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A Study to Analyse Carcinoembryonic Antigen Levels In Relation To Stage and Tumour Characteristics in Colorectal Adenocarcinoma

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Abstract

Colorectal cancer (CRC) is one of the most common forms of gastrointestinal malignancies in the world [1]. CRC ranks as third most common overall cancer. Compared to the Western world, the incidence rates of colorectal cancer are low in India; for colon cancer they vary from 0.7 to 3.7/100,000 among men and 0.4 to 3/100,000 among women, and for rectal cancer from 1.6 to 5.5/100,000 among men and 0 to 2.8/10 0,000 among women[2,3].

Colorectal adenocarcinomas develop in the lining of the colon or rectum, which make up the large intestine. They tend to start in the inner lining and then spread to other layers. Adenocarcinoma of the colon and rectum is the third most common site of new cancer cases.

Carcinoembryonic antigen (CEA) is one of the oldest and best characterized tumor markers of all. Gold and Freedman discovered CEA in 1965 [4]. Initially, CEA was believed to be expressed during fetal life, absent in adult life and re-expressed in cancer cells. Today we know that CEA is expressed in adult tissue as well, but with a restricted expression pat tern found mainly in the epithelial cells in the colon. The protein was detected in only cancer and embryonic tissue; it was given the name Carcinoembryonic antigen [4]. In general, the clinical value of CEA in the management of colorectal cancer can be divided in to preoperative assessment of the extent and outcome of the tumor. This study is done to correlate the preoperative CEA levels with stage and tumor characteristics in colorectal adenocarcinoma.

Aim: To analyze pre-operative CEA levels in relation to stage and tumor (clinic-pathological) characteristics in colorectal adenocarcinoma.

- Age
- Gender
- Pre-operative albumin levels
- Colon vs rectum
- Site of the tumor
- Grading of the tumor.
- Stage of the disease
- Tumor size

Materials and Methods: A total of 50 patients who were diagnosed with colorectal adenocarcinoma undergoing curative resection were included in the study. Serum CEA was measured preoperatively by chemiluminescence immunoassay method (CLIA) in patients undergoing colon and rectal cancer resections.

Inclusion Criteria

- Age group above 18years
- Patients diagnosed to have colorectal adenocarcinoma
- Cases of potentially resectable colorectal adenocarcinomas

Exclusion Criteria

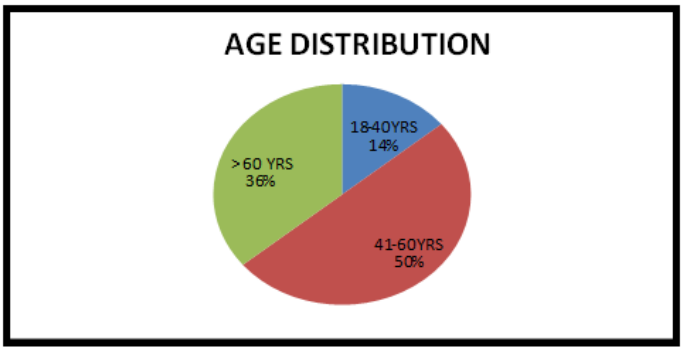
- Patients with non resectable tumors

- Patients underwent neo adjuvant chemotherapy
- Recurrent tumors

Colonic tumour proximal to the splenic flexure was classified as right sided and those between splenic flexure and rectosigmoid junction as left sided. Tumors distal to the rectosigmoid junction were considered to be rectal. The results are analyzed.

Results: A total of 50 patients who were diagnosed with colorectal adenocarcinoma undergoing curative resection were included in the study. Pre operative CEA levels was measured and are analysed with the following variables.

Age with CEA

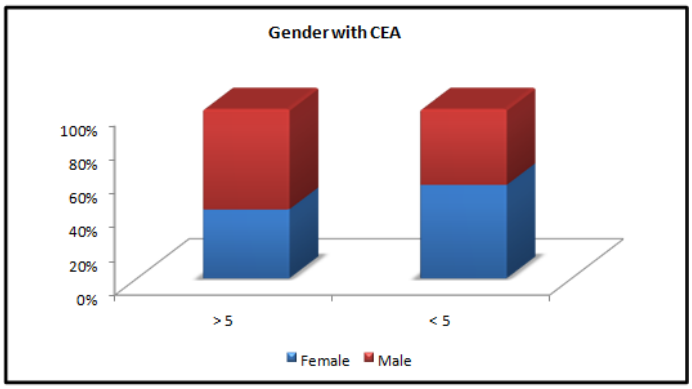


Age (Years)		CEA (ng/ml)		Total
		> 5	< 5	
18 - 40 yrs	Count	2	5	7
	% within CEA	29%	71.4%	100%
41 - 60 yrs	Count	8	17	25
	% within CEA	32%	68%	100%
> 60 yrs	Count	8	10	18
	% within CEA	44.4%	56%	100%
Total	Count	18	32	50
	% within CEA	36%	64%	100.0%

- The mean age of the patients 55.5.
- Of the 50 patients in the study group, majority of the patients were in the age group of **41-60 years** (25), out of which **32%** (8) had CEA >5 ng/ml and **68%** (17) had CEA < 5ng/ml respectively.
- In our study patients **older than 60 yrs** had greater positivity of CEA > 5ng/ml **(44.4%)** in comparison with < 40 yrs where only 29% had CEA >5 ng/ml and was found to be statistically insignificant. (p value = 0.731).

Gender with CEA

Gender		CEA (Ng/Ml)		Total
		> 5	< 5	
Female	Count	7	17	24
	% within CEA	29.1%	70.9%	100%
Male	Count	11	15	26
	% within CEA	42.3%	57.7%	100%
Total	Count	18	32	50
	% within CEA	36%	64%	100.0%

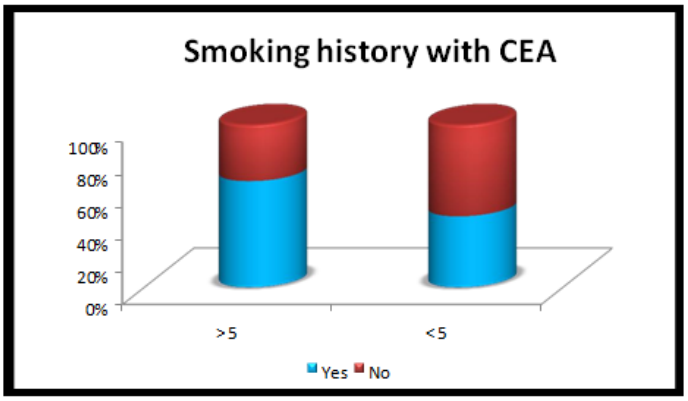


- Majority of the patients in the study group were **males** (26).
- Higher percentage of CEA >5 ng/ml was observed in men **(42.3%)** when compared to females **(29.1%)**, however the p value was 0.388 which was statistically insignificant.

Smoking History With CEA

Smoking History		CEA (ng/ml)		Total
		> 5	< 5	
Non smoker	Count	17	28	45
	% within CEA	37.8%	62.2%	100%

Smoker	Count	1	4	5
	% within CEA	20%	80%	100%
Total	Count	18	32	50
	% within CEA	36%	64%	100.0%



- In the study group, majority of 45 patients were **non smokers** out of which 17 **(37.8%)** had CEA >5ng/ml and 28 (**62.2%)** had CEA <5ng/ml.
- Whereas, Only 5 patients in the study group were **smokers** of whom 1 (**20%)** had CEA >5 ng/ml and 4 (80%) had CEA <5ng/ml, which was statistically insignificant (p value = 0.642)

Albumin Levels With CEA

ALBUMIN LEVELS mg/dl)		CEA (ng/ml)		Total
		> 5	< 5	
< 3.5	Count	11	24	35
	% within CEA	31.4%	68.6%	100%
> 3.5	Count	7	8	15
	% within CEA	46.7%	53.3%	100%
Total	Count	18	32	50
	% within CEA	36%	64%	100.0%

When comparing serum albumin levels with CEA levels, **35 patients** had **hypoalbuminemia** of whom 11 (**31.4%)** had CEA > 5 ng/ml and 24 (68.6%)had CEA < 5 ng/ml.

15 patients had **>3.5 albumin levels** out of which 7 **(46.7%)** had CEA > 5ng/ml and 8 (53.3%) had CEA <5ng/ml.

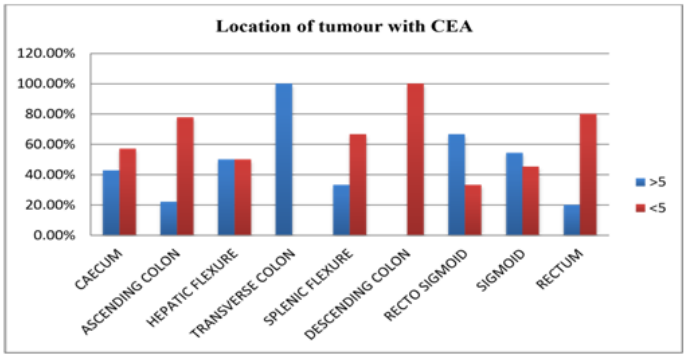
Higher percentage of patients (**46.7%)** with **normal albumin levels** had CEA >5ng/ml in comparison to hypoalbuminemia (31.4%).

- However the comparison between albumin and CEA levels were statistically insignificant. (p value = 0.304).

Location of Tumour with CEA

LOCATION OF TUMOUR		CEA (ng/ml)		Total
		> 5	< 5	
CAECUM	Count	3	4	7
	% within CEA	42.9%	57.1%	100%
ASCENDING COLON	Count	2	7	9
	% within CEA	22.2%	77.8%	100%
HEPATIC FLEXURE	Count	1	1	2
	% within CEA	50%	50%	100%
TRANSVERSE COLON	Count	1	0	1
	% within CEA	100%	0%	100%
SPLENIC FLEXURE	Count	1	2	3
	% within CEA	33.3%	66.7%	100%
DESCENDING COLON	Count	0	3	3
	% within CEA	0.0%	100%	100%
RECTO SIGMOID	Count	2	1	3
	% within CEA	66.7%	33.3%	100%
SIGMOID	Count	6	5	11
	% within CEA	54.5%	45.4%	100%
RECTUM	Count	2	8	10
	% within CEA	20%	80%	100%
Total	Count	18	32	50

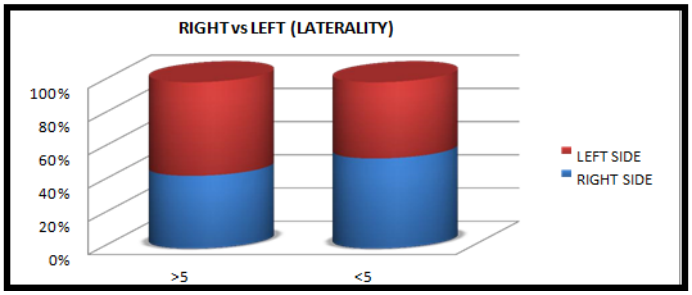
	% within CEA	36%	64%	100.0%



- In this study the most frequent site of malignancy was **sigmoid colon** (11) followed by the **rectum** (10) and **ascending colon** (9).
- Higher percentage of **CEA > 5ng/ml** was noted in the **rectosigmoid (66.7%)** followed by sigmoid (54.5%) when compared to rest of the colon.
- However it was statistically insignificant with the p value of 0.393.

Right Vs Left (Laterality)

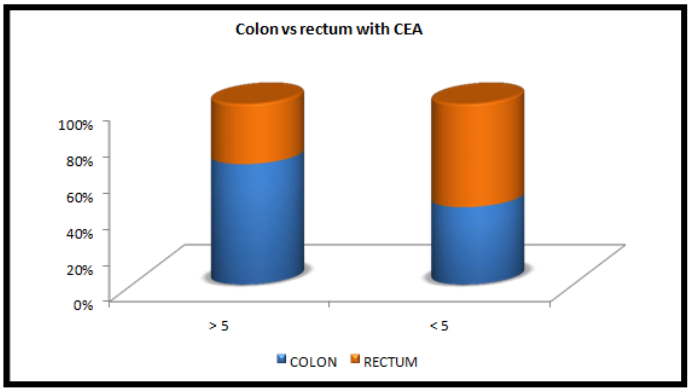
Right VS Left (Laterality)		CEA (ng/ml)		Total
		> 5	< 5	
RIGHT SIDE	Count	7	13	20
	% within CEA	35%	65%	100%
LEFT SIDE	Count	11	19	30
	% within CEA	36.6%	63.4%	100%
Total	Count	18	32	50
	% within CEA	36%	64%	100.0%



- Right and left side of the colon constitutes 20 and 30.
- **Slightly higher percentage** of CEA>5 ng/ml was noted in the **left colon (36.6%)** vs **right colon (35%).**
- However, In this study on comparing right vs left and level of CEA was found to be statistically insignificant.(p value = 0.5).

Colon Vs Rectum with CEA

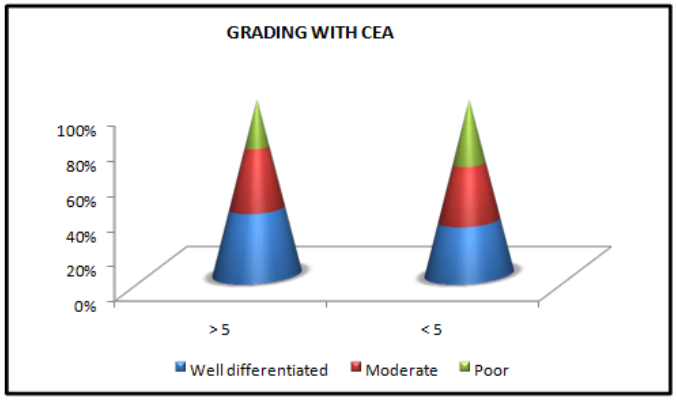
Site Of Tumour		CEA (ng/ml)		Total
		> 5	< 5	
COLON	Count	16	24	40
	% within CEA	40%	60%	100%
RECTUM	Count	2	8	10
	% within CEA	20%	80%	100%
Total	Count	18	32	50
	% within CEA	36%	64%	100.0%



- Out of 50 patients in the study group, **40 patients** constitutes **tumour in the colon** of whom 16 **(40%)** found with CEA >5ng/ml .
- Whereas,**10 patients** constitutes **tumour in the rectum** of whom 2 **(20%)** had CEA > 5ng/ml
- Hence, In this study on comparing colon vs rectum and level of CEA was found to be statistically insignificant with p value = 0.287.

Grading of Tumour

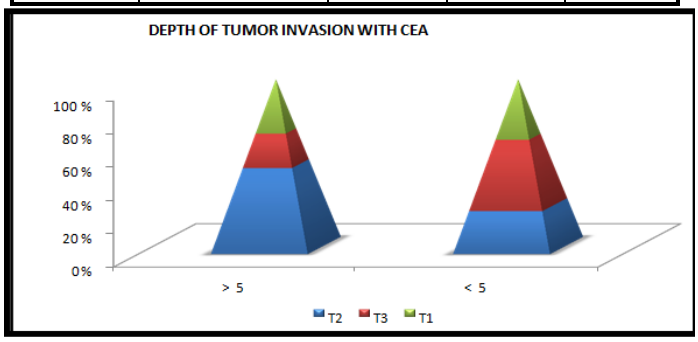
Grading of Tumour		CEA (ng/ml)		Total
		> 5	< 5	
Well differentiated	Count	2	3	5
	% within CEA	40%	60%	100%
Moderate	Count	14	24	38
	% within CEA	36.8%	63.1%	100%
Poor	Count	2	5	7
	% within CEA	28.6%	71.4%	100%
Total	Count	18	32	50
	% within CEA	36%	64%	100.0%



- In this study majority of the patients had **moderately differentiated tumour** (76%).
- Whereas, higher percentage of CEA > 5ng/ml was noted in the **well differentiated tumour** (40%) compared to **moderate (36.8%)** and **poorly differentiated tumour (28.6%)**.
- In this study, on correlation of the tumour differentiation with CEA levels were found to be statistically insignificant (p value = 0.898).

Depth of Tumor Invasion With CEA

Depth of Tumor Invasion		CEA (ng/ml)		Total
		> 5	< 5	
T2	Count	10	9	19
	% within CEA	52.6%	47.3%	100%
T3	Count	4	15	19
	% within CEA	21.0%	78.9%	100%
T4	Count	4	8	12
	% within CEA	33.3%	66.7%	100%
Total	Count	18	32	50
	% within CEA	36%	64%	100.0%

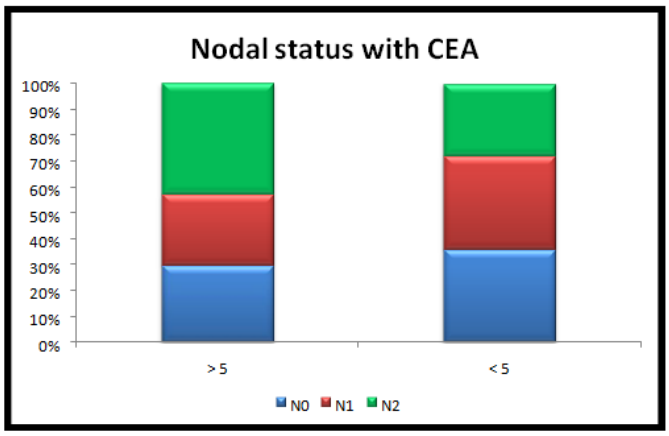


- None of the patients in this study group has T1 lesion.
- Majority belongs to **T2** and **T3 lesion** with 19 patients each.
- On analysis of CEA, patients with **T2 lesions** had higher percentage of CEA > 5 ng/ml **(52.6%)** when compared with other stages.
- On statistical analysis, elevated CEA in T2 was statistically significant with p value= 0.05.

Nodal Status with CEA

NODAL STATUS	CEA(ng/ml)		Total
	> 5	< 5	
Count	8	17	25

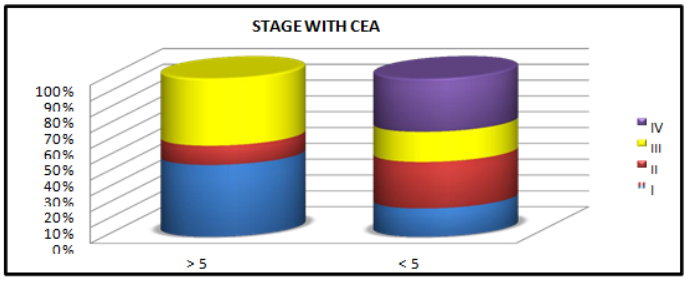
% within CEA		32%	68%	100%
Count		3	7	10
% within CEA		30%	70%	100%
Count		7	8	15
% within CEA		46.7%	53.3%	100%
Total	Count	18	32	50
	% within CEA	36%	64%	100.0%



- In this study majority of patients had N0 disease.
- It was observed that **N2 patients** had higher CEA levels when compared to other nodal status.
- However, on statistical analysis between different nodal status and CEA was statistically insignificant with p value = 0.588.

Stage with CEA

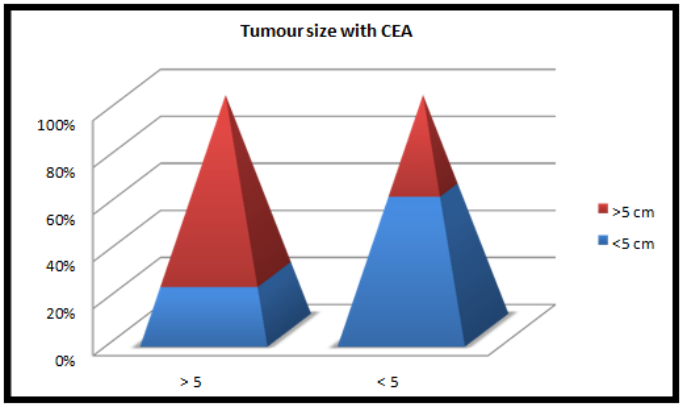
STAGE		CEA(ng/ml)		Total
		> 5	< 5	
STAGE 1	Count	7	8	15
	% within CEA	46.7%	53.3%	100%
STAGE 2	Count	1	7	8
	% within CEA	12.5%	87.5%	100%
STAGE 3	Count	10	13	23
	% within CEA	43.5%	56.5%	100%
STAGE 4	Count	0	4	4
	% within CEA	0.0%	100%	100%
Total	Count	18	32	50
	% within CEA	36%	64%	100.0%



- In this study majority of the patients belongs to **stage 3 (23).**
- **Higher percentage** of elevated CEA level was noted in **stage 1 (46.7%)** and **stage 3 (43.5%)** respectively.
- However on comparison of stage of disease with CEA levels was found to be statistically insignificant with p value = 0.141.

Tumour Size with CEA

Tumour Size (cm)		CEA (ng/ml)		Total
		> 5	< 5	
< 5cm	Count	1	7	8
	% within CEA	12.5%	87.5%	100%
> 5cm	Count	17	25	42
	% within CEA	40.4%	59.5%	100%
Total	Count	18	32	50
	% within CEA	36%	64%	100.0%



- On assessing tumour size with CEA levels, majority of patients **(42)** had **tumour diameter > 5cm.**

- **Higher percentage of CEA** > 5ng/ml **(40.4%)** was noted in patients with tumour diameter of size > 5cm.
- However, the relation between tumour size and CEA levels was not statistically significant (p = 0.06).

Discussion

Colorectal cancer (CRC) accounts for 13% of all cancers, it represents the third most common neoplasia. Prognosis of CRC patients is dependent on several factors: pathological, clinical and biological. Although pathologic stage is useful and essential for predicting prognosis in CRC patients, it is difficult to determine in an accurate way the stage prior to the surgical treatment. Thus, it is necessary to identify promising prognostic factors that could preoperatively identify patients at high risk of recurrences after surgery or with a bad survival prognosis.

Carcinoembryonic Antigen (CEA) an intracellular protein is the most commonly used tumor associated antigens used in pre and post operative surveillance of patients with colorectal cancer.

Primary CRCs are commonly CEA-negative, even though 90% of tumors can be shown to produce CEA. An explanation for this occurrence is that CEA produced by CRCs (except for very low rectal tumors) enters the portal venous circulation and is extracted on the first pass through the liver.

This is a prospective study to analyze the CEA levels in relation to age, gender, location of tumour, Tand N stage of the disease, tumour differentiation, and tumour diameter in colorectal adenocarcinoma, some of which would probably influence the CEA levels.

Patient factor variables like smoking habits, diabetes mellitus, albumin levels were also analyzed with the pre operative of CEA levels.

Age

In our study the age group of patients ranged from 18-80 yrs, and the mean age group of patients was 55.54. Higher percentage of Out of 18 patients with CEA > 5ng/ml, patients in the age group > 60 years had a greater positivity of 44.4%.

In a study done by **Zhenqiang sun et al**[124] showed that the age group < 60 yrs (62.2%) had greater positivity of CEA levels when compared to other age group.

AGE	OUR STUDY		ZHENQIANG SIUN et al	
	CEA >5 ng/ml (N=18)	CEA <5ng/ml (N=32)	CEA>5ng/ml (N=1218)	CEA<5ng/ml (N=817)
< 60 YEARS	31.2%	68.8%	62.2%	37.7%
> 60 YEARS	44.4%	56%	57.9%	42.9%

Gender

- Out of 50 patients in the study group, 52% were males and 48% were females. In this study elevated CEA levels were noted more in males (42.3%) than in females (29.1%), however it was not statistically significant.(p = 0.388).
- **Graziosi et al**[125] reported that slightly higher percentage of elevated CEA levels was noted in females (32.9%) when compared to males (31.7%).

Gender	Our Study		Graziosi Et Al	
	CEA >5 ng/ml (N=18)	CEA <5 ng/ml (N=32)	CEA >5 ng/ml (N=70)	CEA <5 ng/ml (N=147)
Male	42.3%	57.7%	31.7%	68.2%
Female	29%	70.9%	32.9%	67.0%

Albumin Levels With CEA

- In this study, 75% of patients had hypoalbuminemia and 25% had normal albumin levels.
- Higher percentage of elevated CEA levels was noted in patients with normal albumin levels (46.7%) when

compared to hypoalbuminemia (31.4%). however the comparison between albumin and CEA levels are not statistically significant (p = 0.304).

- In the study conducted by **Graziosi et al**[125], 43.8% of patients with hypoalbuminemia and 27.9% with normal albumin levels had CEA >5ng/ml, which showed statistically significant difference between serum albumin and elevated CEA levels.

Albumin With CEA	Our Study		Graziosi Et Al	
	CEA >5 ng/ml (N=18)	CEA <5 ng/ml (N=32)	CEA >5 ng/ml (N=65)	CEA <5 ng/ml (N=135)
< 3.5	31.4%	68.6%	43.8%	56.1%
> 3.5	46.7%	53.3%	27.9%	72.0%

Right Vs Left (Laterality) With CEA

- In this study group of 50 patients right and left side of the colon constitutes 20 and 30 patients. Slightly higher percentage of elevated CEA was noted in the left colon (36.6%) vs right colon (35%), the relationship between the right vs left colon and CEA levels was not statistically significant (p value = 0.5).
- **Graziosi et al**[125] in his study reported to have 31% of patients with tumour in right side and 33.3% in the left side with elevated CEA levels, which was similar to our study.

Right Vs Left (Laterality)	Our Study		Graziosi Et Al	
	CEA >5 ng/ml (N=18)	CEA <5 ng/ml (N=32)	CEA >5 ng/ml (N=70)	CEA <5 ng/ml (N=147)
Right side	35%	65%	31%	68.9%
Left side	36.6%	63.4%	33.3%	66.6%

Colon Vs Rectum with CEA

- Out of 50 patients in this study, 40 patients had tumour in colon and 10 patients had tumour in rectum. Higher percentage of CEA >5ng/ml was noted in the colon (40%) when compared with rectum (20%) however the site of tumour with CEA levels was not statistically significant. p value = 0.287.
- **Zhenqiang Sun et al**[124] showed 61.3% with tumour in the colon and 58.7% in the rectum had CEA > 5ng/ml, which was not significant and correlates with this study.

Site Of Tumour With CEA.	Our Study		Zhenqiang Sun Et Al	
	CEA >5 ng/ml (N=18)	CEA <5 ng/ml (N=32)	CEA >5 ng/ml (N=1218)	CEA <5 ng/ml (N=817)
Colon	40%	60%	61.3%	38.6%
Rectum	20%	80%	58.7%	41.2%

Depth of Tumour Invasion with CEA

- In this study, none of the patients had T1 lesions, T2 and T3 lesions constitutes of 19 patients each and T4 lesions with 12 patients. Higher percentage of elevated CEA levels were noted in T2 (52.6%) when compared to T3 (21%) and T4 (33.3%), no progressive increase in CEA levels was noted with depth of invasion.
- However, Sub analysis showed T2 had higher percentage of patients with CEA>5ng/ml and was statistically significant.(p value=0.05).
- **Graziosi et al**[125] in his study showed higher percentage of elevated CEA levels with progression of depth of invasion (**T1**-0%, **T2**- 21.27%, **T3**- 36.3%, **T4**-50%) and found to have significant association with T stage .

Depth Of Tumor Invasion With CEA	Our Study		Graziosi Et Al	
	CEA >5 ng/ml (N=18)	CEA <5 ng/ml (N=32)	CEA >5 ng/ml (N=70)	CEA <5 ng/ml (N=147)
T1	-	-	0%	100%
T2	52.6%	47.3%	21.27%	78.7%
T3	21%	78.9%	36.3%	63.6%
T4	33.3%	66.7%	50%	50%

Nodal Status with CEA

- Out of 50 patients in this study group, majority of patients had N0 nodal status (25), N1 (10) and N2 (15). N2 patients had higher CEA levels (46.7%) when compared to the other nodal status (N0 32%, N1-30%). On statistical analysis between nodal status and CEA was statistically insignificant (p= 0.588).
- **Graziosi et al[125]** in his study showed higher percentage of elevated CEA levels with increase in number of nodes involved (**N0** -7.4%, **N1**-37.5%, **N2**-42.1%) and was statistically insignificant.

Nodal Status With CEA	Our Study		Graziosi Et Al	
	CEA >5 ng/ml (N=18)	CEA <5 ng/ml (N=32)	CEA >5 ng/ml (N=70)	CEA <5 ng/ml (N=147)
N0	32%	68%	27.4%	72.5%
N1	30%	70%	37.5%	62.5%
N2	46.7%	53.3%	42.1%	57.9%

Stage with CEA

Out of 50 patients in our study, majority of the patients belongs to **stage 3 (23).** Higher percentage of elevated CEA level was noted in **stage 1 (46.7%)** and **stage 3 (43.5%)** respectively. But no statistically significant correlation was detected between CEA levels and stage of disease (p = 0.141).

Topdagi et al[126] reported that higher percentage of elevated CEA levels was noted in stage 4 (48.4%) and stage 2 (38.1%) when compared to other stages.

Stage With CEA	Our Study		Topdagi Et Al	
	CEA >5 ng/ml (N=18)	CEA <5 ng/ml (N=32)	CEA >5 ng/ml (N=98)	CEA <5 ng/ml (N=149)
Stage 1	46.7%	53.3%	31.5%	68.4%
Stage 2	12.5%	87.5%	38.1%	61.8%
Stage 3	43.5%	56.5%	32%	67.9%
Stage 4	-	100%	48.4%	51.5%

Grading of Tumour with CEA

- In this study, with regards to grading of tumours 38 patients had moderately differentiated tumours (76%). Higher percentage of elevated CEA levels was noted in well differentiated tumour (40%) when compared to moderate (36.8%) and poorly differentiated (28.6%) and no statistically significant difference were detected (p = 0.898).
- Study done by **Topdagi et al[126]** revealed that 18.5% had well differentiated tumour, 37.8% had moderately differentiated and 50% had poorly differentiated tumour with CEA > 5 ng/ml.

Grading Of Tumour With Cea	Our Study		Topdagi Et Al	
	CEA >5 ng/ml (N=18)	CEA <5 ng/ml (N=32)	CEA >5 ng/ml (N=92)	CEA <5 ng/ml (N=48)
Well differentiated	40%	60%	18.5%	81.4%
Moderate	36.8%	63.1%	37.8%	62.1%
Poor	28.6%	71.4%	50%	50%

Tumour Size with CEA

- In this study tumour size was evaluated with CEA levels in which 42 patients predominantly had tumour size of > 5cm, 8 patients had tumour size of < 5cm.
- Higher percentage of elevated CEA levels was noted in tumour size > 5cm (40.4%) compared to tumour size < 5cm (12.5%). On statistical analysis between tumour size and CEA was found to be insignificant. (P value = 0.06).

- Study done by **Topdagi et al**[126] reported that 40% of patients to have tumour size of < 5cm, 38.1% with tumour size of > 5cm had CEA > 5 ng/ml, and found no statistical significant correlation was detected.

Tumour Size	Our Study		Topdagi Et Al	
	CEA >5 ng/ml (N=18)	CEA <5 ng/ml (N=32)	CEA >5 ng/ml (N=97)	CEA <5 ng/ml (N=150)
< 5CM	12.5%	87.5%	40%	60%
> 5CM	40.4%	59.5%	38.1%	61.8%

Conclusion

Although elevated CEA levels were observed in males, in patients of the age group >60 years, tumour in rectosigmoid, T2, N2 lesions, stage 1 tumour, well differentiated tumours and tumour size >5cm, statistical analysis of all the above variables was found to be insignificant.

Hence we conclude that there is no correlation between the elevated CEA levels, tumour and clinicopathological variables in colorectal adenocarcinoma in this study.

This being a prospective study in a small population, a similar study with a large sample size may be required to substantiate the results of this study.

References

1. Boyle P, Langman JS. ABC of colorectal cancer: Epidemiology. BMJ 2000;321:805–8.

2. Goh KL, Quek KF, Yeo GT, et al. Colorectal cancer in Asians: a demographic and anatomic survey in Malaysian patients undergoing colonoscopy. Aliment Pharmacol Ther 2005;22:859–64.

3. Mohandas KM, Desai DC. Epidemiology of digestive tract cancers in India.

4. V. Large and small bowel. Indian J Gastroenterol 1999;18:118–21.

5. Gold P, Freedman SO. Specific carcinoembryonic antigens of the human digestive system. J Exp Med 1965;122:467-81.

6. Gold P, Freedman SO. Specific carcinoembryonic antigens of the human digestive system. J Exp Med 1965;122:467-81.

7. Hammarström S. The carcinoembryonic antigen (CEA) family: structures, suggested functions and expression in normal and malignant tissues. Cancer Biology 1999;9:67-81.

8. Horst A K, Wagener C (2004) CEA-related CAMs. In handbook of Experimental Pharmacology, Cell Adhesion Behrens J and Nelson WJ (eds), Vol. 165, pp 283-341. Heidelberg: Springer-Verlag.

9. Benchimol S, Fuks A, Jothy S, Beauchemin N, Shirota K, Stanners CP. Carcinoembryonic antigen, a human tumor marker, functions as an intercellular adhesion molecule. Cell 1989;57:327-34.

10.Nagaishi T, Chen Z, Chen L, Iijima H, Nakajima A, Blumberg RS. CEACAM1 and the regulation of mucosal inflammation. Mucosal Immunol 2008;1:S39-42.

11.Gray-Owen SD, Blumberg RS. CEACAM1: contact-dependent control of immunity. Nat Rev Immunol 2006;6:433-46

12.Neumaier M, Paululat S, Chan A, Matthaes P, Wagener C. Biliary glycoprotein, a potential human cell adhesion molecule, is down-regulated in colorectal carcinomas. Proc Natl Acad Sci U S A 1993;90:10744-48.

13.Osada T, Hsu D, Hammond S, Hobeika A, Devi G, Clay TM, et al. Metastatic colorectal cancer cells from patients previously treated with chemotherapy are sensitive to T-cell killing mediated by CEA/CD3-bispecific T-cell-engaging BiTE antibody. Br J Cancer 2010;102:124-33.

14.Blumenthal RD, Leon E, Hansen HJ, Goldenberg DM.Expression patterns of CEACAM5 and CEACAM6

in primary and metastatic cancers. BMC Cancer 2007:7:2 (Scanlon and Sanders, 2014).

15.Colorectal Cancer Facts & Figures 2014-2016 the American Cancer Society, Atlanta, Georgia. Yeatman T.J. (2001) Colon cancer. eLS.

16.Schwartz principles of surgery 10th edition .F.Charles Brunicardi page 1176- 1178.

17.Schwartz principles of surgery 10th edition .F.Charles Brunicardi page 1179- 1180.

18.Iversen L.H. (2012) Aspects of survival from colorectal cancer in Denmark. Danish medical journal 59(4), B4428-B4428.

19.Iacopetta B. Are there two sides to colorectal cancer? Int J Cancer. 2002;101: 403-408.

20.Winawer SJ, Zauber AG. The advanced adenoma as the primary target of screening. Gastrointest Endosc Clin N Am. 2002;12: 1-9, v.

21.Stryker SJ, Wolff BG, Culp CE, Libbe SD, Ilstrup DM, MacCarty RL. Natural history of untreated colonic polyps. Gastroenterology. 1987;93: 1009-1013.

22.de Heer P. (2007) Molecular and biological interactions in colorectal cancer: Department of Surgery, Faculty of Medicine, Leiden University Medical Center (LUMC), Leiden University.

23.Bond JH. Polyp guideline: diagnosis, treatment, and surveillance for patients with colorectal polyps. Practice Parameters Committee of the American College of Gastroenterology. Am J Gastroenterol. 2000;95: 3053-3063.

24.Schatzkin A, Freedman LS, Dawsey SM, Lanza E. Interpreting pre- cursor studies: what polyp trials tell us about large-bowel cancer. J Natl Cancer Inst. 1994;86: 1053-1057.

25.Levine JS, Ahnen DJ. Clinical practice. Adenomatous polyps of the colon. N Engl J Med. 2006;355: 2551-2557.

26.Risio M. The natural history of adenomas. Best Pract Res Clin Gastro- enterol. 2010;24: 271-280.

27.Pickhardt PJ, Kim DH, Pooler BD, et al. Assessment of volumetric growth rates of small colorectal polyps with CT colonography: a longi- tudinal study of natural history. Lancet Oncol. 2013;14: 711-720.

28.Stewart SL, Wike JM, Kato I, Lewis DR, Michaud F. A popula- tion-based study of colorectal cancer histology in the United States, 1998-2001. Cancer. 2006;107: 1128-1141.

29.Ferlay J., Shin H.R., Bray F., Forman D., Mathers C. and Parkin D.M. (2010) Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. International Journal of Cancer 127(12), 2893-2917.

30.Sjo O.H. (2012) Prognostic factors in colon cancer.

31.Surveillance, Epidemiology and End Results Program. SEER*Stat Database: Incidence – SEER 13 Regs Public Use, Nov 2011 Sub (1992-2010) – Linked to County Attributes – Total US, 1969-2011 Counties. Bethesda, MD: National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch 2013.

32.Wallin U. (2011) Cancer of the Colon and Rectum: Prognostic Factors and Early Detection.

33.Kang W., Lee S., Jeon E., Yun Y.-R., Kim K.-H. and Jang J.-H. (2011) Emerging role of vitamin D in colorectal cancer. World journal of gastrointestinal oncology 3(8), 123.

34.Mattar MC, Lough D, Pishvaian MJ, Charabaty A. Current management of inflammatory bowel disease and colorectal cancer. Gastrointest Cancer Res 2011;4:53-61.

35.Wei EK, Giovannucci E, Wu K, Rosner B, Fuchs CS, Willett WC,et al. Comparison of risk factors for colon and rectal cancer. Int J Cancer 2004;108:433-42.

36.Terry P., Giovannucci E., Michels K.B., Bergkvist L., Hansen H., Holmberg L. and Wolk A. (2001) Fruit,

vegetables, dietary fiber, and risk of colorectal cancer. Journal of the National Cancer Institute 93(7), 525-533.

37.Lin O.S. (2009) Acquired risk factors for colorectal cancer. Cancer Epidemiology: Modifiable Factors361-372.

38.Chao A., Thun M.J., Connell C.J., McCullough M.L., Jacobs E.J., Flanders W.D., Rodriguez C., Sinha R. and Calle E.E. (2005) Meat consumption and risk of colorectal cancer. Jama 293(2), 172-182.

39.Fung T.T. and Brown L.S. (2013) Dietary patterns and the risk of colorectal cancer. Current nutrition reports 2(1), 48-55.

40.Giovannucci E. (2007) Metabolic syndrome, hyperinsulinemia, and colon cancer: a review. The American journal of clinical nutrition 86(3), 836S-842S.

41.Larsson S.C., Orsini N. and Wolk A. (2005) Diabetes mellitus and risk of colorectal cancer: a meta-analysis. Journal of the National Cancer Institute 97(22), 1679-1687.

42.Haggar F.A. and Boushey R.P. (2009) Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. Clinics in colon and rectal surgery 22(4), 191.

43.Zisman A.L., Nickolov A., Brand R.E., Gorchow A. and Roy H.K. (2006) Associations between the age at diagnosis and location of colorectal cancer and the use of alcohol and tobacco: implications for screening. Archives of internal medicine 166(6), 629-634.

44.Pino M.S. and Chung D.C. (2010) The chromosomal instability pathway in colon cancer. Gastroenterology 138(6), 2059-2072.

45.Schwartz principles of surgery 10th edition .F.Charles Brunicardi page 1204- 1205.

46.M.Berretta,L.Alessandrini,C.DeDivitiisetal.,"Seruman dtis- sue markers in colorectal cancer: State of art," Critical Review in Oncology/Hematology, vol. 111, pp. 103–116, 2017.

47.H. T. Lynch and A. de la Chapelle, "Hereditar colorectal can- cer," The New England Journal of Medicine, vol. 348, no. 10, pp. 919–932, 2003.

48.H. F. A. Vasen, J.-P. Mecklin, P. M. Khan, and H. T. Lynch, "The international collaborative group on hereditary non-polyposis colorectal cancer (ICG-HNPCC)," Diseases of the Colon & Rectum, vol. 34, no. 5, pp. 424-425, 1991.

49.A.Mahasneh,F. Al-Shaheri, And E.Jamal,"Molecularbiomark- ers for an early diagnosis, effective treatment and prognosis of colorectal cancer: Current updates," Experimental and Molecular Pathology, vol. 102, no. 3, pp. 475– 483, 2017.

50.A. G. Renehan, J. Jones, C. S. Potten, S. M. Shalet, and S. T. O'Dwyer, "Elevated serum insulin-like growth factor (IGF)-II and IGF binding protein-2 in patients with colorectal cancer," British Journal of Cancer, vol. 83, no. 10, pp. 1344–1350, 2000.

51.J.-M. Liou, C.-T. Shun, J.-T. Liang et al., "Plasma insulin-like growth factorbinding protein-2 levels as diagnostic and prognostic biomarker of colorectal cancer," The Journal of Clinical Endocrinology & Metabolism, vol. 95, no. 4, pp. 1717–1725, 2010.

52.C. Pin ol-Felis, T. Ferna ndez-Marcelo, J. Vin as-Salas, and C. Valls-Bautista, "Telomeres and telomerase in the clinical management of colorectal cancer," Clinical and Translational Oncol- ogy, vol. 19, no. 4, pp. 399–408, 2017.

53.H.R. Hathurusinghe, K.S. Goonetilleke, and A.K. Siriwardena, "Current status of tumor M2 pyruvate kinase (tumor M2-PK) as a biomarker of gastrointestinal malignancy," Annals of Surgical Oncology, vol. 14, no. 10, pp. 2714–2720, 2007.

54.M. Kalia, "Personalized oncology: Recent advances and future challenges," Metabolism - Clinical and Experimental, vol. 62, no. 1, pp. S11–S14, 2013.

55.M. J. Duffy, N. O'Donovan, and J. Crown, "Use of molecular markers for predicting therapy response in cancer patients," Cancer Treatment Reviews, vol. 37, no. 2, pp. 151–159, 2011.

56.R. V. Iaffaioli, G. Facchini, A. Tortoriello et al., "Stop Flow in abdominal and pelvic cancer relapses," Frontiers in Bioscience, vol. 11, no. 2, pp. 1284– 1288, 2006.

57.A. D. Roth, S. Tejpar, M. Delorenzi et al., "Prognostic role of KRAS and BRAF in stage II and III resected colon cancer: results of the translational study on the PETACC-3, EORTC 40993, SAKK 60-00 trial," Journal of Clinical Oncology, vol. 28, no. 3, pp. 466–474, 2010.

58.G. Hutchins, K.Southward, and K. Handley, "Value of mismatch repair, KRAS, and BRAF mutations in predicting recurrence and benefits from chemotherapy in colorectal cancer," Journal of Clinical Oncology, vol. 29, no. 10, pp. 1261–1270, 2011.

59.D.Roock,B.Claes,D.Bernasconietal.,"Effects of KRAS, BRAF, NRAS, and PIK3CA mutations on the efficacy of cetuximab plus chemotherapy in chemotherapy-refractory metastatic col- orectal cancer: a retrospective consortium analysis," Lancet Oncology, vol. 11, no. 8, pp. 753–762, 2010.

60.H.-Y. LuoandR.- H.Xu ,"Predictive and prognostic biomarkers with therapeutic targets in advanced colorectal cancer," World Journal of Gastroenterology, vol. 20, no. 14, pp. 3858–3874, 2014.

61.M.Jhawer,S.Goel,A.J.Wilsonetal.,"PIK3CAMutation/PTEN expression status predicts response of colon cancer cells to the epidermal growth factor receptor inhibitor cetuximab," Cancer Research, vol. 68, no. 6, pp. 1953–1961, 2008.

62.Y. Shirota, J. Stoehlmacher, J. Brabender et al., "ERCC1 and thymidylate synthase mRNA levels predict survival for colorectal cancer patients receiving combination oxaliplatin and fluorouracil chemotherapy," Journal of Clinical Oncology, vol. 19, no. 23, pp. 4298–4304, 2001.

63.P. D. Leiphrakpam, A. Rajput, M. Mathiesen et al., "Ezrin expression and cell survival regulation in colorectal cancer," Cellular Signalling, vol. 26, no. 5, pp. 868–879, 2014.

64.M.Patara, E. M. M. Santos, R. De Almeida Coudry, F.A .Soares, F. O. Ferreira, and B. M. Rossi, "Ezrin expression as a prognostic marker in colorectal adenocarcinoma," Pathology & Oncology Research, vol. 17, no. 4, pp. 827–833, 2011.

65.G.Bulut,S.-H.Hong,K.Chenetal.,"Small molecule inhibitors of ezrin inhibit the invasive phenotype of osteosarcoma cells," Oncogene, vol. 31, no. 3, pp. 269–281, 2012.

66.A. R. Clarke, "Studying the consequences of immediate loss of gene function in the intestine: APC," Biochemical Society Transactions, vol. 33, no. 4, pp. 665-666, 2005.

67.P. Aghagolzadeh and R. Radpour, "New trends in molecular and cellular biomarker discovery for colorectal cancer," World Journal of Gastroenterology, vol. 22, no. 25, pp. 5678–5693, 2016.

68.T.-H. Chen, S.-W. Chang, C.-C. Huang et al., "The prognostic significance of APC gene mutation and miR-21 expression in advanced-stage colorectal cancer," Colorectal Disease, vol. 15, no. 11, pp. 1367–1374, 2013.

69.R. Hamelin, P. Laurent-Puig, S. Olschwang et al., "Association of p53 mutations with short survival in colorectal cancer," Gastroenterology, vol. 106, no. 1, pp. 42–48, 1994.

70.U. Kressner, M. Ingana s, S. Byding.. et al., "Prognostic value of p53 genetic changes in colorectal cancer," Journal of Clinical Oncology, vol. 17, no. 2, pp. 593–599, 1999.

71.G. S. Falchook and R. Kurzrock, “VEGF and dual-EGFR inhibition in colorectal cancer,” Cell Cycle, vol. 14, no. 8, pp. 1129- 1130, 2015.

72.D.J.Jonker,C.J.O’Callaghan,C.S.Karapetisetal.,“Cetuximab for the treatment of colorectal cancer,” The New England Journal of Medicine, vol. 357, no. 20, pp. 2040–2048, 2007.

73.D.Vallbo Hmerand.. H.-J .Lenz, “Epidermal growth factor receptor as a target for chemotherapy,” Clinical Colorectal Cancer, vol. 5, no. 1, pp. S19–S27, 2005.

74.S. Popat and R. S. Houlston, “A systematic review and meta- analysis of the relationship between chromosome 18q genotype, DCC status and colorectal cancer prognosis,” European Journal of Cancer, vol. 41, no. 14, pp. 2060– 2070, 2005.

75.J. Jen, H. Kim, S. Piantadosi et al., “Allelic loss of chromosome 18q and prognosis in colorectal cancer,” The New England Journal of Medicine, vol. 331, no. 4, pp. 213–221, 1994.

76.Y.Du,X.Zhou,Z.Huangetal.,“Meta-analysis of the prognostic value of Smad4 immunohistochemistry in various cancers,” PLoS ONE, vol. 9, no. 10, article e110182, 2014.

77.P. W. Voorneveld, R. J. Jacobs, L. L. Kodach, and J. C. H. Hardwick, “A meta-analysis of SMAD4 immunohistochemistry as a prognostic marker in colorectal cancer,” Translational Oncology, vol. 8, no. 1, pp. 18–24, 2015.

78.N. D. Sigglekow, L. Pangon, T. Brummer et al., “Mutated in colorectal cancer protein modulates the NFκB pathway,” Anti- cancer Reseach, vol. 32, no. 1, pp. 73–79, 2012.

79.Y. Wang, Y. Cao, X. Huang et al., “Allele-specific expression of mutated in colorectal cancer (MCC) gene and alternative susceptibility to colorectal cancer in schizophrenia,” Scientific Reports, vol. 6, article 26688, 2016.

80.Offit K. Genetic prognostic markers for colorectal cancer. N Engl J Med. 2000;342:124-125.

81.Thompson M., Perera R., Senapati A. and Dodds S. (2007) Predictive value of common symptom combinations in diagnosing colorectal cancer. British journal of surgery 94(10), 1260-1265.

82.Richards C.H. (2014) An investigation of the determinants of the local and systemic inflammatory responses in patients with colorectal cancer, University of Glasgow.

83.Cappell M.S. (2005) The pathophysiology, clinical presentation, and diagnosis of colon cancer and adenomatous polyps. Medical Clinics of North America 89(1), 1-42

84.Wactawski-Wende J., Kotchen J.M., Anderson G.L., Assaf A.R., Brunner R.L., O'Sullivan M.J., Margolis K.L., Ockene J.K., Phillips L. and Pottern L. (2006) Calcium plus vitamin D supplementation and the risk of colorectal cancer. New England Journal of Medicine 354(7), 684-696.

85.Mandel JS, Church TR, Bond JH, et al. The effect of fecal occult-blood screening on the incidence of colorectal cancer. N Engl J Med. 2000;343:1603-1607.

86.Winawer SJ, Flehinger BJ, Schottenfeld D, et al. Screening for colorectal cancer with fecal occult blood testing and sigmoidoscopy. J Natl Cancer Inst. 1993;85:1311-1318.

87.Thompson M., Flashman K., Wooldrage K., Rogers P., Senapati A., O'Leary D. and Atkin W. (2008) Flexible sigmoidoscopy and whole colonic imaging in the diagnosis of cancer in patients with colorectal symptoms. British journal of surgery 95(9), 1140-1146.

88.Yeowon choi, Hyosun choi, Chong II sohn. (2012) Optimal number of endoscopic biopsies in diagnosis of

advanced gastric and colorectal cancer. J.Korean med science, 2012 January; 27 (1): 36-39.

89.Yee J, Akerkar GA, Hung RK, et al. Colorectal neoplasia: performance characteristics of CT colonography for detection in 300 patients. Radiology. 2001;219:685-692 .

90.Spratt J.S. and Spjut H.J. (1967) Prevalence and prognosis of individual clinical and pathologic variables associated with colorectal carcinoma. Cancer 20(11), 1976- 1985.

91.Fireman Z, Kopelman Y. The colon: the latest terrain for capsule endoscopy. Dig Liver Dis. 2007;39:895-899.

92.Bernini A, Spencer MP, Wong WD, et al. Computed tomography guided percutaneous abscess drainage in intestinal dis- ease: factors associated with outcome. Dis Colon Rectum. 1997;40:1009-1013.

93.Dukes CE, Bussey HJ. The spread of rectal cancer and its effect on prognosis. Br J Cancer 1958;12:309-20.

94.AJCC. Cancer staging manual, 7th edition, New York, Springer, 2010.

95.Obrocea FL, Sajin M, Marinescu EC, Stoica D. Colorectal cancer and the 7th revision of the TNM staging system: review of changes and suggestions for uniform pathologic reporting. Rom J Morphol Embryol 2011;52:537-44.

96.Swanson RS, Compton CC, Stewart AK, Bland KI, The prognosis of T3 N0 colon cancer is dependent on the number of lymph nodes examined . Annals of surgical oncology 2003; 10 (1); 65-71.

97.Meyerhardt JA, Mayer RJ. Systemic therapy for colorectal cancer. N Engl J Med 2005; 352: 476

98.Gunderson LL, Sargent DJ, Tepper JE, et al. Impact of T and N substage on survival and disease relapse in adjuvant rec- tal cancer: a pooled analysis. Int J Radiat Oncol Biol Phys. 2002;54:386-396.

99.Johnson PM, Porter GA, Ricciardi R, et al. Increasing negative lymph node count is independently associated with improved long-term survival in stage IIIB and IIIC colon cancer. J Clin Oncol. 2006;24:3570-3575.

100. Devita ,Hellman, Rosenbergs cancer principles and practice of oncology 10th edition (2015).pages 778.

101. Sargent DJ, Marsoni S, Monges G, et al. Defective mismatch repair as a predictive marker for lack of efficacy of fluoro- uracil-based adjuvant therapy in colon cancer. J Clin Oncol. 2010;28:3219-3226.

102. Demmy TL, Dunn KB. Surgical and nonsurgical therapy for lung metastasis: indications and outcomes. Surg Oncol Clin N Am. 2007;16:579-605.

103. Francescutti V, Miller A, Satchidanand Y, et al. Management of bowel obstruction in patients with stage IV cancer: predictors of outcome after surgery. Ann Surg Oncol. 2013;20:707-714.

104. Greene FL, Stewart AK, Norton HJ. A new TNM staging for node positive (stage II) colon cancer; an analysis of 50,042 patients. Annals surgicals 2002; 236: 416-21.

105. QUASAR Collaborative group, Gray R, Barnwell J,et al. Adjuvant chemotherapy versus observation in patients with colorectal cancer; a randomized study. Lancet 2007; 370; 2020-9.

106. Dube S,Heyen F,Jenicek M.Adjuvant chemo therapy in colorectal carcinoma ; results of a meta analysis. Dis colon rectum 1997; 40: 35-41.

107. Engstrom P. NCCN Clinical practice guidelines in oncology; colon cancer, Available at: www. Nccn.org/ professionals/physicians_ gls/pdf/colon.pdf .2007.

108. Schwartz principles of surgery 10th edition .F.Charles Brunicardi page 1243.

109. Garcia-Aguilar J, Shi Q, Thomas CR Jr, et al. A phase II trial of neoadjuvant chemoradiation and local excision for T2N0 rectal cancer: preliminary results of

the ACOSOG Z6041 trial. Ann Surg Oncol. 2012;19:384-391.

110. Sauer R, Liersch T, Merkel S, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med. 2004;351:1731-1740.

111. Demmy TL, Dunn KB. Surgical and nonsurgical therapy for lung metastasis: indications and outcomes. Surg Oncol Clin N Am. 2007;16:579-605.

112. Park S.J., Lee K.Y. and Kim S.Y. (2008) Clinical significance of lymph node micrometastasis in stage I and II colon cancer. Cancer Research and Treatment 40(2), 75-80.

113. Chen S.L. and Bilchik A.J. (2006) More extensive nodal dissection improves survival for stages I to III of colon cancer: a population-based study. Annals of surgery 244(4), 602-610.

114. O'Connell J.B., Maggard M.A. and Ko C.Y. (2004) Colon cancer survival rates with the new American Joint Committee on Cancer sixth edition staging. Journal of the National Cancer Institute 96(19), 1420-1425.

115. McDermott F., Hughes E., Pihl E., Milne B. and Price A. (1984) Influence of tumour differentiation on survival after resection for rectal cancer in a series of 1296 patients. Australian and New Zealand Journal of Surgery 54(1), 53-58.

116. Simon G fisher ,Graeme poston, Liver resection for colorectal liver metastasis .Recent advances in surgery,Pages 41-50.

117. Renehan, A.G., Egger, M., Saunders, M.P., and O'Dwyer, S.T. Impact on survival of intensive follow up after curative resection for colorectal cancer: systematic review and meta-analysis of randomised trials. BMJ. 2002 Apr 6;

324: 813

118. Locker, G.Y., Hamilton, S., Harris, J. et al. ASCO 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer. J Clin Oncol. 2006 Nov 20; 24: 5313–5327

119. Duffy, M.J., van Dalen, A., Haglund, C. et al. Tumour markers in colorectal cancer: European Group on Tumour Markers (EGTM) guidelines for clinical use. Eur J Cancer. 2007 Jun; 43: 1348–1360

120. C.J., Aristei, C., Boelens, P.G. et al. EURECCA colorectal: multidisciplinary mission statement on better care for patients with colon and rectal cancer in Europe. Eur J Cancer. 2013 Sep; 49: 2784–2790

121. Hemming, K., Lilford, R., and Girling, A.J. Stepped-wedge cluster randomised controlled trials: a generic framework including parallel and multiple-level designs. Stat Med. 2015 Jan 30; 34: 181–196.

122. C Verbene, Z zhan, E van den Heuvel, I Grossman.Intensified follow-up in colorectal cancer patients using frequent Carcino-Embryonic Antigen (CEA) measurements and CEA-triggered imaging: Results of the randomized "CEAwatch" trial .EJSO for journal of cancer surgery 2015. EJSO 41 (2015) 1188e1196.

123. Pre-operative to post-operative serum carcinoembryonic antigen ratio is a prognostic indicator in colorectal cancer Zhenqiang Sun1,*, Fuqi Wang1,*, Quanbo Zhou1, Shuaixi Yang1, Xiantao Sun1, Guixian Wang1, Zhen Li1, Zhiyong Zhang1, onco target 2017. Vol 8 pp: 54672-54682.

124. Preoperative serum markers prognostic evaluation in colon cancer patients Luigina graziosi, Marino Elisabetta,Albert rebonato,Annibale Donini.J cancer science therapy 2018,Volume 10 (2).

125. Evaluation of the Relationship between Carcinoembryonic Antigen and TNM Stage in

Colorectal Cancer Omer Topdagi, Aysu timuroglu; Eurasian J Med 2018; 50: 96-8

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