Online Submissions: wjg.wjgnet.com
wjg@wjgnet.com
doi:10.3748/wjg.14.6699

World J Gastroenterol 2008 November 21; 14(43): 6699-6703
World Journal of Gastroenterology ISSN 1007-9327

RAPID COMMUNICATION

Peripheral and mesenteric serum levels of CEA and cytokeratins, staging and histopathological variables in colorectal adenocarcinoma

Ivan Gregório Ivankovics, Luis César Fernandes, Sarhan Sydeney Saad, Delcio Matos

Ivan Gregório Ivankovics, Luis César Fernandes, Sarhan Sydeney Saad, Delcio Matos, Coloproctology Group, Discipline of Surgical Gastroenterology, Department of Surgery, Federal University of São Paulo-Escola Paulista de Medicina, São Paulo-SP, 04005-004, Brazil
Author contributions: Ivankovics IG wrote the article; Fernandes LC revised data; Saad SS revised data and writing; Matos D responsible and coordinator of the research.
Correspondence to: Dr. Luis César Fernandes, Discipline of Surgical Gastroenterology, Department of Surgery, Federal University of São Paulo-Escola Paulista de Medicina, Rua Abílio Soares 1160, Apto. 11 Paraíso São Paulo-SP 04005-004, Brazil. luiscfernandes@terra.com.br
Telephone: +55-11-3287-7231 Fax: +55-11-3251-1662
Received: September 12, 2007 Revised: February 12, 2008
Accepted: February 19, 2008
Published online: November 21, 2008

Abstract

AIM: To evaluate the differences that exist between peripheral and mesenteric serum levels of carcinoembryonic antigen (CEA) and cytokeratins in patients with colorectal adenocarcinoma.

METHODS: One hundred and thirty-eight patients with colorectal adenocarcinoma who underwent surgery at Hospital São Paulo (Discipline of Surgical Gastroenterology of UNIFESP-EPM) between December 1993 and March 2000 were retrospectively analyzed. Differences between CEA and cytokeratin (TPA-M) levels in peripheral blood (P) and in mesenteric blood (M) were studied. Associations were investigated between peripheral and mesenteric levels and the staging and histopathological variables (degree of cell differentiation, macroscopic appearance, tumor dimensions and presence of lymphatic and venous invasion).

RESULTS: Differences were observed in the numerical values of the marker levels: CEA (M) (39.10 mg/L ± 121.19 mg/L) *vs* CEA (P) (38.5 mg/L ± 122.55 mg/L), $P < 0.05$; TPA-M (M) (325.06 U/L ± 527.29 U/L) *vs* TPA-M (P) (279.48 U/L ± 455.81 U/L), $P < 0.01$. The mesenteric CEA levels were higher in more advanced tumors ($P < 0.01$), in vegetating lesions (34.44 mg/L ± 93.07 mg/L) ($P < 0.01$) and with venous invasion (48.41 mg/L ± 129.86 mg/L) ($P < 0.05$). Peripheral CEA was higher with more advanced staging ($P < 0.01$) and in lesions with venous invasion (53.23 mg/L ± 158.57 mg/L) ($P < 0.05$). The patients demonstrated increased mesenteric and peripheral TPA-M levels with more advanced tumors ($P < 0.01$ and $P < 0.01$) and in non-ulcerated lesions [530.45 U/L ± 997.46 U/L ($P < 0.05$) and 457.95 U/L ± 811.36 U/L ($P < 0.01$)].

CONCLUSION: The mesenteric levels of the tumor markers CEA and cytokeratins were higher than the peripheral levels in these colorectal adenocarcinoma patients. Higher levels of these biologic tumor markers are associated with an advanced state of cancerous dissemination.

Key words: Colonic neoplasms; Rectal neoplasms; Biological tumor markers; Carcinoembryonic antigen; Cytokeratins

Peer reviewer: Filip Braet, Associate Professor, Australian Key Centre for Microscopy and Microanalysis, Madsen Building (F09), The University of Sydney, Sydney NSW 2006, Australia

Ivankovics IG, Fernandes LC, Saad SS, Matos D. Peripheral and mesenteric serum levels of CEA and cytokeratins, staging and histopathological variables in colorectal adenocarcinoma. *World J Gastroenterol* 2008; 14(43): 6699-6703 Available from: URL: http://www.wjgnet.com/1007-9327/14/6699.asp DOI: http://dx.doi.org/10.3748/wjg.14.6699

INTRODUCTION

The estimates of cancer incidence in Brazil for the year 2006, published by INCA, indicate that colorectal cancer is the fifth most common malignant tumor type among men (11 390 new cases) and the fourth among women (13 970 new cases). The greatest incidence of cases occurs in the age group between 50 and 70 years old, but the possibility of developing this disease is already increasing after the age of 40 years is reached[1-3].

In 2004, in a study carried out in the 25 member countries of the European Union, 2 886 800 new cases of cancer and 1 711 000 deaths were recorded. The most common type was lung cancer (13.3%) followed

by colorectal cancer (13.2%) and breast cancer (13%). Lung cancer was also the greatest cause of death (341 800 cases) followed by colorectal cancer (203 700 cases)[4].

When colorectal cancer is detected in its initial stage, it may even be curable. However, the overall survival of patients with colorectal cancer does not exceed 40%. The mean five-year survival for patients with early diagnosis (stage Ⅰ) is approximately 70%, while it is 6% for advanced cases of the disease (stage Ⅳ)[1,2].

Tumor markers are substances produced by the neoplasia than can be identified in the neoplastic tissue itself and in patients' biological fluids. Many studies have been conducted to evaluate serum tumor markers at different stages of diagnosis and follow-up of colorectal carcinoma cases. Carcinoembryonic antigen (CEA) is distinguished as the most important marker[1,2,5-9].

CEA was first identified in 1965, and is a high-molecular-weight glycoprotein that is found in the cytoplasmic membrane of digestive system cells in the fetal phase and in neoplastic cells[10]. Cytokeratins form part of the microtubules of the cellular cytoskeleton, and they are released into the bloodstream during processes in which there is intense cell proliferation or apoptosis[11].

There is controversy regarding whether or not there are differences in the serum levels of the markers according to the location of the blood sample collection: from peripheral veins or from blood flowing directly out of the lesions. If there were a difference between the mesenteric and peripheral serum levels of such markers, the former might more accurately reflect the real levels produced by the tumors than would the latter. Some authors have found a significant difference between the mesenteric and peripheral levels of CEA, while others have not reproduced these results. Some studies have also demonstrated relationships between high marker levels in mesenteric serum and the histopathological variables of colorectal tumors[12-16].

The objective of the present investigation was to analyze the mesenteric and peripheral levels of CEA and cytokeratins in patients with colorectal adenocarcinoma and observe their correlation with the staging and certain histopathological variables.

MATERIALS AND METHODS

The patients were volunteers and were treated in accordance with a protocol approved by the Research Ethics Committee of the institution. In this study, 138 patients with colorectal adenocarcinoma were retrospectively analyzed. These patients were attended to and surgically treated by the Coloproctology Group, Discipline of Surgical Gastroenterology, Department of Surgery, Federal University of São Paulo-Escola Paulista de Medicina (UNIFESP-EPM). The operations were performed at Hospital São Paulo between December 1993 and March 2000. Surgical resection was performed on 124 patients, while the tumors were considered irresectable in 14 patients.

Patients who had had some other benign or malignant neoplasia at some previous time, and those for whom it was not possible to collect the data needed for the proposed analysis, were not included in the study.

With regard to the ethnic group to which the patients belonged, 68.1% were white, 22.5% brown, 6.5% yellow and 2.8% black. With regard to gender, 57.2% were female. The patients' ages ranged from 19 to 87 years, with a mean of 61.7 years.

The variables analyzed in the present investigation were: staging of the colorectal neoplasia by means of the TNM classification, degree of cell differentiation, diameter of the neoplasia, presence or absence of venous invasion and presence or absence of lymphatic invasion.

According to the TNM classification, 34 patients were in stage Ⅰ, 21 in Ⅱ, 34 in Ⅲ and 49 in Ⅳ. With regard to the degree of cell differentiation, there were 55 patients with well-differentiated tumors, 66 with moderately-differentiated tumors and three with poorly-differentiated tumors. Regarding the diameter of the neoplasia, 16 patients had tumors of $\leqslant$ 3.9 cm; 76 of 4.0-7.9 cm and 32 $\geqslant$ 8.0 cm. The presence of venous invasion was identified in the lesions of 23 patients, while lymphatic invasion was identified in 41 patients.

The collection of peripheral venous blood was done by means of direct puncture in the arm that was free of endovenous hydration, while anesthesia was being induced. Samples of 10 mL of blood were collected in dry tubes. These were centrifuged to obtain the serum from the sample, and this was stored at -20℃.

The mesenteric blood for assaying the marker levels was collected by dissection, sectioning and catheterization of the inferior mesenteric vein, when the tumor was located in the left colon or the rectum. For tumors in the right colon, collection was *via* the wide tributary vein of the superior mesenteric vein, and for tumors in the transverse colon, collection was *via* the middle colic vein. The corresponding vein was dissected and repaired with 00 cotton thread; the vein was sectioned obliquely and the catheter was introduced towards the tumor, with the collection of 10 mL of blood. This procedure was carried out before any manipulation of the tumor. The blood was centrifuged, with separation of the serum and storage in the same way as done for the peripheral blood samples.

The method utilized for assaying the CEA levels was DELFIA®. The CEA levels were considered to be normal when they were less than the limit of 5.0 mg/L.

For assaying the cytokeratin (TPA-M) levels, the LIA-mat® TPA-M Prolifigen® method was utilized, (AB Sangtec Medical®), which utilizes a reference value of 72 U/L as the cutoff point between normal and abnormal values, and this point was taken for the present investigation. The apparatus utilized for carrying out the serum assays was the Lumat LB 9501® luminometer, (EG&G Berthold).

Statistical analysis

For the statistical analysis of the data obtained in this study, *t* test and the marginal homogeneity test were

Table 1 Descriptive measurements of the tumor markers and the histopathological variables and staging of the colorectal adenocarcinoma (mean ± SD)

Variables	CEA (M) ug/L	CEA (P) ug/L	TPA-M (M) U/L	TPA-M (P) U/L
TNM				
Ⅰ	14.96 ± 43.02	15.82 ± 52.37	178.91 ± 116.08	168.44 ± 137.84
Ⅱ	3.71 ± 3.23	3.10 ± 2.63	148.56 ± 79.25	126.13 ± 82.13
Ⅲ	11.33 ± 21.21	8.00 ± 16.71	214.94 ± 164.20	151.55 ± 131.75
Ⅳ	90.28 ± 190.14	90.69 ± 190.88	578.52 ± 812.53	511.02 ± 692.70
P	0.001	0.001	0.001	0.001
Cell differentiation				
PD	22.06 ± 72.07	22.40 ± 72.24	227.35 ± 214.74	197.28 ± 234.32
MD	40.95 ± 116.87	40.52 ± 127.30	392.67 ± 695.62	338.50 ± 589.94
BD	11.40 ± 17.84	9.97 ± 14.84	111.67 ± 46.50	72.53 ± 43.22
P	0.816	0.632	0.212	0.164
Diameter (cm)				
Up to 3.9	44.80 ± 155.57	53.88 ± 190.73	194.84 ± 139.81	193.03 ± 230.85
4.0 to 7.9	27.96 ± 86.94	27.18 ± 85.14	331.94 ± 645.83	294.35 ± 561.49
⩾ 8.0	34.63 ± 89.26	31.51 ± 89.48	325.34 ± 314.19	248.44 ± 234.79
P	0.106	0.186	0.104	0.197
Macroscopic ulcerated				
No	38.21 ± 103.39	36.82 ± 108.08	530.45 ± 997.46	457.95 ± 811.36
Yes	30.01 ± 96.84	30.26 ± 104.16	248.99 ± 257.75	214.44 ± 276.23
P	0.433	0.736	0.014	0.009
Vegetating				
No	29.19 ± 103.53	30.94 ± 114.16	233.59 ± 229.94	217.40 ± 284.20
Yes	34.44 ± 93.07	32.51 ± 95.45	388.99 ± 706.77	319.81 ± 583.88
P	0.035	0.197	0.057	0.18
Infiltrative				
No	15.71 ± 41.64	15.22 ± 45.76	281.19 ± 394.86	244.83 ± 376.19
Yes	47.00 ± 129.00	47.23 ± 137.53	341.94 ± 637.18	292.49 ± 532.86
P	0.132	0.07	0.415	0.321
Venous invasion				
Present	48.41 ± 129.86	53.23 ± 158.57	347.10 ± 282.17	255.56 ± 477.84
Absent	28.09 ± 89.57	26.85 ± 88.36	304.68 ± 575.348	330.35 ± 391.40
P	0.034	0.029	0.163	0.094
Lymp. invasion				
Present	49.76 ± 129.89	46.75 ± 125.35	447.89 ± 845.14	227.83 ± 286.49
Absent	23.02 ± 77.03	24.33 ± 92.70	245.69 ± 251.79	353.65 ± 691.80
P	0.095	0.15	0.137	0.527

utilized. To study the correlations using the TNM variable, the Bonferroni multiple comparisons method was utilized.

In the tests utilized, the level of statistical significance for rejection of the nullity hypothesis was set at 0.05% or 5% ($\alpha \leqslant 0.05$), thereby indicating the results that were considered significant.

RESULTS

Analysis of the mesenteric and peripheral levels of the markers

Two statistical analysis methods were performed (one numerical and the other categorical), and each of the markers was analyzed in relation to its peripheral and mesenteric concentrations. With regard to the numerical descriptive measurements of the CEA levels, the mean for CEA (M) was 39.10 mg/L ± 121.19 mg/L and the mean for CEA (P) was 38.5 mg/L ± 122.55 mg/L, with a statistically significant difference ($P < 0.05$). Comparison between the proportions of positive rates of mesenteric and peripheral CEA was done by means of the marginal homogeneity test. No statistical difference was found from this.

With regard to the numerical descriptive measurements of the TPA-M levels, the mean for TPA-M (M) was 325.06 U/L ± 527.29 U/L and the mean for TPA-M (P) was 279.48 U/L ± 455.81 U/L ($P < 0.01$). To compare the evaluations of mesenteric and peripheral TPA-M, the marginal homogeneity test was utilized, from which it was found that rate of positive results was greater for mesenteric TPA-M ($P < 0.05$).

Associations

For both markers and for both mesenteric and peripheral blood, the levels were related to advanced stage of the neoplasia, and especially to stage Ⅳ of TNM. In addition to this association, CEA (M) and CEA (P) presented correlations with venous invasion, and CEA (M) alone correlated with vegetating lesions. Both the mesenteric and peripheral levels of TPA-M were high in non-ulcerated lesions (Table 1).

DISCUSSION

Many studies have been conducted on tumor markers, seeking greater understanding of all the possible ways of using them in diagnoses, staging, prognoses and

detection of neoplastic recurrences[1,5-7,14,17]. Even the location for sample collection has been analyzed, seeking the site that would best translate the serum levels of tumor markers and identify groups of patients with more limited prognoses (with or without liver micrometastases), and also to identify the patients who would most benefit from adjuvant therapy, for example[8,17-20].

Studies have analyzed samples from different markers collected from different points: peripheral veins or the main drainage vein from the neoplasia. The levels of these markers have been found to be higher when sampled closer to the tumors, and thus the peripheral levels do not provide a true reflection of the production of these markers.

The production of markers by diseased cells, the release of these markers and their passage through adjacent tissue, their entry into lymphatic vessels and the bloodstream, the formation of immunocomplexes, metabolism of these markers, their excretion from the liver and absorption by the colorectal wall, are factors that would influence the peripheral levels of these markers[12,13].

The way in which markers arrive in the peripheral blood has still not been clearly established. It could be *via* the portal vein system, the lymphatic system, or both. Previous studies have suggested that CEA arrives in the peripheral blood *via* the portal system[12,13]. These studies have shown that there is a strong association between the mesenteric and peripheral CEA levels and the extent of venous invasion and degree of penetration of this invasion into the colorectal wall. They have also shown that there is a significant increase in the portal levels of CEA soon after the manipulations carried out during the surgical resection of the neoplasia.

In the case of colorectal adenocarcinoma, CEA has become prominent in demonstrating usefulness for following up patients who have undergone surgery with curative intent, with increases in its levels in the event of probable tumor recurrence or development of liver metastases[7,17-19,21].

Cytokeratins have shown greater sensitivity than that of CEA in the initial diagnosis, staging, establishment of prognoses and detection of recurrence in colorectal adenocarcinoma cases[1,2,5].

The studies performed by Tabuchi *et al*[12,13] in Japan have established that there is a statistically significant difference between the mesenteric and peripheral CEA levels, and thus the authors postulate that this marker reaches the peripheral blood *via* the portal system. Positive rates were correlated with certain histopathological variables, such as venous invasion and Dukes classification. These studies have also demonstrated that patients with high mesenteric CEA levels are potentially at risk of developing liver metastases and that such levels have a negative impact on patient survival.

The mesenteric-peripheral CEA gradient has also been utilized, together with the mesenteric levels, for assessing the impact on postoperative survival among patients with colorectal cancer. A study published in Japan in 1990 demonstrated that patients with a mesenteric-peripheral CEA gradient greater than 10 ng/mL would have a worse prognosis[18].

Another study of interest showed that the mesenteric levels and the mesenteric-peripheral gradient were more effective than the utilization of the peripheral levels alone for predicting liver metastases. A study published in Japan in 1998 compared patients with advanced colorectal cancer divided into two groups: with and without liver metastases. The mean mesenteric CEA level and mesenteric-peripheral gradient were greater than the peripheral level in the group with postoperative liver metastases. This suggests that mesenteric assaying of this marker would be more effective for predicting this event[22].

Subsequent studies conducted by other authors have not shown significant differences between the peripheral and mesenteric CEA levels[14-16]. This may be related to the small size of the samples analyzed in these studies.

In the present investigation, the sample was composed of 138 patients who were analyzed retrospectively. All of them underwent peripheral and mesenteric assaying of the CEA and cytokeratin (TPA-M) levels, which were evaluated in relation to seven histopathological variables. Statistically significant differences were found between the peripheral and mesenteric CEA and cytokeratin levels when numerical analysis was performed. When only the positive frequency of the markers was investigated, there was only a difference for cytokeratins. This may signify that the main drainage route for the markers is the portal system.

Both of these markers had high levels in TNM stage IV, both for mesenteric and for peripheral blood. Thus, the markers had significantly higher levels when the neoplastic disease was no longer limited to the colon. This corroborates the findings of Fernandes *et al*[1] (2005), which showed higher marker levels in cases of patients with extra-colonic disease, perhaps signifying the presence of liver or occult lymph node micrometastases[17].

The mesenteric and peripheral CEA levels were higher in the presence of venous invasion, and this reproduces the results from previous studies. This may corroborate the hypothesis that drainage *via* the portal vein system is the fundamental principle for the distribution of this marker[12-16].

In the present study, the cytokeratin levels were also higher in the presence of non-ulcerated lesions. No studies presenting an association between peripheral and mesenteric CEA and cytokeratin levels and the macroscopic characteristics of the lesion were found in a search of the medical literature. In the present investigation, there were associations between mesenteric CEA and vegetating lesions and between mesenteric and peripheral cytokeratins and non-ulcerated lesions. It is believed that subsequent studies will be necessary, in order to analyze and compare ulcerated, vegetating and infiltrative lesions in relation

to survival and the peripheral and mesenteric levels of biological tumor marker, so as to obtain greater depth for the conclusions.

In summary, the present results allow it to be concluded that, for the patients analyzed, there was a significant difference between the CEA and cytokeratin tumor marker levels, with higher levels in the samples collected from the portal vein system than in those obtained from the peripheral blood. The levels increased in accordance with the progression of neoplastic dissemination. High mesenteric and peripheral CEA levels were associated with venous invasion. There were higher assayed cytokeratin levels in patients with non-ulcerated colorectal adenocarcinoma lesions.

REFERENCES

1 **Fernandes LC**, Kim SB, Matos D. Cytokeratins and carcinoembryonic antigen in diagnosis, staging and prognosis of colorectal adenocarcinoma. *World J Gastroenterol* 2005; **11**: 645-648

2 **Fernandes LC**, Kim SB, Saad SS, Matos D. Value of carcinoembryonic antigen and cytokeratins for the detection of recurrent disease following curative resection of colorectal cancer. *World J Gastroenterol* 2006; **12**: 3891-3894

3 **Wilmink AB**. Overview of the epidemiology of colorectal cancer. *Dis Colon Rectum* 1997; **40**: 483-493

4 **Boyle P**, Ferlay J. Cancer incidence and mortality in Europe, 2004. *Ann Oncol* 2005; **16**: 481-488

5 **Correale M**, Arnberg H, Blockx P, Bombardieri E, Castelli M, Encabo G, Gion M, Klapdor R, Martin M, Nilsson S. Clinical profile of a new monoclonal antibody-based immunoassay for tissue polypeptide antigen. *Int J Biol Markers* 1994; **9**: 231-238

6 **Forones NM**, Tanaka M, Machado D, Falcão JB, Giovanoni M. [Carcinoembryonic antigen in diagnosis and monitoring of colorectal cancer] *Arq Gastroenterol* 1997; **34**: 3-6

7 **Kim SB**, Fernandes LC, Saad SS, Matos D. Assessment of the value of preoperative serum levels of CA 242 and CEA in the staging and postoperative survival of colorectal adenocarcinoma patients. *Int J Biol Markers* 2003; **18**: 182-187

8 **Lindmark G**, Gerdin B, Påhlman L, Bergström R, Glimelius B. Prognostic predictors in colorectal cancer. *Dis Colon Rectum* 1994; **37**: 1219-1227

9 **Plebani M**, De Paoli M, Basso D, Roveroni G, Giacomini A, Galeotti F, Corsini A. Serum tumor markers in colorectal cancer staging, grading, and follow-up. *J Surg Oncol* 1996; **62**: 239-244

10 **Gold P**, Freedman SO. Demonstration of tumor-specific antigens in human colonic carcinomata by immunological tolerance and absorption techniques. *J Exp Med* 1965; **121**: 439-462

11 **Björklund B**. Tissue polypeptide antigen (TPA): Biology, biochemistry, improved assay methodology, clinical significance in cancer and other conditions, and future outlook. *Antibiot Chemother* 1978; **22**: 16-31

12 **Tabuchi Y**, Deguchi H, Imanishi K, Saitoh Y. Comparison of carcinoembryonic antigen levels between portal and peripheral blood in patients with colorectal cancer. Correlation with histopathologic variables. *Cancer* 1987; **59**: 1283-1288

13 **Tabuchi Y**, Deguchi H, Imanishi K, Saitoh Y. Carcinoembryonic antigen levels of peripheral and draining venous blood in patients with colorectal cancer. Correlation with survival. *Cancer* 1992; **69**: 2411-2417

14 **Harłozińska A**, Rachel F, Gawlikowski W, Richter R, Kołodziej J. CEA and NCA levels in peripheral and tumour venous blood of patients with gastric and colonic carcinomas estimated by RIA and EIA methods. *Eur J Surg Oncol* 1991; **17**: 59-64

15 **Moura RM**, Matos D, Galvão Filho MM, D'Ippólito G, Sjzenfeld J, Giuliano LM. Value of CEA level determination in gallbladder bile in the diagnosis of liver metastases secondary to colorectal adenocarcinoma. *Sao Paulo Med J* 2001; **119**: 110-113

16 **Waisberg J**, Contim-Neto L, Oliveira Mda S, Matheus Cde O, Nagashima CA, Goffi FS. Determination of carcinoembryonic antigen levels in peripheral and draining venous blood in patients with colorectal carcinoma. *Arq Gastroenterol* 2004; **41**: 88-92

17 **Finlay IG**, McArdle CS. The identification of patients at high risk following curative resection for colorectal carcinoma. *Br J Surg* 1982; **69**: 583-584

18 **Deguchi H**, Tabuchi Y, Saitoh Y. [CEA levels of draining venous blood and draining-peripheral CEA gradient in colorectal cancer patients: correlation with postoperative survival] *Nippon Geka Gakkai Zasshi* 1990; **91**: 575-580

19 **Finlay IG**, Meek DR, Gray HW, Duncan JG, McArdle CS. Incidence and detection of occult hepatic metastases in colorectal carcinoma. *Br Med J* (Clin Res Ed) 1982; **284**: 803-805

20 **Koch M**, Weitz J, Kienle P, Benner A, Willeke F, Lehnert T, Herfarth C, von Knebel Doeberitz M. Comparative analysis of tumor cell dissemination in mesenteric, central, and peripheral venous blood in patients with colorectal cancer. *Arch Surg* 2001; **136**: 85-89

21 **Hünerbein M**. The value of tumor markers in colorectal cancer. *Recent Results Cancer Res* 1998; **146**: 48-55

22 **Tabuchi Y**, Nakamura T, Kuniyasu T. A predictive value of carcinoembryonic antigen in draining venous blood for colorectal cancer patients with postoperative hematogenous metastases. *Cancer Detect Prev* 1998; **22**: 57-61

S- Editor Li JL **L- Editor** Logan S **E- Editor** Zheng XM