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Correlation Between Histopathological Grading and Appearance of Obstruction With Level of Carsino-Embryonic Antigen (CEA) in Colorectal Carcinoma

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Abstract

CEA (*Carcinoembryonic Antigen)* is a blood colorectal tumor marker test that widely used in a clinical setting. The aim of this research is to assess the correlation between carcinoembryonic antigen (CEA) and the degree of tumor differentiation, and between obstruction and age of patients and colorectal adenocarcinoma. This research was a retrospective analytic observational study with a cross-sectional approach. This research used medical record of colorectal carcinoma patients without other malignancy obtained from Wahidin Sudirohusodo Hospital having complete medical records from 2015 to 2017. Initial anamnesis, the result of radiology, laboratory, and the result of pathology were obtained and analyzed using univariate and bivariate analyses with the value of CEA cutoff 5ng/ml. The result of 107 samples, most of the subjects examined is female (60.7%), between the ages of 41-60 years (48.6%) with the levels of CEA >= 5 (55.1%). Histopathology examination results showed most of the differentiate were moderate (68.2%). While the obstruction was found in 34 subjects (31.8%). We found a significant relationship between the presence of an obstruction with levels of CEA ($p < 0.001$), and degree of differentiating with the CEA levels also showed a significant relationship ($p < 0.001$). The result of the analysis indicates that there is a significant correlation between CEA level and the degree of differentiation and obstruction. Obstruction has a more significant correlation with high CEA level. There is no significant correlation between age group and CEA level.

Keywords: Carcinoembryonic antigen; colorectal adenocarcinoma; obstruction; the degree of differentiation; age.

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1. Introduction

Colorectal cancer is one of the world's health problems can be cured if diagnosed early. Research in the last fifteen years has demonstrated the existence of a specific genetic change in the transformation of normal colonic epithelium anti-neoplastic activities into a benign adenoma until being adenocarcinoma [1]. Colorectal cancer is the third leading cause of death due to cancer in the world. The decline in the number of deaths of colorectal cancer although small but tend to remain achievable, one through the program early detection of population-based screening [2].

In Indonesia alone, up to this point, there has been no definite figures for the incidence of colorectal cancer by the absence of data-based population. From various reports only showed a rise in the number of cases of colorectal cancer in the ten types of cancer. Data from the Ministry of Health obtained figure 1.8/100.000 population. In Makassar based on data on Surgical Division Digestif an increase in colorectal cancer cases almost every year. In the year 2005 colorectal cancer ranks fourth of the whole year 2006, the violence recorded 107 cases and occupies third place while in 2008 found 272 cases and ranks second after breast cancer [3].

Examination of a blood test for colorectal tumor alert that is often used is the CEA (Carcinoembryonic Antigen) [4]. Recommendations of the American Society of Clinical Oncology (ASCO) in 2006 stated that the CEA examined before the operation if it assists in the determination of the stadium or the plan of action also in monitoring therapy response during treatment. Some of the factors affecting the levels of CEA in sufferers of the colorectal cancers include tumor stage, the degree of the tumor, liver function, the location of the tumor, intestinal obstruction, and history of smoking [5].

Effect of tumorigenesis CEA includes inhibition of cell differentiate, cell polarization to block, interfere with the network architecture and inhibits anoikis (cell death due to loss of contact of cells with cells). However, the molecular mechanisms of metastasis in the induction by CEA is still unclear and can involve some mechanism [6]. Several studies have shown that the colorectal cancers with degrees of histopathology differentiate well ("well-differentiated colorectal cancers") produce CEA higher compared to differentiate bad ("poorly differentiated"). A study by Sugarbaker concluded that intestinal obstruction gives higher levels of CEA in the case of the colorectal cancers with obstruction compare with non-obstruction [7]. A lot of things that affect the prognosis of the colorectal cancers, one of them is histopathology examination results obtained from Anatomic Pathology (PA) [8]. In the handling of the colorectal cancers in particular, examination of the PA for determining histopathology is required. Some things that are assessed in the examination of histopathology, among others, the type and degree of differentiating [5]. This research aims to know the relationship between the degree of differentiation and obstruction by the age and the levels of CEA in colorectal cancer patients.

2. Materials and Method

2.1. Collection of Samples

This research is an observational analytic approach of cross-sectional with a retrospective design. This design was chosen because of the measurement on the free variables and bound at the same time at Wahidin

Sudirohusodo Hospitals Makassar in 2015-2017.

The data used in the form of secondary data that is derived from the Hospital medical record at Wahidin Sudirohusodo Makassar in 2015-2017. The data is taken in the form of initial anamnesis of the patient, laboratory and radiology results, examination of pathology results of colorectal carcinoma at Wahidin Sudirohusodo Hospital.

2.2. Data Analysis

Data analysis using the SPSS (Statistical Package for Social Science) version 22. Analysis of patient's characteristics and clinical response using chi-square.

2.3. Ethical Clearance

Ethical approval for this study was obtained from the Research Ethics Committee, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia. Number; 1098/H4.8.4.5.31/PP36-KOMETIK/2018.

3. Results

Based on the distribution characteristics of 107 samples, most of the subjects examined are female (60.7%), between the ages of 41-60 years (48.6%) with the levels of CEA >= 5 (55.1%). Histopathology examination results showed most of the differentiate were moderate (68.2%). While the obstruction was found in 34 subjects (31.8%) characteristic of samples can be seen in the following table 1.

Table 1: Distribution characteristic of the sample (n=107)

Variable		N	%
Gender	Male	65	60.7
	Female	42	39.3
Age (year)	<40	24	22.4
	41-60	52	48.6
	>60	31	29.0
Differentiate	Good	22	20.6
	Moderate	73	68.2
	Poor	12	11.2
Obstruction	Yes	34	31.8
	No	73	68.2
CEA	>=5	59	55.1
	<5	48	44.9

The Chi-Square test results against the degree of differentiating with the CEA levels showed a significant

relationship ($p < 0.001$), where the percentage of subjects with CEA >= 5 most significant high on moderate differentiate (75.3%) as shown in table 2.

Table 2: Relationship of histopathology grade with CEA level

			CEA			
Differentiate			>=5	<5	Total	p
	Good	N	4	18	22	
		%	18.2%	81.8%	100.0%	
	Moderate	N	55	18	73	
		%	75.3%	24.7%	100.0%	
	Poor	N	0	12	12	
		%	0.0%	100.0%	100.0%	
Total		N	59	48	107	0.000
		%	55.1%	44.9%	100.0%	

On the study also found a significant relationship between the presence of an obstruction with levels of CEA ($p < 0.001$), where the percentage of subjects with CEA > = 5 significantly higher on obstruction (85.3%) than there is no obstruction (41.1%) as shown in table 3.

Table 3: Relationship of obstruction with CEA level

			CEA			
Obstruction			>=5	<5	Total	p
	Yes	n	29	5	34	
		%	85.3%	14.7%	100.0%	
	Non	n	30	43	73	
		%	41.1%	58.9%	100.0%	
Total		n	59	48	107	
		%	55.1%	44.9%	100.0%	0.000

Distribution according to the age of the CEA levels showed no significant differences ($p > 0.05$), although the visible percentage of subjects with CEA >= 5 is highest at age < 40 years (62.5%) and the lowest at > 60 years (51.6%) as shown in table 4.

Table 4: Distribution of CEA level according to age

Age (year)			CEA >=5	CEA <5	Total	p
	<40	N	15	9	24	
		%	62.5%	37.5%	100.0%	
	41-60	N	28	24	52	
		%	53.8%	46.2%	100.0%	
	>60	N	16	15	31	
		%	51.6%	48.4%	100.0%	
Total		N	59	48	107	0.699
		%	55.1%	44.9%	100.0%	

The results of the analysis above show that the degree of differentiation and obstruction has a significant relationship with levels of CEA. To find out if differentiate or obstruction has the most significantly associated with levels of CEA, then performed multivariate analysis using Logistic Regression. As shown in table 5 it looks that at Step 2 only obstruction associated significantly with levels of CEA ($p < 0.001$). So it could be inferred that the **obstruction** is more correlated significantly with the CEA levels compared to the degree of differentiation.

Table 5: Multivariate analysis result

Variable		B	Wald	P
Step 1	Differentiate	0.31	0.64	0.422
	Obststruction	2.23	15.81	0.000
	Constant	-4.66	10.96	0.001
Step 2	Obstruction	2.12	15.41	0.000
	Constant	-3.88	15.10	0.000

4. Discussion

From some libraries are obtained that the male gender has the risk of suffering from colorectal cancer that is a little higher than in women. Based on national seminar 2 Colorectal Cancer year 2011 Makassar obtained a male-female appeal of 1.3:1 and based on research Lusikooy the year 2013 brings about male-female appeal 1.8:1 [3].

According to research conducted by Hafiz, the lowest levels of CEA is 0, the highest 652 ng/ml and the mean was 102.69 ng/ml [9]. Increased CEA pre-operative learning outcomes associated with the bad prognosis post surgery, besides of course the affected by staging and grading of tumor histopathology[10]. This research shows a positive correlation has a staging with the tumor marker and an increased level of CEA, has a worse prognosis with a cutoff point of the CEA is 5 ng/ml.

This research in accordance with the results of previous research by Michael JD which concluded that colorectal carcinoma with a good differentiation produces higher levels of CEA compared colorectal carcinomas specimens that differentiate bad [7]. Serum CEA reported increases in patients with tumors that are well-differentiated tumor than patients with poorly differentiated tumors [11]. Similarly, with research by Rizaldi A, at Pringadi hospital Medan, concluded that declining levels of CEA on a tumor that differentiate bad [12]. When viewed from the sequences process, supposedly more expression of CEA will give histopathology grade worse, but it seems the degree of differentiation is not only are affected by one of the above factors but is also influenced by several other pathways involves a molecular alert role in. Duffy reported on patients with lack of differentiation or finding a poorly shows concentrations of CEA does not increase [13]. According to research done by Saito, with the use of cutoff point levels of CEA 5 ng/ml, no meaningful difference between age, gender, grading histopathology, lymphatic and vascular invasions, the location of the tumor, stage and location of the first tumor to the occurrence of recurrence [14].

This study showed that intestinal obstruction gives CEA levels higher in the case of the colorectal carcinoma with bowel obstruction compared with cases of non-bowel obstruction. Decompression in the case of obstruction lower the levels of CEA. No doubt the size of the tumor causing obstruction symptoms that gave the elevation of CEA levels associated with colonic dilation [15]. So, in the relationship among the level of CEA and the size of the tumor, the levels of CEA in patients with colonic obstruction is higher compared to patients who were non-obstruction. There also study from our center reported a significant relationship between COX-2 expression and patient's tumor size and the degree of differentiation of CRC Patients, but not with age, tumor location and TNM stage [16].

5. Conclusion

From the results of research on 107 samples, some conclusions can be drawn that there is a significant relationship between the degrees of differentiating with the levels of CEA, there is a significant relationship between. Obstruction with levels of CEA, There is no significant relationship between the age with the levels of CEA, and obstruction associated significantly with high levels of CEA as compared to the degree of differentiation.

6. Recommendations

This research can also be a basis for further research on a variety of factors that can affect the levels of CEA.

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7. Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare

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