

Gastrointestinal Cancer

Role of Serum Carcinoembryonic Antigen in Predicting Recurrent Disease following Curative Resection of Rectal Cancer

Srikanth Soma¹ Sachin Gurnule²

¹Department of Surgical Oncology, Chalmada Anand Rao Cancer Hospital and Research Centre, Karimnagar, Telangana, India

²Department of Community Medicine, Chalmada Anand Rao Institute of Medical Sciences, Karimnagar, Telangana, India

Address for correspondence Soma Srikanth, MCh, Department of Surgical Oncology, Chalmada Anand Rao Cancer Hospital and Research Centre, Karimnagar 505001, Telangana, India (e-mail: soma_986@yahoo.co.in).

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Abstract



Srikanth Soma

Keywords

- ▶ carcinoembryonic antigen
- ▶ early detection
- ▶ rectal cancer
- ▶ recurrence
- ▶ serum CEA

Introduction Surveillance of patients following definitive treatment of rectal malignancy is based on the predicament that early detection of recurrence may provide an opportunity for cure. Available methods for monitoring include clinical, radiological, and serum tests. The purpose of this study was to determine the effectiveness of CEA in detecting recurrences.

Materials and Methods Retrospective analysis of patients with adenocarcinoma rectum treated with curative intent between 2012 to 2020 at our institute was performed. Postoperatively, patients were followed with CEA measurements according to our institution protocol and elevation of serum CEA above 5 ng/dL was considered as suspicious of recurrence.

Results One hundred ninety patients who received curative treatment were deemed eligible for the analysis. Among these 61 patients had recurrences during the follow-up period and postoperative CEA measurements at the time of recurrence were analyzed in all the patients. Sensitivity, specificity, positive predictive value, and negative predictive value of postoperative CEA to detect recurrences are 81.9, 92.2, 83.3, and 91.5%, respectively.

Conclusion CEA surveillance following definitive management of rectal cancer detects recurrences in majority of the patients and hence strongly recommended.

Introduction

Carcinoembryonic antigen (CEA) is the most widely used tumor marker for colorectal malignancies. Higher serum CEA levels during surveillance is associated with increased recurrence rates and worse prognosis. The diagnosis of recurrent disease may be made several months earlier by investigating the first abnormal CEA level, although any benefit in terms of survival remains to be proven.

The purpose of our study was to assess the role of CEA in the detection of recurrences in rectal cancer.

Materials and Methods

This is a retrospective analysis of patients with adenocarcinoma rectum treated with curative intent between 2012 and 2020 at our institute.

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Staging work-up was performed before initiating definitive treatment in all patients, which included digital rectal examination, serum CEA levels, colonoscopy, imaging of abdomen and pelvis. Patients with early localized malignancies underwent upfront surgery while those locally advanced at presentation underwent neoadjuvant therapy (-chemoradiation/radiation) followed by definitive surgery.

Postoperatively, patients were followed with 3 monthly CEA measurements for the first 3 years followed by biennial measurements for the years 3 to 5 and then, annually thereafter and annual computed tomography (CT) scan of the abdomen for the first 3 years. During follow-up, elevation of serum CEA above 5 ng/dL was considered as suspicious of recurrence. In this situation, the test would be repeated after 1 to 2 months. Serial elevation of serum CEA was an indication for further evaluation in the form of imaging (CT scan or PET-CT) with or without colonoscopy.

Data was collected focusing on CEA at diagnosis, number and nature of recurrences, CEA at the time of recurrence, and also details regarding false positive CEA elevations.

We calculated the sensitivity, specificity, and positive and negative predictive value for CEA as an index of tumor recurrence.

Results

Among the 350 patients who presented to the institution during this time period, 190 patients completed definitive treatment, either in the form of upfront surgery or surgery following neoadjuvant therapy and were thus eligible for the study. There were 116 male and 74 female patients. Mean age was 50.86 years (range: 16–85 years).

Recurrence of disease took place in 61 patients (32%) following definitive treatment. Median follow-up period was 33 months (range: 0–84 months).

Local recurrences manifested in 20 patients and distant metastases in 41 patients.

Among patients with recurrences, preoperative CEA was ≥ 5 ng/mL in 41 patients and >5 ng/mL in 20 patients.

Fifty cases had elevated CEA with recurrence while 11 patients had normal CEA levels. False positive CEA elevations were noted in 10 patients. Among 50 patients with elevated CEA at the time of recurrence, approximately 31 patients had normal CEA values at diagnosis and 19 patients had elevated CEA levels. Sensitivity, specificity, positive predictive value, and negative predictive value of postoperative CEA to detect recurrences are 81.9, 92.2, 83.3, and 91.5%, respectively.

Discussion

CEA was identified in fetal colonic cells and colon adenocarcinoma by Gold and Freedman in 1965.^{1,2} Since this was identified only in cancerous and embryonic tissue, it was named as CEA. Further research, however, showed that CEA was also present in certain healthy tissues, although the concentrations in tumors were significantly much higher.³

The gene that encodes CEA is classified as a member of the immunoglobulin supergene family.^{4,5}

CEA has been used as a tumor marker in the follow-up of colorectal cancer for more than four decades. Controversy still exists today regarding its diagnostic applicability due to a relatively low sensitivity and a questionable effect on mortality. The serum levels of CEA at diagnosis have low sensitivity as patients with colorectal cancer can have normal levels of serum CEA. The relationship between elevated CEA values in the preoperative period and poor prognosis has been investigated in several studies with no definite conclusion. Most of the institutions do CEA surveillance monitoring during follow-up of their patients following surgery as it has been shown to be the most frequent indicator of recurrence in asymptomatic patients and also appears to be the most cost-effective test for the detection of potentially curative recurrences.

Studies have shown that longitudinal CEA measurements detect recurrent cancer with a sensitivity of approximately 80% (range, 17–89%) and specificity of approximately 70% (range, 34–91%).⁶ In a prospective randomized trial conducted by Pietra et al.,⁷ CEA was found to be superior to endoscopy and imaging in detecting local recurrences. Berman and colleagues in their analysis regarding post-surgical surveillance found that CEA elevation occurred at least 5 months (range: 4–10 months) prior to symptomatic recurrences.⁸ Few studies have shown immense value of CEA determinations in detecting liver metastases. Jones et al.⁹ found that increased CEA concentrations had a sensitivity of 94% and specificity of 96% in detecting liver metastases in a prospective study of 305 patients. The CEA watch trial, a randomized controlled multicenter prospective study which included 3,223 patients assessed the role of intensive CEA monitoring (every 2 months) during follow-up of their patients and concluded that the CEA watch protocol detects recurrent disease after colorectal cancer earlier, in a phase in which a significantly higher proportion of recurrences can be treated with curative intent.¹⁰

A prospective comparison of various modalities to detect recurrent cancer by Sugarbaker et al.¹¹ concluded that serial CEA assays and routine visits to a physician's office were the most useful tests for earliest detection of recurrent cancer.

Of the 1,356 Eastern Cooperative Oncology Group patients in Intergroup Protocol 0089 who underwent surgical resection for Dukes' B2 and C colon carcinoma, 421 patients who developed recurrent disease were reviewed.¹² Similar to the above study various modalities were compared and found that CEA measurement was the most cost-effective test in detecting potentially curable recurrent disease while a routine physician examination had no added benefit.

Conclusion

In this study serum CEA was an indicator for recurrence in 82% cases while at the same time elevated CEA at the time of diagnosis did not predict increased recurrence rates. Considering such high predictive value of CEA in detecting recurrences in asymptomatic patients as proven in our study, we recommend serial CEA monitoring following definitive treatment of rectal cancer.

Conflict of Interest

None declared.

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