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Opposite variation tendencies of serum CA724 levels in patients with colon and rectal carcinoma

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Abstract. The aim of this study was to investigate tumor biomarker carbohydrate antigen 724 (CA724) in the serum of patients with carcinomas of the colon and rectum at various clinical stages. Serum was collected from 51 patients with colon carcinoma (CC) and 49 patients with rectal carcinoma (RC). CA724 levels were then measured in the different groups according to site, TNM classification, gender, age and metastastic status of the patients. The statistical significance of the differences between the groups was calculated by non-parametric statistics (Mann-Whitney and Kruskall-Wallis tests). We observed a close association between the serum CA724 levels and tumor migration in colorectal carcinoma (CRC) and opposite variation tendencies of CA724 in the evolution of CC and RC. In conclusion, we identified a close association between the serum levels of CA724 and tumor migration in CRC. The opposite variation tendencies of CA724 in the different evolution groups of CC and RC may reflect the differences between these two types of cancer. The evaluation of serum CA724 may be of monitoring and and predictive value and may also assist in the development of treatment strategies for CRC patients.

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Introduction

Colorectal carcinoma (CRC) remains one of the most common malignancies worldwide and represents a global health problem (1). An increasing number of Asian countries, including China, Japan, South Korea and Singapore, have experienced a 2- to 4-fold increase in the incidence of CRC over the last few decades (2). The pathogenesis of CRC ordinarily occurs in a staged progression from normal colonic mucosa to adenoma and finally to carcinoma over a period of ~7-10 years (3-5). This sequenced progression over time provides an opportunity for early diagnosis and treatment.

It has previously been indicated that delayed diagnosis is the main reason for a poor prognosis (6). The traditional non-invasive and invasive methods of screening modalities include fecal occult blood testing, fecal immunochemical test, double-contrast barium enema, flexible sigmoidoscopy and colonoscopy (7-9). Although some of these screening modalities have been demonstrated to reduce the rates of malignancy or mortality, there remains the issue of reducing cancer-related mortality by removing premalignant adenomas and early localized cancer prior to the onset of more advanced stages. Therefore, an effective approach to early screening, diagnosis and follow-up monitoring of CRC is required.

Over the last few years, extensive investigations have focused on serum tumor markers (STMs). In patients with CRC, single STMs exhibit low sensitivity and specificity, whereas the simultaneous measurement of several STMs may increase their diagnostic accuracy (10). It was demonstrated that the combined use of carcionembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9 was effective in the screening and diagnosis of CRC (11). CA724 was previously identified as a type of STM specific for gastric cancer (12) and the correlation between CA724 and CRC has been attracting increasing attention (13).

Furthermore, due to the numerous characteristics shared by colon carcinoma (CC) and rectal carcinoma (RC), the two are discussed as a single entity. Whether CC and RC should be considered as a single or two distinct entities remains controversial (14). The aim of the present study was to investigate serum CA724 levels in patients with different clinical stages of CC and RC and analyze the correlation between serum CA724 levels and the clinical stages of CRC.

Patients and methods

Patients. In this study, a total of 100 patients (63 male and 37 female) with histologically confirmed CRC were investigated. The patient sample was comprised of 51 patients with CC (32 male and 19 female) and 49 patients with RC (31 male and 18 female). The CC and RC patients were classified into four stages according to the 2003 TNM classification. Stages I and II were considered as early-stage, whereas stages III and IV were considered as advanced-stage disease. The patients in the advanced-stage group had either lymph node (stage III) or distant metastases (stage IV). Patient information, such as gender, age and pathological TNM staging, is summarized in Table I. The ethics committee for the Second Affiliated Hospital of Dalian Medical University provided approval for this study (Dalian, China)

Serum collection and CA724 assay. The values of CA724 were measured prior to the patients receiving radiation treatment or chemotherapy. Blood samples were collected, separated by centrifugation and the serum samples were stored at -20˚C until assays were performed. The CA724 kit was provided by Diagnostic Products Corporation (DPC, Tianjin, China). The serum CA724 levels were determined with an immunoradiometric gamma counter (DPC-GAMMA-C12; DPC). The patient details were furnished by the First and Second Hospitals affiliated to Dalian Medical University, between 2010 and 2012.

Statistical analysis. The CA724 levels were assessed in different groups according to different site, TNM classification, gender, age and metastatic status of the patients. Since the serum CA724 levels in each group did not follow a normal distribution, the statistical significance of the differences between the groups was calculated by non-parametric statistics (Mann-Whitney and Kruskall-Wallis tests). The centralized tendency of each group was described as means plus standard error of the mean (SEM). All statistical tests were performed using SPSS software, version 11.5 (SPSS Inc., Chicago, IL, USA). $P<0.05$ was considered to indicate a statistically significant difference.

Results

Differences among CRC patients in different groups. The mean serum CA724 values ± SEM were 6.808±1.462 U/ml in CC patients and 5.524±1.151 U/ml in RC patients, with no statistically significant difference. Therefore, we first analyzed the two types of cancer as a single entity. The different CA724 levels among CRC patients in different groups are presented in Table II. The differences in the CA724 values between CRC clinical stages were compared (Fig. 1). Further investigations indicated that the mean serum CA724 concentrations ± SEM in patients with early- and advanced-stage disease were 5.414±1.317 and 6.689±1.281 U/ml, respectively. The differences between the two groups were not statistically significant. However, the differences between the CRC patient group with and that without distant metastasis was statistically significant (P=0.043).

To determine whether gender and age affected the results in CRC patients mentioned above, the differences in the serum

Table I. Clinicopathological characteristics of 100 CRC patients.

Variables	No. of CC	No. of RC
Gender		
Male	32	31
Female	19	18
Age (years)		
≤50	9	11
>50	42	38
Lymph node metastasis		
No	18	22
Yes	33	27
Distant metastasis		
No	35	39
Yes	16	10
Stage		
I	6	14
II	12	8
III	17	17
IV	16	10

CC, colon carcinoma; RC, rectal carcinoma; CRC, colorectal carcinoma.

Table II. Differences in CA724 levels among patients with colorectal carcinoma in different groups.

Variables	Pt no. (CA724 levels[a])	P-value
Site		NS
Colon	51 (6.808±1.462)	
Rectum	49 (5.524±1.151)	
Lymph node metastasis		NS
No	40 (5.414±1.317)	
Yes	60 (6.689±1.281)	
Distant metastasis		0.043
No	74 (4.835±0.791)	
Yes	26 (10.005±2.677)	
Stage		NS
I	20 (7.464±2.156)	
II	20 (3.364±1.426)	
III	34 (4.153±0.760)	
IV	26 (10.005±2.677)	
Gender		NS
Male	63 (5.771±1.039)	
Female	37 (7.148±1.798)	
Age		NS
30-50	20 (5.026±1.560)	
>50	80 (6.467±1.096)	

[a]Mean ± standard error of the mean, U/ml. Pt, patient; CA, carbohydrate antigen; NS, not significant.

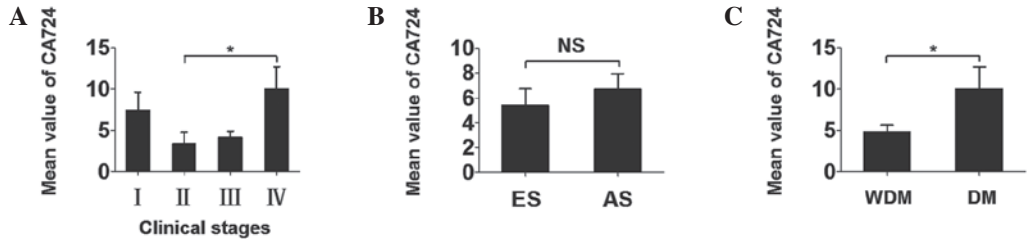

Figure 1. Different mean carbohydrate antigen (CA) 724 values among colorectal carcinoma (CRC) patients in different groups. (A) The graph shows the variation trend of CA724 levels among the four different clinical stages. Only the differences between stages II and IV were statistically significant (*P=0.025). (B) There were no statistically significant differences between patients with early-stage (ES) and advanced-stage (AS) disease. (C) There were statistically significant differences between patients without distant metastasis (WDM) and those with distant metastasis (DM) (*P=0.043). The results are presented as means + standard error of the mean.

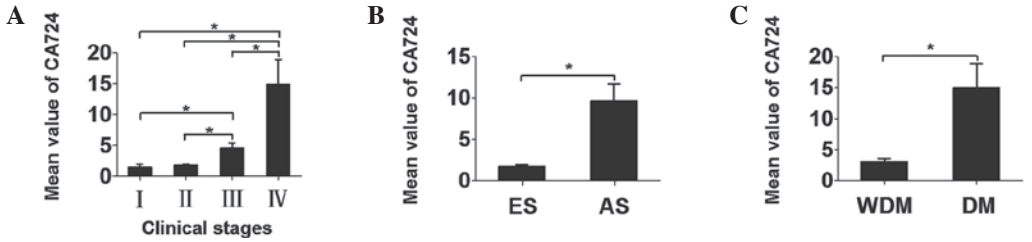

Figure 2. Different mean carbohydrate antigen (CA) 724 values among colon carcinoma patients in different groups. (A) The graph shows an ascending variation trend of CA724 values with increasing clinical stage. Multiple comparisons among clinical stages revealed statistically significant differences (*P<0.05), except between stages I and II. (B) The CA724 values in early-stage (ES) were higher compared to those in advanced-stage (AS) disease, with a statistically significant difference (*P<0.001). (C) A similar phenomenon was observed between patients with distant metastasis (DM) and those without distant metastasis (WDM). This difference was also considered to be statistically significant (*P<0.001). The results are presented as means + standard error of the mean.

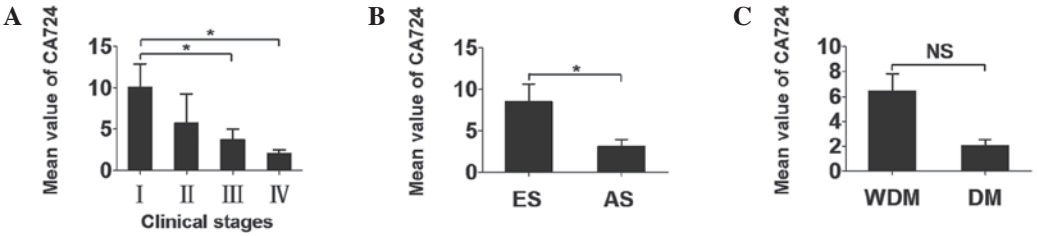

Figure 3. Different mean carbohydrate antigen (CA) 724 values among rectal carcinoma patients in different groups. (A) The graph shows a descending variation trend of CA724 values with increasing clinical stage. Multiple comparisons among clinical stages indicate that the differences between stages I and III (*P=0.003) and those between stages I and IV (*P=0.009) reached a statistical significance. (B) The level of CA724 values in early-stage (ES) were lower compared to those in advanced-stage (AS) disease, with a statistically significant difference (*P=0.011). (C) A similar phenomenon was observed between patients with distant metastasis (DM) and those without distant metastasis (WDM). However, the difference was not statistically significant. The results are presented as means + standard error of the mean.

CA724 values between genders was also assessed. Table III shows that there were no significant differences between male and female CRC patients. Furthermore, there were no significant differences between CRC patients aged 30-50 years and those aged >50 years. Therefore, the variables of gender and age were eliminated (Table II). Since there were distinct differences among CRC patients, in order to interpret the differences described above when assessing the two groups as a single entity, we proceeded to analyze CC and RC separately.

Ascending gradient among CC patients. The different CA724 levels among CC patients in different groups are presented in Table III. There was an ascending gradient of serum CA724 values with increasing clinical stage, except for the difference between stages I and II (Fig. 2). The mean CA724 values ± SEM for each stage were as follows: stage I, 1.437±0.535 U/ml; stage II, 1.777±0.249 U/ml; stage III, 4.559±0.855 U/ml; and stage IV, 14.985±3.875 U/ml. The differences in the CA724 values between early- and advanced-stage disease were statistically significant (P<0.001), as were those between patients with and those without distant metastasis (P<0.001) (Fig. 2).

Descending gradient among RC patients. The different CA724 levels among CC patients in different groups are presented in Table IV. The mean serum CA724 values ± SEM for each stage were as follows: stage I, 10.046±2.819 U/ml; stage II, 5.745±3.506 U/ml; stage III, 3.748±1.277 U/ml; and stage IV, 2.036±0.491 U/ml, these results are based on the data provided in Table V. Therefore, a descending gradient was identified among RC patients when each clinical stage was separately analyzed (Fig. 3). Similarly, analysis with SPSS software, version 11.5, revealed a significant correlation between early- and advanced-stage disease (P=0.010). However, the differences in the CA724 values between patients with and those without distant metastasis did not reach a statistical significance (Fig. 3).

Table III. Differences in CA724 levels among CC patients.

Variables	Pt no. (CA724 levels[a])	P-value
Lymph node metastasis		<0.001
No	18 (1.663±0.237)	
Yes	33 (9.614±2.109)	
Distant metastasis		<0.001
No	35 (3.143±0.493)	
Yes	16 (14.985±3.875)	
Stage		<0.001
I	6 (1.437±0.535)	
II	12 (1.777±0.249)	
III	17 (4.559±0.855)	
IV	16 (14.985±3.875)	
Gender		NS
Male	32 (6.451±1.508)	
Female	19 (7.409±3.051)	
Age (years)		NS
30-50	9 (4.664±1.160)	
>50	42 (7.267±1.755)	

[a]Mean ± SEM, U/ml. Pt, patient; CC, colon carcinoma; CA, carbohydrate antigen; NS, not significant.

Table IV. Differences in CA724 levels among RC patients.

Variables	Pt no. (CA724 levels[a])	P-value
Lymph node metastasis		0.011
No	22 (8.482±2.196)	
Yes	27 (3.114±0.830)	
Distant metastasis		NS
No	39 (6.419±1.396)	
Yes	10 (2.036±0.491)	
Stage		0.022
I	14 (10.046±2.819)	
II	8 (5.745±3.506)	
III	17 (3.748±1.277)	
IV	10 (2.036±0.491)	
Gender		NS
Male	31 (5.069±1.442)	
Female	18 (6.308±1.905)	
Age (years)		NS
30-50	11 (5.322±2.739)	
>50	38 (5.583±1.261)	

[a]Mean ± SEM, U/ml. Pt, patient; RC, rectal carcinoma; CA, carbohydrate antigen; NS, not significant.

Discussion

This comprehensive integrative analysis of 100 CRC patients indicated that serum CA724 levels may be of predictive value in CRC, particularly in the analysis of clinical stage. As regards CA724, recent studies have mainly focused on the sensitivity and specificity of its diagnostic and early detection value for recurrences. The combinations of CA724 with other STMs were considered to be satisfactory (10,13,15-17). In our study, we focused on the differences in the CA724 levels among patients with different disease stages.

The differences in serum CA724 values between patients with early- and advanced-stage disease suggest that CA724 may be associated with the metastasis of CC and RC. A similar association was observed between CEA levels and CRC metastasis (18,19). When comparing and analysing CC and RC, we may surmise that the differences in the serum levels of CA724 represent a sign of distant metastasis in CC. However, we did not observe a statistically significant difference between RC patients with and those without distant metastasis. We then compared the clinical stages of CC and RC. Although we were unable to verify a statistically significant difference for each stage transition, there was a distinct variation tendency among the stages. Therefore, we consider that monitoring serum CA724 levels may be indicative of clinical stage, particularly in patients for whom the determination of the pathological stage is difficult. The CA724 value may reflect advanced stage, progression and metastasis of CRC. Due to the widely variable prognosis of CRC, a previous study attempted to identify a parameter useful in the selection of patients who may be candidates for more tailored treatment (20). Whether CA724 is such a parameter requires further verification; however, our results suggest that it has potential as a tumor marker. Considering the association between CA724 and CRC, we may surmise the presence of similar associations between other STMs and carcinomas.

Our study demonstrated the presence of two opposite trends in the levels of CA724 according to the progression of the clinical CRC stage. As was mentioned previously, there was an ascending gradient among CC patients and a descending gradient among RC patients. These two opposite trends possibly reflect biological, advancing and metastatic differences between CC and RC. Due to the similarities in morphology and configuration and the fact that one is considered to be the continuation of the other, CC and RC are often considered as a single disease entity. However, an increasing number of studies refer to the differences between these two types of cancer. Firstly, the colon embryologically originates from the midgut and hindgut, whereas the rectum originates from the cloaca. Furthermore, relevant studies have demonstrated that there were differences regarding blood supply, biological function, histochemical reactions and the level of mRNA expression (21-26). Those studies indicated that the normal colon and rectum are different. A previous study also reported that the prognosis of CC is better compared to that of RC and that RC exhibits a higher expression of CEA15. Additionally, a gene-level analysis demonstrated that methylation and mutations were more common in the right colon (27). All those results suggested that there are biological differences between CC and RC. The exact mechanism underlying the descending gradient in the CA724 levels among RC patients has not been elucidated.

Although this study included a small number of patients, the results regarding the association between CA724 levels

Table V. Clinicopathological characteristics of 100 patients with colorectal carcinoma.

No.	Pathological diagnosis	Site	Pathological TNM staging	Lesion	Age/gender	CA724
1	Adenocarcinoma	Colon	T2N0M0	Primary tumor	61/M	4.05
2	Adenocarcinoma	Colon	T2N0M0	Primary tumor	77/M	1.19
3	Adenocarcinoma	Colon	T2N0M0	Primary tumor	61/M	1.13
4	Adenocarcinoma	Colon	T1N0M0	Primary tumor	63/F	1.09
5	Adenocarcinoma	Colon	T2N0M0	Primary tumor	69/M	0.59
6	Adenocarcinoma	Colon	T2N0M0	Primary tumor	58/F	0.57
7	Adenocarcinoma	Colon	T4N0M0	Primary tumor	65/F	3.44
8	Adenocarcinoma	Colon	T4N0M0	Primary tumor	61/F	3.04
9	Adenocarcinoma	Colon	T4N0M0	Primary tumor	56/F	2.78
10	Adenocarcinoma	Colon	T3N0M0	Primary tumor	75/F	1.81
11	Adenocarcinoma	Colon	T4N0M0	Primary tumor	64/M	1.71
12	Adenocarcinoma	Colon	T3N0M0	Primary tumor	48/M	1.67
13	Adenocarcinoma	Colon	T3N0M0	Primary tumor	33/M	1.49
14	Adenocarcinoma	Colon	T4N0M0	Primary tumor	51/F	1.38
15	Adenocarcinoma	Colon	T3N0M0	Primary tumor	55/M	1.24
16	Adenocarcinoma	Colon	T4N0M0	Primary tumor	67/M	1.10
17	Adenocarcinoma	Colon	T3N0M0	Primary tumor	69/M	0.85
18	Adenocarcinoma	Colon	T4N0M0	Primary tumor	48/F	0.81
19	Adenocarcinoma	Colon	T4N1M0	Primary tumor	65/M	11.90
20	Adenocarcinoma	Colon	T3N1M0	Primary tumor	64/M	10.22
21	Adenocarcinoma	Colon	T3N1M0	Primary tumor	45/M	8.92
22	Adenocarcinoma	Colon	T4N1M0	Primary tumor	52/F	8.44
23	Adenocarcinoma	Colon	T3N1M0	Primary tumor	60/F	6.44
24	Adenocarcinoma	Colon	T4N1M0	Primary tumor	45/F	6.31
25	Adenocarcinoma	Colon	T3N1M0	Primary tumor	51/M	4.78
26	Adenocarcinoma	Colon	T3N2M0	Primary tumor	61/M	3.86
27	Adenocarcinoma	Colon	T3N2M0	Primary tumor	62/F	3.38
28	Adenocarcinoma	Colon	T3N1M0	Primary tumor	35/M	2.90
29	Adenocarcinoma	Colon	T3N2M0	Primary tumor	55/M	2.05
30	Adenocarcinoma	Colon	T3N2M0	Primary tumor	54/F	1.82
31	Adenocarcinoma	Colon	T3N1M0	Primary tumor	70/F	1.74
32	Adenocarcinoma	Colon	T3N1M0	Primary tumor	68/M	1.67
33	Adenocarcinoma	Colon	T3N1M0	Primary tumor	67/M	1.09
34	Adenocarcinoma	Colon	T3N1M0	Primary tumor	66/M	1.03
35	Adenocarcinoma	Colon	T4N1M0	Primary tumor	67/F	0.95
36	Adenocarcinoma	Colon	T2N0M1	Primary tumor	66/F	57.79
37	Adenocarcinoma	Colon	T3N0M1	Primary tumor	81/M	43.30
38	Adenocarcinoma	Colon	T2N0M1	Primary tumor	70/F	19.99
39	Adenocarcinoma	Colon	T4N2M1	Primary tumor	61/M	19.90
40	Adenocarcinoma	Colon	TxNxM1	Primary tumor	64/F	16.56
41	Adenocarcinoma	Colon	T4N2M1	Primary tumor	56/M	16.17
42	Adenocarcinoma	Colon	TxNxM1	Primary tumor	59/M	15.15
43	Adenocarcinoma	Colon	T4N1M1	Primary tumor	80/M	12.23
44	Adenocarcinoma	Colon	T3N2M1	Primary tumor	37/M	10.76
45	Adenocarcinoma	Colon	T4N2M1	Primary tumor	75/M	7.37
46	Adenocarcinoma	Colon	TxNxM1	Primary tumor	74/M	7.03
47	Adenocarcinoma	Colon	T4N1M1	Primary tumor	42/M	5.54
48	Adenocarcinoma	Colon	T4N0M1	Primary tumor	42/M	3.58
49	Adenocarcinoma	Colon	T4N0M1	Primary tumor	74/F	2.43
50	Adenocarcinoma	Colon	TxNxM1	Primary tumor	36/M	1.32
51	Adenocarcinoma	Colon	T3N0M1	Primary tumor	61/M	0.64

Table V. Continued.

No.	Pathological diagnosis	Site	Pathological TNM staging	Lesion	Age/gender	CA724
52	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	66/M	29.60
53	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	72/M	26.03
54	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	79/M	24.86
55	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	56/F	18.30
56	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	55/M	16.02
57	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	67/F	6.48
58	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	73/F	3.93
59	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	65/M	3.91
60	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	57/M	2.35
61	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	78/M	2.14
62	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	62/F	2.07
63	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	59/M	1.95
64	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	79/F	1.88
65	Adenocarcinoma	Rectum	T2N0M0	Primary tumor	72/F	1.13
66	Adenocarcinoma	Rectum	T3N0M0	Primary tumor	55/F	29.85
67	Adenocarcinoma	Rectum	T3N0M0	Primary tumor	67/F	5.92
68	Adenocarcinoma	Rectum	T4N0M0	Primary tumor	54/M	4.27
69	Adenocarcinoma	Rectum	T3N0M0	Primary tumor	55/F	2.06
70	Adenocarcinoma	Rectum	T3N0M0	Primary tumor	67/M	1.40
71	Adenocarcinoma	Rectum	T3N0M0	Primary tumor	66/F	0.95
72	Adenocarcinoma	Rectum	T3N0M0	Primary tumor	67/F	0.83
73	Adenocarcinoma	Rectum	T4N0M0	Primary tumor	73/M	0.68
74	Adenocarcinoma	Rectum	T4N2M0	Primary tumor	38/F	15.27
75	Adenocarcinoma	Rectum	T3N1M0	Primary tumor	79/F	14.91
76	Adenocarcinoma	Rectum	T3N1M0	Primary tumor	68/M	13.70
77	Adenocarcinoma	Rectum	T4N2M0	Primary tumor	48/M	3.14
78	Adenocarcinoma	Rectum	T3N1M0	Primary tumor	72/M	3.13
79	Adenocarcinoma	Rectum	T4N2M0	Primary tumor	73/M	2.93
80	Adenocarcinoma	Rectum	T4N1M0	Primary tumor	57/M	1.48
81	Adenocarcinoma	Rectum	T3N1M0	Primary tumor	55/M	1.14
82	Adenocarcinoma	Rectum	T2N1M0	Primary tumor	71/M	1.13
83	Adenocarcinoma	Rectum	T3N1M0	Primary tumor	54/M	1.05
84	Adenocarcinoma	Rectum	T3N1M0	Primary tumor	47/F	1.00
85	Adenocarcinoma	Rectum	T3N1M0	Primary tumor	48/M	0.96
86	Adenocarcinoma	Rectum	T4N1M0	Primary tumor	69/M	0.91
87	Adenocarcinoma	Rectum	T4NxM0	Primary tumor	76/M	0.86
88	Adenocarcinoma	Rectum	T4N1M0	Primary tumor	43/M	0.80
89	Adenocarcinoma	Rectum	T3N2M0	Primary tumor	44/M	0.67
90	Adenocarcinoma	Rectum	T3N2M0	Primary tumor	72/M	0.63
91	Adenocarcinoma	Rectum	TxNxM1	Primary tumor	74/F	5.80
92	Adenocarcinoma	Rectum	TxN1M1	Primary tumor	54/M	2.34
93	Adenocarcinoma	Rectum	T4N1M1	Primary tumor	67/F	0.95
94	Adenocarcinoma	Rectum	T3N1M1	Primary tumor	62/M	3.33
95	Adenocarcinoma	Rectum	T4NxM1	Primary tumor	43/F	1.59
96	Adenocarcinoma	Rectum	T4NxM1	Primary tumor	61/M	2.26
97	Adenocarcinoma	Rectum	T4N1M1	Primary tumor	67/M	1.32
98	Adenocarcinoma	Rectum	TxNxM1	Primary tumor	39/M	1.10
99	Adenocarcinoma	Rectum	T4NxM1	Primary tumor	62/M	1.04
100	Adenocarcinoma	Rectum	T3N2M4	Primary tumor	53/F	0.63

Age is presented in years and CA724 values in U/ml. CA, carbohydrate antigen; M, male; F, female.

and CRC patients were considered to be statistically significant. Due to the small number of stage I CC patients (n=6), further investigations are required to confirm these findings. Furthermore, the exact nature of the association and the underlying pathophysiological mechanisms of the opposite trends of serum CA724 in CC and RC require further investigation by future large prospective studies.

In conclusion, we demonstrated a close correlation between serum CA724 levels and tumor migration in CRC. The opposite variation tendencies of CA724 levels in the different evolution groups of CC and RC may reflect the differences between these two types of cancer. The evaluation of serum CA724 levels, particularly elevation in patients with CC, may be of monitoring and predictive value and may also assist in the development of treatment strategies for CRC patients.

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References

1. Jemal A, Siegel R, Ward E, *et al*: Cancer statistics, 2009. CA Cancer J Clin 59: 225-249, 2009.
2. Sung JJ, Lau JY, Goh KL, *et al*: Increasing incidence of colorectal cancer in Asia: implications for screening. Lancet Oncol 6: 871-876, 2005.
3. Hofstad B and Vatn M: Growth rate of colon polyps and cancer. Gastrointest Endosc Clin N Am 7: 345-363, 1997.
4. Winawer SJ, Fletcher RH, Miller L, *et al*: Colorectal cancer screening: clinical guidelines and rationale. Gastroenterology 112: 594-642, 1997.
5. Wong JJ, Hawkins NJ and Ward RL: Colorectal cancer: a model for epigenetic tumorigenesis. Gut 56: 140-148, 2007.
6. Diallo Owono FK, Nguema Mve R, Ibaba J, Mihindou C and Ondo N'dong F: Epidemiological and diagnostic features of colorectal cancer in Libreville, Gabon. Med Trop (Mars) 71: 605-607, 2011 (In French).
7. U.S. Preventive Services Task Force: Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 149: 627-637, 2008.
8. Levin B, Lieberman DA, McFarland B, *et al*; American Cancer Society Colorectal Cancer Advisory Group; US Multi-Society Task Force; American College of Radiology Colon Cancer Committee: Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. CA Cancer J Clin 58: 130-160, 2008.
9. Dominic OG, McGarrity T, Dignan M and Lengerich EJ: American College of Gastroenterology Guidelines for Colorectal Cancer Screening 2008. Am J Gastroenterol 104: 2626-2627; author reply 2628-2629, 2009.
10. Lumachi F, Marino F, Orlando R, Chiara GB and Basso SM: Simultaneous multianalyte immunoassay measurement of five serum tumor markers in the detection of colorectal cancer. Anticancer Res 32: 985-988, 2012.
11. Wang JY, Lu CY, Chu KS, *et al*: Prognostic significance of pre- and postoperative serum carcinoembryonic antigen levels in patients with colorectal cancer. Eur Surg Res 39: 245-250, 2007.
12. Chen XZ, Zhang WK, Yang K, *et al*: Correlation between serum CA724 and gastric cancer: multiple analyses based on Chinese population. Mol Biol Rep 39: 9031-9039, 2012.
13. Nicolini A, Ferrari P, Duffy MJ, *et al*: Intensive risk-adjusted follow-up with the CEA, TPA, CA19.9, and CA72.4 tumor marker panel and abdominal ultrasonography to diagnose operable colorectal cancer recurrences: effect on survival. Arch Surg 145: 1177-1183, 2010.
14. Li M, Li JY, Zhao AL and Gu J: Colorectal cancer or colon and rectal cancer? Clinicopathological comparison between colonic and rectal carcinomas. Oncology 73: 52-57, 2007.
15. Filella X, Molina R, Mengual PJ, *et al*: Significance of CA72.4 in patients with colorectal cancer. Comparison with CEA and CA19.9. J Nucl Biol Med 35: 158-161, 1991.
16. Yu JK, Yang MQ, Jiang TJ and Zheng S: The optimal combination of serum tumor markers with bioinformatics in diagnosis of colorectal carcinoma. J Zhejiang Univ 33: 407-410, 2004 (In Chinese).
17. Newton KF, Newman W and Hill J: Review of biomarkers in colorectal cancer. Colorectal Dis 14: 3-17, 2012.
18. Wiggers T, Arends JW, Verstijnen C, *et al*: Prognostic significance of CEA immunoreactivity patterns in large bowel carcinoma tissue. Br J Cancer 54: 409-414, 1986.
19. Kitadai Y, Radinsky R, Bucana CD, *et al*: Regulation of carcinoembryonic antigen expression in human colon carcinoma cells by the organ microenvironment. Am J Pathol 149: 1157-1166, 1996.
20. Seregni E, Ferrari L, Martinetti A and Bombardieri E: Diagnostic and prognostic tumor markers in the gastrointestinal tract. Semin Surg Oncol 20: 147-166, 2001.
21. Araki K, Furuya Y, Kobayashi M, *et al*: Comparison of mucosal microvasculature between the proximal and distal human colon. J Electron Microsc (Tokyo) 45: 202-206, 1996.
22. Skinner SA and O'Brien PE: The microvascular structure of the normal colon in rats and humans. J Surg Res 61: 482-490, 1996.
23. Devesa SS and Chow WH: Variation in colorectal cancer incidence in the United States by subsite of origin. Cancer 71: 3819-3826, 1993.
24. Shamsuddin AM, Phelps PC and Trump BF: Human large intestinal epithelium: light microscopy, histochemistry, and ultrastructure. Hum Pathol 13: 790-803, 1982.
25. Macfarlane GT, Gibson GR and Cummings JH: Comparison of fermentation reactions in different regions of the human colon. J Appl Bacteriol 72: 57-64, 1992.
26. Mercurio MG, Shiff SJ, Galbraith RA and Sassa S: Expression of cytochrome P450 mRNAs in the colon and the rectum in normal human subjects. Biochem Biophys Res Commun 210: 350-355, 1995.
27. Cancer Genome Atlas Network: Comprehensive molecular characterization of human colon and rectal cancer. Nature 487: 330-337, 2012.