ORIGINAL ARTICLE

Retrospective Study

Carcinoembryonic antigen, carbohydrate antigen 199 and carbohydrate antigen 724 in gastric cancer and their relationship with clinical prognosis

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Abstract

BACKGROUND

Gastric cancer (GC) is a common malignant tumor of the digestive system with a high degree of malignancy. It usually develops insidiously without any specific symptoms in the early stages. As one of the diseases caused by abnormal gene changes, GC has abnormal expression of various oncogenes and products during its development. Tumor markers such as carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA199) and carbohydrate antigen 724 (CA724) are not expressed or lowly expressed in normal people, but significantly increased after carcinogenesis. Monitoring the changes in the levels of tumor markers such as CEA, CA199 and CA724 is conducive to early diagnosis and evaluation of the occurrence of some solid tumors.

AIM

To investigate the expression of CEA, CA199 and CA724 in GC and their correlation with clinical features, hoping to provide more effective markers for the early preventive diagnosis of GC.

METHODS

Of 87 patients with GC admitted to our hospital from September 2020 to December 2021 were included in the GC group, and another 80 healthy people who came to our hospital for physical examination with normal results during the same period were selected as the control group. The serum CEA, CA199, and CA724 levels were compared between the two groups, and the serum CEA, CA199, and CA724 levels were compared in patients with GC at different TNM stages, and the differences in the positive rates of CEA, CA199, and CA724 alone and in combination in detecting TNM stages of GC and GC were compared. In addition, the relationship between the levels of tumor markers CEA, CA199 and

CA724 and the clinicopathological characteristics of GC patients was also analyzed. The relationship between the serum levels of CEA, CA199 and CA724 and the survival period of GC patients was analyzed by Pearson.

RESULTS
The serum levels of CEA, CA199 and CA724 in GC group were significantly higher than those in control group ($P < 0.05$). With the increase of TNM stage, the serum CEA, CA199 and CA724 expression levels in GC patients increased significantly, and the differences between groups were statistically significant ($P < 0.05$). The positive rate of the CA724 single test was higher than that of CEA and CA199 single test ($P < 0.05$). The positive rate of the three combined tests was 95.40% (83/87), which was higher than that of CEA, CA199 and CA724 single tests. The difference was statistically significant ($P < 0.05$). The combined detection positive rates of CEA, CA199, and CA724 in stages I, II, III, and IV of GC were 89.66%, 93.10%, 98.85%, and 100.00% respectively, all of which were higher than the individual detection rates of CEA, CA199, and CA724. The differences were statistically significant ($P < 0.05$). There was no significant difference in serum CEA, CA199 and CA724 levels between GC patients with different genders, smoking history and alcohol history ($P > 0.05$). However, the serum CEA, CA199 and CA724 levels were significantly higher in GC patients aged ≥ 45 years, TNM stage III-IV, with lymph node metastasis and tumor diameter ≥ 5 cm than in GC patients aged < 45 years, TNM stage I-II, without lymph node metastasis and tumor diameter < 5 cm ($P < 0.05$).

CONCLUSION
The expression levels of serum tumor markers CEA, CA199 and CA724 in patients with GC are high and rise with the increase of TNM stage. The levels of CEA, CA199 and CA724 are related to age, TNM stage, lymph node metastasis and tumor diameter. The combined detection of CEA, CA199 and CA724 is helpful to improve the diagnostic accuracy of GC with high clinical guidance value.

Key Words: Carcinoembryonic antigen; Carbohydrate antigen 199; Carbohydrate antigen 724; Gastric cancer; TNM stage; Clinicopathologic

Core Tip: In this retrospective analysis, the expression levels of tumor markers carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA199) and carbohydrate antigen 724 (CA724) in gastric cancer (GC) patients and normal people were detected. In addition, the serum CEA, CA199 and CA724 levels in GC patients with different TNM stages, and the differences in the positive rates of TNM stages of GC and GC detected by CEA, CA199 and CA724 alone and in combination were compared. The relationship between tumor markers CEA, CA199 and CA724 levels and clinicopathological characteristics of GC patients was analyzed.

INTRODUCTION

Gastric cancer (GC) is a common malignant tumor of the digestive system originating from gastric epithelial cells, which can occur at any age, especially in the middle-aged and elderly population aged 40 to 60 years, and is more common in males than in females[1], with greater clinical harm, more than 1 million new cases each year worldwide, advanced GC has a high mortality rate, and the prognosis is unsatisfactory, seriously threatening the life safety and quality of life of patients[2,3]. According to authoritative literature, GC as a disease with high molecular and phenotypic consistency, the etiological factors are diverse, of which age, smoking, *Helicobacter pylori* infection, low fruit and vegetable intake and high salt intake are all high risk factors for the incidence of GC[4,5]. Timely adjustment of diet, smoking cessation and appropriate exercise are expected to be effective means to prevent the incidence of GC, while for patients who have suffered from GC, early examination of tumor markers is more beneficial to early diagnosis of the disease, which is of great significance for improving the survival rate and prognosis of patients[6].

Carcinoembryonic antigen (CEA), first extracted from colon cancer and embryonic tissues, is an acidic glycoprotein with human embryonic antigen characteristics, and can also exist in the form of membrane structural proteins on the surface of cancer cells and surrounding body fluids[7]. It is a common marker of solid tumors such as colon cancer, lung cancer, breast cancer and GC, and the change of its expression level can be used as an effective indicator to evaluate the therapeutic effect and prognosis of malignant tumor diseases[8,9]. Carbohydrate antigen 199 (CA199), an oligosaccharide tumor-associated antigen, is a high-molecular weight glycoprotein mixture, a glycolipid substance on the cell membrane.

It can be secreted by the human colon, stomach, pancreas and other epithelia, and significantly increased expression in digestive tract tumors. It can be used as a monitoring index to predict the treatment, follow-up and judgment of recurrence of digestive tract tumors[10]. Carbohydrate antigen 724 (CA724) is a specific glycoprotein of tumor cells. As a high molecular glycoprotein CEA, CA724 is an important indicator for staging tumor and judging digestive tract tumors. Previous studies have also suggested that patients with GC often show elevated expression of CA724. Monitoring changes in CA724 levels has a high guiding value for the screening and treatment of GC[11]. Although a large number of studies have found that CEA, CA199 and CA724 have the potential to be used as markers to predict the development of digestive tract tumors[12,13], there are few reports on the expression of CEA, CA199 and CA724 in GC and their correlation with clinical features. Based on this, this study analyzed the clinical data of patients with GC admitted to our hospital retrospectively in order to investigate the expression levels of tumor markers such as CEA, CA199 and CA724 in patients with GC and their correlation with clinical parameters. It is expected to provide more data to support the early prevention, screening and treatment of GC.

MATERIALS AND METHODS

General information
Of 87 patients with GC admitted to our hospital from September 2020 to December 2021 were selected as the study subjects and included in the GC group, including 46 males and 41 females; aged 35 to 80 years, mean age (59.11 ± 6.02) years; 52 patients with smoking history, 35 patients without smoking history; 56 patients with alcohol history, 31 patients without alcohol history; TNM stage[14] was 20 patients in stage I, 23 patients in stage II, 28 patients in stage III, and 16 patients in stage IV. Another 80 healthy people who came to the hospital for physical examination during the same period and had normal results were selected as the control group, including 42 males and 38 females; aged 35-79 years, mean age (58.94 ± 5.76) years; 43 cases with smoking history, 37 cases without smoking history; 45 cases with alcohol history, 35 cases without alcohol history. There was no significant difference in gender, age, smoking and alcohol history between the two groups ($P > 0.05$), and the balance was comparable, as shown in Table 1.

Inclusion and exclusion criteria
Inclusion criteria: All patients in the GC group were pathologically confirmed as GC; no radiotherapy, chemotherapy, immunotherapy and other anti-tumor treatment were received before admission; the control group was normal physical examination results and healthy people; aged ≥ 18 years; clinical history and data were complete.

Exclusion criteria: Patients with heart, liver, kidney and other vital organ dysfunction; combined with other malignant tumor diseases; combined autoimmune diseases, blood diseases; combined cognitive dysfunction or mental illness; pregnant, lactating women.

Tumor marker detection method
Of 5 mL of fasting cubital venous blood was collected from patients in the GC group in the morning on the next day after admission and from the control group in the morning on the day of physical examination. The whole blood was centrifuged at 3000 r/min using a high-speed centrifuge for 10 min to obtain the upper layer of serum, which was stored at -80 °C thereafter for future use. Serum CEA, CA199 and CA724 levels were measured by automatic electrochemilumin-escence immunoassay analyzer (manufacturer: Roche Biotechnology, Switzerland, model: cobas e601) in the two groups of subjects, respectively. All kits were purchased from Shanghai Enzyme Linked Immunology Co., Ltd. All experimental procedures were performed in strict accordance with the kit instructions. The criteria for positive detection were as follows: CEA > 3.4 ng/mL, CA199 > 39 U/mL, CA724 > 9.8 U/mL, and if one of the indicators in the combined detection was positive, it was judged as positive.

Statistical analysis
SPSS 22.0 software was used to process and analyze all data in this study. Measurement data were expressed as (mean ± SD). One-way analysis of variance was used to compare multiple groups. t test was used to compare two groups. Enumeration data were expressed as percentage and χ^2 test was used. Pearson analysis was performed to analyze the relationship between CEA, CA199 and CA724 levels and the survival period of GC patients. $P < 0.05$ was considered statistically significant.

Ethical approval
This study has obtained approval from the Ethics Committee of The First People's Hospital of Lianyungang, and has been conducted in accordance with the principles outlined in the Helsinki Declaration and Good Clinical Practice guidelines. All patients information are strictly confidential, so the informed consent was waived by the Ethics Committee.

RESULTS

Comparison of serum CEA, CA199 and CA724 levels between the two groups
The expression levels of serum tumor markers CEA, CA199 and CA724 in the two groups were compared. The results

Table 1 Comparison of general data between the two groups

Group	n	Gender (n)		Age (yr)	Smoking history (case)		Alcohol history (n)	
		Male	Female		Yes	No	Yes	No
Gastric cancer group	87	46	41	59.11 ± 6.02	52	35	56	31
Control group	80	41	39	58.94 ± 5.76	43	37	45	35
χ^2		0.044		0.186	0.616		1.149	
P value		0.834		0.853	0.433		0.284	

showed that the serum CEA, CA199 and CA724 levels in the GC group were significantly higher than those in the control group, and the differences were statistically significant ($P < 0.05$), as shown in Table 2.

Comparison of serum CEA, CA199 and CA724 levels in patients with different stages of GC

The differences in the expression levels of serum tumor markers CEA, CA199 and CA724 between patients with different TNM stages of GC were compared, and the results showed that the expression levels of serum CEA, CA199 and CA724 in patients with GC increased significantly with TNM stage, and the differences between groups were statistically significant ($P < 0.05$), as shown in Table 3.

Comparison of the positive rates of single and combined detection of CEA, CA199 and CA724 in patients with GC

The differences in the positive rates of GC detected by serum tumor markers CEA, CA199 and CA724 alone and in combination were compared. The results showed that the positive rate of CA724 single detection was higher than that of CEA and CA199 single detection ($P < 0.05$); the positive rate of the three combined detection was 95.40% (83/87), higher than that of CEA, CA199 and CA724 single detection, and the differences were statistically significant ($P < 0.05$), as shown in Table 4.

Comparison of the positive rates of single and combined detection of CEA, CA199 and CA724 in patients with different stages of GC

The positive rates of CEA, CA199 and CA724 in detecting different TNM stages of GC were compared. The results showed that the positive rates of CEA, CA199 and CA724 in detecting I, II, III and IV stages of GC were 89.66%, 93.10%, 98.85% and 100.00%, respectively, which were higher than those in CEA, CA199 and CA724. The differences were statistically significant ($P < 0.05$) in Table 5.

Relationship between Serum CEA, CA199 and CA724 levels and clinicopathology of Patients with GC

The differences in serum CEA, CA199 and CA724 levels between GC patients with different genders, ages, smoking history, alcohol history, TNM stage of tumor, lymph node metastasis and tumor diameter were compared, and the correlation between the changes in their levels and clinicopathological characteristics was analyzed. The results showed that there was no significant difference in serum CEA, CA199 and CA724 levels between GC patients with different genders, smoking history and alcohol history ($P > 0.05$), while the serum CEA, CA199 and CA724 Levels in GC patients with age ≥ 45 years, TNM stage III-IV, lymph node metastasis and tumor diameter ≥ 5 cm were significantly higher than those in GC patients with age < 45 years, TNM stage I-II, no lymph node metastasis and tumor diameter < 5 cm. The differences were statistically significant ($P < 0.05$), as shown in Table 6.

Serum CEA, CA199 and CA724 levels in patients with GC before and after radical gastrectomy

In order to investigate the relationship between serum CEA, CA199 and CA724 levels and prognosis in patients with GC, we measured serum CEA, CA199 and CA724 levels in 87 patients with GC before and 3 mo after radical gastrectomy. The results showed that the serum levels of CEA, CA199 and CA724 decreased in patients 3 mo after surgery compared with those before surgery, and the differences were statistically significant ($P < 0.05$) in Table 7.

Pearson analysis of the relationship between serum levels of CEA, CA199, and CA724 in GC and patient survival

Of 10 patients were selected from GC patients, and the relationship between the serum levels of CEA, CA199, and CA724 in GC and the survival rate of GC patients was analyzed using Pearson. The results showed that the levels of CEA, CA199 and CA724 were negatively correlated with the survival period of GC patients (Figures 1A-C).

DISCUSSION

GC is one of the malignant tumors of the digestive tract originating from the epithelial cells of the surface mucosa of the gastric wall, mostly occurring in the antrum, pylorus, cardia and other parts[15,16]. The advanced GC has a very high degree of malignancy and is a great threat to the patient's survival cycle and quality of life[17,18]. Early GC has insignificant symptoms and low diagnostic yield. Most patients are often diagnosed in the late stage, missing the optimal

Table 2 Comparison of serum carcinoembryonic antigen, carbohydrate antigen 199 and carbohydrate antigen 724 levels between the two groups

Group	n	CEA (ng/mL)	CA199 (U/mL)	CA724 (U/mL)
Gastric cancer group	87	23.69 ± 4.83	52.75 ± 8.52	41.32 ± 6.53
Control group	80	2.58 ± 0.79	4.62 ± 1.49	5.10 ± 1.27
t value		38.611	49.819	48.759
P value		< 0.001	< 0.001	< 0.001

CEA: Carcinoembryonic antigen; CA199: Carbohydrate antigen 199; CA724: Carbohydrate antigen 724.

Table 3 Comparison of serum carcinoembryonic antigen, carbohydrate antigen 199 and carbohydrate antigen 724 levels in patients with different stages of gastric cancer

Group	n	CEA (ng/mL)	CA199 (U/mL)	CA724 (U/mL)
Gastric cancer stage I group	20	18.05 ± 4.16	46.31 ± 6.78	34.29 ± 5.46
Gastric cancer stage II group	23	21.43 ± 4.22[a]	50.25 ± 5.27[a]	39.41 ± 5.89[a]
Gastric cancer stage III group	28	25.58 ± 5.37[a,b]	54.33 ± 7.64[a,b]	43.68 ± 6.03[a,b]
Gastric cancer stage IV group	16	30.68 ± 4.83[a,b,c]	61.63 ± 8.11[a,b,c]	48.72 ± 6.95[a,b,c]
F value		29.482	21.709	25.139
P value		< 0.001	< 0.001	< 0.001

[a]$P < 0.05$, compared with stage I gastric cancer group.
[b]$P < 0.05$, compared with stage II gastric cancer group.
[c]$P < 0.05$, compared with stage III gastric cancer group.
CEA: Carcinoembryonic antigen; CA199: Carbohydrate antigen 199; CA724: Carbohydrate antigen 724.

Table 4 Comparison of the positive rates of single and combined detection of carcinoembryonic antigen, carbohydrate antigen 199 and carbohydrate antigen 724 in patients with gastric cancer

Indicators	Number of positive tests	Positive rate (%)
CEA	46	52.87
CA199	48	55.17
CA724	62	71.26[a,b]
Combined	83	95.40[a,b,c]

[a]$P < 0.05$, compared with carcinoembryonic antigen.
[b]$P < 0.05$, compared with carbohydrate antigen 199.
[c]$P < 0.05$, compared with carbohydrate antigen 724.
CEA: Carcinoembryonic antigen; CA199: Carbohydrate antigen 199; CA724: Carbohydrate antigen 724.

surgical period, and the therapeutic effect is greatly reduced[19]. At present, clinical treatment of advanced GC is mostly performed by adjuvant chemoradiotherapy, molecular targeted therapy and immunotherapy, but because patients with advanced GC are mostly accompanied by distant metastasis and chemotherapy resistance[20-22], the therapeutic effect of chemoradiotherapy is poor. Thus, it is of great significance to find new molecular targets for early diagnosis and treatment of GC.

With the continuous exploration of GC, more and more scholars have found that a variety of highly expressed tumor markers, such as CEA, CA199, CA724, *etc.* can be detected in tumor tissues and serum samples of patients with GC. The abnormal changes of these tumor markers can not only be used as an effective indicator for the diagnosis and evaluation of GC progression, but also predict the prognosis of patients to a certain extent[23-25]. Ma *et al*[26] found that CEA is an independent prognostic factor in patients with GC, and the establishment of a CNLR prognostic scoring system combined with CEA and neutrophil-lymphocyte ratio can accurately predict the 3-year and 5-year survival rates of patients with GC. It has also been pointed out that the incidence of GC is significantly correlated with gender, age, CEA, alpha-fetoprotein (AFP), CA125, CA199 and CA242 positive levels, and AFP, CEA, CA125, CA199 and CA242 positive levels are

Table 5 Comparison of positive rates of single and combined detection of serum carcinoembryonic antigen, carbohydrate antigen 199 and carbohydrate antigen 724 in patients with different stages of gastric cancer, *n* (%)

Indicators	Gastric cancer stage I	Gastric cancer stage II	Gastric cancer stage III	Gastric cancer stage IV
CEA	45 (51.72)	44 (50.57)	47 (54.02)	48 (55.17)
CA199	42 (48.28)	48 (55.17)	50 (57.47)	52 (59.77)
CA724	59 (67.82)	60 (68.97)	64 (73.56)	65 (74.71)
Combined	78 (89.66)[a,b,c]	81 (93.10)[a,b,c]	86 (98.85)[a,b,c]	87 (100.00)[a,b,c]

[a]$P < 0.05$, compared with carcinoembryonic antigen.

[b]$P < 0.05$, compared with carbohydrate antigen 199.

[c]$P < 0.05$ compared with carbohydrate antigen 724.

CEA: Carcinoembryonic antigen; CA199: Carbohydrate antigen 199; CA724: Carbohydrate antigen 724.

Table 6 Relationship between serum carcinoembryonic antigen, carbohydrate antigen 199 and carbohydrate antigen 724 levels and clinicopathology in patients with gastric cancer

Clinical pathology		*n*	CEA (ng/mL)	CA199 (U/mL)	CA724 (U/mL)
Gender	Male	46	23.42 ± 4.65	52.49 ± 7.83	41.29 ± 6.18
	Female	41	23.99 ± 5.12	53.04 ± 7.67	41.35 ± 6.22
Age	< 45 years old	60	20.47 ± 8.53	49.18 ± 9.13	39.02 ± 6.45
	≥ 45 years old	27	30.85 ± 8.77[a]	60.68 ± 8.85[a]	46.43 ± 6.76[a]
Smoking history	Yes	52	23.51 ± 4.43	52.66 ± 8.41	41.57 ± 6.17
	No	35	23.96 ± 4.50	52.88 ± 8.35	40.95 ± 6.03
Alcohol history	Yes	56	23.49 ± 4.81	52.69 ± 7.41	41.30 ± 5.94
	No	31	24.05 ± 4.87	52.86 ± 9.03	41.36 ± 6.12
TNM staging	Phase I-II	43	21.02 ± 4.65	48.63 ± 8.75	37.25 ± 6.88
	Phase III-IV	44	26.30 ± 4.72[b]	56.78 ± 9.24[b]	45.30 ± 7.13[b]
lymphatic metastasis	No	45	20.83 ± 4.23	46.16 ± 7.36	38.11 ± 6.59
	Yes	42	26.75 ± 4.88[c]	59.81 ± 8.48[c]	44.76 ± 6.13[c]
Tumor diameter	< 5 cm	49	19.61 ± 4.67	47.02 ± 8.55	35.26 ± 6.62
	≥ 5 cm	38	28.95 ± 5.01[d]	60.14 ± 9.31[d]	49.13 ± 6.89[d]

[a]$P < 0.05$, compared with age < 45 years.

[b]$P < 0.05$, compared with TNM stage I-II.

[c]$P < 0.05$, compared with no lymph node metastasis.

[d]$P < 0.05$, compared with tumor diameter < 5 cm.

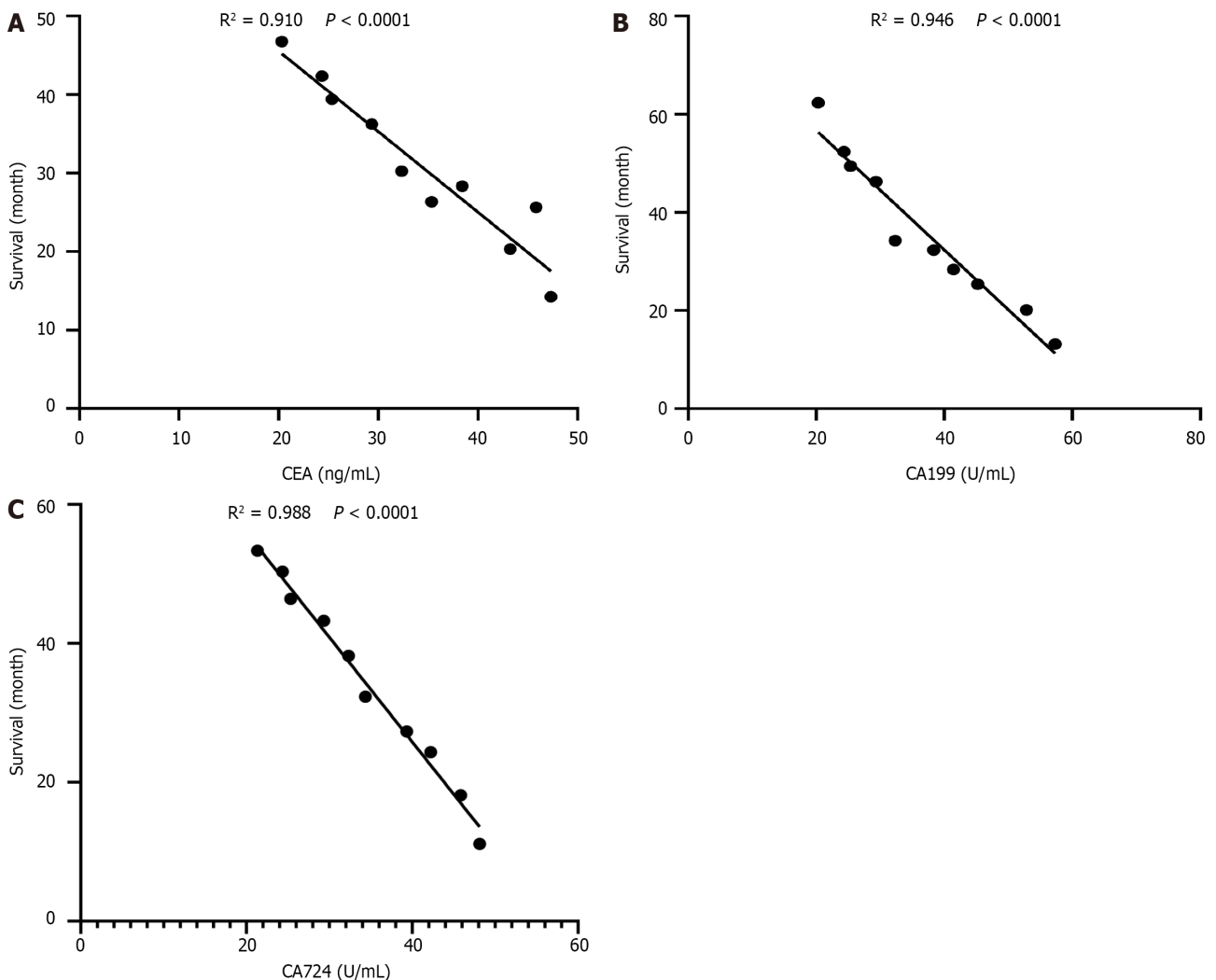CEA: Carcinoembryonic antigen; CA199: Carbohydrate antigen 199; CA724: Carbohydrate antigen 724.

significantly higher in M1 GC patients than in M0 patients[27]. Wang *et al*[28] compared the serum CA724 levels between patients with benign gastric lesions and patients with GC, and the results showed that the expression of CA724 in the serum of patients with GC was significantly increased, and the area under the curve of serum CA724 in the diagnosis of GC was 0.849, with high sensitivity and specificity in differentiating GC, which is an important indicator for early screening and auxiliary diagnosis of GC. The above studies suggest that tumor markers such as CEA, CA199, and CA724 have the potential to be used as targets for the diagnosis and treatment of GC, and based on this, this study investigated the expression of serum CEA, CA199, and CA724 in GC with their correlation with clinicopathological features in order to prevent and control the incidence of GC early and improve the survival rate and quality of life of patients with GC.

In this study, serum CEA, CA199 and CA724 levels were detected and compared between 87 patients with GC and 80 healthy subjects, and serum CEA, CA199 and CA724 levels were compared between patients with different TNM stages of GC. The results showed that serum CEA, CA199 and CA724 levels in patients with GC were significantly higher than those in the control group, and with the increase of TNM stage, serum CEA, CA199 and CA724 expression levels in patients with GC were significantly increased, and the differences between the groups were statistically significant ($P < 0.05$). In addition, the positive rate of CA724 single detection was higher than that of CEA and CA199 single detection, and the positive rate of the three combined detection was higher than that of CEA, CA199 and CA724 single detection.

Table 7 Comparison of serum carcinoembryonic antigen, carbohydrate antigen 199 and carbohydrate antigen 724 levels before and after operation in 87 patients with gastric cancer

Group	*n*	CEA (ng/mL)	CA199 (U/mL)	CA724 (U/mL)
Before procedure	87	33.11 ± 3.63	57.72 ± 6.64	31.23 ± 3.45
After procedure	87	7.24 ± 1.81	14.23 ± 2.37	4.12 ± 1.12
t value		59.488	57.536	69.712
P value		< 0.001	< 0.001	< 0.001

CEA: Carcinoembryonic antigen; CA199: Carbohydrate antigen 199; CA724: Carbohydrate antigen 724.

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Figure 1 Pearson analysis detected the linear relationship between carcinoembryonic antigen, carbohydrate antigen 199 and carbohydrate antigen 724 and survival time. A: Pearson analysis showed a negative correlation between carcinoembryonic antigen and survival time. R^2 = 0.910, $P < 0.0001$; B: Pearson analysis showed a negative correlation between carbohydrate antigen 199 and survival time. R^2 = 0.946, $P < 0.0001$; C: Pearson analysis showed a negative correlation between carbohydrate antigen 724 and survival time. R^2 = 0.988, $P < 0.0001$. CEA: Carcinoembryonic antigen; CA199: Carbohydrate antigen 199; CA724: Carbohydrate antigen 724.

The positive rates of CEA, CA199 and CA724 in stage I, II, III and IV of GC were higher than those in CEA, CA199 and CA724 ($P < 0.05$). This suggests that tumor markers CEA, CA199 and CA724 are significantly highly expressed in patients with GC and are closely related to the severity of the disease. Monitoring CEA, CA199 and CA724 levels is helpful for clinical differentiation of the incidence and progression of GC. The combined use of the three tumor markers in GC has a higher detection rate and has a higher clinical application value. CEA is one of the most widely used tumor markers in clinical practice, which was first extracted and isolated from colon cancer metastases by Canadian scholars gold and

Freedman[29] and first applied in the diagnosis of colorectal cancer. With the continuous development of molecular diagnosis, CEA has also been gradually applied in the clinical differentiation of breast cancer, lung cancer, extrahepatic cholangiocarcinoma and GC[30-33]. Similar to CEA, CA199 was first discovered in colon cancer cells in 1979, and its main active components are salivary glycolipids and salivary glycoproteins, which are not or rarely expressed in normal tissues [34,35], while they are significantly highly expressed in tumor tissues such as breast cancer and gastrointestinal adenocarcinoma and have the potential to diagnose gastrointestinal tumor diseases such as GC[36]. CA724 is one of the novel tumor markers, which was first discovered in 1981 and is widely used in the diagnosis of breast cancer and gastrointestinal tumor diseases. CA724 has a high sensitivity in the diagnosis of GC and can be detected in all stages, and is slightly superior to other tumor markers in the diagnostic efficacy of GC[37,38]. The results of this study were also consistent with that. In this study, the expression of tumor markers CEA, CA199 and CA724 in the serum of patients with GC was significantly increased, and rised with the increase of TNM stage. For GC with different TNM stages, CA724 had a better detection ability, the diagnostic rate of CA724 was better than that of CEA and CA199, and the accuracy of the three combined detection was better.

In addition, in order to further investigate the relationship between tumor markers CEA, CA199 and CA724 and clinicopathological characteristics, we collected basic data such as age, gender, smoking history, alcohol history, TNM stage, lymph node metastasis and tumor diameter of GC patients to compare the differences in serum CEA, CA199 and CA724 expression in GC patients with different characteristics. The result shows that there was no significant statistical difference in serum CEA, CA199 and CA724 levels between GC patients with different genders, smoking history and alcohol history ($P > 0.05$), while serum CEA, CA199 and CA724 levels in GC patients aged ≥ 45 years, TNM stage III-IV, with lymph node metastasis, and tumor diameter ≥ 5 cm were significantly higher than those in GC patients aged < 45 years, TNM stage I-II, without lymph node metastasis, and tumor diameter < 5 cm ($P < 0.05$). This indicates that the expression of tumor markers CEA, CA199 and CA724 is closely related to the age, TNM stage, lymph node metastasis and tumor diameter of patients with GC, and rises with the increase of patient age, TNM stage and deterioration of the disease. It suggests that the expression levels of tumor markers CEA, CA199 and CA724 can be closely detected in clinical work, so as to effectively diagnose GC, and evaluate the severity of the patient's disease, which is conducive to guiding the clinical development of effective treatment options. However, this study also has some limitations, such as failure to deeply investigate the effect of tumor markers CEA, CA199 and CA724 expression on the prognosis of patients with GC due to enrollment time constraints, which will be further supplemented subsequently.

On the other hand, we also assessed the prognostic value of tumor markers in GC. The data showed that serum CEA, CA199, and CA724 levels decreased significantly after 3 mo of radical gastrectomy for GC. This has been shown in the study by Jing *et al*[39]. In addition, Pearson analysis showed a negative correlation between serum levels of CEA, CA199, and CA724 and survival in GC patients. These markers may be of value in predicting secondary progression. However, due to the small number of patients in this study, CEA, CA199, and CA724 data all need to be treated with caution.

CONCLUSION

In summary, the expression levels of serum tumor markers CEA, CA199 and CA724 in patients with GC were significantly higher than those in the normal population, and the serum levels of CEA, CA199 and CA724 rised with the increase of TNM stage. In addition, the serum levels of CEA, CA199 and CA724 in patients with GC of different ages, TNM stages, lymph node metastases and tumor diameters were different, and the serum tumor markers were significantly highly expressed in patients with older age, more advanced TNM stages, lymph node metastases and larger tumor diameters. The combined detection of the three items helped to improve the diagnostic accuracy of GC, and could predict the progression of patients to a certain extent, providing a new molecular target and ideas for the clinical treatment and prognosis evaluation of GC, which is worthy of clinical promotion and reference.

ARTICLE HIGHLIGHTS

Research background
Tumor markers carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA199) and carbohydrate antigen 724 (CA724) are rarely expressed or not expressed in normal tissues, but significantly increased in solid cancers such as gastric cancer (GC), and monitoring the levels of tumor markers such as CEA, CA199 and CA724 is of some value for early screening and treatment of GC.

Research motivation
Tumor markers CEA, CA199, and CA724 are highly expressed in GC and are associated with clinicopathology.

Research objectives
This study aims to investigate the expression levels of serum CEA, CA199 and CA724 in patients with GC and analyze their correlation with clinical practice.

Research methods

The differences of serum CEA, CA199 and CA724 between patients with GC and normal people and the differences of each index between patients with GC at different TNM stages were compared to determine the positive rates of tumor markers alone and in combination in the diagnosis of GC and GC stages, and the correlation between CEA, CA199 and CA724 and the clinicopathology of patients with GC was analyzed.

Research results

The serum levels of CEA, CA199 and CA724 in patients with GC were significantly higher than those in the control group, and the expression levels of various indicators raised significantly with the increase of TNM stage. The positive rate of CA724 single test was higher than that of CEA and CA199 single test, and the positive rate of three combined tests was higher than that of CEA, CA199 and CA724 single test. The positive rates of CEA, CA199 and CA724 in stage I, II, III and IV of GC were higher than those in CEA, CA199 and CA724. The levels of serum CEA, CA199, and CA724 were significantly higher in GC patients aged ≥ 45 years, TNM stage III to IV, with lymph node metastasis, and tumor diameter ≥ 5 cm than GC patients aged < 45 years, TNM stage I to II, without lymph node metastasis, and tumor diameter < 5 cm.

Research conclusions

The expression levels of CEA, CA199 and CA724 in serum of patients with GC were high and increased with the increase of TNM stage. The expression levels of tumor markers were related to age, TNM stage, lymph node metastasis and tumor diameter. The combined detection of the three items was helpful to improve the diagnostic accuracy of GC.

Research perspectives

The number of enrolled patients should be further expanded, and prognostic data should be collected to investigate the effect of tumor marker CEA, CA199 and CA724 expression levels on the prognosis, which is more valuable and comprehensive guidance for clinical treatment and disease evaluation.

FOOTNOTES

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