEA, CA19-9 and CA50 were 24.0%, 18.9% and 24.5%, respectively. The positivity rate of serum CEA was significantly correlated with age (P < 0.001), sex (P = 0.022), tumor size (P = 0.007) and depth of invasion (P = 0.018); CA19-9 with tumor size (P = 0.042) and lymph node metastasis (P < 0.001); and CA50 only

with lymph node metastasis (P = 0.001). In multivariate analysis, tumor size, T category, N category, vascular or neural invasion, and adjuvant chemotherapy were independent prognostic factors for overall survival. CA19-9 had an independent prognostic significance in patients without adjuvant chemotherapy (P = 0.027).

CONCLUSION: Preoperative serum CEA, CA19-9 and CA50 are prognostic in patients with gastric cancer. Only CA19-9 is an independent prognostic factor after surgery without adjuvant chemotherapy.

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Key words: Gastric cancer; Carcinoembryonic antigen; Cancer antigen 19-9; Cancer antigen 50; Prognosis

Core tip: Recent researches have investigated the prognostic value of tumor markers in gastric cancer. The results were not conclusive and consistent. Most researchers did not account for some confounding factors, especially the use of adjuvant chemotherapy, so we investigated the prognostic value of carcinoembryonic antigen, carbohydrate antigen (CA)19-9 and CA50 in Chinese gastric cancer patients when considering the use of adjuvant chemotherapy. CA19-9 is an independent prognostic factor for gastric cancer patients after surgery without adjuvant chemotherapy.

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#### INTRODUCTION

Gastric cancer has shown a significant decline in incidence



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Table 1 Previous studies reporting the association between preoperative tumor markers and oncologic outcomes

Ref.	CEA	CA199	CA50	Number of	Pr	Prognostic impact in overall survival (P value)				
	cut-off value	cut-off value	cut-off value	patients	Univ	Univariate analysis		Multivariate analysis		
	(ng/mL)	(U/mL)	(U/mL)		CEA	CA19-9	CA50	CEA	CA19-9	CA50
Ishigami et al <sup>[10]</sup>	10	74	NA	549	< 0.0001	< 0.0001		0.040	0.150	
Nakane et al <sup>[18]</sup>	10	NA	NA	865				0.001		
Kochi et al <sup>[6]</sup>	5	37	NA	434	< 0.01	< 0.01		0.044	0.169	
Schauer et al <sup>[11]</sup>	NA	45	NA	120		0.007				
Marrelli et al <sup>[7]</sup>	5	37	NA	153	< 0.0005	< 0.0001		< 0.05	< 0.05	
Park et al <sup>[8]</sup>	7	NA	NA	810	< 0.001			0.005		
<sup>1</sup> Liu et al <sup>[12]</sup>	10	37	20	273	0.000	0.000	0.000	0.000	0.000	0.006
Liu et al <sup>[13]</sup>	10	35	25	391	0.000	0.000	0.001	0.006	> 0.05	> 0.05
Gaspar et al <sup>[23]</sup>	5	35	NA	82				0.770	0.630	
Ucar et al <sup>[19]</sup>	5	35	NA	95				0.500	0.600	
Tachibana et al <sup>[14]</sup>	5	NA	NA	196	< 0.0001			0.000		
Duraker et al <sup>[15]</sup>	5	37	NA	168	0.003	0.014		0.145	0.174	
Tocchi et al <sup>[16]</sup>	3	37	NA	59	< 0.03	< 0.05		0.000	0.014	
Lai et al <sup>[9]</sup>	5	37	NA	196				0.867	0.230	
Dilege et al <sup>[17]</sup>	5	33	NA	75	> 0.05	> 0.05				

<sup>&</sup>lt;sup>1</sup>Prognostic significance of tumor markers in T4a gastric cancer. NA: Not available; CEA: Carcinoembryonic antigen; CA: Carbohydrate antigen.

and mortality over the past decades, but due to its poor prognosis, it is still the second leading cause of cancer-related death worldwide<sup>[1]</sup>. Surgery is the main approach for gastric cancer, and the most important prognostic factor of gastric cancer is tumor node metastasis (TNM) classification<sup>[2]</sup>. However, it is difficult to obtain complete data preoperatively. For this reason, it may be important to find some other preoperative prognostic factors for evaluating the outcome of gastric cancer patients.

Tumor markers, including carcinoembryonic antigen (CEA), carbohydrate antigen (CA)19-9 and CA50, are not applied to TNM staging according to the American Joint Committee on Cancer (AJCC) 7th edition, but they have been applied in clinical practice for several decades and shown to have prognostic value in gastric cancer. CEA, a member of the immunoglobulin superfamily, was originally used as a serum marker for colorectal cancer<sup>[3]</sup>. Now, it is widely used in the diagnosis and monitoring of gastric cancer. CA19-9 is one of the antigens of the Lewis family and has been reported to be elevated in the sera of patients with gastrointestinal cancer, particularly in pancreatic cancer<sup>[4]</sup>. CA50 is a glycolipid antigen that plays an important role in cell growth and differentiation and can also be observed in a variety of malignancies, especially gastrointestinal cancers<sup>[5]</sup>. According to previous studies of the association between preoperative tumor markers and outcome of gastric cancer (Table 1), a high preoperative CEA or CA19-9 level is associated with high tumor recurrence<sup>[6-9]</sup> and poor survival rates<sup>[6-8,10-17]</sup>. Some studies have suggested that preoperative CEA, CA19-9 or CA50 level is an independent prognostic factor of gastric cancer [6-8,10,12-14,18]. However, some of these studies did not calculate the disease-free survival (DFS) time, which could indirectly reflect tumor recurrence. Moreover, most studies did not account for other factors, especially the use of adjuvant chemotherapy, which may be expected to be associated with long-term oncological outcomes.

In this retrospective study, we investigated the relationship between preoperative serum levels of CEA, CA19-9 and CA50 and clinicopathological features, and the prognostic value of these three tumor markers in patients who underwent D2 resection for gastric cancer with adjuvant chemotherapy.

#### **MATERIALS AND METHODS**

#### Patient data

We included 363 patients who underwent D2 surgical resection at the First Affiliated Hospital of Nanjing Medical University between January 2006 and December 2009. The patient inclusion criteria in this study were as follows: (1) pathological diagnosis of gastric cancer; (2) D2 surgical resection; (3) Stage I - III cancer; (4) adjuvant chemotherapy regimen of cisplatin or oxaliplatin combined with 5-fluorouracil; (5) death due to gastric cancer; and (6) availability of follow-up data. The end of follow-up was April 2013. The study protocol was approved by the Ethics Committee of this hospital. Patients were staged according to the criteria of the AJCC 7th edition. CEA, CA19-9 and CA50 were assayed by enzyme linked immunosorbent assay. Blood samples were obtained from each patient within 1 wk before surgery. CEA, CA19-9, and CA50 were assayed with magnetic particle enzyme immunoassay in UniCel<sup>TM</sup> DxI 800 Access immunoassay system (Beckman Coulter Inc. Miami, United States). The cut-off values for serum CEA, CA19-9 and CA50 were 5 ng/mL, 37 U/mL and 20 U/mL, respectively, according to the manufacturer's instructions. These patients were monitored every 3 mo for the first 2 years after surgery, and every 6 mo thereafter. Follow-up examinations included physical examination, ultrasonic inspection, chest radiography, computed tomography, positron emission tomography, magnetic resonance imaging, endoscopy, and histological biopsy. Recurrence was determined by clinical and radiological examinations or by histological confirmation.

#### Statistical analysis

The  $\chi^2$  test was used to evaluate the associations between



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Table 2 Correlation between tumor makers and major clinicopathologic characteristics of 363 patients with gastric cancer n (%)

Patient characteristics	Cases	CEA (+)	P	CA19-9 (+)	P	CA50 (+)	P
Age (yr)			< 0.001		0.213		0.134
< 60	169 (46.6)	26 (15.4)		36 (21.7)		40 (28.4)	
≥ 60	194 (53.4)	61 (31.4)		31 (16.5)		31 (20.8)	
Gender			0.022		0.800		0.375
Male	266 (73.3)	72 (27.1)		48 (18.6)		48 (23.1)	
Female	97 (26.7)	15 (15.5)		19 (19.8)		23 (28.0)	
Tumor size (cm)			0.007		0.042		0.051
< 6	243 (66.9)	48 (19.8)		38 (16.0)		40 (20.9)	
≥ 6	120 (33.1)	39 (32.5)		29 (25.0)		31 (31.3)	
Tumor location			0.463		0.737		0.662
Cardia or fundus	117 (33.1)	33 (28.2)		21 (18.6)		20 (22.0)	
Corpus or angulus	131 (37.1)	31 (23.7)		22 (17.2)		26 (25.2)	
Antrum	103 (29.2)	21 (20.4)		22 (21.8)		24 (28.2)	
Whole stomach	2 (0.6)	1 (50.0)		0 (0.0)		0 (0.0)	
Differentiation			0.65		0.671		0.701
Well/moderate	61 (16.8)	16 (26.2)		10 (16.9)		10 (22.2)	
Poorly	302 (83.2)	71 (23.5)		57 (19.3)		61 (24.9)	
T category			0.018		0.058		0.308
pT1-pT2	48 (13.2)	5 (10.4)		4 (8.7)		7 (17.9)	
pT3-pT4	315 (86.8)	82 (26.0)		63 (20.5)		64 (25.5)	
N category			0.109		< 0.001		0.001
pN0	61 (16.8)	14 (23.0)		10 (16.7)		10 (21.3)	
pN1	73 (20.1)	10 (13.7)		5 (6.9)		10 (16.9)	
pN2	100 (27.5)	29 (29.0)		12 (12.5)		10 (13.5)	
pN3	129 (35.5)	34 (26.4)		40 (31.7)		41 (37.3)	
Vascular/nerves invasion			0.997		0.950		0.763
Negative	171 (47.1)	41 (24.0)		31 (18.8)		30 (23.6)	
Positive	192 (52.9)	46 (24.0)		36 (19.0)		41 (25.2)	
AJCC stage	,		0.347	. ,	0.084	. ,	0.187
I	2 (0.6)	0 (0.0)		0 (0.0)		0 (0.0)	
П	97 (26.7)	19 (19.6)		11 (11.7)		13 (17.6)	
Ш	264 (72.7)	68 (25.8)		56 (21.7)		58 (27.1)	

AJCC: American Joint Committee on Cancer; CEA: Carcinoembryonic antigen.

tumor markers and the existing prognostic factors. Univariate survival analysis was performed using the Kaplan-Meier method. Survival curves were compared with the log-rank test. Multivariate analysis was performed using the Cox proportional hazards regression model. P < 0.05 was considered significant. All statistical analyses were performed using SPSS version 18.0.

#### **RESULTS**

#### Patient characteristics

The characteristics of 363 patients are presented in Table 2. These patients had a median age of  $60.67 \pm 11.91$  years (range: 24-93 years) and included 266 (73.3%) men and 97 (26.7%) women. Only two patients (0.6%) had Stage I cancer, 97 (26.7%) were Stage II, and 264 (72.7%) were Stage III. Poorly differentiated tumors were observed in 302 patients (83.2%), and moderately and well-differentiated tumors in 61 (16.8%). And 261 patients (71.9%) received platinum-based adjuvant chemotherapy.

## Association between clinicopathological features and tumor markers

Preoperative serum CEA levels were assayed in all 363 patients, however, for some unknown reasons, CA19-9 was assayed for 354 patients and CA50 for 290. The

preoperative serum positive rates of CEA, CA19-9 and CA50 were 24.0%, 18.9% and 24.5%, respectively. As shown in Table 2, positivity rate of CEA was significantly correlated with age (P < 0.001), sex (P = 0.022) and tumor size (P = 0.007), while CA19-9 was correlated with tumor size (P = 0.042). Compared with CA19-9 and CA50, CEA showed a more significant difference in depth of invasion (P = 0.018). In contrast, lymph node metastasis was significantly more frequent in patients with elevated levels of CA19-9 (P < 0.001) and CA50 (P = 0.001). Nevertheless, the tumor location, tumor differentiation, and vascular or neural invasion did not influence the positivity of the three tumor markers.

#### Survival and tumor markers

Overall survival (OS) was recorded for all patients, and DFS was recorded for 160. At the end of follow-up in May 2013, 167 (46.0%) patients were still alive.

On univariate analysis, by Kaplan-Meier method with the log-rank test, the OS of all patients was lower in those with elevated CEA, CA19-9 and CA50 compared to those with normal tumor marker levels (P = 0.023, P = 0.009 and P = 0.004, respectively). DFS showed no significant difference between elevated tumor marker levels and normal ones (Table 3). We divided these patients into two groups: those with and those without adjuvant che-



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Table 3 Univariate model for disease-free survival and overall survival by log-rank test

Tumor markers	DFS (P)	OS (P)
CEA (+)	0.197	0.023
CA19-9 (+)	0.236	0.009
CA50 (+)	0.335	0.004
CEA (+) and CA19-9 (+)	0.236	0.026
CA50 (+) and CEA (+)	0.236	0.100
CA19-9 (+) and CA50 (+)	0.236	0.021
CEA (+) and CA19-9 (+) and CA50 (+)	0.397	0.751
CEA (+) or CA19-9 (+) or CA50 (+)	0.302	0.002

CEA: Carcinoembryonic antigen; CA: Carbohydrate antigen; DFS: Disease-free survival; OS: Overall survival.

Table 4 Univariate model for disease-free survival and overall survival by log-rank test when considering the adjuvant chemotherapy

Tumor	DFS	( <i>P</i> )	OS (P)		
markers	Adjuvant	Non-adjuvant	Adjuvant	Non-adjuvant	
	chemotherapy	chemotherapy	chemother apy	chemotherapy	
CEA (+)	0.878	0.116	0.297	0.017	
CA19-9 (+)	0.961	0.116	0.179	< 0.001	
CA50 (+)	0.828	0.182	0.069	0.001	
CEA (+) and	0.961	0.116	0.304	0.004	
CA19-9 (+)					
CA50 (+)	0.991	0.132	0.383	0.065	
and CEA (+)					
CA19-9 (+)	0.991	0.132	0.303	< 0.001	
and CA50 (+)					
CEA (+) and	0.991	0.132	0.867	0.298	
CA19-9 (+)					
and CA50 (+)					
CEA (+) or	0.742	0.196	0.107	< 0.001	
CA19-9 (+)					
or CA50 (+)					
( )					

CEA: Carcinoembryonic antigen; CA: Carbohydrate antigen; DFS: Disease-free survival; OS: Overall survival.

motherapy (Table 4). In the non adjuvant chemotherapy group, patients with elevated CEA, CA19-9 and CA50 had a significantly worse prognosis than patients with normal tumor marker levels. The adjuvant chemotherapy group did not show similar results. To evaluate combination assays of serum CEA, CA19-9 and CA50 levels, cumulative survival was compared among five groups: all three tumor markers elevated (CA50<sup>+</sup>/CEA<sup>+</sup>/CA19-9<sup>+</sup>), at least two markers elevated (CEA<sup>+</sup>/CA19-9<sup>+</sup>, CA50<sup>+</sup>/CEA<sup>+</sup>, CA19-9<sup>+</sup>/CA50<sup>+</sup>), and at least one marker elevated (CEA<sup>+</sup>, CA19-9<sup>+</sup> or CA50<sup>+</sup>). As shown in Tables 2 and 4, the CEA<sup>+</sup>/CA19-9<sup>+</sup>, CA19-9<sup>+</sup>/CA50<sup>+</sup> and CEA<sup>+</sup>, CA19-9<sup>+</sup> or CA50<sup>+</sup> groups displayed poor OS rates in all patients and in the adjuvant chemotherapy group.

On multivariate analysis, tumor size, T category, N category, vascular or neural invasion, and adjuvant chemotherapy were independent prognostic factors for OS. Meanwhile, only tumor size was a significant risk factor for DFS. Preoperative serum CEA, CA19-9 and CA50 were not independent prognostic factors for OS (Table 5), but CA19-9 was an independent prognostic factor

in patients without adjuvant chemotherapy (P = 0.027) (Table 6).

#### DISCUSSION

Tumor markers are often used to determine the prognosis of cancer patients after radical surgery, but the role of tumor markers in gastric cancer is still controversial. α-Fetoprotein, CEA, CA19-9, CA50 and CA72-4 were considered as relatively specific markers for gastric cancer in some studies<sup>[12]</sup>. In our hospital, we began to use the preoperative serum levels of CEA, CA19-9 and CA50 to evaluate the prognosis of gastric cancer patients several years ago. That is the reason why we chose these three tumor markers in the present retrospective study.

The preoperative rate of positivity for serum CEA was 24.0%, which is similar to other studies using the same cutoff value<sup>[7,19,20]</sup>. The corresponding proportion of patients with elevated serum CA19-9 and CA50 levels was 18.9% and 24.5%, respectively, which was also similar to previous studies [6,9,12]. Some authors have reported that tumor marker positivity is associated with tumor stage [6]. However, no such correlation was found in our study. The reason may be that most of our samples were Stage II or III tumors, and there was no patient with Stage IV disease. Nevertheless, we found that CA19-9 and CA50 were associated with pN stage, and CEA with pT stage, which indicated that the positive rates of tumor markers increased as the tumor progressed. Our analysis showed that the positive rate of CEA was higher in male and elderly patients. The proportion of patients with elevated serum CEA and CA19-9 was significantly higher in those with large tumors. Also, there was a tendency for CA50 to be a marker for tumor size. It has been reported in animal studies that the elevation of serum CEA was caused by the increase in weight of primary cancer, as well as the increase in CEA production in cancer tissues<sup>[21]</sup>. It has also been reported that elevated CEA levels are related to the degree of differentiation<sup>[22]</sup>. However, we did not find any correlation between the tumor markers studied and the degree of differentiation. Similar to our findings, tumor location has previously been noted to have no association with tumor marker positivity<sup>[23]</sup>.

On the basis of our univariate analysis, patients positive for CEA, CA19-9 and CA50 had significantly poorer OS than those who were the marker negative. We found that the correlations between CEA, CA19-9, CA50 and OS were consistent with previous studies [6,7,10,13,15,16]. These correlations reflected the worse prognosis in patients with positive values for tumor markers. Marrelli et al<sup>[7]</sup> observed that the combined assay of CEA and CA19-9 provided more useful prognostic information than CEA or CA19-9 alone. Combination of these three markers, with positivity for at least two, resulted in a significant difference in OS, and proved to be a better prognostic indicator with respect to the three markers used alone. This finding suggests the complementary role of the three markers, which is also supported by the increase in overall sensitivity obtained with their concomitant use.

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Table 5 Independent prognostic factors for predicting disease-free survival and overall survival by multivariate analysis using Cox model

Factors		DFS			OS			
	HR	95%CI	P	HR	95%CI	P		
Age	1.028	0.825-1.770	0.331	0.932	0.667-1.303	0.682		
Gender	1.072	0.634-1.814	0.795	0.791	0.543-1.151	0.220		
Tumor size	1.718	1.159-2.546	0.007	1.998	1.433-2.785	< 0.001		
Differentiation	1.398	0.685-2.853	0.357	0.714	0.398-1.281	0.258		
T category	0.796	0.213-2.978	0.734	6.042	2.190-16.668	0.001		
N category	1.014	0.836-1.231	0.884	1.734	1.429-2.014	< 0.001		
Vascular/nerves invasion	0.930	0.606-1.426	0.739	1.515	1.045-2.195	0.028		
Adjuvant chemotherapy	0.931	0.614-1.411	0.736	0.618	0.425-0.898	0.012		
CEA	3.045	0.401-23.157	0.282	0.902	0.618-1.316	0.592		
CA19-9	0.392	0.045-3.384	0.394	0.836	0.449-1.556	0.571		
CA50	1.058	0.546-2.050	0.868	1.470	0.842-2.569	0.176		

CEA: Carcinoembryonic antigen; CA: Carbohydrate antigen; DFS: Disease-free survival; OS: Overall survival.

Table 6 Multivariate analysis of overall survival of patients without chemotherapy

Factors	OS				
	HR	95%CI	P		
Age	1.525	0.765-3.041	0.230		
Gender	1.229	0.559-2.701	0.608		
Tumor size	4.758	2.339-9.678	< 0.001		
Differentiation	0.784	0.259-2.379	0.668		
T category	4.566	0.570-36.569	0.153		
N category	2.096	1.506-2.916	< 0.001		
Vascular/nerves invasion	2.861	1.247-6.566	0.013		
CEA	1.329	0.670-2.637	0.415		
CA19-9	5.077	1.203-21.427	0.027		
CA50	0.671	0.183-2.463	0.547		

CEA: Carcinoembryonic antigen; CA: Carbohydrate antigen; OS: Overall survival.

On the contrary, there was no significant difference in OS when all three markers were positive. This may have been due to the limitations of the small sample size and that the levels of the three markers in the patients were not high in our analysis. We found that when CA50 was positive, there was a 77.5% chance for at least one of the other two markers to be positive. This revealed that all three markers were sensitive in gastric cancer. Also, there may be similarities in the mechanism of generation of the three markers. We also intended to compare cumulative survival in patients who were positive for only one of the tumor markers, but the numbers of these patients were too small to reach statistical significance. Not many previous studies considered the confounding factors such as the use of adjuvant chemotherapy. Therefore, to exclude the potential bias of adjuvant chemotherapy, we observed the oncological outcomes in patients without chemotherapy after surgery. As a result, these patients who were positive for CEA, CA19-9 or CA50 had a poor prognosis by univariate analysis, while there was no association between tumor markers and oncological outcomes in patients with adjuvant chemotherapy. This may have been because adjuvant chemotherapy after surgery improved the prognosis of gastric cancer patients. In our multivariate analysis, adjuvant chemotherapy was an independent prognostic factor. To evaluate whether CEA, CA19-9 and CA50 could provide information about tumor recurrence, we compared cumulative survival curves for DFS. Choi *et al*<sup>22</sup> reported that patients with an elevated tumor marker were at higher risk for recurrence. However, in our study, we did not find any correlation between recurrence and tumor markers.

In order to clarify the value of tumor markers in prognosis of gastric cancer patients, we performed multivariate analysis using a Cox proportional hazards model. The results showed that tumor size, T category, N category, vascular or neural invasion, and adjuvant chemotherapy had independent prognostic value for OS. However, the three tumor markers that we studied did not provide independent predictive value for recurrence and OS. Nevertheless, Tocchi et al<sup>[16]</sup> reported that preoperative serum CEA and CA19-9 were independent prognostic factors in gastric cancer patients. Liu et al<sup>12</sup> showed that CA50 had prognostic significance in T4a gastric cancer. Other studies did not show similar results<sup>[13]</sup>. This may have been because of the heterogeneity of patients included in these studies. Our study revealed that adjuvant chemotherapy played an important role in prognosis of gastric cancer patients. When excluding the impact of chemotherapy, increased preoperative CA19-9 level was associated independently with oncological outcomes in patients without adjuvant chemotherapy. Duraker et al<sup>24</sup> assessed CEA when investigating adjuvant chemotherapy in patients with colon cancer, but found no difference in patients with or without chemotherapy. Thus, we suppose that increased preoperative CA19-9 level could be a reason for initiating adjuvant chemotherapy in gastric cancer patients after surgery.

There were some limitations to our study. We did not obtain sufficient details about recurrence, and just calculated the DFS, which might not provide sufficient information about the correlation between tumor markers and recurrence. Also, not all three tumor markers were assayed in all the patients, so there was loss of some data. Further research with a more complete patient data is needed to obtain definitive results.

In conclusion, preoperative serum levels of CEA,



CA19-9 and CA50 can provide prognostic information in patients with gastric cancer. Furthermore, only CA19-9 is an independent prognostic factor for gastric cancer patients after surgery without adjuvant chemotherapy.

#### **COMMENTS**

#### Background

Gastric cancer is the second leading cause of cancer-related death worldwide. To predict the outcome of patients before surgery, it is important to find some preoperative prognostic factors. Tumor markers have prognostic significance in several neoplasms. This retrospective study evaluated the prognostic value of preoperative carcinoembryonic antigen (CEA), carbohydrate antigen (CA)19-9 and CA50 in patients who underwent D2 resection for gastric cancer.

#### Research frontiers

Many tumor markers are widely used clinically. CEA, CA19-9 and CA50 are relatively important in gastric cancer. The preoperative levels of these markers may indirectly reflect tumor load and prognosis. Therefore, it is becoming more important to explore the prognostic value of these tumor markers. Especially for clinicians, these markers can help them to choose appropriate treatment strategy.

#### Innovations and breakthroughs

Many studies have investigated the prognostic value of tumor markers, but most researches did not account for the confounding factors, especially the use of adjuvant chemotherapy. The authors investigated the prognostic value of CEA, CA19-9 and CA50 in gastric cancer patients when considering the use of adjuvant chemotherapy. To eliminate the influence of chemotherapy, the authors divided the patients in non-adjuvant chemotherapy and adjuvant chemotherapy groups for subgroup analysis.

#### **Applications**

CA19-9 is an independent prognostic factor for gastric cancer patients after surgery without adjuvant chemotherapy. The authors suggest that patients with a high preoperative level of CA19-9 may relapse earlier than those with a normal level; therefore, for patients with a high level of markers, more frequent physical examinations are needed.

#### Terminology

Tumor markers, including CEA, CA19-9 and CA50, have been applied in clinical practice for several decades and shown to have prognostic value in gastric cancer. Adjuvant chemotherapy: it is additional treatment given after surgery to lower the risk of the cancer recurrence.

#### Peer review

The authors evaluated the prognostic value of preoperative CEA, CA19-9 and CA50 in patients who underwent D2 resection for gastric cancer. They concluded that CA19-9 is an independent prognostic factor for gastric cancer patients after surgery without adjuvant chemotherapy. This study was important and interesting.

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