

## **Difference of Cea Level Before, after Surgery and After Chemotherapy with Folfox Regime on Colorectal Stage IIB-III in H. Adam Malik General Hospital Medan**

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**Abstract : Introduction** Colorectal carcinoma is the fourth most common cancer in the world and is the second leading cause of death in the United States. In 2012, there are an estimated 103,170 new cases of Colorectal Cancer. Management of colorectal carcinoma in the form of surgery, chemotherapy and radiotherapy have a good effect. Post-operative CEA level measurement is often performed as a monitoring indicator in stage III colorectal cancer patients. The purpose of postoperative CEA measurements and chemotherapy is to assess prognostics, assess recurrence as well as assess the response of chemotherapy.

**Materials and Methods** We collected 58 patients who met the inclusion criteria. Demographic studies of patient characteristics and histopathology were performed. We then measured the patient's CEA levels before the surgery, after the surgery and after receiving FOLFOX chemotherapy and performed the analysis of the CEA level against any given therapy.

**Results** We obtained the most common age distribution in colorectal patients at the age of 51-60 years, Adeno Ca Rekti with the most diagnosis found with stage IIIB dominating the sample, and well differentiated histopathology into the most demographic type of histology. The average CEA level was much lower after surgery 11.35 than before surgery with a mean of 15.6 ( $p < 0.0001$ ), and after surgery and after FOLFOX chemotherapy using the Wilcoxon test, a significant CEA result after chemotherapy became 5.4 ( $p < 0.001$ ).

**Conclusion** Combination therapy in colorectal cancer patients with surgery and chemotherapy provides significant decrease in CEA levels.

**Keywords:** Colorectal cancer, combination therapy, chemotherapy FOLFOX, Carcino-Embryonic Antigen (CEA).

### **Introduction**

In Indonesia, in 2006 colorectal carcinoma was ranked third with the number of cases 1.8 / 100.000 population. In the hospital. Haji Adam Malik in the year 2013 was found the prevalence of colorectal carcinoma as many as 87 cases. The mortality rate of colorectal cancer also decreased by almost 35% from 1990 to 2007, due to an early detection effort as well as better screening and therapeutic modalities.<sup>1,2</sup>

Management of colorectal carcinoma in the form of surgery, chemotherapy and radiotherapy. Surgical treatment is effective when done on a localized disease. The development of chemotherapy and radiotherapy at this time, allows the opportunity for adjuvant therapy for patients with advanced stage or on the occurrence of relapse.<sup>2</sup>

Carcino-Embryonic Antigen (CEA) is a widely accepted oncofetal antigen for its use as a tumor marker and is an easy and inexpensive method of measurement. Post-operative CEA level measurements are often performed as monitoring indicators for stage III colorectal cancer patients. The purpose of postoperative CEA measurements and chemotherapy is to assess prognostics, assess recurrence as well as assess the response of chemotherapy.

## Method

We calculated the formula and got a large sample of 58 patients. Patients who met the inclusion criteria were included in the study and processed through SPSS 20. Colorectal cancer patients were given combination therapy interventions in the form of surgery and chemotherapy. Then we measured the decrease in CEA levels after each stage of the therapy, then analyzed and looked for the relationship statistically.

## Processing and Analysis of Data

Differences in pre and post operative CEA and post-chemotherapy levels were analyzed by Friedmann ANOVA. Meanwhile, further analysis for the different CEA sequences (pre and post surgery) and (postoperative and post-chemotherapy) was performed with chi-square test. A difference was found to be significant when  $p < 0.05$ .

## Results

### Demographic Study

Obtained colorectal stadium IIB-III colorectal patients undergoing surgery and chemotherapy male sex as much as 32 people (55.2%) and female patients female 26 people (44.8%).

Patients with colorectal carcinoma in the age range 21-30 years were as many as 4 people, colorectal carcinoma patients in the age range 31-40 years were as many as 6 people, colorectal carcinoma patients in the age range 41-50 years were as many as 11 people, patients in the age range 51-60 years old is the most that is 18 people, followed by age group 61-70 years old as many as 16 people, and last patient with age range 71 - 80 as many as 3 people.

Adenocarcinoma Caecum colorectal carcinoma of 2 people, Adenocarcinoma Colon Ascenden type 9 people, Adenocarcinoma Colon Descenden as many as 8 people, Adenocarcinoma Colon Transversum as many as 10 people, most types found in this research are Adenocarcinoma Rekti counted 24 people and Adenocarcinoma colon sigmoid 9 person.

As many as 3 people suffered from disease at stage IIB, in stage IIIA as many as 7 people, colorectal carcinoma patients mostly in stage IIIB that is 31 people, and last at stage IIIC as many as 17 patient.

The most surgical action performed on the patients in this study was Left Hemicolectomy as many as 15 people, followed by Miles procedure as many as 13 people, Right hemicolectomy as many as 10 people, right Extended Hemikolektomi 6 people, 4 people LAR, LAR action with ileostomy as many as 4 people, Hartmann's procedure and sigmoidostomy diversified as many as 3 people, and a subtotal of 1 person's colectomy.

The results of anatomic pathology examination showed the most histopathologic type was Adenocarcinoma Well Differentiated that is as many as 31 people, followed by type Adenokarsinoma

Moderate Differentiated as many as 18 people, the third sequence of Adenokarsinoma Poorly Differentiated as many as 5 people, then type Adenokarsinoma Mucinous as many as 3 people, and the lowest one is Adenocarcinoma type Undifferentiated as much as 1 person.

Statistical Annalysis

**Table 1. The Difference between CEA Level Before and After Surgery**

	<b>Before Surgery</b>	<b>After Surgery</b>	<b>P</b>
CEA Level	15.6 (0.2 – 1000)	11.35 (0.5 – 1000)	<0.001

Because the distribution of research data for CEA levels before and after surgery is not normal, therefore the analysis used was Wilcoxon test. Based on the analysis using Wilcoxon test, we found a significant difference of mean CEA level before and after surgery (p<0.001). The Mean CEA level is much lower after surgery which was 11.35 compared to before surgery with the mean 15.6.

**Table 2. The difference between CEA Level before and after surgery with the histopathology of Well-Differentiated**

<b>Variable</b>	<b>Before Surgery</b>	<b>After Surgery</b>	<b>P value</b>
CEA Level	9.4 (0.2 – 1000)	5.4 (0.3 – 1000)	< 0.001

Based on the analysis using Wilcoxon test, we found a significant difference between the mean CEA level before and after surgery in colorectal carcinoma with the histopathology of *Well Differentiated* (p<0.001).

**Table 2.1. The difference between CEA Level before and after surgery with the histopathology of Moderate-Differentiated**

<b>Variable</b>	<b>n</b>	<b>Before Surgery</b>	<b>After Surgery</b>	<b>P value</b>
CEA Level	18	21.85 (0.2 – 693.2)	16.45 (0.9 – 447.5)	0.002 <sup>w</sup>

Because the distribution of research data for CEA levels before and after surgery is not normal, therefore the analysis used was Wilcoxon test. Based on the analysis using Wilcoxon test, we found a significant difference between the mean CEA level before and after surgery in colorectal carcinoma with the histopathology of *Moderate Differentiated* (p = 0.002).

**Table 2.2 The difference between CEA Level before and after surgery with the histopathology of Poor Differentiated**

<b>Variable</b>	<b>N</b>	<b>Before Surgery</b>	<b>After Surgery</b>	<b>P value</b>
CEA Level		6.8 (0,9 – 32.3)	4.1 (0.5 – 7.22)	0.043 <sup>w</sup>

Because the distribution of research data for CEA levels before and after surgery is not normal, therefore the analysis used was Wilcoxon test. Based on the analysis using Wilcoxon test, we found a significant difference between the mean CEA level before and after surgery in colorectal carcinoma with the histopathology of *Poorly Differentiated* (p=0,043).

**Table 2.3 The difference between CEA Level before and after surgery with the histopathology of Mucinous**

<b>Variable</b>	<b>N</b>	<b>Before Surgery</b>	<b>After Surgery</b>	<b>P value</b>
CEA Level	3	19.5 (7.1 – 25.7)	21.4 (8.2 – 24.6)	0.593 <sup>w</sup>

Because the distribution of research data for CEA levels before and after surgery is not normal, therefore the analysis used was Wilcoxon test. Based on the analysis using Wilcoxon test, we did not find a significant difference between the mean CEA level before and after surgery in colorectal carcinoma with the histopathology of *Mucinous* (p=0,593).

**Table 3. The difference between CEA Level Before and After Chemotherapy**

Variable	n	Before Chemotherapy	After Chemotherapy	P value
CEA Level	58	10.05 (0 – 545.1)	5.4 (0 – 586.3)	0.009

Because the distribution of research data for CEA levels before and after chemotherapy is not normal, therefore the analysis used was Wilcoxon test. Based on the analysis using Wilcoxon test, we found a significant difference of mean CEA level before and after chemotherapy (p=0,009). The mean CEA level is much lower after administration of chemotherapy which was 5.4 compared to before chemotherapy administration with the mean of 10.05.

**Table 3.1 The difference between CEA Level before and after chemotherapy with the histopathology of Well Differentiated**

Variable	N	Before Chemotherapy	After Chemotherapy	P value
CEA Level	31	8.7(0 – 324.3)	4.8(0 – 280.5)	0.039

Because the distribution of research data for CEA levels before and after surgery is not normal, therefore the analysis used was Wilcoxon test. Based on the analysis using Wilcoxon test, we found a significant difference between the mean CEA level before and after chemotherapy in colorectal carcinoma with the histopathology of *Well Differentiated* (p=0,039).

**Table 3.2 The difference between CEA Level before and after chemotherapy with the histopathology of Moderate Differentiated**

Variable	n	Before Chemotherapy	After Chemotherapy	P value
CEA Level	18	14.95(1.3 – 545.1)	8 (1.2 – 567.4)	0.078 <sup>w</sup>

<sup>w</sup>Wilcoxon Test

Because the distribution of research data for CEA levels before and after surgery is not normal, therefore the analysis used was Wilcoxon test. Based on the analysis using Wilcoxon test, we found a significant difference between the mean CEA level before and after chemotherapy in colorectal carcinoma with the histopathology of *Moderate-Differentiated* (p=0,078).

**Table 3.3 The difference between CEA Level before and after chemotherapy with the histopathology of Poorly Differentiated**

Variabile	n	Before Chemotherapy	After Chemotherapy	P value
Kadar CEA	5	3.8 (0.5 – 6.8)	1.8 (0.3 – 4.2)	0.043

Because the distribution of research data for CEA levels before and after surgery is not normal, therefore the analysis used was Wilcoxon test. Based on the analysis using Wilcoxon test, we found a significant difference between the mean CEA level before and after chemotherapy in colorectal carcinoma with the histopathology of *Poorly Differentiated* (p=0,043).

**Table 3.4. The difference between CEA Level before and after chemotherapy with the histopathology of Mucinous**

Variable	N	Before Chemotherapy	After Chemotherapy	P value
CEA Level	3	50.6 (5.1 – 97.8)	243.4 (1.6 – 586.3)	0.285

<sup>w</sup>Wilcoxon Test

Because the distribution of research data for CEA levels before and after surgery is not normal, therefore the analysis used was Wilcoxon test. Based on the analysis using Wilcoxon test, we found a significant difference between the mean CEA level before and after chemotherapy in colorectal carcinoma with the histopathology of *Mucinous* (p=0,285).

**Table 4. The difference between CEA Levels Before, After Surgery and After Chemotherapy**

Variable			<i>P value overall</i>	<i>p value intergroup</i>
	n	CEA Level		
Before surgery	58	69,72 ± 168.92	< 0.001 <sup>a</sup>	Reference
After Surgery	58	52.33 ± 150.27		< 0.001 <sup>w</sup>
After Chemotherapy	58	73.97 ± 176.30		< 0.001 <sup>w</sup>

<sup>a</sup>Friedmann Anova, <sup>w</sup>Wilcoxon

Because the distribution of research data for CEA levels before, after surgery and after chemotherapy was not normal, the test used was Friedmann Annova test. By surgery and after chemotherapy (p<0,001). Then from the result of further analysis, we compared the CEA level before and after surgery, before and after chemotherapy by using Wilcoxon test, we found a significant result. ( p < 0.001).

**Discussion**

There were patients with colorectal carcinoma stage IIB-III who underwent surgery and chemotherapy, consisting of male 32 patients (55,2%) and female 26 patients (44,8%).

**Conclusion**

There was a difference between CEA level before and after surgery with the regimen FOLFOX in patients with colorectal carcinoma Stage IIB-III in Haji Adam Malik Central General Hospital Medan.

**References**

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