Int J Clin Exp Med 2016;9(10):20109-20113
www.ijcem.com /ISSN:1940-5901/IJCEM0010963

Original Article

CEA, CA125, CA153 and TSGF act as diagnostic tumor biomarkers for patients with rectal carcinoma

Wen-Bin Ji[1], Jin Chen[1], Yu-Che Mi[1], Gui-Liang Wang[1], Xin-Jiang Xu[1], Wei-Zheng Wang[2]

Departments of [1]Radiology, [2]Vascular Surgery, Affiliated Taizhou Hospital of Wenzhou Medical University, Taizhou 317000, Zhejiang, China

Received June 1, 2015; Accepted December 6, 2015; Epub October 15, 2016; Published October 30, 2016

Abstract: Many studies indicate that the biomarkers, such as CA27, carcinoembryonic antigen (CEA), (tumor specific growth factor) TSGF, CA153 could be helpful in making decisions in diagnosing the cancers. However, the biomarkers used as the diagnostic marker have not been discovered in the rectal carcinoma. This study aims to explore and analyze the biomarkers in rectal cancer. In this study, 100 cases of rectal cancer patients in were collected from January 2010 to 2013 February in affiliated Taizhou Hospital of Wenzhou Medical University. Serum tumor markers, including CA125, CEA, CA153 and TSGF were detected by using the ELISA kit on the automatic chemiluminescence immunoassay analyzer. The specificity and sensitivity of the above biomarkers were also analyzed. The results indicated that the levels of CEA, CA125, CA153 and TSGF were significantly higher compared to the level in control group ($P<0.05$). The specialty of CEA, CA153, TSGF, CA125 in these two groups had significant difference ($\chi^2=3.22$, 3.29, 3.11, 3.14, $P<0.05$). The sensitivity of CEA, CA153, TSGF, CA125 between two groups showed significant difference ($\chi^2=4.23$, 2.81, 3.04, 4.12, $P<0.05$). In conclusion, the tumor biomarkers (CA125, CA153, CEA and TSGF) could be employed as the predictor for the rectal carcinoma diagnosis in clinical.

Keywords: Rectal carcinoma, detection, carbohydrate antigen, tumor specific growth factor

Introduction

In recent years, along with the accelerated pace of life, eating disorders, environmental and metal factors, the incidence of rectal cancer showed a rising trend, which had a high mortality rate and resulted in serious harm on people's health. Cancer is a serious hazard to human health [1]. In the early diagnostic time, the appropriate treatment can prevent cancer getting worsen. When we diagnosed the cancer by cytology and the histology method, most patients had been in the middle-late stage of cancer. So searching for effective method on the early detection of cancer has the important clinical significance. Serum tumor markers (TM) and the detection of malignant tumor factors are effective methods on the early diagnosis of cancer. When the tumor proliferation occurs, tumor cells or host cells will release a number of biochemical substances such as the tumor markers (TM), tumor specific growth factor. Serum tumor markers in the early diagnosis of cancer raised concerns. One tumor marker can appeared in many kinds of tumors. One kind of tumor can have a variety of tumor markers. One tumor marker in diagnosing tumor usually showed low accuracy and less information. Single detector will cause higher false and might result in higher false positive rate and false negative rate. The detection of a variety of tumor markers can compensate for the errors that caused by a single detector. Currently multiple tumors makers were used to help diagnose cancer. A variety of tumor markers detection can improve the positive rate when we detected cancer recurrence and drug treatment studies. Common clinical detection of tumor markers could be useful in the diagnosis of tumors, screening of antitumor efficacy evaluation, tumor recurrence, follow-up therapy and other anti-cancer therapy. There are some common tumor markers such as carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), carbohydrate antigen 19-9 (CA19-9), carbohydrate antigen 72-4 (CA72-4), vascular

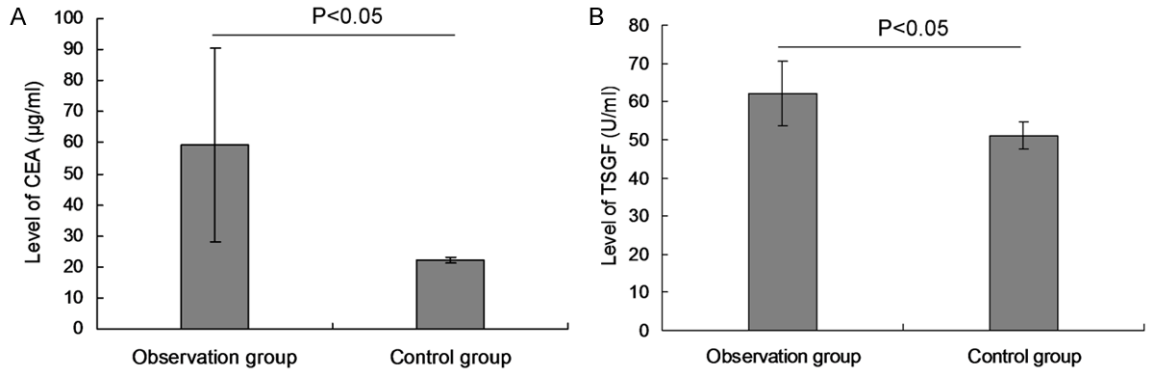

Figure 1. Examination of the CEA and TSGF tumor marker levels. A. Examination of serum CEA levels. B. Examination of serum TSGF levels. *P<0.05 represents the values in observation group compared to the control group.

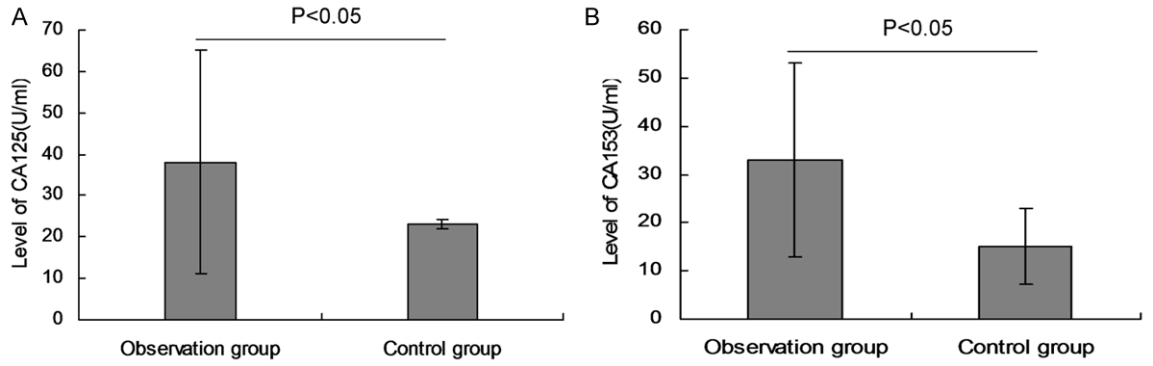

Figure 2. Examination of CA125 and CA153 serum tumor marker levels. A. Examination of serum CA125 levels. B. Examination of serum CA153 levels. *P<0.05 represents the values in observation group compared to the control group.

endothelial growth factor (VEGF), interleukin -6 (IL-6), carbohydrate antigen 153 (CA-153), M2-PK, CEA, CYFRA 21-1, NSE and SCC. CA 19-9 was considered as the most extensively biochemical marker in the diagnosis of pancreatic cancer [2-6]. Many studies predicted the diagnostic markers by searching and analyzing the related medline literature. Lyndsay Harris held an opinion that CA15-3 and CA 27.29 could be helpful in making decisions in diagnosing the breast cancer. But carcinoembryonic antigen (CEA) is not recommended [7]. In this article, we studied 100 cases of rectal cancer patients in our hospital from January 2010 to 2013 February. At the same period we also studied 100 healthy patients on detection of carbohydrate antigen (CA125), carcinoembryonic antigen (CEA), (tumor specific growth factor) TSGF, CA153. We detected and analyzed the results and evaluated rectal cancer diagnostic value of serum tumor markers (TM) with the malignant tumor factors.

Materials and methods

Clinical data and diagnostic method

100 cases of rectal cancer patients in our hospital were collected from January 2010 to 2013 February. They were diagnosed as rectal cancer by cytology and the histology. There were 47 males and 53 females. They were between ages of 25-65. The mean age was 45 ± 4 years old. At the same period, 100 patients of benign diseases were studied as the control group. There were 45 males and 55 females. They were between ages of 31 to 73 years. The mean age was 52 ± 3 years old. Patients knew about this trial and signed the voluntary consent. This trial was approved by our hospital ethics committee.

Table 1. Joint detection markers compared with single detection (%)

Category	Sensibility	Specificity	PPV	NPV	Veracity
CEA	78.7*	76.8*	64.3	71.5	53.7*
CA153	24.8*	63.5*	71.4	55.9	42.4*
TSGF	44.7*	63.6*	43.6	64.4	53.6*
CA125	32.4*	62.4*	41.4	49.5	41.7*
Joint detection	85.7	46.5	59.3	60.6	82.6

*P<0.05 represents the values compared to the joint detection.

Serum tumor markers were provided by the new Biotechnology Co. Ltd. Qingdao Bo. Testing instrument was Stratec Biomedical Systems AG's ZX6 Lumino automatic chemiluminescence immunoassay analyzer. Test items mainly contained carbohydrate antigen (CA125), carcinoembryonic antigen (CEA), (tumor specific growth factor) TSGF, CA153.

Detection for markers

Patients were given 3 ml by fasting venous blood in the early morning. Then the serum was get by centrifugal separation and placed at -20°C. Blood carbohydrate antigen (CA125), carcinoembryonic antigen (CEA) and CA153 was test by ZX6 Lumino-automatic chemiluminescence immunoassay analyzer. TSGF (tumor specific growth factor) was test through biochemical colorimetric assay. Detection step was based on the operational sequence of reagents. Carbohydrate antigen (CA125), Carcinoembryonic antigen (CEA), tumor specific growth factor (TSGF) and CA153 in two groups were detected and the data were analyzed statistically. According to the standard: CEA>5 ng/ml, CA153>25 U/ml, CA125>40 U/ml, TSGF>.

Statistical analysis

SPSS16.0 software was used for data processing and analysis. Measurement data was expressed by ($\overline{x} \pm s$). Groups were compared by using the t test. Count data was expressed by rate (%). Groups were compared by using the χ^2 test. P<0.05 indicates that the results had statistical significance difference.

Results

The level of CEA, CA125, CA153 and TSGF

The testing results of carbohydrate antigen (CA125), Carcinoembryonic antigen (CEA), (tumor specific growth factor) TSGF, CA153 in two groups were compared. The levels of CEA (**Figure 1A**) in patients with colorectal cancer was significantly higher than the level in control group (t=5.14, P<0.05). TSGF in colorectal cancer was significantly higher, the difference was statistically significant (**Figure 1B**, t=2.13, P<0.05). The CA125 (**Figure 2A**) and CA153 (**Figure 2B**) in patients with colorectal cancer was significantly higher than the level in control group. The results had significant difference (t=3.12, 3.23, P<0.05).

Specificity and sensitivity of CEA, CA153, TSGF, CA125 for rectal carcinoma detection

In the detection of rectal carcinoma, the detection of marker show higher specialty than the joint detection. The specialty of CEA, CA153, TSGF, CA125 in these two groups had significant difference (χ^2=3.22, 3.29, 3.11, 3.14, P<0.05). The detection of marker show lower accuracy and sensitivity than the joint detection. Compared with the single detection, joint detection showed higher accuracy and sensitivity. The accuracy of CEA, CA153, TSGF, CA125 in these two groups had significant difference (χ^2=3.13, 3.44, 3.22, 3.11, P<0.05). The sensitivity of CEA, CA153, TSGF, CA125 between two groups showed significant difference (χ^2=4.23, 2.81, 3.04, 4.12, P<0.05), the results showed as shown in **Table 1**.

Discussion

Tumor markers which were produced by tumor cells referred the active substances such as enzymes, proteins, hormones, glycoproteins and cellular metabolites. The content of these markers was closely related to the malignant tumor. So by observing the change of the content of tumor markers, we could diagnose malignant tumors. In present study a variety of multi-tumor marker detection method was commonly used in diagnosing and researching malignant tumors. In recent years rectal cancer had high morbidity and mortality.

This article detected carbohydrate antigen (CA125), carcinoembryonic antigen (CEA), (tumor specific growth factor) TSGF and CA15-3 in the diagnosis of rectal cancer. Joint detection showed higher sensitivity and accuracy and better than the single tests (P<0.05). This

article detected CEA, CA153, TSGF and CA125. Their sensitivities were 28.7%, 24.8%, 44.7% and 32.4% respectively. The sensitivity of combined detection sensitivity was 85.7%. The accuracy of joint detection was 82.6%, which was better than the single detection of tumor markers. CEA is a glycoprotein. It appeared the endothelial cells of fetal gastrointestinal tract of 3 to 6 months infant and gradually disappeared with fetal growth. When the body had a tumor, CEA will reappear. CEA is commonly used in the diagnosis of gastrointestinal cancer [8, 9]. The levels of CEA in patients with article gastric cancer, rectal cancer, duodenal cancer, colon cancer were higher than patients with benign gastrointestinal diseases. The single detection of CEA levels showed high false positive, low sensitivity and accuracy in the diagnosis malignancy tumors. The article the sensitivity and accuracy of CEA were 28.7%, 53.7%. Some article showed that the patients with pneumonia, smokers, gastrointestinal inflammation had the high levels of CEA.

CA199, CA125, CA153 and CD133, CD166 and CD44s are the common tumor markers in diagnosing the patients with cancer who usually had high serum levels. The main components of these tumor makers are sialic acid glycoprotein and glycolipid sialic acid, cancer-associated antigen, which exist on the cell membrane in the form lipid or lipoprotein. These tumor makers are often used in clinical diagnosis and monitoring of cancer [9-11]. This article detected TSGF in patients with rectal cancer. The content of TSGF was higher than in patients with benign gastrointestinal diseases, and the difference was statistically significant ($P<0.05$). In control group, 2 patients had the high TSGF. Because a false positive caused by inflammation. When the inflammation disappeared, TSGF levels of patients returned to normal. Tumor specific growth factor (TSGF) is produced by the malignant cells, which can promote tumor growth, and stimulate the proliferation of capillaries surrounding the cells. TSGF would be released gradually into the bloodstream along with the growth of the tumor. It is a specific marker of malignancy. It can be detected in early time of cancer. A variety of tumor markers detection method is often used in early diagnosis of breast cancer, pancreatic cancer, stomach cancer and liver cancer. This article found that multiple tumor marker levels in the serum of patients with rectal cancer were significantly higher than levels in patients with benign gastrointestinal diseases. Compared to the single detection, combined detection showed high sensitivity diagnostic yield, and reduced the false positive rate in early time of the tumor diagnosis. We draw a conclusion that the joint detection of CA125, CEA, TSGF and CA153 could improve the early diagnostic yield of rectal carcinoma. This method of detection had a certain guiding significance and showed application values in the early diagnosis of rectal carcinoma. This method should be widely applied in clinical practice.

Acknowledgements

This study was granted by the project of science and Technology Agency of Zhejiang Province (2014C33156). This study was also supported by Doctor Kuifeng Wang in the experiments design and data collection.

Disclosure of conflict of interest

None.

Address correspondence to: Wei-Zheng Wang, Department of Vascular Surgery, Affiliated Taizhou Hospital of Wenzhou Medical University, Taizhou 317000, Zhejiang, China. E-mail: wangweizhengtz@qq.com

References

[1] Li Y, Yu Y, Kang L, Lu Y. Effects of chlorine e6-mediated photodynamic therapy on human colon cancer SW480 cells. Int J Clin Exp Med 2014; 7: 4867-4876.

[2] Goonetilleke KS, Siriwardena AK. Systematic review of carbohydrate antigen (CA 19-9) as a biochemical marker in the diagnosis of pancreatic cancer. Eur J Surg Oncol 2007; 33: 266-270.

[3] Schneider J, Velcovsky HG, Morr H, Katz N, Neu K, Eigenbrodt E. Comparison of the tumor markers tumor M2-PK, CEA, CYFRA 21-1, NSE and SCC in the diagnosis of lung cancer. Anticancer Res 2000; 20: 5053-5058.

[4] Susumu S, Tanaka K, Toiyama Y, Yokoe T, Okugawa Y, Miki C, Kusunoki M. Correlation of CD133,OCT4, and SOX2 in rectal cancer and their association with distant recurrence after chemoradiotherapy. Ann Surg Oncol 2009; 16: 3488-3498.

[5] Lin PC, Lin JK, Lin CC, Wang HS, Yang SH, Jiang JK, Lan YT, Lin TC, Li AF, Chen WS, Chang SC.

Carbohydrate antigen 19-9 is a valuable prognostic factor in colorectal cancer patients with normal levels of carcinoembryonic antigen and may help predict lung metastasis. Int J Colorectal Dis 2012; 27: 1333-1338.

[6] Moore LE, Pfeiffer RM, Zhang Z, Lu KH, Fung ET, Bast RC. Proteomic biomarkers in combination with CA 125 for detection of epithelial ovarian cancer using prediagnostic serum samples from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial. Cancer 2012; 118: 91-100.

[7] Harris L, Fritsche H, Mennel R, Norton L, Ravdin P, Taube S, Somerfield MR, Hayes DF, Bast RC. American Society of Clinical Oncology 2007 Update of Recommendations for the Use of Tumor Markers in Breast Cancer. J Clin Oncol 2007; 25: 5287-5312.

[8] Molina R, Filella X, Augé JM, Fuentes R, Bover I, Rifa J, Moreno V, Canals E, Viñolas N, Marquez A, Barreiro E, Borras J, Viladiu P. Tumor Markers (CEA, CA 125, CYFRA 21-1, SCC and NSE) in Patients with Non-Small Cell Lung Cancer as an Aid in Histological Diagnosis and Prognosis. Tumor Biol 2003; 24: 209-218.

[9] Liu GL, Liu X, Lv XB, Wang XP, Fang XS, Sang Y. miR-148b functions as a suppressor in non-small lung cancer by targeting carcinoembryonic antigen (CEA). Int J Clin Exp Med 2014; 7: 1990-1999.

[10] Lugli A, Iezzi G, Hostettler I, Muraro MG, Mele V, Tornillo L, Carafa V, Spagnoli G, Terracciano L, Zlobec I. Prognostic impact of the expression of putative cancer stem cell markers CD133, CD166, CD44s, EpCAM, and ALDH1 in colorectal cancer. Br J Cancer 2010; 103: 382-390.

[11] Aggarwal C, Meropol NJ, Punt CJ, Iannotti N, Saidman BH, Sabbath KD, Gabrail NY, Picus J, Morse MA, Mitchell E, Miller MC, Cohen SJ. Relationship among circulating tumor cells, CEA and overall survival in patients with metastatic colorectal cancer. Ann Oncol 2013; 24: 420-428.