# Evaluation of the Relationship between Carcinoembryonic Antigen and TNM Stage in Colorectal Cancer

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## ABSTRACT

**Objective:** We aimed to examine the relationship between carcinoembryonic antigen (CEA) levels in the preoperative period and TNM (T: primary tumor, N: lymph node, M: distant metastasis or metastasis) staging in patients with colorectal cancer in our region.

**Materials and Methods:** In the present study, 752 cases diagnosed with colorectal cancer between January 1992 and December 2010 we analyzed retrospectively.

**Results:** Data of 752 patients diagnosed with colorectal cancer between 1992 and 2010 were evaluated; of the 752 patients, 427 (56.8%) were males and 325 (43.2%) were females with the mean age of 56.8±14.9 years. CEA levels of 316 cases were measured; 52.2% of the samples were within normal limits. Cases with CEA ≤5 ng/mL were majorly in Stage III, whereas those with CEA >5 ng/mL were predominantly in Stage IV. The TNM stage, tumor diameter, and differentiation levels were defined, and no statistically significant relationship was detected between these parameters and CEA levels.

**Conclusion:** While the CEA levels of 52.2% of participating cases were within normal limits, there was no statistically significant relationship between the CEA levels and differentiation level of tumor, tumor diameter, and TNM staging. According to the data, CEA levels may be within normal limits in the majority of patients with colorectal cancer. Therefore, normal levels of CEA will not rule out colorectal cancer diagnosis, and it can be concluded that these patients should be investigated in detail.


**Keywords:** Colorectal cancer, carcinoembryonic antigen, disease stage

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***Cite this article as:*** *Topdagi O, Timuroglu A. Evaluation of the Relationship between Carcinoembryonic Antigen and TNM Stage in Colorectal Cancer. Eurasian J Med 2018; 50 96-8*

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**Received:** June 18, 2017
**Accepted:** November 12, 2017

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DOI 10.5152/eurasianjmed.2018.17093



## Introduction

Colorectal cancer is an important cause of mortality and morbidity worldwide [1]. It is the fourth cancer type among women and men, and it ranks second among cancer-related deaths [2]. Serum carcinoembryonic antigen (CEA) is a glycolyzed antigen, which is secreted into the lumen after expression on the apical surface of colonic epithelial cells [3]. It is an oncofetal antigen, and its serum levels are increased at a rate of 75% in colorectal cancer recurrence. While CEA levels are highly sensitive in hepatic and retroperitoneal metastases, local recurrences are less sensitive in peritoneal and lung metastases [4]. Preoperative CEA levels in patients with colorectal cancer may be normal or high, and high CEA levels are reported to be closely related to recurrence and poor prognosis [5].

In our study, the presence of a relationship between preoperative CEA levels and tumor stage was investigated in patients with colorectal cancer.

## Materials and Methods

Patients diagnosed with colorectal cancer as pathological results of examinations performed in our institution between 1992 and 2010 were retrospectively screened. The tumor, node, metastasis (TNM) stage of 320 patients were defined. The TNM classification (T: primary tumor, N: lymph node, M: distant metastasis or metastasis) of American Joint Committee on Cancer/ Union for International Cancer Control was used in colorectal cancer staging. Patients with colorectal cancer were classified as Stage I (presence of tumor without lymph node involvement extending to subserosa), Stage II (presence of tumor without lymph node involvement extending beyond subserosa), Stage III (presence of tumor without lymph node involvement without metastasis), and Stage IV (metastatic tumor) by using this method. The CEA levels of patients

**Table 1.** Median age, gender, tumor localization, and TNM stages of cases

| | |
|---|---|
| **Median age, years** | 56 (21-92) |
| Gender | |
| Male | 427 (56.8%) |
| Female | 325 (43.2%) |
| Total | 752 (100%) |
| Tumor localization | |
| Cecum | 33 (4.4%) |
| Ascending colon | 66 (8.9%) |
| Transverse colon | 21 (2.8%) |
| Descending colon | 81 (10.9%) |
| Sigmoid colon | 134 (18%) |
| Rectum | 410 (%55) |
| Total | 745 (%100) |
| TNM staging | |
| I | 22 (6.9%) |
| II | 68 (21.3%) |
| III | 100 (31.3%) |
| IV | 130 (40.6%) |
| Total | 320 (100%) |

T: primary tumor; N: lymph node; M: metastasis

**Table 2.** CEA levels and frequency values

| CEA | Frequency | % |
|---|---|---|
| ≤5 ng/mL | 188 | 59.5 |
| >5 ng/mL | 128 | 40.5 |
| Total | 316 | 100 |

CEA: carcinoembryonic antigen

were also measured in the preoperative period. According to the reference range of our institution's hormone laboratory, values <3.4 ng/mL were accepted as normal, whereas those >3.4 ng/mL were accepted as high.

The Statistical Package for Social Sciences (SPSS Inc.; Chicago, IL, USA) 15.0 program was used in data analysis. Statistical analysis of mean ($\bar{X}$), frequency value (F), p value, Chi square ($X^2$), and t test were used in the analyses. The p values were obtained as the results of statistical analysis of data, and the level of significance was accepted as

All participants were informed about the study and written consent was obtained. The ethics committee approved the study protocol.

## Results

In the present study, data from 752 patients diagnosed with colorectal cancer between 1992 and 2010 were evaluated. Of the 752 patients, 427 (56.8%) were males and 325 (43.2%) were females. The mean age was 56.8±14.9 years, and the median age was 56 years. The youngest patient was 21 years old, whereas the oldest was 92 years old. Patient data are summarized in Table 1.

The CEA levels of 316 patients could be defined; the CEA levels of samples were within normal limits (CEA= 0-3.4 ng/mL). When literature was reviewed generally, it was observed that patients were classified according to CEA levels below or about 5 g/mL. Therefore, the second classification was performed in the study and it was defined that 59.5% of cases had CEA ≤5 ng/mL (Table 2).

The relationship between CEA levels and TNM staging of patients is shown in Table 3. Cases with CEA ≤5 ng/mL were predominantly in the Stage III, whereas those with CEA >5 ng/mL were intensely in the Stage IV. Chi square analysis was performed, and no statistically significant correlation was detected between TNM staging and CEA levels (p>0.05; Table 3).

**Table 3.** CEA levels and TNM staging

| CEA | TNM staging | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Stage I | | Stage II | | Stage III | | Stage IV | | Total | |
| | Freq. | % | Freq | % | Freq | % | Freq | % | Freq | % |
| ≤5 ng/mL | 13 | 8.7 | 34 | 22.8 | 53 | 35.6 | 49 | 32.9 | 149 | 100 |
| >5 ng/mL | 6 | 6.1 | 21 | 21 | 25 | 25.5 | 46 | 46.9 | 98 | 100 |
| Total | 19 | 7.7 | 55 | 22.3 | 78 | 31.6 | 95 | 38.5 | 247 | 100 |

T: primary tumor; N: lymph node; M: metastasis; CEA: carcinoembryonic antigen Freq: frequency

**Table 4.** CEA level and differentiation degree

| | Differentiation degree | | | | |
|---|---|---|---|---|---|
| CEA | Mild | Moderate | Well | Undifferentiated | Total |
| ≤5 ng/mL | 9 | 60 | 22 | 1 | 92 |
| >5 ng/mL | 10 | 32 | 5 | 1 | 48 |
| Total | 19 | 92 | 27 | 2 | 311 |

CEA: carcinoembryonic antigen

**Table 5.** CEA level and tumor diameters

| | CEA level | | |
|---|---|---|---|
| Tumor diameter | ≤5 ng/mL | >5 ng/mL | Total |
| < 3 cm | 32 | 29 | 61 |
| 3-6 cm | 58 | 31 | 89 |
| 6-9 cm | 31 | 21 | 52 |
| >9 cm | 29 | 16 | 45 |
| Total | 150 | 97 | 247 |

CEA: carcinoembryonic antigen

When CEA levels were evaluated with tumor differentiation degrees, no statistically significant correlation was detected between cases with CEA ≤5 ng/mL and those with >5 ng/mL in the Chi square analysis (p>0.05; Table 4).

When the correlation between CEA levels and tumor diameters of patients was compared, no statistically significant correlation was detected in the Chi square analysis (p>0.05; Table 5).

## Discussion

CEA, which was first defined by Gold and Feedman in 1965, is an intracellular protein, and can be defined normal at low concentrations in the embryonic and fetal intestines or normal adult human cells. CEA can be detected at high levels in breast and lung cancers as well as in the serum levels are detected high at 90% of primary colorectal cancer cases. CEA is an important structure regulating promoter functions in intracellular adhesion and aggregation. Therefore, it has been believed that CEA has an important role in tumor invasion and in defining metastasis [5, 6]. Filiz et al. [7] reported in their study on 151 colorectal cancer patients in 2009 that 58.8% of patients had normal preoperative CEA levels. No statistically significant correlation was detected between tumor size, localization, and differentiation degree and preoperative CEA levels in that study. In another study conducted by Duffy [8], correlation between CEA levels of patients and differentiation degree was investigated. While CEA levels were high in cases with well and moderately differentiated tumors, they were low in the cases with poor and mild differentiations. This condition was believed to be due to low CEA levels in patients with undifferentiated or poorly differentiated tumors at the advanced stage. When CEA levels and differentiation degrees of patients were compared in the aforementioned study, it was observed that tumor differentiation was mild or undifferentiated in patients with CEA levels of >5 ng/mL; it was generally well or moderate in cases with CEA levels of <5 ng/mL. However, the condition was not statistically significant.

Huh et al. [5] investigated the correlation between CEA levels and TNM staging in 474 patients with colorectal cancer. Patients were divided into two groups according to CEA levels of above or below 5 ng/mL. However, only patients with non-metastatic colorectal cancer were included in the study. As result of the study, a statistically significant correlation between CEA levels and TNM staging of patients was defined. While CEA levels were high in 33.1% of patients preoperatively, they were normal in the rest of patients. No significant correlation was detected between CEA levels, tumor localization, and differentiation degrees of patients. Lee et al. [6] accepted a preoperative CEA level of 5 ng/mL as the cut-off value. CEA levels were low among patients with Stage I and II TNM classification (66%), but they were high in patients with more advanced disease; the correlation was statistically significant. In our study, CEA levels were detected within normal limits in 52.2% of cases; no statistically significant correlation was detected between CEA levels and tumor differentiation degree, tumor diameter, and TNM staging. In the light of this information, it should be considered that CEA levels may be within normal limits in many patients with colorectal disease; hence, in suspected cases for colorectal cancer, normal levels of CEA cannot rule out colorectal cancer diagnosis. Moreover, a clear correlation between CEA levels and TNM staging of patients has not been revealed, clearly indicating that further studies are required about this issue.

Retrospective design is a limitation of this study. And inadequate care in keeping patient records is another limitation of our study.

In conclusion, colorectal cancer is a cancer type, in which more studies should be performed because it is an important mortality and morbidity cause in the world and in our country. There is a meaningful link between TNM stage and CEA level.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Atatürk University.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - O.T., A.T.; Design - O.T., A.T.; Supervision - O.T., A.T.; Resources - O.T., A.T.; Materials - O.T., A.T.; Data Collection and/or Processing - O.T., A.T.; Analysis and/or Interpretation O.T., A.T.; Literature Search - O.T., A.T.; Writing Manuscript - O.T., A.T.; Critical Review O.T., A.T.; Other - O.T., A.T.

**Conflict of Interest:** Authors have no conflict of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

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