Research

The Relationship between Tumor Size and Carcinoembryonic Antigen (CEA) Levels in Stage IV Colorectal Adenocarcinoma Patients at Dr. Moewardi Hospital, Indonesia

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ABSTRACT

Background: Colorectal adenocarcinoma is one of the most common types of colorectal cancer based on histopathology, accounting for about 10% of cancer cases diagnosed worldwide each year. Tumor size and levels of carcinoembryonic antigen (CEA) are used to determine the presence and evaluation of colorectal cancer. However, studies on the correlation between the size of colorectal cancer based on CT scan abdominal with contrast and the CEA levels are still very minimal in the Indonesian population. This study aimed to analyze the relationship between tumor size examined by abdominal CT scan with contrast and carcinoembryonic antigen (CEA) levels in stage IV colorectal adenocarcinoma patients.

Subjects and Method: A cross-sectional study was conducted at the radiology department, Dr. Moewardi hospital, Surakarta, from February 2021 to July 2021. A total of 40 patients with stage IV colorectal adenocarcinoma were selected in this study. The patient already had the examination results of blood CEA levels and performed an abdominal CT scan with contrast. The dependent variable was blood CEA levels. The independent variable was tumor size. Data were collected from medical records and analyzed by the Spearman test.

Results: There was a positive and significant relationship between tumor size and CEA levels (r= 0.47; p= 0.003).

Conclusion: Tumor size is positively correlated to blood CEA levels in patients with stage IV colorectal adenocarcinoma.

Keywords: colorectal adenocarcinoma, contrast abdominal CT scan, carcinoembryonic antigen (CEA).

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BACKGROUND

Colorectal cancer is an abnormal growth of malignant cells originating from the large intestine (colon) or rectum (American Cancer Society, 2018). Colorectal adenocarcinoma is one of the most common types of colorectal cancer based on histopathology. The annual incidence of colorectal cancer is high, with around 10% of cancer cases diagnosed worldwide each year (Bray et al., 2018). Colorectal cancer is also the second most diagnosed cancer in women and the

third in men worldwide (Bray et al., 2018; Dekker et al., 2019). Colorectal cancer is cancer with the 4th most incidence in Indonesia, with 8.6% of cancer cases. This cancer is the second most common cancer in men and the fifth in women in Indonesia (Bray et al., 2018). Type A referral Dr. Moewardi has a very high number of colorectal cancer cases. In 2020, there were 465 colorectal cancer cases based on histopathological results dominated by stage IV colorectal adenocarcinoma, where the death occurred in 57 patients.

With the number of cases increasing every year, especially in developing countries, it is estimated that colorectal cancer worldwide will reach 2-5 million new cases by 2035 (Arnold et al., 2017). The death rate from colorectal cancer is the third-highest death rate from cancer worldwide with 10.2%, while in Indonesia, it is the fifth-highest death rate from cancer with 7.7% (Bray et al., 2018).

Computed tomography (CT) abdominal scan with contrast is the gold standard for detecting colorectal cancer and measuring the size of the tumor. In addition, it can evaluate the patient's response after therapy (Yu et al., 2018). Based on the criteria from the Response Evaluation Criteria in Solid Tumors (RECIST 1.1), a contrast abdominal CT scan should be performed every 2-3 months for the evaluation of colorectal cancer therapy. However, using abdominal CT scan with contrast as an evaluation of therapeutic response also has several weaknesses, including the presence of radiation and inaccuracy of results when there is diffuse peritoneal dissemination (Hermunen et al., 2018).

Carcinoembryonic antigen (CEA) is a colorectal tumor marker biomarker that can be a diagnostic and prognostic marker, especially in metastatic colorectal cancer (Hermunen et al., 2018). CEA has been considered for its accuracy in evaluating the prognosis of liver cancer therapy with metastases in Europe (Duffy et al., 2014). Several studies, mainly conducted on European and American populations, have shown a correlation between CEA levels and abdominal CT scans with contrast in assessing colorectal cancer, including cancer size (de Haas et al., 2010; Hermunen et al., 2018).

However, studies on the correlation of colorectal cancer size with CEA levels are still very minimal in Asian populations, especially Indonesian populations. Therefore, in this study, the researchers aimed to find a correlation between tumor size in stage IV colorectal adenocarcinoma patients based on abdominal CT scan with contrast and the CEA levels at Dr. Moewardi Hospital, Surakarta.

SUBJECTS AND METHOD

1. Study Design
The cross-sectional study was conducted at the Radiology installation, Dr. Moewardi Hospital, Surakarta, from February 2021 to July 2021.

2. Population and Sample
The subjects of this study were patients with stage IV colorectal adenocarcinoma. A total of 40 patients had their blood CEA levels checked and had undergone abdominal CT scan with contrast at the Radiology installation of Dr. Moewardi Hospital.

3. Study Variable
The dependent variable was the level of Carcinoembryonic Antigen (CEA) in the blood. The independent variable was tumor size.

4. Operational Definition of Variable
Measurement of blood CEA levels using the Vidas Bromeriaeux IVD 3002596. Tumor size was measured by CT scan 64 slices with contrast through the Picture Archiving and

Communication System (PACS). Data collected from medical records.

5. Data Analysis

The relationship between tumor size and blood CEA levels was analyzed by Spearman's test.

6. Ethical Clearance

The ethical suitability letter was issued by the Health Research Ethics Commission of Dr. Moewardi Hospital, Surakarta, with the letter number: 419/IV/HREC/2021.

RESULTS

1. Sample Characteristics

This study involved 40 patients with stage IV colorectal adenocarcinoma who had undergone the abdominal CT scan with contrast and blood CEA levels at the Radiology installation of Dr. Moewardi Hospital, Surakarta. The characteristics of the subjects of this study are the basic description of the research data, including age, sex, smoking habits, tumor size, and CEA levels. Data in the form of categorical data is presented in the value of the frequency distribution and percentage. The numerical data is presented in the median value. The results of the description of the characteristics of the research subjects are shown in Tables 1 and 2.

Table 1 showed that the mean age of the patients was 56 years (Mean= 56.35; SD= 11.24), the mean tumor size was 720 cm³ (Mean= 720.37; SD= 1345.35), and the mean blood CEA level was 45 mg /mL (Mean= 44.97; SD= 65.65).

Table 2 showed that most of the patients were male (60.0%). Half of the patients were smokers (50%). Most tumors were located in the rectosigmoid location (45%), followed by the rectum (32.5%).

Table 1. Description of continuous data samples

Variables	n	Mean	SD	Min.	Max.
Age (year)	40	56.35	11.24	26	80
Tumor size (cm³)	40	720.37	1345.35	40.6	1925.7
CEA level (mg/mL)	40	44.97	65.65	0.61	200

Table 2. Description of the categorical data sample

Variables	n	%
Gender		
Male	24	60.0%
Female	16	40.0%
Smoking		
Not smoking	20	50.0%
Smoking	20	50.0%
Tumor size		
<317.55 cm3	20	50.0%
≥317.55 cm3	20	50.0%
Location		
Anorectal	1	2.5%
Ascending-transverse colon	1	2.5%
Ascending colon	4	10.0%
Rectosigmoid	18	45.0%
Rectum	13	32.5%
Sigmoid	3	7.5%

Based on Table 3, it is known that patients with tumor size 317.55 cm³ (70%) are more likely to have blood CEA levels of ≥10.22 mg/mL than patients with tumor

size of <317.55 cm^3 (70%). Tumor size of 317.55 cm^3 increased the risk of blood CEA level of 10.22 mg/mL by five times, and it was statistically significant (OR= 5.44; p= 0.015).

**Table 3. Cross-tabulation of tumor size description with CEA levels**

Tumor Size	CEA Level				OR	p
	<10.2 mg/ml		≥10.22 mg/ml			
	n	%	n	%		
<317.55 cm^3	14	70%	6	30%	5.44	0.015
≥317.55 cm^3	6	30%	14	70%		

Table 4 showed that tumor size was positively correlated with blood CEA levels in patients with stage IV colorectal adeno- carcinoma and was statistically significant (r= 0.47; p= 0.003).

Table 4. Spearman analysis of the relationship between tumor size and blood CEA levels in patients with stage IV colorectal adenocarcinoma

Variable	r	p
Tumor Size	0.47	0.003
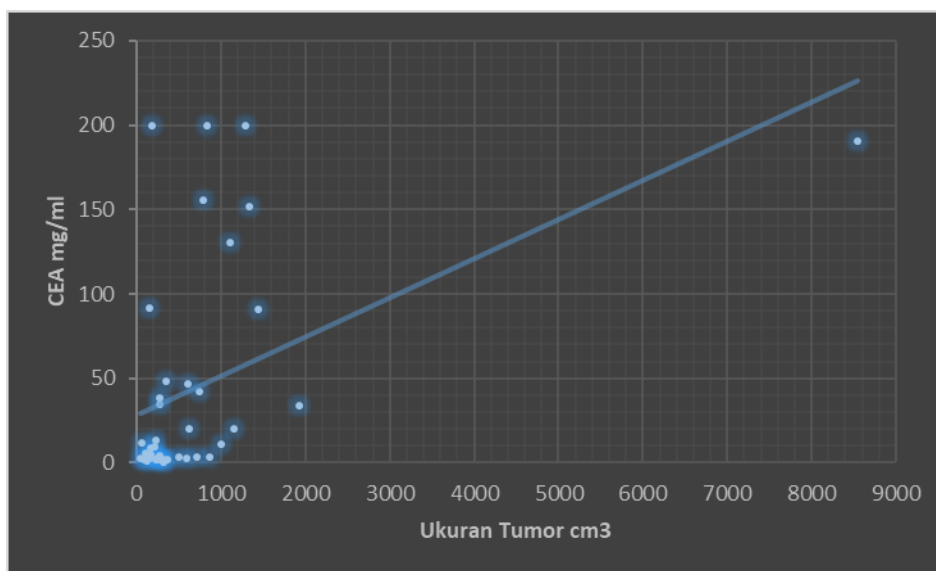
Figure 1. Diagram of the relationship between tumor size and CEA levels in patients with stage IV colorectal adenocarcinoma

DISCUSSION

This study showed that the average age of the patients was 56 years. Most of them were male and had a history of smoking. These patient characteristics align with previous studies' findings related to colorectal adenocarcinoma predisposing factors (Amersi et al., 2005; Japaries, 2012).

Most tumors are located in the rectosigmoid. This location corresponds to the location of the predilection for colorectal adenocarcinoma, which is the most frequently inflamed (Amersi et al., 2005).

The results of this study indicated that there is a positive and significant relationship between tumor size and blood CEA levels in patients with stage IV colorectal adenocarcinoma. Carcinoembryonic antigen (CEA) is a colorectal tumor biomarker that has the potential as a diagnostic and prognostic marker, especially in metastatic colorectal cancer (Hermunen et al., 2018). CEA has been considered for its accuracy in evaluating the prognosis of liver cancer therapy with metastases in Europe (Duffy et al., 2014). Several studies, mainly conducted on European and American populations, have shown a correlation between CEA levels and contrast abdominal CT scans in the assessment of colorectal cancer, including cancer size (de Haas et al., 2010; Hermunen et al., 2018). However, CEA examination cannot be used as a single criterion for confirming the diagnosis of colorectal cancer because the inflammatory process or tissue damage can also increase CEA levels (Gan and Zheng, 2011).

Elevated CEA levels were positively associated with grade 1 and 2 colorectal adenocarcinoma, advanced stage, and organ metastases. CEA is known as a prognostic marker. CEA levels can be very significant in ongoing postoperative evaluation (Sayuti, 2019; Bohorquez et al., 2016).

Clinicians can apply the clinical application of the results of this study in the post-treatment evaluation of colorectal adenocarcinoma (either surgery, chemotherapy, or radiotherapy). In post-treatment, if CEA is still high, the possibility of recurrence should be considered. So it is advisable to immediately do a CT scan of the abdomen again with contrast (within three months).

Another clinical application of the significant relationship between tumor size and CEA levels is in the case of high CEA levels with undetectable tumor size. Ideally, a Positron Emission Tomography (PET) scan is used to evaluate. But, a PET scan is not necessarily available for all cases in health facilities. Therefore, it can be suggested to the clinician to re-evaluate the CT-Scan sooner than recommended (faster than three months).

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