

# Individualized Cutoff Value of the Serum Carcinoembryonic Antigen Level According to TNM Stage in Colorectal Cancer

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Serum carcinoembryonic antigen (CEA) is the most widely used tumor marker for the management of colorectal cancer. The preoperative serum CEA level has been reported to be one of prognostic parameters for the recurrence of colorectal cancers [1, 2]. Postoperative monitoring of the serum CEA level has been commonly used in the follow-up for colorectal cancers [3]. However, whether the preoperative serum CEA level has a prognostic significance according to individual stages in patients with colorectal cancer is controversial [4-7]. Harrison et al. [6] analyzed a large cohort of node-negative colon cancer patients (T1-4, N0, M0) to determine prognostic factors. The study demonstrated that the preoperative serum CEA elevation (>5 ng/mL) had a poor prognostic value in node-negative patients (T1-4, N0, M0). Another study showed that 5 ng/mL, as cutoff value for serum CEA, had no significant prognostic value within the different Dukes' stages and had borderline prognostic value in the Dukes' C stage [7]. Those trials to identify the prognostic value of serum CEA elevation within individual stages have some limitations. The biochemical characters of serum CEA are not well known. For those trials, hypotheses are necessary. Serum CEA has other biochemical characters, but not as a marker to predict increasing size of tumor or metastasis to lymph nodes. Serum CEA might be a sensitive marker, represents size and metastasis.

Few studies have reported optimal cutoff values for serum CEA levels in patients with colorectal cancer. Reiter et al. [8] reported the results of a multivariate analysis of the prognostic value of serum CEA level in colorectal cancer. For preoperative serum CEA

levels of  $\geq 4$  ng/mL vs.  $< 4$  ng/mL, the relative risk was 1.4 ( $P < 0.07$ ). The 2-year survival rates in the groups of patients with preoperative serum CEA levels  $> 4$  ng/mL and  $< 4$  ng/mL were 16% and 38%, respectively, for patients with Dukes' stage D cancer, 73% and 91% for patients with Duke's stage B/C cancer, and 100% and 98% for patients with Dukes' stage A cancer. Also, Takagawa et al. [2] reported that the relapse-free survival was significantly different in patients with stage II and III according to preoperative CEA level ( $> 10$  ng/mL vs.  $< 10$  ng/mL). However, in patients with stage I, there was no significant difference in relapse-free survival. Park et al. [9] divided patients with colorectal cancer into four subgroups by using serum CEA cutoff values of 3, 6, and 17 ng/mL. Their 5-year disease free survival rates were 85.3% ( $< 3.0$  ng/mL), 70.0% (3-6 ng/mL), 64.2% (6-17 ng/mL), and 55.2% ( $> 17$  ng/mL) ( $P < 0.001$ ). According to stage, a significant difference in survival was observed only in patients with stage III tumors ( $P = 0.007$ ).

In this study, the authors tried to determine the individual optimal cutoff value of CEA according to TNM stage [10]. The conventional cutoff value of CEA (5 ng/mL) has no significant prognostic value in stage T1-2, N0 and stage T1-4, N2. Optimal cutoff values from the receiver operating characteristic curve were 7.4, 5.5 and 4.5 ng/mL for TNM stages I, II and III, respectively. Those for stages N0, N1 and N2 were 5.5, 4.8 and 3.5 ng/mL, respectively. The 5-year disease free survivals were significantly different with these cutoff values for each TNM and N stages. However, one has to consider that a sub-normal CEA level may be a cutoff value that can be used as a prognostic marker.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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