ORIGINAL RESEARCH

Evaluation of Clinical Diagnostic and Prognostic Value of Preoperative Serum Carcinoembryonic Antigen, CA19-9, and CA24-2 for Colorectal Cancer

Shenghuai Hou, MM; Jiexian Jing, MM; Yan Wang, MM; Lili Du, MM; Baoguo Tian, MM; Xiaoqin Xu, MD; Ting Sun, MM; Yanchun Shi, MM

ABSTRACT

Objective • To investigate the clinical diagnostic and prognostic value of preoperative serum tumor markers in patients with colorectal cancer (CRC).

Methods • From September 2013 to September 2016, we enrolled 980 patients diagnosed with CRC and 870 healthy subjects from The Affiliated Cancer Hospital of Shanxi Medical University. Patients were grouped and compared in accordance with tumor stage, tumor location, lymph node metastasis, distant metastasis, histological type, depth of invasion, growth type, and other factors. Serum carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), and carbohydrate antigen 24-2 (CA24-2) concentrations in patient peripheral blood were measured, and the diagnostic value of the tumor markers in diagnosing CRC was assessed by receiver operating characteristic analysis.

Results • The sensitivity of serum tumor markers in combination was significantly higher than serum tumor markers detected individually. CA19-9 levels were significantly correlated with CA24-2 levels ($r = 0.884$; $P < .001$) in patients with CRC. The preoperative CEA, CA19-9, and CA24-2 levels in patients with colon cancer were significantly higher than in patients with rectum cancer (all $P < .001$). The CA19-9 and CA24-2 levels were significantly higher in patients with lymph node metastasis than without (both $P < .001$). In addition, the CEA, CA19-9, and CA24-2 levels in patients with distant metastasis were significantly higher than those in patients without metastasis (all $P < .001$). Stratified analysis showed that CEA, CA19-9, and CA24-2 levels were significantly correlated with TNM staging ($P < .05$). With regard to the depth of tumor invasion, CEA, CA19-9, and CA24-2 levels in tumors outside the serosa were significantly higher than those in other tumor types ($P < .05$). In terms of diagnostic performance, CEA had a sensitivity of 0.52 and a specificity of 0.98, CA19-9 had a sensitivity of 0.35 and a specificity of 0.91, and CA24-2 had a sensitivity of 0.46 and a specificity of 0.95.

Conclusion • The detection of serum tumor markers CEA, CA19-9, and CA24-2 is a good method for supporting diagnosis, making treatment decisions, judging therapeutic effect, and predicting prognosis when managing patients with CRC. (*Altern Ther Health Med.* 2023;29(6):192-197).

Shenghuai Hou, MM, Department of Colorectal and Anal Surgery, Shanxi Province Cancer Hospital/ Shanxi Hospital Affiliated to Cancer Hospital, Chinese Academy of Medical Sciences/ Cancer Hospital Affiliated to Shanxi Medical University. **Jiexian Jing,** MM; **Yan Wang,** MM; **Lili Du,** MM; **Baoguo Tian,** MM; **Xiaoqin Xu,** MD; **Ting Sun,** MM; **Yanchun Shi,** MM; Department of Etiology and Tumor Markers Laboratory, Shanxi Province Cancer Hospital/ Shanxi Hospital Affiliated to Cancer Hospital, Chinese Academy of Medical Sciences/ Cancer Hospital Affiliated to Shanxi Medical University.

Corresponding author: Yan Wang, MM
E-mail: 1015743258@qq.com

INTRODUCTION

Colorectal cancer (CRC) is the third-most-common cancer worldwide, with high rates of incidence and mortality for all genders. In China, the incidence of CRC has gradually increased in recent years, and patients with CRC are 12- to 18-years younger than those in Western countries. Previous multiple regression analysis suggested that pathological staging, TNM staging, and tumor differentiation were the prognostic factors of CRC.[1,2] Researchers have yet to explore the relationship between the main clinical features of patients with CRC and the levels of preoperative tumor markers, which could be used for monitoring recurrence and metastasis and assessing prognosis.

Serum tumor markers, such as carcinoembryonic antigen (CEA), have been commonly used for auxiliary diagnosis and disease monitoring of various tumor types. However, previous studies have reported that elevated CEA

alone is not a prognostic indicator of CRC. The serum levels of carbohydrate antigen 19-9 (CA19-9) and carbohydrate antigen 24-2 (CA24-2) have often been used in combination with CEA in the management and treatment of patients with CRC.[3-10] The low cost and ease of measurement also makes these biomarkers favorable for clinical application.[11,12] Previous CRC-zz related studies have focused on the auxiliary diagnostic role of various tumor markers, but there is a lack of relevant studies that analyze the levels of tumor markers together with clinical characteristics in patients with CRC. Exploring tumor marker levels in patients with CRC while distinguishing their clinical characteristics provides a theoretical basis for accurate patient management.

Therefore, we aimed to investigate the relationship between preoperative serum tumor markers and clinical characteristics of patients with CRC and to further explore the clinical predictive value of preoperative serum tumor markers in patients with CRC.

MATERIALS AND METHODS

From September 2013 to September 2016, we enrolled 980 patients diagnosed with CRC and 870 healthy subjects from The Affiliated Cancer Hospital of Shanxi Medical University. The study protocol was formulated in accordance with the requirements of the Declaration of Helsinki of the World Medical Association and approved by the Ethics Committee of The Affiliated Cancer Hospital of Shanxi Medical University. Informed consent forms were obtained from all patients and healthy subjects.

Inclusion and exclusion criteria

Inclusion criteria: (1) patient diagnosed with CRC by histopathology after surgery; and (2) patient received curative tumor resection; and (3) patient signed informed consent.

Exclusion criteria: (1) patient received chemotherapy or radiotherapy before surgery; or (2) patient had dysfunction of major organs, such as the liver, kidneys, or bone marrow; or (3) patients did not receive the results of their preoperative CEA, CA19-9, or CA24-2 levels.

Sample collection, testing, and evaluation

Peripheral blood from patients was obtained at the preoperative workup. The samples were centrifuged for 10 minutes at 3000 rpm, and the serum was immediately separated for testing. Serum CEA, CA19-9, and CA24-2 were detected by enzyme-linked immunosorbent assay using a Tecan system and Fujirebio diagnostics AB (Gothenburg, Sweden).

CEA >3.0 μg/mL, CA19-9 >20.0 U/mL, and CA24-2 >12.0 U/mL were deemed elevated. The cutoff values for these tumor markers were previously established by our laboratory by considering factors such as diet, living conditions, and patient-selection criteria.

Follow-up program

All patients were followed up at the outpatient clinic after hospital discharge. The follow-up program included measurement of serum tumor markers at 3-month intervals for the first 2 years and at 6-month intervals thereafter; abdominal ultrasound or chest computed tomography (CT) and pelvic CT every 6 months; colonoscopy every 1 to 2 years for 5 years. CT or positron emission tomography scans were performed on patients with increased serum CEA concentrations or when the patients developed symptoms.

Criteria for the establishment of recurrent disease were histological confirmation, radiographic progression, supportive biochemical indicators suggesting significant disease progression, or palpable disease. The follow-up end date was September 30, 2021. All surviving patients were followed up for at least 3 years. The primary endpoint of the study was overall survival (OS), defined as the time from diagnosis to death from any cause.

Statistical analysis

All the data collected in this study were analyzed using SPSS 26.0 software (IBM Corp, Armonk, NY, USA). The normality of continuous variables was tested by the Shapiro-Wilk test and visualized by histograms and Q-Q plots. Normally distributed measurement data were expressed as mean (SD), nonnormally distributed measurement data were expressed as median (IQR), and comparisons were examined by Student *t* test and Mann-Whitney test (nonparametric distribution). Categorical data were expressed as n (%), and the differences between two groups were examined by chi-square test or Fisher exact test. The predictive value of CEA, CA19-9, and CA24-2 in CRC diagnosis was evaluated by receiver operating characteristic (ROC) analysis. Multivariate analysis by the Cox proportional hazards model was used to establish the association between prognostic risk factors and 5-year survival, and the results were expressed as odds ratios (ORs) and 95% CIs. The OS rates were calculated by the Kaplan-Meier method. The statistical significance level was set at $P<.05$ for a 2-sided test.

RESULTS

Patient characteristics

A total of 980 patients and 870 healthy subjects were enrolled in this study. The study group consisted of 980 patients with CRC with a median (IQR) age of 58.6 (13.2) years (range, 20-78 years); 512 (52.2%) were male and 468 (47.8%) were female. The control group consisted of 870 healthy subjects with a median (IQR) age of 56.6 (12.1) years (range 20-77 years); 512 (52.2%) were male and 468 (47.8%) were female. There were 98 (10.0%) patients with liver-only metastasis, 21 (2.1%) with lung-only metastasis, 6 (0.6%) with bone metastasis, 8 (0.8%) with peritoneal metastasis, and 9 (0.9%) with 2 or more sites of metastases. Specific clinical characteristics are shown in Table 1.

ROC analysis of the predictive value of serum tumor markers in the diagnosis of CRC

Figure 1 shows the ROC curves for CEA, CA19-9, and CA24-2 and the correlation among preoperative serum CEA, CA19-9, and CA24-2 concentrations in patients with CRC. We

Table 1. Characteristics of Patients With Colorectal Cancer Enrolled in This Study (N = 980)

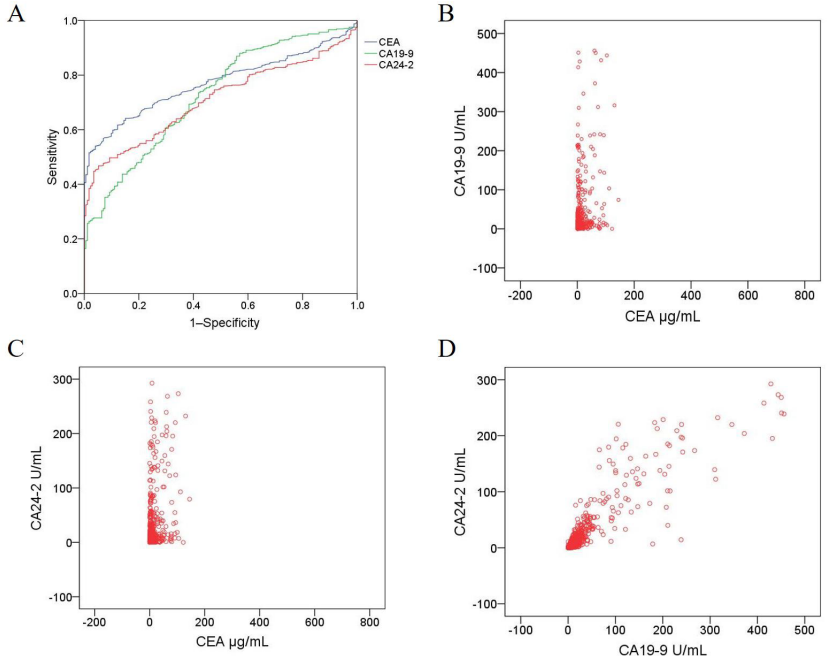
Characteristics	n
Sex	
Male	512
Female	468
Age, y	
≤40	261
>40	719
Location of primary tumor	
Rectum	775
Colon	205
TNM stage	
I	65
II	308
III	377
IV	230
Histological type	
Papillary tubular adenocarcinoma	325
Canalicular adenocarcinoma	512
Mucinous adenocarcinoma	67
Signet-ring cell carcinoma	53
Other type	23
Lymph node metastasis	
Yes	460
No	520
Distant metastasis	
Yes	142
No	838
Depth of invasion	
Outside of serosa	314
All layers	464
Deep muscularis	138
Superficial muscularis	64
Growth type	
Ulcer	501
Fungating	337
Invasive	102
Shrinkage tube	40
Tumor size, cm	
≤4 cm	474
>4 cm	506
Status at last follow-up	
Alive	389
Dead	301
Lost	290

Table 2. Preoperative Serum Tumor Marker Positivity Rates of Patients With Colorectal Cancer by TNM Stage

	Stage I (n = 65)	Stage II (n = 308)	Stage III (n = 377)	Stage IV (n = 230)	χ^2	*P* value
CEA, No. (%)	9 (14%)	63 (20.5%)	138 (36.6%)	106 (46.1%)	10.4	<.005
CA19-9, No. (%)	10 (15%)	105 (34.1%)	201 (53.4%)	160 (69.5%)	13.9	<.005
CA24-2, No. (%)	11 (17%)	94 (30.5%)	188 (49.8%)	147 (63.9%)	12.3	<.005
CEA + CA19-9 + CA24-2, No. (%)	16 (25%)	100 (32.5%)	225 (59.7)	181 (78.6%)	20.5	<.005

Abbreviations: CA19-9, carbohydrate antigen 19-9; CA24-2, carbohydrate antigen 24-2; CEA, carcinoembryonic antigen.

Figure 1. Receiver Operating Characteristic (ROC) Analysis of the Predictive Value of Carcinoembryonic Antigen (CEA), Carbohydrate Antigen 19-9 (CA19-9), and Carbohydrate Antigen 24-2 (CA24-2) Serum Tumor Markers for the Diagnosis of Colorectal Cancer (CRC). **A.** ROC curves of CEA, CA19-9, and CA24-2 for CRC diagnosis. **B, C, D.** Correlation among preoperative serum CEA, CA19-9, and CA24-2 concentrations in patients with CRC.



calculated the areas under the ROC curves to be 0.779 (95% CI, 0.74-0.84) for CEA, 0.724 (95% CI, 0.71-0.74) for CA19-9, and 0.709 (95% CI, 0.70-0.72) for CA24-2 for CRC diagnosis. The positivity rates of CEA were 14%, 20.5%, 36.6%, and 46.1% for TNM stages I to IV, respectively. The positivity rates of CA19-9 were 15%, 34.1%, 53.4%, and 69.5% for TNM stages I to IV, respectively. The positivity rates of CA24-2 were 17%, 30.5%, 49.8%, and 63.9% for TNM stage I to IV, respectively. Further analysis revealed a remarkable increase in the positivity rate with increased TNM stage ($P < .005$)(Table 2).

In terms of diagnostic performance, CEA had a sensitivity of 0.52 and a specificity of 0.98, CA19-9 had a sensitivity of 0.35 and a specificity of 0.91, and CA24-2 had a sensitivity of 0.46 and a specificity of 0.95. In addition, the sensitivity of serum tumor markers detected in combination had a sensitivity of 0.67 and a specificity of 0.84.The sensitivity of serum tumor markers detected in combination was significantly higher than markers detected individually (Figure 1).

Relationship between serum CEA, CA19-9, and CA24-2 levels in patients with CRC and their clinical characteristics

Table 3 shows the relationship between serum CEA, CA19-9, and CA24-2 levels in patients with CRC and their clinical characteristics. The preoperative CEA, CA19-9, and CA24-2 levels in patients with colon cancer were significantly higher than in patients with rectum cancer (all $P < .001$). CA19-9 and CA24-2 were significantly higher in patients with lymph node metastasis than without (both $P < .001$). In addition, the CEA, CA19-9, and CA24-2 levels in patients with distant metastasis were significantly higher than those

Table 3. Correlation Between Serum CEA, CA19-9, and CA24-2 Levels in Patients With Colorectal Cancer and Their Clinical Characteristics

Variable	Case, n	CEA, mean (SD)	*P* value	CA19-9, mean (SD)	*P* value	CA24-2, mean (SD)	*P* value
Sex							
Male	512	14.38 (2.23)	>.05	39.24 (6.12)	>.05	30.02 (3.03)	>.05
Female	468	12.04 (1.46)		35.98 (3.64)		28.79 (2.85)	
Age, y							
≤40	261	11.98 (2.17)	>.05	34.88 (5.91)	>.05	29.62 (4.90)	>.05
>40	719	12.97 (1.69)		52.66 (16.26)		28.61 (2.25)	
Location			<.001		<.001		<.001
Colon	205	24.29 (7.64)		45.11 (6.24)		41.27 (6.23)	
Rectum	775	11.13 (1.99)		33.43 (3.06)		25.06 (2.18)	
Lymph node metastasis			>.05		<.001		<.001
Yes	460	14.05 (1.41)		47.11 (5.04)		37.70 (3.89)	
No	520	12.54 (3.36)		22.38 (2.57)		18.99 (2.15)	
Distant metastasis			<.001		<.001		<.001
Yes	142	31.52 (3.02)		92.34 (12.20)		69.08 (7.85)	
No	838	9.76 (1.61)		25.05 (2.56)		22.80 (1.80)	
TNM staging							
Stage I	65	1.33 (0.45)[a]	<.005	9.34 (2.04)[d]	<.05	5.52 (1.51)[h]	<.05
Stage II	308	11.39 (1.2)[b]	<.001	18.47 (2.05)[d]	<.05	16.91 (2.23)[i]	<.05
Stage III	377	13.80 (4.64)		39.84 (4.99)[e]	<.001	30.16 (3.59)[j]	<.001
Stage IV	230	24.29 (2.99)		73.44 (10.17)		57.48 (6.84)	
Histological type			>.05		>.05		>.05
Papillary tubular adenocarcinoma	325	14.03 (3.79)		34.78 (4.72)		28.19 (3.39)	
Canalicular adenoma	512	12.65 (1.43)		37.03 (4.25)		30.15 (3.32)	
Mucinous adenocarcinoma	67	17.94 (4.96)		34.87 (8.94)		26.12 (6.63)	
Signet-ring cell carcinoma	53	9.17 (2.92)		40.43 (13.46)		29.48 (11.18)	
Other type	23	3.52 (1.73)		17.36 (8.26)		12.75 (5.12)	
Depth of invasion							
Outside of serosa	314	13.52 (1.87)[c]	<.005	50.05 (8.96)[f]	<.05	39.93 (6.47)[k]	<.001
All layers	464	14.77 (2.79)[c]	<.005	31.92 (3.25)		26.71 (2.64)	
Deep muscularis	138	7.03 (2.32)		17.51 (2.32)		10.93 (1.58)	
Shallow muscularis	64	4.62 (3.52)		7.23 (1.87)		4.97 (1.32)	
Growth type			>.05		<.05		<.01
Ulcer	501	14.50 (2.58)		35.85 (3.64)		29.57 (2.90)	
Fungating	337	10.22 (1.80)		24.88 (3.80)		19.02 (2.67)	
Invasive	102	10.7 (4.19)		104.32 (38.05)[g]		81.9 (20.77)	
Shrinkage tube	40	4.05 (1.39)		16.44 (3.67)		12.65 (2.61)	
Tumor size, cm			>.05		<.001		<.001
≤4	474	13.29 (9.09)		21.33 (5.21)		14.67 (3.54)	
>4	506	13.79 (1.21)		43.62 (3.38)		33.39 (2.98)	

[a]compared with II, III, and IV.
[b]compared with IV.
[c]compared with deep muscularis and superficial muscularis.
[d]compared with III and IV.
[e]compared with IV.
[f]ompared with all layers, deep muscularis, and superficial muscularis.
[g]compared with ulcer, fungating, and shrinkage tube.
[h]compared with II, III, and IV.
[i]compared with III and IV.
[j]compared with IV.
[k]compared with all layers, deep muscularis, and superficial muscularis.
[l]compared with ulcer, fungating, and shrinkage tube.

Abbreviations: CA19-9, carbohydrate antigen 19-9; CA24-2, carbohydrate antigen 24-2; CEA, carcinoembryonic antigen.

in patients without metastasis (all $P < .001$). Stratified analysis showed that CEA, CA19-9, and CA24-2 were significantly correlated with TNM staging ($P < .05$). With regard to the depth of tumor invasion, CEA, CA19-9, and CA24-2 levels in tumors outside the serosa were significantly higher than those in other tumor types ($P < .05$). CA19-9 and CA24-2 levels in tumors with an invasive growth type were significantly higher than those in other growth types (both $P < .05$). Tumor size was strongly correlated with the levels of CA19-9 and CA24-2 (both $P < .002$). There were no significant differences in the levels of tumor markers in CRC by sex, age, or histological type (all $P > .05$).

Follow-up results

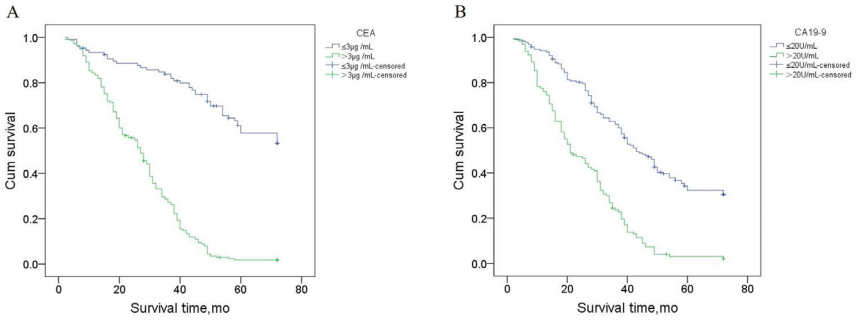
A total of 301 patients died during the follow-up period. Multivariate Cox proportional hazards regression analysis indicated that the statistically significant independent prognostic factors for 5-year OS of CRC were preoperative serum CEA (Wald = 68.77; $P = .000$), CA19-9 (Wald = 60.870; $P < .001$), tumor location (Wald = 4.727; $P = .030$), TNM staging (Wald = 11.224; $P = .001$), and lymph node metastasis (Wald = 10.039; $P = .002$) (Table 4). During follow-up, tumor marker levels generally increased and metastasis and patient deterioration increased. The median survival time of patients with CRC with ≤3 μg/mL preoperative CEA was 48 months and the median survival time of patients with >3 μg/mL preoperative CEA was 27 months ($P < .0001$). Similarly, the median survival time of patients with CRC with ≤20 U/mL preoperative CA19-9 was 43 months, and the median survival time of patients with >20 U/mL preoperative CA19-9 was 21 months ($P < .0001$). Figure 2 shows the cumulative survival curves of patients grouped by their preoperative CEA and CA19-9 concentrations.

Table 4. Multivariate Analysis of Prognostic Factors for Patients With Colorectal Cancer

Factors	B	SE	Wald	*P* value	Exp(B)
CEA >3 μg/mL	0.42	0.002	68.77	<.001	2.82
CA19-9 >20 U/mL	0.41	0.001	60.87	<.001	2.71
Location (colon vs rectum)	0.29	0.13	4.73	.03	1.31
TNM stage (III, IV vs I, II)	0.30	0.09	11.22	.001	1.36
Lymph node metastasis (yes vs no)	0.25	0.08	10.04	.002	1.29

Abbreviations: CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen.

Figure 2. Cumulative Survival Curves for Patients With Colorectal Cancer (CRC). **A.** OS curves for patients with preoperative CEA ≤3 μg/mL and >3 μg /mL. **B.** OS curves for patients with preoperative CA19-9 ≤20 U/mL and <20 U/mL.



DISCUSSION

Colorectal cancer is a common malignant tumor often discovered in the later stages of disease. Early detection of CRC can improve cure rates and decrease mortality rates and is a hot topic of current medical research. The diagnosis of CRC remains difficult, and physical examinations and standard inspection methods are not sufficient to identify early lesions. Therefore, research on early diagnostic indicators of CRC has important clinical significance.

Tools commonly used for screening CRC include the fecal immunochemical test, fecal target-DNA detection, and colonoscopy. The fecal immunochemical test has a low sensitivity for precancerous lesions, and fecal target-DNA detection is expensive. Colonoscopy is considered the gold standard for screening, but it is an invasive examination and patients have poor compliance. Therefore, rapid and accurate diagnosis of CRC is important for early diagnosis and treatment. Serum tumor markers have played an important role in the diagnosis and prognosis evaluation of CRC, and measuring these markers is noninvasive and efficient.

Tumor markers have been widely used in clinical practice for the diagnosis, treatment evaluation, and recurrence monitoring of CRC, but each tumor marker has its limitations in diagnostic value when applied alone. The results of this study show that the combined detection of CEA, CA19-9, and CA24-2 improved the specificity of diagnostic prediction, and the combined detection of CEA, CA19-9, and CA24-2 had the highest diagnostic prediction value for CRC. This result was similar to previous studies,[6-8] and detection of these tumor markers individually was not statistically significant.[13] Our study showed the preoperative levels of serum CEA, CA19-9, and CA24-2 in patients with colon cancer were significantly higher than those in patients with rectum cancer. A Cox proportional hazards model with forward stepwise regression showed the survival time for patients with colon cancer was significantly lower than that in patients with rectum cancer. Our study found that serum CA19-9 and CA24-2 levels were higher in patients with CRC with lymph node metastasis, and CEA, CA19-9, and CA24-2 levels were higher in patients with CRC with distant metastasis. Therefore, we believe that these serum tumor markers can play an important role in monitoring tumor metastasis, thus predicting the development of clinically insignificant distant metastasis and providing a basis for surgical intervention for clinicians, similar to the results reported in previous studies.[14-16] Recent studies have reported that the OS of patients with isolated peritoneal metastatic CRC or patients with 2 or more sites of metastasis was significantly reduced.[17] However, we did not analyze OS in patients with peritoneal metastasis because of the small number of these patients recruited. It has also been reported that patients with a high TNM stage and elevated preoperative serum CEA and CA19-9 levels are more likely to have poor survival.[9,13,18,19] Rao and coauthors found that serum CEA, CA19-9, and CA24-2 concentrations were positively correlated with TNM stage,[13] consistent with our results.

Our results show that CEA, CA19-9, and CA24-2 levels increased with tumor progression and were related to tumor load, similar to the results of other studies that showed that CEA was an independent risk factor predicting the survival of CRC.[20] Our Cox regression analysis showed that elevated serum CEA and CA19-9 levels before surgery were closely associated with poor prognosis, and the 5-year survival rate of patients with CRC with preoperatively elevated CEA and CA19-9 levels was significantly lower than that of other patients. Therefore, we suggest that the preoperative tumor markers CEA and CA19-9 could be used to predict 5-year survival in the clinic.

Univariate analysis showed that preoperative serum CEA, CA19-9, and CA24-2 levels had no relationship with histological type but were significantly correlated with the depth of tumor invasion, and the levels of tumor markers increased with increased depth of tumor invasion. In this study, we investigated serum levels of CEA, CA19-9, and CA24-2 in combination in patients with CRC. Although the sensitivity for detecting CRC of each marker was relatively low, the specificity of the three markers in combination was extremely high. Therefore, preoperative levels of relevant tumor markers could provide clinicians with useful evidence to recommend surgery and adjuvant chemotherapy.

Our results showed a relationship between the growth type of CRC tumors and the levels of tumor markers. CA19-9 and CA24-2 levels were significantly increased in the serum of patients with tumors that had an invasive growth type. A previous report showed that the 5-year OS rate was significantly lower in patients with tumors that had an invasive growth type than in patients with noninvasive CRC.[9] In addition, we showed that tumor size could affect CA19-9 and CA24-2 levels but not CEA levels, which was consistent with a previous report.[22]

Although we compared different groups of patients, a limitation of our study was that we did not compare baseline data at the same time to prove the data were comparable, which may affect the generalization of our conclusions. Another limitation was that the inclusion criteria did not control for patient staging and typing, so our results may be limited in their widespread applicability.

CONCLUSION

The detection of serum tumor markers in combination had diagnostic value for patients with CRC, and the levels of tumor markers were closely related to lymph node metastasis, distant metastasis, depth of invasion, and tumor stage, location, size, and growth type. Serum CEA and CA19-9 were independent predictors of prognosis in patients with CRC. The detection of the serum tumor markers CEA, CA19-9, and CA24-2 can support diagnosis, aid in treatment decisions and judging of therapeutic effects, and predict prognosis to manage patients with CRC.

ACKNOWLEDGEMENTS

The authors would like to thank the Department of Etiology and Tumor Markers Laboratory, The Affiliated Cancer Hospital of Shanxi Medical University.

FUNDING

No funding was received.

CONFLICT OF INTEREST STATEMENT

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We declare that we have no conflicts of interest.

ETHICAL APPROVAL

All procedures performed in this study involving human participants were performed in accordance with the ethical standards of The Affiliated Cancer Hospital of Shanxi Medical University and with the 1964 Helsinki declaration and its later amendments.

AVAILABILITY OF DATA AND MATERIAL

The data sets generated and analyzed during the current study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

SH and YW contributed to the conception and design of the study; JJ, LD, BT, XX, and TS performed the experiments and collected and analyzed the data; SH and YW wrote the manuscript; and SH, YS, and YW revised the manuscript. All authors reviewed and approved the final version of the manuscript.

REFERENCES

1. Nfonsam V, Wusterbarth E, Gong A, Vij P. Early-onset colorectal cancer. *Surg Oncol Clin N Am*. 2022;31(2):143-155. doi:10.1016/j.soc.2021.11.001
2. Low EE, Demb J, Liu L, et al. Risk factors for early-onset colorectal cancer. *Gastroenterology*. 2020;159(2):492-501.e7. doi:10.1053/j.gastro.2020.01.004
3. Yang XQ, Chen C, Peng CW, Liu SP, Li Y. Carbohydrate antigen 242 highly consists with carbohydrate antigen 19-9 in diagnosis and prognosis of colorectal cancer: study on 185 cases. *Med Oncol*. 2012;29(2):1030-1036. doi:10.1007/s12032-011-9967-z
4. Byström P, Berglund Å, Nygren P, et al. Evaluation of predictive markers for patients with advanced colorectal cancer. *Acta Oncol*. 2012;51(7):849-859. doi:10.3109/0284186X.2012.705020
5. Lumachi F, Marino F, Orlando R, Chiara GB, Basso SM. Simultaneous multianalyte immunoassay measurement of five serum tumor markers in the detection of colorectal cancer. *Anticancer Res*. 2012;32(3):985-988.
6. Diamandis EP. Towards identification of true cancer biomarkers. *BMC Med*. 2014;12(1):156. doi:10.1186/s12916-014-0156-8
7. Schiffman JD, Fisher PG, Gibbs P. Early detection of cancer: past, present, and future. *Am Soc Clin Oncol Educ Book*. 2015;(35):57-65. doi:10.14694/EdBook_AM.2015.35.57
8. Tokunaga R, Sakamoto Y, Nakagawa S, Yoshida N, Baba H. The utility of tumor marker combination, including serum P53 antibody, in colorectal cancer treatment. *Surg Today*. 2017;47(5):636-642. doi:10.1007/s00595-016-1464-8
9. Zhao XW, Jiang B, Han CZ, Jing JX. [Detection and clinical study of serum tumor markers in patients with colorectal cancer]. *Zhonghua Zhong Liu Za Zhi*. 2005;27(5):286-288.
10. Zhang XC, Zhang JH, Wang RF, et al. [Diagnostic value of ^{18}F-FDG PET/CT and tumor markers (CEA, CA19-9, CA24-2) in recurrence and metastasis of postoperative colorectal moderately differentiated adenocarcinoma]. *Beijing Da Xue Xue Bao*. 2019;51(6):1071-1077. doi:10.19723/j.issn.1671-167X.2019.06.017
11. Zhang Y, Qin X, Chen W, et al. Risk factors for developing peritoneal metastases after curative surgery for colorectal cancer: A systematic review and meta-analysis. *Colorectal Dis*. 2021;23(11):2846-2858. doi:10.1111/codi.15880
12. Kawamura H, Honda M, Takano Y, et al. Prognostic role of carcinoembryonic antigen and carbohydrate antigen 19-9 in stage IV colorectal cancer. *Anticancer Res*. 2022;42(8):3921-3928. doi:10.21873/anticanres.15886
13. Rao H, Wu H, Huang Q, Yu Z, Zhong Z. Clinical value of serum CEA, CA24-2 and CA19-9 in patients with colorectal cancer. *Clin Lab*. 2021;67(4):1079-1089. doi:10.7754/Clin.Lab.2020.200828
14. Zhang D, Yu M, Xu T, Xiong B. Predictive value of serum CEA, CA19-9 and CA125 in diagnosis of colorectal liver metastasis in Chinese population. *Hepatogastroenterology*. 2013;60(126):1297-1301. doi:10.5754/hge121125
15. Mitsuyama Y, Shiba H, Haruki K, et al. Carcinoembryonic antigen and carbohydrate antigen 19-9 are prognostic predictors of colorectal cancer with unresectable liver metastasis. *Oncol Lett*. 2012;3(4):767-771. doi:10.3892/ol.2012.574
16. Dong H, Tang J, Li LH, et al. Serum carbohydrate antigen 19-9 as an indicator of liver metastasis in colorectal carcinoma cases. *Asian Pac J Cancer Prev*. 2013;14(2):909-913. doi:10.7314/APJCP.2013.14.2.909
17. Franko J, Shi Q, Meyers JP, et al; Analysis and Research in Cancers of the Digestive System (ARCAD) Group. Prognosis of patients with peritoneal metastatic colorectal cancer given systemic therapy: an analysis of individual patient data from prospective randomised trials from the Analysis and Research in Cancers of the Digestive System (ARCAD) database. *Lancet Oncol*. 2016;17(12):1709-1719. doi:10.1016/S1470-2045(16)30500-9
18. Jiang B, Nie ZS, Liu DB, et al. Evaluation of serum tumor markers in diagnosis of colorectal cancer. *Cancer Research and Clinic*. 2002;14(3):199-201.
19. Huh JW, Kim CH, Lim SW, Kim HR, Kim YJ. Factors predicting long-term survival in colorectal cancer patients with a normal preoperative serum level of carcinoembryonic antigen. *J Cancer Res Clin Oncol*. 2013;139(9):1449-1455. doi:10.1007/s00432-013-1459-4
20. Selcukbiricik F, Bilici A, Tural D, et al. Are high initial CEA and CA 19-9 levels associated with the presence of K-ras mutation in patients with metastatic colorectal cancer? *Tumour Biol*. 2013;34(4):2233-2239. doi:10.1007/s13277-013-0763-6
21. Yu H, Son GM, Joh YG. The clinical significance of preoperative serum levels of carbohydrate antigen 19-9 in colorectal cancer. *J Korean Surg Soc*. 2013;84(4):231-237. doi:10.4174/jkss.2013.84.4.231
22. Kim YJ, Park SC, Kim DY, et al. No correlation between pretreatment serum CEA levels and tumor volume in locally advanced rectal cancer patients. *Clin Chim Acta*. 2012;413(3-4):511-515. doi:10.1016/j.cca.2011.11.019