Clinical Chemistry 47:4
624–630 (2001)

Minireview

Carcinoembryonic Antigen as a Marker for Colorectal Cancer: Is It Clinically Useful?

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Background: **Carcinoembryonic antigen (CEA) is one of the most widely used tumor markers worldwide. Its main application is mostly in gastrointestinal cancers, especially in colorectal malignancy. Although in use for almost 30 years, the clinical value of CEA in colorectal cancer is still not clear.**

Methods: **The literature relevant to the clinical value of CEA in colorectal cancer was reviewed. Particular attention was paid to studies involving metaanalyses and guidelines issued by Expert Panels.**

Results: **Although of little use in detecting early colorectal cancer, high preoperative concentrations of CEA correlate with adverse prognosis. Serial CEA measurements can detect recurrent colorectal cancer with a sensitivity of ~80%, a specificity of ~70%, and can provide a lead time of ~5 months. CEA is the most frequent indicator of recurrence in asymptomatic patients and currently is the most cost-effective test for the preclinical detection of resectable disease. CEA is most useful for the early detection of liver metastasis in patients with diagnosed colorectal cancer. Overall, however, little evidence is available that monitoring of all patients with diagnosed colorectal cancer leads to enhanced patient outcome or quality of life.**

Conclusions: **Currently, the most useful application of CEA is in the detection of liver metastasis from colorectal cancers. Because of the relative success of surgery in resecting hepatic metastases, serial determinations of the marker are recommended for detecting cancer spread to the liver. In the future, preoperative concentrations of CEA may be included with the standard staging procedures for assessing prognosis.**

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Received October 12, 2000; accepted January 29, 2001.

Carcinoembryonic antigen (CEA) was first described in 1965 by Gold and Freedman *(1, 2)*, when they identified an antigen that was present in both fetal colon and colon adenocarcinoma but that appeared to be absent from healthy adult colon. Because the protein was detected in only cancer and embryonic tissue, it was given the name carcinoembryonic antigen, or CEA. Subsequent work showed that CEA, or at least a CEA-like molecule, was also present in certain healthy tissues, although concentrations in tumors were on average 60-fold higher than in the nonmalignant tissues *(3)*.

In one of the first reports on CEA in serum, Thomson et al. *(4)* found increased concentrations in 35 of 36 patients with colorectal cancer. In contrast, high values were not found in "normal" subjects, pregnant women, patients with nongastrointestinal cancers, or in patients with miscellaneous benign gastrointestinal diseases.

Although these findings were not confirmed, they nevertheless prompted widespread use of CEA as a marker for colorectal cancer. Thirty years after its initial detection in serum, CEA is one of the most widely used tumor markers worldwide and certainly the most frequently used marker in colorectal cancer. The aim of this report is to provide a critical and updated review on the value of CEA as a marker for colorectal cancer, with a introductory discussion on the structure and biological function of the CEA molecule.

Structure and Biological Function of CEA

The gene encoding CEA is now classified as a member of the immunoglobulin supergene family [for reviews, see Refs. *(5, 6)*]. This family includes genes coding for adhesion proteins such as intercellular adhesion molecule 1 (ICAM-1) and lymphocyte function-associated antigen 1 as well as the major histocompatibility antigens *(6)*. The human CEA gene family is clustered on chromosome 19q and comprises 29 genes. Of these, 18 are expressed, with 7 belonging to the CEA subgroup and 11 to the pregnancy-specific glycoprotein subgroup *(6)*.

When isolated from liver metastasis, CEA is a glycoprotein consisting of ~60% carbohydrate and a molecular mass of ~180–200 kDa *(5)*. CEA exhibits considerable

heterogeneity, which appears to be attributable to variations in its carbohydrate side chains *(5)*. Most of the carbohydrate is composed of mannose, galactose, *N*-acetylglucosamine, fucose, and sialic acid *(5)*.

As mentioned above, CEA is a member of the immunoglobulin superfamily. Two types of immunoglobulin domains are found: an N-terminal domain of 108 amino acids homologous to the immunoglobulin variable domain (IgV-like) and six domains homologous to the immunoglobulin constant domain of the C-2 set (IgC2-like) *(6, 7)*. CEA is attached to the cell membrane by a glycosyl phosphatidylinositol anchor and probably is released as a soluble form by a phospholipase C or phospholipase D *(6)*.

Structural similarity of CEA to certain immunoglobulin-related proteins, such as ICAM-1 and ICAM-2, initially suggested that CEA might act as an adhesion molecule. In vitro experiments showed that CEA was capable of both homophilic (CEA binding to CEA) and heterophilic (CEA binding to non-CEA molecules) interactions *(6–8)*. Because alterations in cell adhesion are causally involved in cancer invasion and metastasis, it was further suggested that CEA may play a role in these processes *(8)*. Evidence for a role in cancer dissemination was obtained recently by Hostetter et al. *(9)*, who showed that after transplantation of colorectal tumors into nude mice, the number of liver metastases increased from 2% to 48% following injection of mice with CEA. There is, however, no direct evidence that CEA is causally involved in cancer dissemination.

Although in vitro data implicate CEA in cell adhesions *(6, 7)*, its localization to the apical surface of mature enterocytes in healthy human colon is difficult to reconcile with this role. In the healthy colon, CEA has been found to bind certain strains of *Escherichia coli*. According to Thompson et al. *(6)*, this binding may facilitate bacterial colonization of the intestine. Hammarstrom *(7)*, on the other hand, suggested that CEA may play a role in protecting the colon from microbial infection, possibly by binding and trapping infectious microorganisms.

Factors Affecting Serum CEA Concentrations in Patients with Colorectal Cancer

TUMOR STAGE

As with most tumor markers, both the concentration and proportion of patients with increased values tend to increase with increasing disease stage. Thus, in one typical early study *(10)*, the proportion of patients with increased CEA concentrations (>2.5 μg/L) were as follows: Dukes' A disease, 28%; Dukes' B, 45%; Dukes' C, 75%; and Dukes' D, 84%. Using a cutoff point of 5 μg/L, the authors found that the proportions of patients with increased values were 3%, 25%, 45%, and 65% for patients with Dukes' A, B, C, and D disease, respectively *(10)*.

TUMOR GRADE

Several studies have shown that well-differentiated colorectal cancers produce more CEA per gram of total protein than poorly differentiated specimens *(11, 12)*. For example, in a recent report *(12)*, mean concentrations of CEA in well-differentiated, moderately differentiated, and poorly differentiated colorectal neoplasms were 18.0, 5.5, and 2.2 μg/g of protein, respectively. Similarly, serum concentrations of CEA tend to be higher in patients with well-differentiated tumors compared with those with poorly differentiated tumors *(13)*. A lack of differentiation or poor differentiation may explain why some patients with advanced colorectal cancer do not have increased serum CEA values.

LIVER STATUS

The liver is the primary site for the metabolism of CEA. Initially, uptake occurs in the Kupffer cells, which modify CEA by removing its sialic acid residues *(5)*. The asialo CEA is then endocytosed by liver parenchymal cells where it is degraded *(5)*. Certain benign liver diseases impair liver function and, thus, the clearance of CEA. Consequently, CEA can be increased in serum from patients with nonmalignant liver disease *(5, 14)*.

TUMOR SITE WITHIN THE COLON

Patients with tumors in the left side of the colon generally have a higher incidence of increased CEA concentrations than those with malignancies on the right-hand side of the colon *(10, 15)*.

PRESENCE OR ABSENCE OF BOWEL OBSTRUCTION

Sugarbaker *(16)* showed that bowel obstruction per se gives rise to higher CEA concentrations in patients with colorectal malignancy. Decompression alone reduced serum CEA values *(16)*.

SMOKING

In a recent study of >700 apparently healthy volunteers, the median CEA values for male smokers and nonsmokers were 6.2 and 3.4 μg/L, respectively. The median concentrations for female smoker and nonsmokers were 4.9 and 2.5 μg/L, respectively *(17)*. Thus, smoking appears to almost double the serum concentration of CEA.

PLOIDY STATUS OF TUMOR

Patients with aneuploid colorectal cancers have been shown to produce higher concentrations of CEA than those with tumors with a near diploid pattern *(18)*.

CEA as a Marker for Colorectal Cancer

SCREENING

In screening for colorectal cancer, the aim should be to detect disease at either Dukes' A or B stage. Malignancy detected at more advanced stages is unlikely to be more treatable than that detected through the usual course of events. Using an upper limit of normal of 2.5 μg/L, Fletcher *(19)* calculated that CEA has a sensitivity of 36% and a specificity of 87% in screening for Dukes' A and B colorectal cancer. These findings, combined with the low

prevalence of this malignancy in unselected populations, render the positive predictive value of CEA unacceptably low and thus of little value in screening healthy subjects. For the present, therefore, we must rely on fecal occult blood and endoscopy to screen for colorectal cancer *(20)*.

DIAGNOSIS

As in screening, lack of sensitivity and specificity limit the application of CEA in diagnosing colorectal cancer, especially early disease. As mentioned above, at a cutoff of 2.5 μg/L, sensitivity ranges from ~30% to 80%, depending on the stage of disease. However, as pointed out by Fletcher *(19)*, sensitivity in symptomatic subjects is likely to be higher than in asymptomatic patients because the former group is likely to have more advanced disease.

Regarding specificity, it is important to mention that CEA can be increased in most types of advanced adenocarcinomas as well as in multiple benign disorders *(14, 21)*. Frequently, the benign conditions with increased concentrations are disorders that require differentiation from cancer. Benign diseases, however, only rarely give rise to serum values >10 μg/L. Therefore, in patients with appropriate symptoms, a highly increased concentration (e.g., >5 times the upper limit of normal) should be considered strongly suggestive for the presence of cancer in that particular patient *(22)*. In this situation, which is likely to be found in the presence of advanced disease, additional tests are necessary to establish a definite diagnosis *(22)*.

ASSESSING PROGNOSIS

The Dukes' staging system, either in its original form or as one of its modifications (Table 1), has for many decades been the gold standard for predicting outcome in patients with newly diagnosed colorectal cancer [for review, see Ref. *(23)*]. For a new prognostic factor to be clinically useful in colorectal cancer it should (*a*) provide information that is independent of existing staging systems, (*b*) be a stronger indicator of patient outcome than the existing systems, or (*c*) provide prognostic information within the subgroups of the existing systems. Additional prognostic factors are particularly required for the Dukes' B (stage II or node-negative) category of patients. Approximately 40–50% of patients from this subgroup have aggressive disease and thus might benefit from adjuvant chemotherapy. Although several studies have shown that adjuvant chemotherapy extends survival in Dukes' C colon cancer patients, the effectiveness of this therapy is less clear for the Dukes' B group *(20)*. Rather than administer adjuvant chemotherapy to all patients with Dukes' B disease, it would be desirable to have a marker capable of differentiating patients with aggressive from those with indolent disease within this group. Patients with aggressive disease could then be considered for treatment with adjuvant chemotherapy, whereas those likely to have a good outcome could be spared the costs and side effects of the cytotoxic agents.

Multiple studies have shown that patients with high preoperative concentrations of CEA have a worse outcome than those with low concentrations of the marker [for review, see Refs. *(24, 25)*]. In at least seven different reports, the prognostic impact of the marker was investigated in either node-negative or Dukes' B patients *(10, 26–31)* (Table 2). In five of these *(10, 26, 28, 30, 31)*, including the only two prospective studies *(30, 31)*, high CEA concentrations predicted adverse prognosis. In the remaining two *(27, 29)*, however, no significant relationship was found between marker concentrations and patient outcome. In one of these negative studies *(27)*, only a subset of the Dukes' B patients was analyzed, i.e., those with stage B2 disease or where tumor invaded into or through the serosa or perirectal fat. In the other negative study *(29)*, although CEA alone was not prognostic in Dukes' B patients, when combined with CA 242, the two markers together yielded significant prognostic information in this subgroup of patients. Thus, the majority of studies suggest that preoperative CEA can provide prognostic data in patients with Duke's B colorectal cancer. CEA may thus be able to help identify the subset of patients with aggressive disease who might benefit from adjuvant chemotherapy. However, it is important to point

Table 1. Pathological staging systems used for colorectal cancer.[a]

Dukes'	UICC/AJCC[b]	
A	I	Tumors invading submucosa or muscularis propria
B	II	Tumors invading through muscularis propria
C	III	Invasion of tumor to regional lymph nodes
D[c]	IV	Metastasis to distant sites

[a] Taken from McLeod and Murray *(23)* with permission from the publisher, Churchill Livingstone.

[b] UICC, International Union Against Cancer; AJCC, American Joint Committee on Cancer.

[c] Stage D was not included in the original Dukes' staging system but now is commonly used to denote distant metastasis.

Table 2. Studies evaluating preoperative serum CEA as a prognostic marker in low-risk (Dukes' B or node-negative) colorectal cancer patients.

Authors	No. of patients	*P*	Type of study[a]
Wanebo et al. *(10)*	50	<0.02	R
Blake et al. *(26)*	30	<0.001	R
Moertel et al.[b] *(27)*	162	NS[c]	R
Chu et al. *(28)*	126	0.03	R
Carpelan-Holmstrom et al. *(29)*	100	NS	R
Harrison et al.[d] *(30)*	572	0.001	P
Carriquiry et al. *(31)*	57	0.03	P

[a] R, retrospective study; P, prospective study.

[b] Analysis confined to patients with Dukes' B2 disease only, i.e., tumors invading into or through the serosa or perirectal fat. In addition, in this study, only multivariate analysis was performed.

[c] NS, not significant.

[d] Prognostic value confirmed using both univariate and multivariate analysis.

out that there currently are no reports showing a benefit from the use of adjuvant therapy based solely on an increased preoperative CEA concentration.

It is of interest that the American Joint Committee on Cancer at a recent Consensus Conference suggested that CEA be added to the TNM staging system for colorectal cancer *(31, 32)*. The CEA concentration should be designated as follows: CX, CEA cannot be assessed; CO, CEA not increased (<5 μg/L) or CEA1, CEA increased (>5 μg/L). It should be pointed out that these suggestions were for the purpose of discussion only and are not yet formal proposals *(31, 32)*.

A College of American Pathologists Expert Groups ranked preoperative serum CEA concentration as a category I prognostic marker for colorectal cancer *(33)*. Category I factors include those "definitely proven to be of prognostic import based on evidence from multiple statistically robust published trials and generally used in patient management". Also included in the category I group were local extent of tumor assessed pathologically (i.e., TNM staging), regional lymph node metastasis, blood or lymphatic vessel invasion, and residual tumor following surgery with curative intent *(33)*.

Although less work has been carried out to investigate the prognostic value of postoperative CEA concentrations, the available evidence suggests that high concentrations at this time also predict adverse outcome. After successful surgical resection of colorectal cancer, an increased CEA concentration should return to normal within 4–6 weeks *(34)*. Failure of an increased preoperative value to decrease to normal concentrations within 6 weeks of surgery frequently is associated with early recurrent disease *(34)*.

CEA may also provide prognostic data in patients who develop liver metastasis following curative resection for colorectal cancer. The liver is the main site for metastatic disease from colorectal cancer, with ~60% of patients developing metastasis in this organ *(35)*. In ~40% of patients who die from colorectal cancer, the liver appears to be the only site of metastatic disease *(35)*. Approximately 25% of these patients are candidates for hepatic resection, and the 5-year survival for patients who undergo surgery is 21–48% *(36)*. Hepatic resection is thus the most successful and currently the only potential curative form of treatment for metastatic colorectal cancer *(36)*.

Unfortunately, 50–80% of patients who undergo hepatic resection develop further recurrences. It is therefore important to have preoperative prognostic factors that might predict those patients likely to develop recurrent disease. In a review of the literature, Cromheecke et al. *(36)* (Table 3) found that high concentrations of preoperative CEA predicted a poor outcome in 8 of 11 studies reviewed. High concentrations of CEA 1–3 months after hepatectomy has also been shown to correlate with adverse prognosis *(37, 38)*.

Table 3. Dukes' stage and serum CEA as prognostic factors for recurrence after resection for liver metastasis from colorectal cancer.[a]

Authors	Dukes' stage[b]	CEA[b]
Fortner et al. 1984	Y	N
Doci et al. 1991	Y	N
Younes et al. 1991	ND	Y
Rosen et al. 1992	N	N
Cady et al. 1992	N	Y
Scheele et al. 1995	ND	Y
Seifert et al. 1996	Y	Y
Wang et al. 1996	ND	Y
Fong et al. 1997	Y	Y
Cady et al. 1998	ND	Y
Ohlsson et al. 1998	ND	Y

[a] Adapted from Cromheecke et al. *(36)* with permission of the publisher, WB Saunders.

[b] Y, significant prognostic factor; N, not a significant prognostic factor; ND, not done.

Surveillance of Patients with Diagnosed Colorectal Cancer

The aim of CEA monitoring after curative resection of colorectal cancer is to detect recurrent disease at an early and treatable stage. Although many studies have addressed the value of serial CEA determinations for this purpose, most contained relatively small numbers of patients and were retrospective in design [for reviews, see Refs. *(19, 39)*]. Despite these limitations, several conclusions have emerged regarding the use of CEA in the follow-up of patients with colorectal cancer. These include:

- Longitudinal CEA measurements detect recurrent cancer with a sensitivity of ~80% (range, 17–89%) and specificity of ~70% [range, 34–91%; for review, see Ref. *(19)*]. The wide ranges of sensitivities and specificities are likely to be attributable to factors such as frequency of CEA assay and definition of a CEA increase.
- Serial CEA determinations are most useful in detecting liver metastasis. For example, in a prospective study of 305 patients, Arnoud et al. *(40)* showed that increased CEA concentrations had a sensitivity of 94% and specificity of 96% in diagnosing liver metastasis. In a further prospective evaluation, using 196 patients, CEA was reported to have a sensitivity of 100% in detecting metastatic liver disease *(41)*.
- CEA exhibits relatively poor sensitivity for the detection of locoregional recurrences, i.e., ~60% *(30)*. Despite this limited sensitivity for locoregional disease, Pietra et al. *(41)* recently showed in a prospective randomized trial that CEA was superior to endoscopy, computerized tomography, and ultrasound in diagnosing local recurrences.
- Monitoring with CEA can detect recurrent colorectal cancer with an average lead time of 5 months (range, 4–10 months) *(19, 39)*.

- CEA is the most frequent indicator of recurrence in asymptomatic patients *(30, 41)*.
- CEA appears to be the most cost-effective test for the detection of potentially curable recurrent disease *(42)*.

On the basis of the above findings, we can conclude that CEA currently is the most cost-effective and sensitive method for diagnosing recurrent disease in patients with previously diagnosed colorectal cancer. An important question therefore is: do these results justify the routine assay of CEA in patients who undergo curative resection for colorectal cancer? To answer this question it would be necessary to carry out a large prospective randomized trial comparing patient outcome, quality of life, and cost of care in patients with and without CEA monitoring. To my knowledge, results from such a study have never been published.

In the absence of data from a large randomized trial, a metaanalysis of small randomized or nonrandomized studies provides the most reliable data. In 1998, Rosen et al. *(43)* reported the results of such an analysis based on a review of the published literature from 1972 to 1996. The aim of this study was to compare outcomes in patients with intensive follow-up vs those with no follow-up. Intensive follow-up was defined as (*a*) at least history, physical examination, and serial CEA assays; (*b*) an interval for these follow-up periods of at least three times per year for the first 2 years; and (*c*) mean follow-up after initial resection of at least 2 years. The control group had no routine follow-up, with physicians responding only to changes in symptoms. From the literature review, two randomized and three comparative cohort studies, comprising 2005 patients, met the above criteria. After evaluation in a metaanalysis, the following conclusions emerged:

- The cumulative 5-year survival was 1.16 times higher in patients who underwent intensive follow-up than in the controls ($P = 0.003$).
- More than twice as many curative re-resections were performed for recurrent cancer in the group with intensive follow-up than in the controls ($P = 0.0001$).
- Patients who underwent intensive follow-up had a survival rate 3.6 times higher than that of the control group ($P = 0.0004$).
- Similar results were obtained from a metaanalysis of 14 single cohort studies (total number of patients, 6641) comparing intensive follow-up with minimum or no follow-up, consisting of historical controls *(43)*.

Although this metaanalysis concluded that intensive follow-up diagnosed a greater number of resectable recurrences and led to enhanced patient outcome, it did not investigate the specific benefit of CEA. However, in a separate metaanalysis based on seven nonrandomized studies with a total of 3283 patients, Bruinvels et al. *(44)* showed that patients who underwent intensive follow-up had a 9% better 5-year survival rate than those with minimal or no follow-up only when the intensive follow-up group had CEA assayed.

The value of CEA, or indeed of any other procedure for the preclinical detection of recurrent/metastatic disease, depends primarily on whether outcome is improved as a result of early diagnosis. As mentioned above, hepatic resection for isolated liver metastasis achieves long-term survival in ~20–50% of patients and may be the only curative therapy for metastatic colorectal cancer. Because of the success of surgery in treating liver metastasis from colorectal cancer, an American Society of Clinical Oncology panel recommended CEA monitoring in "only those patients who would be willing and able to undergo a hepatic resection for recurrent disease" *(25)*. For this subset of patients, it was recommended that CEA testing be performed every 2–3 months for at least 2 years after diagnosis. Testing was to be confined to those patients with stage II (Dukes' B) and III (Dukes' C) disease. Patients with Dukes' A disease were excluded from CEA monitoring because the probability of developing recurrences is low in this subgroup.

Finally, it is important to address (*a*) the proportion of patients who are likely to benefit from CEA monitoring, and (*b*) the cost of this monitoring. On the basis of the assumptions that ~50% of patients with colorectal cancer develop liver metastasis, that 25% of these patients are candidates for resection, and that 25% of these have 5-year survival rates, Ballantyne and Modlin *(45)* calculated that at most only 3% of patients with colorectal cancer benefit from surgical resection of liver metastasis. Similar conclusions were also reached by other authors *(46, 47)*.

Regarding costs, Kievit and van de Velde *(48)* in 1990 concluded that monitoring with CEA provided a minor improvement in survival but at a high cost ($22 936 to $4 888 208 per quality-adjusted life-years saved). A further analysis in 1999 estimated a cost of $500 000 per cure of recurrence *(49)*. Despite these apparently high costs, it is important to point out that monitoring with CEA is likely to be cheaper and more convenient to patients than either radiology or endoscopy.

Monitoring Chemotherapy in Patients with Advanced Disease

There are now at least three different metaanalyses showing that the use of fluorouracil-based chemotherapy enhances outcome in patients with advanced colorectal cancer *(50–52)*. Because CEA can be increased in >80% of patients with distant metastasis, it is a potential marker for monitoring response to chemotherapy. Several studies have shown that patients who exhibited a decrease in CEA while on chemotherapy had a better overall survival compared with those whose CEA concentrations failed to decrease *(14, 16, 25)*. Conversely, increases in CEA while receiving chemotherapy generally predict progressive disease. There is, however, no study showing that CEA testing in patients undergoing chemotherapy for ad-

vanced colorectal cancer has an impact on survival, quality of life, or cost of care *(25)*.

Despite this, an American Society of Clinical Oncology Panel *(25)* recommended the following with respect to the use of CEA in monitoring therapy in patients with advanced colorectal cancer: (*a*) a baseline CEA value before treatment; and (*b*) serial monitoring every 2–3 months while on active treatment (if no other simple test is available to indicate a response). According to the Panel, two values above the baseline are adequate to document progressive disease and discontinuation of therapy, even in the absence of corroborating radiological evidence.

It is important to mention that administration of fluorouracil-based therapy can cause transient increases in CEA concentrations in the absence of disease progression. For example, in a study by Moertel et al. *(53)*, among 99 patients who developed liver toxicity while on chemotherapy, 19 had false-positive CEA increases. These CEA values ranged from 5.1 to 34 μg/L and returned to normal after cessation of therapy.

Conclusion

On the basis of available evidence, it would appear that monitoring of all colorectal cancer patients with serial CEA assays has only a modest effect on patient outcome. However, a definite study such as a large prospective randomized trial to address the effect of CEA testing on overall survival, quality of life, or cost of care has never been carried out, or at least its results have not been reported.

The question therefore remains whether CEA should be used in the surveillance of patients who have undergone curative resection for colorectal cancer. According to Macdonald *(54)*, monitoring may be of benefit if the subject is a potential candidate for aggressive curative surgery if metastases were to develop. It was mentioned above that removal of liver metastases from patients with no extra metastatic deposits produces 5-year survivals of 21–48%. Consequently, the American Society of Clinical Oncology Guidelines have recommended CEA monitoring in patients if resection of liver metastasis would be clinically indicated.

Finally, it should be mentioned that most of the data relating to the use of CEA in the follow-up of patients with colorectal cancer were obtained before the relatively widespread use of chemotherapy for this malignancy. In recent years, both chemotherapy for metastatic disease and adjuvant chemotherapy for patients with Dukes' C malignancy have found increasing use. Currently, there is no evidence that monitoring these patients with CEA values enhances prognosis. However, should more effective chemotherapy for colorectal cancer become available or should there be an increase in the use of second-line chemotherapy in the future, it is likely that CEA would be used more widely to monitor its effects.

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