

Original Article

Clinical value of CEA and CA19-9 in colorectal cancer by Kaplan-Meier survival curve

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Abstract: Objective: Using Kaplan-Meier survival curves to analyze the value of CEA and CA19-9 in evaluating the prognosis of colorectal carcinoma. Methods: We selected 136 cases of colorectal cancer patients who were hospitalized in The Second Affiliated Hospital of Shandong First Medical University during January 2012~December 2018, they were followed up and CEA and CA19-9 were tested regularly. Kaplan-Meier survival curves were used to analyze the correlation between CEA, CA19-9 and colorectal cancer recurrence or metastasis. All data were analyzed by SPSS 17.0 statistical software package. Results: 1. The positive expression of CEA and CA19-9 is related to the recurrence or metastasis of colorectal cancer, and the combined detection of the two can improve the positive rate of detection; 2. The combined detection of CEA and CA19-9 could predict the recurrence or metastasis of colorectal cancer after radical resection earlier than previously; 3. CEA and CA19-9 are related to the adverse prognosis of colorectal cancer. Conclusions: Combined detection of serum CEA and CA19-9 levels in patients with colorectal cancer after radical resection may be a predictive method for predicting recurrence or metastasis, and diagnosing progression-free survival, and overall survival of colorectal cancer.

Keywords: Kaplan-Meier survival curve, CEA/CA19-9, colorectal cancer

Introduction

At present, the incidence of colorectal cancer (CRC) in China is on the rise year by year. The 5-year survival rate is only 50%~60% [1-4]. Surgical resection is the main treatment for colorectal cancer. According to statistics, 20%~50% of patients still die of tumor recurrence or metastasis after CRC radical surgery [5, 6]. Therefore, there is an urgent need for a method to predict the changes and progression of colorectal cancer. The purpose of this study is to analyze and study the clinical significance of CEA and CA19-9 in determining the prognosis of colorectal cancer by monitoring the levels of CEA and CA19-9 in the serum of patients after CRC radical surgery, so as to provide more accurate prediction methods for clinical assessment to evaluate the prognosis of colorectal cancer.

Materials and methods

Reagents and instruments

Clinical data: Retrospective analysis of 136 patients with colorectal cancer who were hospi-

talized in the Second Affiliated Hospital of the First Medical University of Shandong Province from January 2012 to December 2018. These 136 patients had surgical and colonoscopy pathological diagnosis. ① In total, 91 males and 45 females, aged 34-81 years, with a median age of 59.6 years; ② 52 cases of colon cancer and 84 cases of rectal cancer; ③ according to the 7th edition of American Joint Cancer Committee (AJCC), there were 6 cases in stage I, 39 cases in stage II, 47 cases in stage III and 44 cases in stage IV. ④ All patients underwent CRC radical surgery in 92 cases, and 51 cases had recurrence or metastasis during the follow-up, including 8 cases of local recurrence and 43 cases of distant metastasis.

Research methods

Tumor marker monitoring method: (1) monitoring method: laboratory venous blood collection; (2) monitoring cycle: ① patients undergoing radical resection of colorectal cancer: within 1 week before operation and 1 month after operation; ② postoperative adjuvant chemotherapy

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Table 1. Correlation between positive rate of CEA and CA19-9 and recurrence or metastasis of colorectal cancer

Group	Case	CEA			CA19-9			CEA+CA19-9		
		Positive cases	Positive rate (%)	P	Positive cases	Positive rate (%)	P	Positive cases	Positive rate (%)	P
Recurrence and metastasis group	51	36	70.6	< 0.05	34	66.7	< 0.05	43	84.3	< 0.05
No recurrence and metastasis group	41	12	29.3		4	9.7		13	31.7	

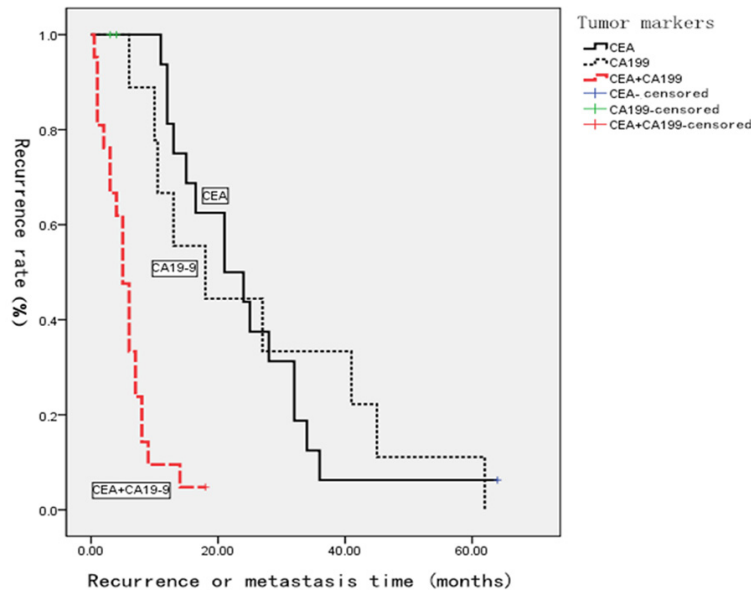


Figure 1. Survival curves of elevated time to recurrence and metastasis in CEA, CA19-9 and CEA+CA19-9 groups.

and palliative chemotherapy: 1 day before each cycle of chemotherapy; ③ follow-up of patients discharged from hospital after treatment: within 2 years after operation: once every 3 months; from the 3rd year to the 5th year after the operation: testing every 6 months; from the 6th year after the operation: once a year.

Detection methods: CEA and CA19-9 are all determined by Abbott Laboratories Unified Standard Kit. Normal value of tumor markers: CEA: 0~5 ng/ml; CA19-9: 0~37 U/ml.

Statistical methods

Chi-square test was used to analyze the positive rate between the separate test group and the combined test group of CEA and CA19-9. The survival function (Kaplan-Meier) and related survival analysis were applied: ① statistical significance of the time between CEA, CA19-9 single detection group and combined detection group to relapse or metastasis; ② correlation

between CEA, CA19-9 and PFS (progression-free survival) and OS (overall survival total survival) of colorectal cancer. All data were processed by SPSS 17.0. $P < 0.05$ means there is statistical significance.

Results

Correlation between CEA, CA19-9 positive rate and recurrence or metastasis of colorectal cancer

The positive rates of CEA, CA19-9 single detection group and combined detection group related to recurrence or metastasis of colorectal cancer were analyzed by χ^2 test, and the results are shown in **Table 1**.

Correlation between tumor markers rise and recurrence or metastasis time

The time between the CEA and CA19-9 single test group and the combined test group increased to the time of recurrence or metastasis. After the survival function test, the results are shown in **Figure 1**.

Correlation between CEA, CA19-9 and the PFS, OS in colorectal cancer

Correlation between CEA and PFS, OS in colorectal cancer: after the survival function and relevant Log Rank tests, the results are shown in **Figures 2 and 3**.

Correlation between CA19-9 and PFS, OS in colorectal cancer: after the survival function and relevant Log Rank tests, the results are shown in **Figures 4 and 5**.

Correlation between CEA and CA19-9 combined detection and the PFS, OS in colorectal

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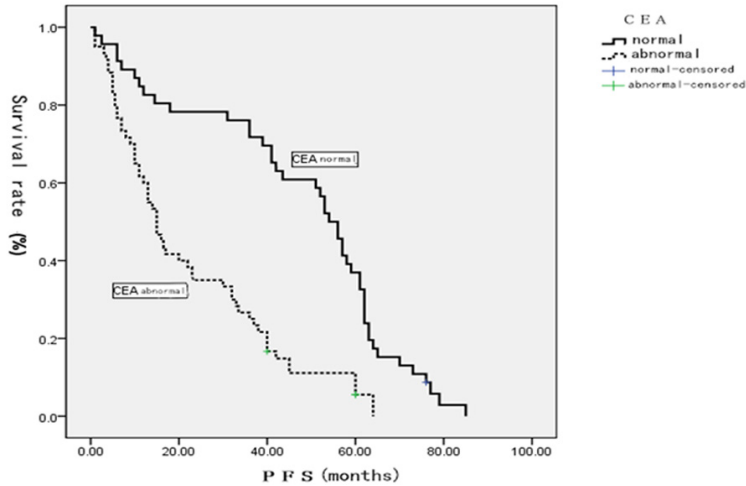


Figure 2. PFS survival curve of CEA normal group and abnormal group.

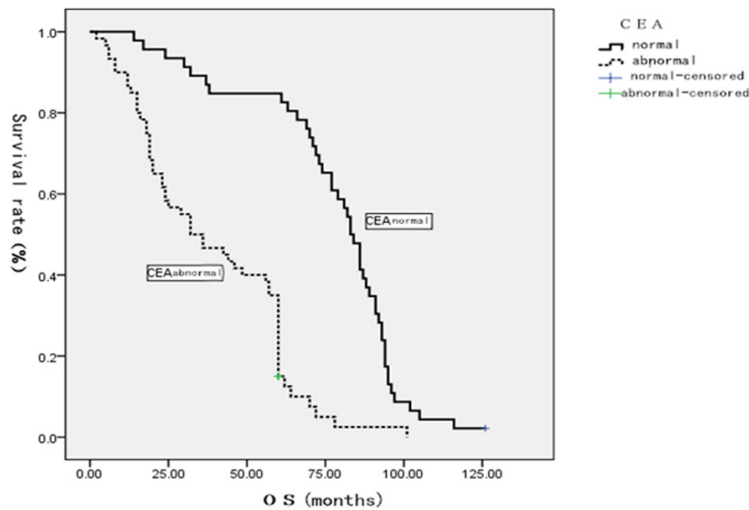


Figure 3. OS survival curve of CEA normal group and abnormal group.

cancer: the results obtained by survival function and relevant Log Rank tests are shown in **Figures 6 and 7.**

Discussion

In recent years, the morbidity and mortality of colorectal cancer (CRC) have increased year by year. The vast majority of deceased patients died due to recurrence or metastasis after treatment, which urgently requires a prediction method to predict CRC recurrence or metastasis. Serum tumor marker monitoring, as a convenient, rapid, minimally invasive and inexpensive detection method, has been widely used in the auxiliary diagnosis, curative effect evalua-

tion and prognosis evaluation of malignant tumors.

CEA is a broad spectrum tumor marker and is one of the most commonly used tumor markers for CRC [7]. CEA is widely used in the diagnosis and prognosis evaluation of CRC, especially in monitoring the recurrence or metastasis after CRC operation. Many studies show that the increase of serum CEA in colorectal cancer patients indicates a worse prognosis than normal CEA patients. For patients with positive serum CEA before CRC radical surgery, if CEA decreases to normal levels after surgery but increases continuously during follow-up, it indicates the possibility of recurrence or metastasis. Therefore, once serum CEA level rises in CRC patients after operation, a comprehensive examination should be carried out immediately to determine whether there is recurrence or metastasis [8-10]. Chen L et al [11] studied 266 patients with stage II~III colorectal cancer after radical surgery. Compared with normal CEA patients before surgery, the 5-year disease-free survival rate and 5-year overall survival rate of patients with elevated CEA were significantly reduced. In

this paper, 136 patients after CRC radical surgery were followed up and analyzed, and the results were similar to the above research conclusions: among 51 patients with recurrence and metastasis, 36 patients were monitored for CEA elevation before operation, with a positive rate of 70.6%. It is concluded that the increase of CEA is correlated with the recurrence and metastasis of colorectal cancer patients after operation. The PFS and OS of patients with positive CEA monitoring before operation are shorter than those of patients with negative CEA monitoring before operation. The difference is statistically significant by Kaplan-Meier and related Log Rank tests. The positive expression of CEA can predict PFS and

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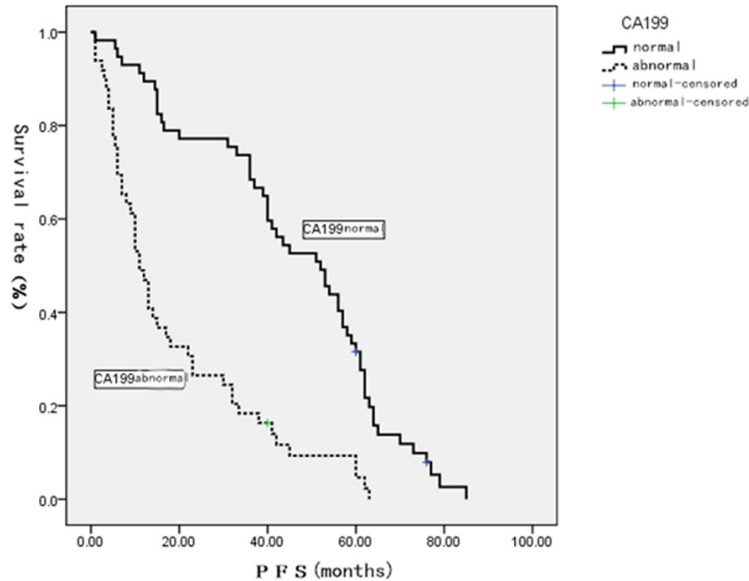


Figure 4. PFS survival curve of CA19-9 normal group and abnormal group.

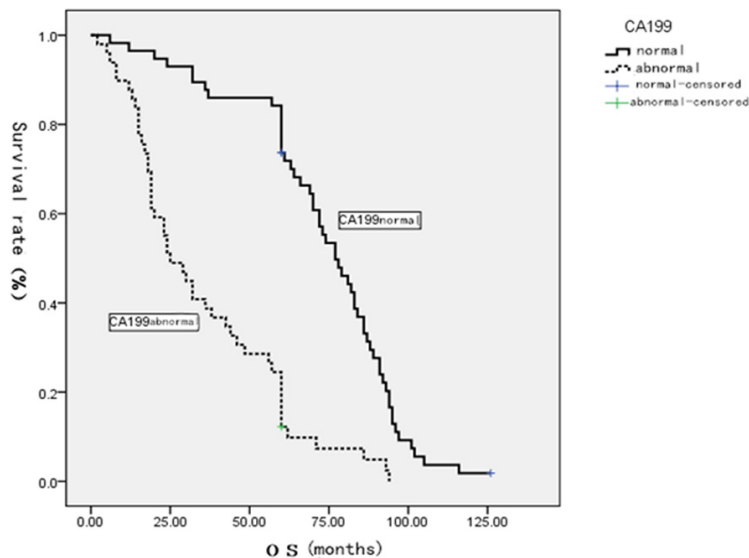


Figure 5. OS survival curve of CA19-9 normal group and abnormal group.

OS of patients after CRC radical operation to a certain extent.

CA19-9 can be elevated in different degrees in various digestive tract malignant tumors, especially in pancreatic cancer and CRC with high sensitivity and specificity [12]. Shin Nishiumi et al [13]. Pointed out that The expression of CA19-9 in patients with colorectal cancer contributes to the diagnosis of the colorectal cancer. László Herszényi et al [14] also concluded

through research that in some CRC patients clinicians detect the continuous increase of serum CEA and CA19-9 levels about 2-5 months before they are found to have relapse or metastasis. The results of this study are basically consistent with the above studies: 51 patients with recurrence and metastasis after CRC radical surgery, of which the positive rate of CA19-9 monitored pre-operatively is 66.7%, and the positive expression of CA19-9 can predict the recurrence and metastasis of CRC patients to some extent; dynamic monitoring of CA19-9 is helpful for early detection of CRC recurrence or metastasis. PFS and OS in patients with positive monitoring of CA19-9 before operation are shorter than those in patients with negative monitoring of CA19-9 before operation. The difference is statistically significant by Kaplan-Meier and relevant Log Rank tests. It is concluded that the positive expression of CA19-9 can predict PFS and OS in colorectal cancer patients to some extent.

Tumor markers are sensitive indicators to predict tumor progression. However, due to the poor specificity of positive expression of a single marker, two or more markers are usually used in clinical detection [15, 16]. In this study, we found that

by comparing and analyzing the changes of serum CEA and CA19-9 levels after CRC radical surgery, the combined detection of serum CEA and CA19-9 can predict the recurrence or metastasis of CRC earlier than separate detection. Moreover, combined detection of CEA and CA19-9 is more sensitive than separate detection in evaluating CRC prognosis. We believe that the combined monitoring of CEA and CA19-9 can be used as a routine preoperative detection method for colorectal cancer, and the

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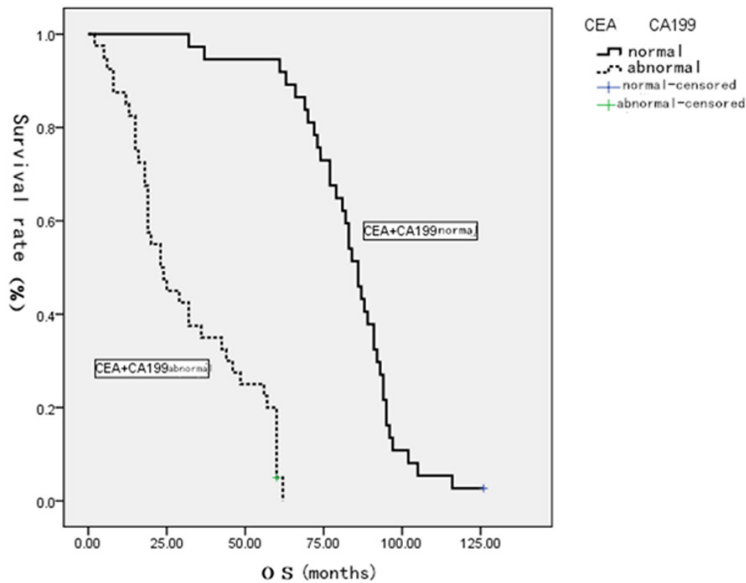


Figure 6. PFS survival curve of CEA+cA19-9 normal group and abnormal group.

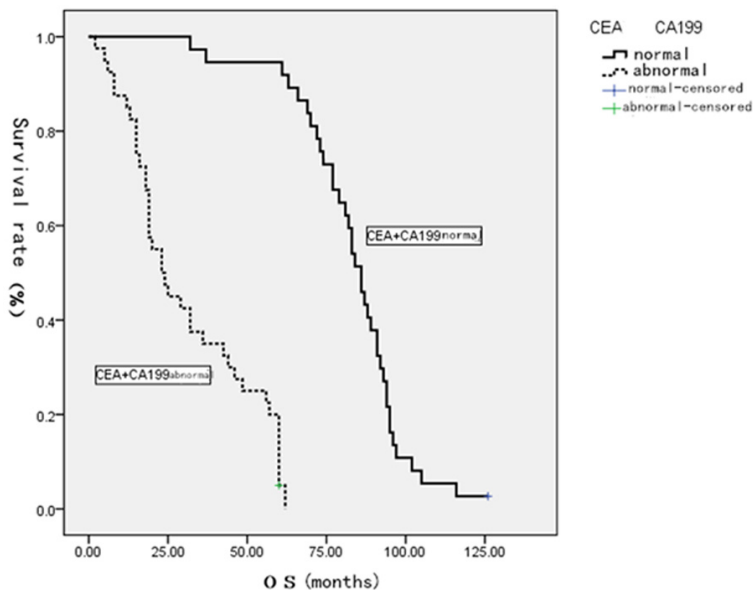


Figure 7. OS survival curve of CEA+CA19-9 normal group and abnormal group.

dynamic changes of CEA and CA19-9 can be applied to evaluate PFS and OS of patients after CRC. The combined detection of CEA and CA19-9 can be used as a prognosis prediction method for patients after CRC. Destri G L and others pointed out through research [17]: after CRC radical surgery, serum CEA gradually decreased and could rise again if there was recurrence. However, CA19-9 is not as sensi-

tive as CEA in detecting recurrence and metastasis after CRC operation. Reports show that combined detection of CEA and CA19-9 are helpful to improve the accuracy of CRC prognosis evaluation. Stiksmas J [18] and others have pointed out through research that the combined detection of CEA and CA19-9 can be used as a good indicator to evaluate whether tumor metastasis occurs before CRC. At the same time, it can be found that continuous monitoring of the two levels after treatment can evaluate the curative effect and prognosis, indicating the occurrence of recurrence and metastasis, providing a more objective clinical standard for the prognosis evaluation of CRC, which is consistent with the results of this study.

In a few words, the positive expression of serum CEA and CA19-9 is closely related to postoperative recurrence or metastasis of colorectal cancer through Kaplan-Meier and related Log Rank test analysis. Regular monitoring of both may become a prediction method for judging progression-free survival and overall survival of colorectal cancer, and is a sensitive, simple and effective indicator for judging prognosis of colorectal cancer.

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Disclosure of conflict of interest

None.

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