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Comparison of Carcinoembryonic Antigen Levels Among Degree of Differentiation and Colorectal Cancer's Location in Medan

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Abstract

BACKGROUND: The most widely used tumour markers, especially in colorectal malignancy, is Carcinoembryonic antigen (CEA).

AIM: This study was aimed to investigate CEA value among the degree of differentiation and tumour location.

METHODS: A cross-sectional analytical study was used in this study on eighty consecutive patients with colorectal carcinoma (CRC) at Adam Malik General Hospital and Permata Bunda Hospital, Medan, Indonesia. All data were analysed using SPSS for Windows version 21.

RESULTS: They were rectal cancer 49.4%, left-sided colon cancer 43.2% and right-sided colon cancer 6.2%. Histopathology findings were well-differentiated 40.7%, moderate differentiated 32.1% and poorly differentiated 25.9%. There were no correlations between CEA level and haemoglobin level, white blood cells count, and platelet count. There was no significant difference between CEA and location of the tumour ($p = 0.70$), although CEA level was significantly differenced among histopathology findings ($p = 0.03$). CEA levels were and associated with the degree of differentiation.

CONCLUSION: CEA levels increased in well-differentiated colorectal carcinoma especially in rectal cancer.

Introduction

Cancer is a disease characterized by the unchecked division and survival of abnormal cells. When this abnormal growth occurs in colon or rectum, it is called colorectal cancer (CRC) [1]. CRC is one of the common tumour types in the world, which accounts for 400 000 deaths annually [2]. The incidence rates of CRC were 19.1 for men and 15.6 for women per 100.000 populations in Indonesia [3] with a major risk factor for CRC are smoking, alcoholism, physical inactivity and obesity [4].

In 1965 Gold and Freedman demonstrated that a CEA presents in extracts of tumours from the gastrointestinal tract and fetal gut tissues but not in extracts of adult intestinal tissues. CEA modulates intercellular adhesion of colon epithelial cell-collagen interactions. Since high concentrations of CEA presents in fetal tissues and tumours, it disrupts normal intercellular or cell-collagen adhesion forces allowing more cell movement and the development of less ordered tissues architecture and greater cell-cell interaction. CEA appears to have the greatest clinical use as evaluation of treatment efficacy and in follow-up for recurrent disease.

Carcinoembryonic antigen (CEA) is the most commonly used tumour marker for CRC diagnosis, prognosis evaluation or after treatment recurrence [5]. CEA is found in normal fetal gastrointestinal tissue and at very low concentrations in adult blood plasma. Its concentration increases in many tumours, such as CRC. Increased CEA concentrations were also reported in gastric, bronchial, uterine and ovarian cancers, and lymphomas as well [6].

American Society of Clinical Oncology (ASCO) defined right-sided colon cancer of cecum and ascending colon up to the hepatic flexure. Left-sided colon cancer comprises of cancers in splenic

flexure and regions distal to the splenic flexure, including the rectum. The transverse colon connects left and right-sides and on average is appreciably shorter than the right and left-sides. Colorectal adenocarcinoma can be divided into three distinct disease entities: right colon cancer, left colon cancer and rectal cancer [3].

High CEA production by tumours is associated with increased tumour growth and poorer prognosis [2], [3]. CEA can be detected and quantitatively measured in the serum and the tumour tissues of CRC patients although its role in the prognosis of CRC (Figure 1) remains controversial [7].

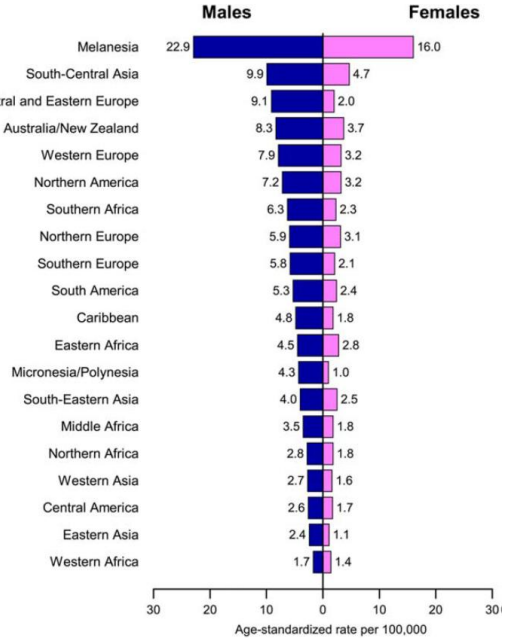

Figure 1. Colorectal Cancer Incidence, 2012

Current ASCO guidelines recommend that CEA examinations be routinely obtained at 3-month intervals during postoperative surveillance and at 1–3-month intervals during systemic treatment for metastatic CRC [2].

Normal value of CEA is 5 ng/mL in serum. Patients with appropriate symptoms, a highly increased concentration (e.g., 5 times the upper limit of normal reference value) should be considered strongly suggestive for the presence of cancer in that particular patient.

Factors affecting serum CEA levels in patients with CRC are tumour stage, tumour grade, liver status, tumour site within colon, presence or absence of bowel obstruction, smoking, ploidy status of the tumour. Well-differentiated CRC produces higher CEA level than poorly differentiated one. Certain benign liver diseases impair liver function and, thus, CEA clearance. Consequently, CEA increased in serum of patients with nonmalignant liver diseases. Smoking appears to double CEA serum concentration [6].

Material and Methods

Serum CEA levels in CRC patients were measured using CEA Elecsys analysers (Roche Diagnostics GmbH, United States) with a reference range of 5.0 ng/mL. CRC patients were then divided into two groups, those with normal serum CEA levels (e.g., ≤ 5 ng/mL) and those with elevated serum CEA levels (> 5 ng/mL)

A cross-sectional analytical study was used in this study on eighty consecutive patients with CRC at Adam Malik General Hospital and Permata Bunda Hospital, Medan, Indonesia. All data were analysed with SPSS for Windows version 21. Data were examined using the Kruskal Wallis test.

Results

Demographic characteristics of the patient are shown in Table 1. The recruited patients consisted of 48 males (60%), and 32 females (40%). The median age of these patients was 53 (25-80) years old. The majority of patients' education level was senior high school (43.2%), elementary school (25.9%), university (16%) and junior high school (13.6%).

The most common tumor location were rectal cancer (49.4%), left-sided colon cancer (43.2%) and right-sided colon cancer (6.2%). Histopathology examinations showed well-differentiated 41,3%, moderate differentiated 32.1% and poorly differentiated 25.9% CRCs.

Table 1. Demographic and clinical characteristics of the patients

Variable	N = 80
Gender	
Male	48 (60%)[a]
Female	32 (40%)[a]
Age	53 (25-80)[b]
education level	
Elementary School	21 (26.3%)[a]
Junior High School	11 (13.8%)[a]
Senior High School	35 (43.8%)[a]
University	13 (16.3%)[a]
Tumour Location	
Rectal cancer	40 (50%)[a]
Left-sided colon cancer	35 (43.8%)[a]
Right-sided colon cancer	5 (6.3%)[a]
Histopathology	
Well-differentiated	33 (41.3%)[a]
Moderately differentiated	26 (32.5%)[a]
Poorly differentiated	21 (26.3%)[a]
Haemoglobin	11 (5-19)[b]
White blood cells	8850 (1650-25 750)[b]
Platelet	32 5178 ± 135 551[c]
CEA	6.93(0.42-3340.08)[b]

[a] Categoric data: n (%); [b] Numeric data, abnormal distribution: median (min-max); [c] Numeric data, normal distribution: mean ± SD.

The correlation between routine blood count with CEA is shown in Table 2. Hb, WBC and platelet, showed no difference (p > 0.05).

Table 2. Correlation of routine blood test with CEA

Variable	CEA Levels	
	Correlation Coefficient	p
Hb	-0.111	0.32
WBC	0.002	0.98
Platelet	-0.109	0.33

Table 3 shows a comparison of CEA to tumor locations and histopathology grades. Mean of CEA level at rectal 223.90 ng/mL, left-sided cancer 156.79 ng/mL, and right-sided cancer 2.61 ng/mL ng/mL (p = 0.70). Histopathology examinations showed that there were well differentiated 387.66 ng/mL, moderately differentiated 36.62 ng/mL and poorly differentiated 33.90 ng/mL with significant differences among them (p = 0.03).

Table 3. Comparison of carcinoembryonic antigen (CEA) levels on histopathology classifications and tumour locations in colorectal cancer

	CEA Level Unit	F	p
Tumour location		0.37	0.70
Rectal cancer	223.90 ± 741.98		
Left-sided colon	156.79 ± 378.31		
Right-sided colon	2.61 ± 0.84		
Histopathology			
Well	387.66 ± 865.33	3.83	0.03
Moderate	36.62 ± 73.50		
Poorly	33.90 ± 66.22		

Discussion

Mostly sample is male (60%). This is according to the research of American cancer society 2012 obtained majority of gender is male than female. The localisation a large number of patients had colorectal cancer in rectal cancer 50% and Left-sided colon cancer 43.8% [10], [11] found that 44 cancers were in rectal region and 68 cancers were in other regions of the colon.

In this study differentiated histopathology findings the mostly well-differentiated 41.3%, this is similarly from the research of Aru W. Sudoyo et al. while the majority of colorectal carcinoma was well-differentiated [8].

CEA is the most widely used tumour marker worldwide and certainly the most frequently used marker in CRC [9]. In this study, there was a significant difference (p = 0.03) mean CEA among well differentiated 387.66 ng/ml, moderate 36.62 ng/ml and poorly 33.90 ng/ml. Well-differentiated CRC produces more CEA than poorly differentiated. Similarly, CEA tends to be higher in patients with well-differentiated compared to poorly differentiated [12], [13], [14], [15]. Thus, a lack of differentiation or poorly differentiated may explain why some patients with advanced CRC do not have increased CEA value (Park JW et al., 2013). Mean of CEA of location tumour obtained CEA increased to rectal cancer 223.90 and left-sided colon cancer 156.79. Some reports suggest that patients with tumours in the left-sided of colon cancer generally have a higher incidence of increased CEA than right-sided of colon cancer (Nicholson BD et al., 2015, Jeon BG et al., 2013) [16], [17].

In conclusion, CEA levels increased in well-differentiated colorectal carcinoma especially in rectal cancer.

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