United Journal of Surgery

Research Article

A Study of CEA, CRP & Albumin as Prognostic Indicators in Colorectal Carcinomas

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Volume 1 Issue 1 - 2020

Received Date: 14 Feb 2020

Accepted Date: 05 Mar 2020

Published Date: 11 Mar 2020

2. Keywords:

Hematologic; Sigmoidoscopy; Carcinoembryonic

1. Introduction

Colorectal carcinoma is the most common malignancy of the gastrointestinal tract [1]. Early detection and subsequent prompt treatment of colorectal carcinoma provide a better 5 years survival rate. Colon cancer screening not only detects the disease at an early, more favourable stage, but also prevents disease by removing premalignant polyps[2]. Higher detection rate can be achieved if patients over 40 years of age with symptoms are submitted to a series of investigations including sigmoidoscopy, barium enema and colonoscopy[2]. Colorectal cancer is responsible for approximately 15% of all cancer deaths [3]. Corrected 5-year survival is less than 50% [3]. Determination of hematologic, immunological, and nutritional measurements are described with increasing frequency as associated with prognosis in cancer [5].

The patient-dependent parameters, such as age, medical co morbidities, extent of distant metastases, and local invasion are the well-established factors that may influence the decision making on whether a curative or palliative operation or a non-operative treatment should be selected in such cases. However, postoperative survival cannot be accurately predicted.

Prognosis is determined by several factors, of which the specific tumour stage and biology- and patient-related factors are particularly important, and the prognosis can potentially be modified by treatment.

3. Methodology

A. STUDY DESIGN: Prospective observational study.

B. STUDY PERIOD: NOVEMBER 2017 – MAY 2019.

C. PLACE: Department of General Surgery, in hospitals attached to Bangalore medical college and Research Institute, Bangalore.

D. SAMPLE SIZE: It is a hospital based study to include a minimum of 30 patients who fulfil the inclusion and exclusion criteria.

E. INCLUSION CRITERIA:

1. Patients willing to give written informed consent for the study undertaken (Annexure I).
2. Patients > 18years of age and both sexes.
3. All histologically proven cases of colorectal carcinomas.

F. EXCLUSION CRITERIA:

1. Patients subjected to non-curative treatment.
2. Patients with fever, arthritis, inflammatory bowel disease, uraemia.

G. METHODLOGY:

- After obtaining institutional ethics committee clearance, Cases will be selected as per the inclusion criteria mentioned above and informed consent (Annexure I) will be taken. Clinical examination will be done. Following investigations will be done at the hospital:
- Routine blood investigations
- Preoperative Carcinoembryonic antigen (CEA), C-reactive protein (CRP) and albumin will be assessed.

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Citation: Abhilash L, A Study of CEA, CRP & Albumin as Prognostic Indicators in Colorectal Carcinomas. United Journal of Surgery. 2020; 1(1): 1-6.

- Further Carcinoembryonic antigen (CEA), C-reactive protein (CRP) and albumin assessment will be done during 1st (3rd to 5th week postoperatively) and 2nd (3rd to 5th month postoperatively) follow up visits.

H. STATISTICAL ANALYSIS: Data collected will be analyzed by descriptive statistics and chi-square test for association of three categorical variables. Quantitative data will be analyzed by student paired t test and ANOVA test as applicable.

4. Results

This prospective observational study was conducted in hospitals attached to Bangalore Medical College and Research Institute during the period from November 2017 to May 2019. A total of 30 patients fulfilling inclusion and exclusion criteria were included in the study. In all the 30 patients estimation on CEA (Carcinoembryonic antigen), CRP(C- reactive protein) and Albumin levels in pre-operative and 1st (3rd-5th week) and 2nd (3rd- 5th month) Post-Operative follow up period was done (Table 1).

Table 1: Estimation of CEA,CRP and Albumin[10,4,11]

Investigations	Normal Value	Baseline (Pre operatively)	1st Followup Visit (3rd to 5th week post operatively)	2nd Followup Visit (3rd to 5th month post operatively)
Carcino embryonic antigen (CEA)	4ng/ml			
C-r e ac t iv e Protein (CRP)	6ng/ml			
Albumin	3.5-4.5g/ml			

4.1. Gender Distribution: In this study 19(63.3%) were males and 11(36.6%) were females (Table 2 and Figure 1).

4.2. Age Distribution: In this Study, Patients in the age more than 18 years were included. Mean age at presentation was 57.4 years. The youngest patient diagnosed was 45 years old while the oldest was 72 years old (Table 3 and Figure 2).

Table 2: Gender distribution of study population.

Males n (%)	Females n (%)
19(63.3%)	11(36.6%)

Table 3: Age distribution of study population

Age < 60 years	Age >60 years
18 (60%)	12 (40%)

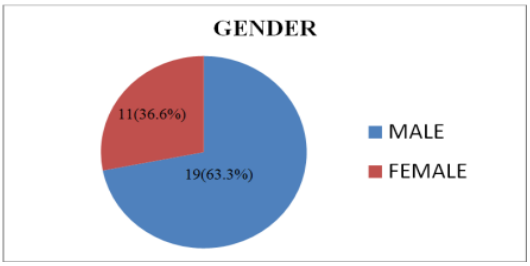

Figure 1 : Gender distribution of study population.

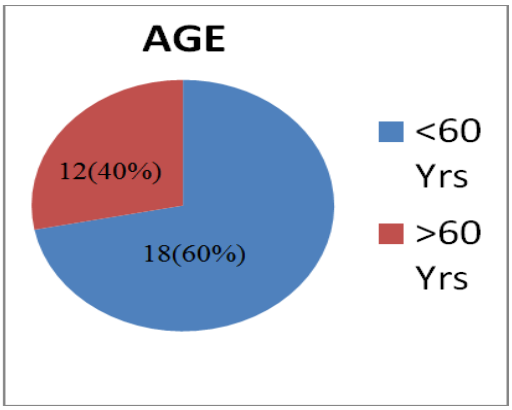

Figure 2: Age distribution of study population.

4.3. Location of Colorectal Carcinoma: A total of 17 (56.6%) of 30 patients were diagnosed to have colorectal carcinomas were located in the right colon, 11 (36.6%) in left colon, 2 (6.6%) in the rectum only. The most common location of colorectal carcinoma was found to be on the right colon.

4.4. Histological Differentiation of Colorectal Carcinomas: The most common histological differentiation of colorectal carcinoma observed was moderately differentiated type, accounting for 13(43.3%) cases followed by well differentiated 11(36.6%) and least being the poorly differentiated type 6(20%) cases (Figure 3 and 4).

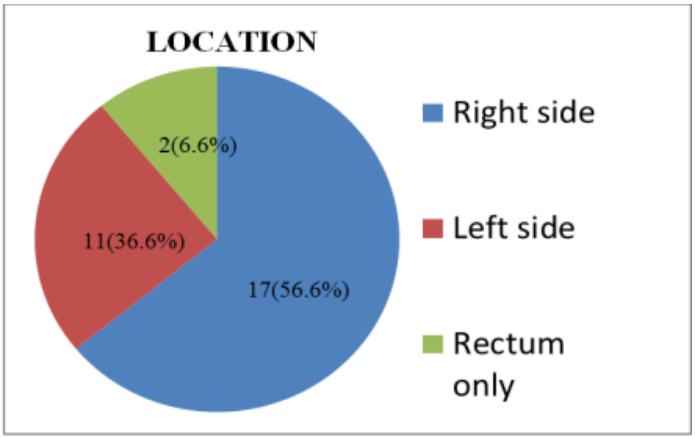

Figure 3: Location of colorectal carcinomas in the study population.

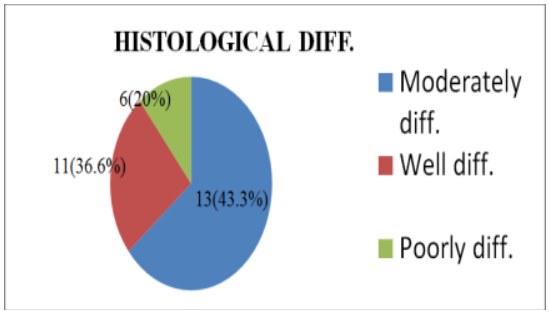

Figure 4: Histological differentiation of colorectal carcinomas in the study population.

4.5. Gross Tumor Size in Colorectal Carcinomas: Nineteen (63.3%) cases had tumor size of > 5.2 cms while 11 (36.6%) cases had tumor size of less than or equal to 5.2 cms at the time diagnosis (Figure 5).

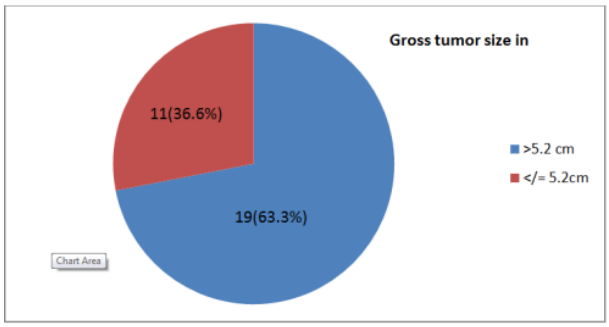

Figure 5: Gross tumor size in colorectal carcinomas in study population.

4.6. Gross Type of Colorectal Carcinomas: The most common gross type observed was ulcerative type accounting for 22 (73.3%) of the 30 cases. Five (16.6%) cases presented with polypoidal lesions and 3 (10%) cases had infiltrative lesions (Figure 6).

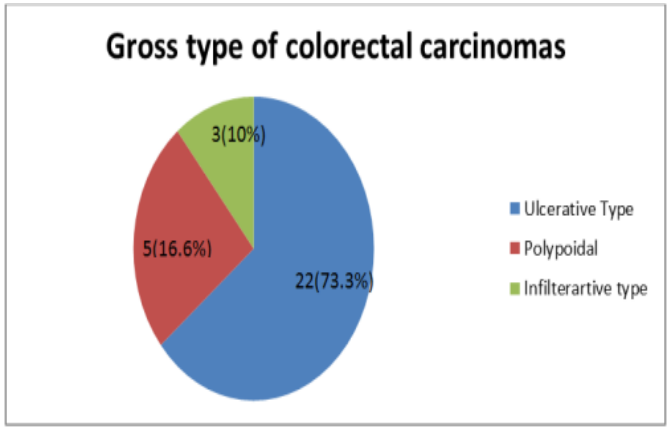

Figure 6: Gross type of colorectal carcinomas in study population.

4.7. Distribution of Colorectal Carcinomas Based on AJCC Staging: Most of the patients presented with stage III and stage IV disease accounting for 19 (63.3%) and 5 (16.6%) cases respectively. Two (6.6%) and Four (13.3%) cases presented in stage I and stage II respectively (Figure 7).

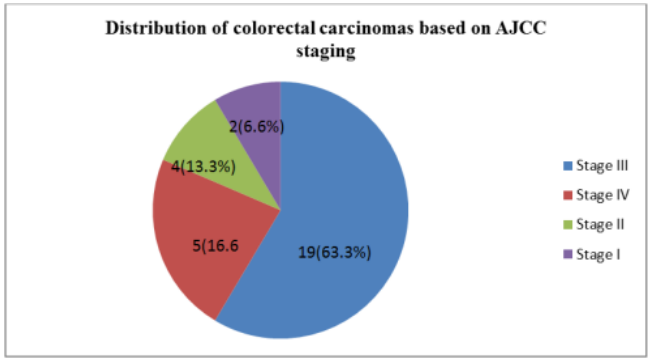

Figure 7: Distribution of colorectal carcinomas based on AJCC staging.

4.8. Histopathological Distribution of Colorectal Carcinomas: The most common histopathological type was adenocarcinoma, accounting for 26 (86.6%). Three (10%) cases had mucinous adenocarcinoma while only 1(3.3%) had signet ring cell adenocarcinoma (Figure 8 and Table 4).

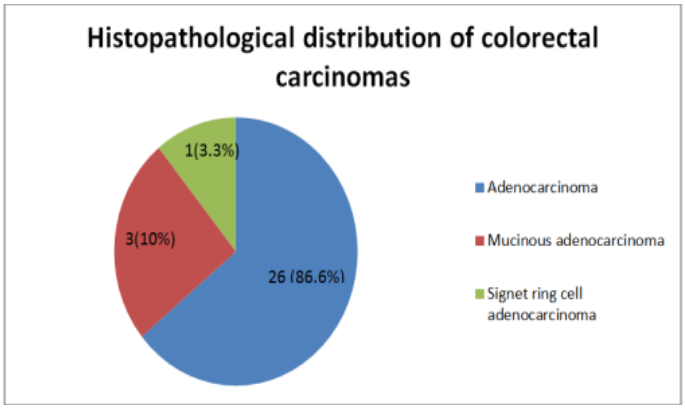

Figure 8: Histological distribution of colorectal carcinomas in the study population.

Table 4: Treatment modalities advocated for colorectal carcinomas in the study population

Procedure	n(30)
Right hemicolectomy	10(33.3%)
Right extended hemicolectomy	7(23.3%)
Left extended hemicolectomy	5(16.6%)
Left Hemicolectomy	4(13.3%)
Anterior resection	2(6.6%)
Abdominoperineal resection	2(6.6%)

4.9. Data Analysis: Collected data analyzed using ANOVA test and results were found as follows (Table 5, 6, 7 and Figure 9, 10, 11).

Table 5: Association of mean preoperative , postoperative and follow up CEA levels in colorectal carcinomas in the study population

	Mean	Standard deviation	n	p- value
Preoperative CEA	29.03	4.33	30	<0.001
Postoperative CEA	15.53	3.46	30	<0.001
Followup CEA	6.66	2.03	30	<0.001

Table 6: Association of mean preoperative, postoperative and followup CRP levels in colorectal carcinoms

	Mean	Standard deviation	n	p-value
Preoperative CRP	10.63	3.124989	30	<0.001
Postoperative CRP	5.4	1.959592	30	<0.001
Followup CRP	1.93	0.891939	30	<0.001

Table 7: Association of mean preoperative, postoperative and follow up albumin levels in colorectal carcinomas.

	Mean	Standard deviation	n	p-value
Preoperative	3.02	0.29	30	<0.001
Postoperative	2.55	0.29	30	<0.001
Followup	2.16	0.22151	30	<0.001

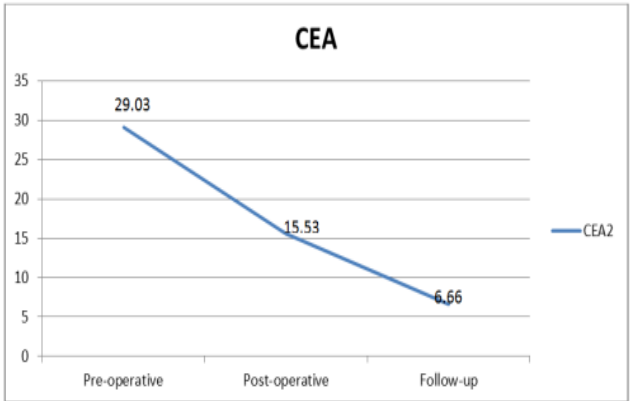

Figure 9: Association of mean preoperative, postoperative and followup CEA levels in colorectal carcinomas.

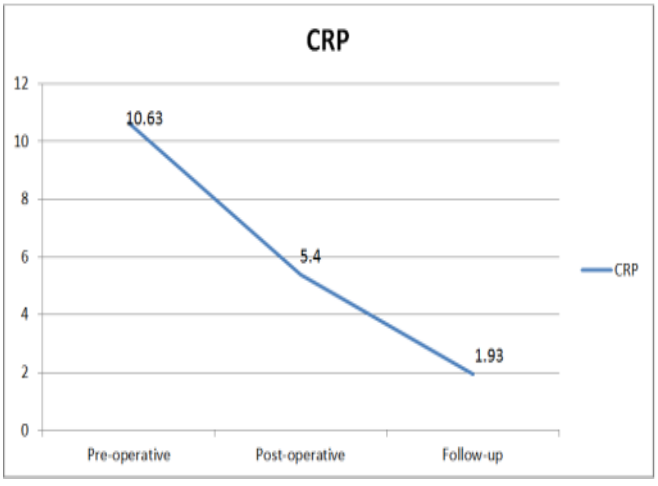

Figure 10: Association of mean preoperative, postoperative and followup CRP levels in colorectal carcinoma.

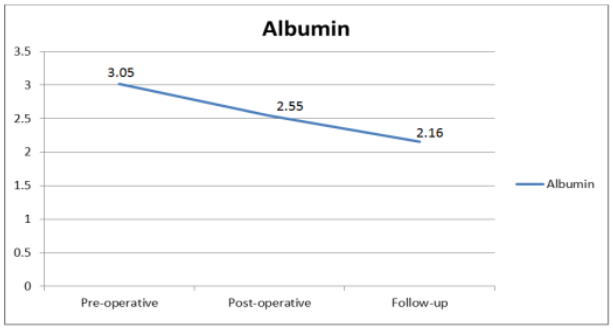

Figure 11: Association of mean preoperative, postoperative and follow up albumin levels in colorectal carcinomas.

5. Discussion

This prospective observational study was conducted in hospitals attached to Bangalore Medical College and Research Institute, Bangalore. The study was undertaken to evaluate Carcinoembryonic antigen, C-reactive protein and Albumin as prognostic indicators in colorectal carcinomas. Results and observations are discussed and compared with various other studies.

A total of 30 patients fulfilling inclusion and exclusion criteria were included in the study. In all these 30 patients levels of Carcinoembryonic antigen, C-reactive protein and Albumin were estimated in preoperative, postoperative(3^{rd} -5^{th} week) and follow up(3^{rd} -5^{th} month) period.

5.1. Demographic Data

In this study colorectal carcinomas were more common in males (63.3%) compared to females (36.6%). In this study patients age >18 years were included. Mean age of the patients at the time of presentation in the study was found to be 57.4 years. In our study maximum number of patients were in fifth decade of life. Sixty percentage of patients belonged to age group <60 years and only 40 % belonging to the age group of >60 years.

This was comparable to other studies (Figure 8).

6. Objectives of the Study

The main objective of this study is to study CEA, CRP and Albumin as prognostic indicators in Colorectal Carcinoma.

The proportion of patients with elevated CEA levels at the time of presentation was 55.5% and 84.2% in Astler Coller B and C groups respectively as per our study. There was a significant increase in the progressive stages of the disease ($p<0.05$). This is in strong agreement with the data from other studies, Wanebo et al, Goslin et al, Janusz et al and Nair et al (Table 9).

Table 8: Comparison of demographic data in other studies.

	Present study 2019	Yu-Chen Shiu et al 2001	Nair et al 2011
Male (%) Female (%)	63.3/36.6	60.3/39.7	62.3/37.7
Mean age in years	57.4	56.2	55.6

Table 9: Comparison of preoperative CEA levels in various studies.

Study	Stage B		Stage C	
	Total no. of patients	No. of patients with raised preoperative CEA	Total no. of patients	No. of patients with raised preoperative CEA
Wanebo et al	51	13(25%)	63	28(44%)
Robert Goslin et al	71	11(15%)	46	21(46%)
Janusz J.et al	41	12(30%)	127	75(59%)
Nair et al	23	13(56.5%)	46	37(80.4%)
Present study	9	5(55.5%)	19	16(84.2%)

The present study was compared with the study done by Yu-Chen Shiu et al and Nair et al. According to their study, the CRP level, differentiation and gross type were the independent prognostic factors. It also showed that CRP was significant for Stage III and Stage IV disease. In the study by Yu-Chen Shiu et al , CRP level was considered as an independent variable and in the study by Nair et al there was a positive relation of change in CRP with Stage IV disease [8, 6].

In the present study also raise in CRP is significant for Stage III and Stage IV disease.

CEA elevation along with CRP elevation had shown statistical significance in the present study. Furthermore it was concluded that though CEA alone could not be used as a prognostic tool, the combined values of CEA and CRP was a strong predictor of prognosis in colorectal carcinomas (Table 10).

Table 10: Comparison of various factors in present study with Yu-Chen et al

		Yu-Chen Shiu et al 2001		Present study	
		Patient number(%)		Patient number(%)	
		CRP<6	CRP>6	CRP <6	CRP>6
Age	<60	58(27.4)	47(22.2)	4(22.2)	14(77.7)
	>60	45(21.2)	62(29.2)	2(16.6)	10(83.3)
Gender	Male	66(31.3)	74(34.9)	5(26.3)	14(73.6)
	Female	37(17.5)	35(16.5)	2(18.1)	9(81.1)
Histological differentiation	Well	1(0.5)	1(0.5)	2(18.1)	9(81.8)
	Moderate	90(42.5)	90(42.5)	2(15.3)	11(84.6)
	Poor	12(5.7)	18(8.5)	1(16.6)	5(83.3)
Gross Type	Polypoidal	35(16.5)	19(9)	1(20.0)	4(80.0)
	Ulcerative	60(28.3)	83(39.2)	2(9.09)	20(90.0)
	Infiltrative	8(3.8)	7(3.3)	1(33.3)	2(66.6)
Location	Right colon	26(12.3)	37(17.5)	2(11.7)	15(88.2)
	Left Colon	35(16.5)	44(20.8)	1(9.09)	11(90.9)
	Rectum	42(19.8)	28(13.2)	1(50.0)	1(50.0)
AJCC Staging	Stage I	22(10.4)	7(3.3)	1(50.0)	1(50.0)
	Stage II	32(15.1)	32(15.1)	1(25.0)	3(75.0)
	Stage III	33(15.6)	34(16)	2(10.5)	17(89.4)
	Stage IV	16(7.5)	36(17)	1(20.0)	4(80.0)

When relating to the cancer specific survival, our patients were followed up for a short period (about 3 to 6 months). Our study is mainly relating to CRP levels with advanced stage of the disease also the inflammatory response increases as tumor increases in size and becomes bigger and more advanced, which is similar to the study reported by Chung and Chang and Nair et al.

All the patients in AJCC stage III and IV had hypoalbuminemia preoperatively with a strong association. Postoperative period Stage III disease patients persisted to have hypoalbuminemia, 18 of the 19 patients in this group persisted to have low albumin levels (94.7%).

This is concordance with the study as per Heys, et al. which showed that serum albumin was an individual prognostic indicator in detecting advanced disease preoperatively, outcome and recurrence rates.

In the present study hypoalbuminemia is strongly associated with poorer prognosis and poor histopathological variants. Which is in concordance with study done by Truong et al, in which persistent hypoalbuminemia is advanced cases of colorectal cancers are associated with poorer prognosis.

7. Conclusion

The present study was conducted in hospitals attached to Bangalore Medical College and Research Institute,Bangalore, involving 30 patients with the earliest followup at 3 weeks postoperatively and the latest at 6 months. Serial preoperative, postoperative and followup CEA, CRP and albumin levels were analysed.

Following were the conclusions made in the present study.

7.1. Carcino Embryonic Antigen (CEA)

Poor histology carcinomas patients tend to have higher CEA levels as compared to others. (Signet ring>mucinous>adenocarcinoma)

The present study findings indicate that an abnormal pre and postoperative serum CEA level observed significantly correlated with the depth of tumor invasion, advanced stages, and higher postoperative relapse.

7.2. C- Reactive Protein (CRP)

Polypoidal lesions seemed to have higher CRP levels as compared to patients with ulcerative and infiltrative lesions.

Higher CRP values were observed in patients with poorer differentiation of tumor.

There was statistical significance with combined CRP and CEA values as prognostic indicators.

7.3. Albumin

Hypoalbuminemia was also strongly associated with poorer prognosis and poor histopathological variants.

Persistent hypoalbuminemia is a feature of advanced disease and should be monitored serially and for longer period to arrive at a consensus.

To conclude CEA, CRP and Albumin were found to have statistical significance as preoperative and postoperative indicators of prognosis of colorectal carcinomas and should be followed up serially in all patients who have undergone surgery with curative intent.

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