ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor: 5.2
IJAR 2015; 1(13): 28-37
www.allresearchjournal.com
Received: 19-10-2015
Accepted: 21-11-2015

BJ Sharath Chandra
Professor and Unit chief, Department of General Surgery, JSSMH, JSS University, Mysore.

Sanjay Kumar
Post graduate, Department of General Surgery, JSSMH, JSS University, Mysore.

Suraj Girish
Undergraduate student JSSMH, JSS University, Mysore.

Correspondence
BJ Sharath Chandra
Professor and Unit chief, Department of General Surgery, JSSMH, JSS University, Mysore.

Evaluation of C- reactive protein as an early predictor of septic complications after elective colorectal Surgery

BJ Sharath Chandra, Sanjay Kumar, Suraj Girish

Abstract
Introduction: Intestinal resection and anastomosis is still by far the most common alimentary tract surgery done by the present day general surgeons. Resection done for various pathological causes, require an anastomosis method for the restoration of continuity of the intestine. This is associated with varied degree of morbidity and mortality. The breakdown of the suture line may result in peritonitis, fecal fistula formation and other fatal septic complications.
Safety in the gastrointestinal surgery may thus depend to a great extent on the factors that influence the healing of anastomosis, technical expertise of the operating surgeon in performing anastomosis and the type of anastomosis. However, with adequate supervision, there is little difference between the outcomes of anastomosis performed by trainees and those performed by established surgeons.
Aim and Objectives: To assess the changes occurring in the level of CRP with respect to the septic complications among patients undergoing elective colorectal surgery.

1. To assess the accuracy of C-reactive protein as an early predictor of septic complications after elective colorectal surgery.

Methods: Patients admitted in JSS medical college and hospital, Mysore during the study period i.e. October 2013 to October 2015, satisfying inclusion and exclusion criteria were studied. Who have undergone elective colorectal surgery.

- A standard Performa will be used during the initial evaluation of the patient to Obtain the relevant information.
- One Blood sample for CRP before surgery and other samples on postoperative days 2, 4, 6 and 9 will be taken.

All the measurements are done using SPSS version 21.0. The graphs were made using Microsoft Excel.
Results: In our study, APR accounted for majority of the procedure, in which 4 out of 10 cases had septic complications, 8 patients underwent LAR and 2 of them had septic complication. In total 30 colonic procedures 6 developed complication i.e. 20% (p-0.4), which is statistically less significant, probably as they are all elective surgeries.
In our study after elective colorectal surgery, surgical site infections were 16.7%, anastomotic leak 6.7% and mortality occurred in one patient i.e., 3.33%.
The diagnostic accuracy of CRP on POD 2 and POD 4 as a predictor of septic complications after elective colorectal surgery.
Our study showed CRP level, reached maximum on POD 4. So POD 4 CRP level has maximum sensitivity of (83.33%), specificity of (91.67%) and positive predictive value of 71.43% in the prediction of postoperative septic complications.
The mean cut of value of CRP in our study was 125 mg/l.
Conclusion: Our study suggested that serial CRP measurements after elective colorectal surgery could be used as a diagnostic biomarker in the early prediction of postoperative septic complications.
The present study shows that measurement of CRP on 4th POD can be used as an indicator for safe discharge from hospital after colorectal surgery.

Key words: Colorectal surgery, C-reactive protein, septic complications.

Introduction
Intestinal resection and anastomosis is still by far the most common alimentary tract surgery done by the present day general surgeons. Resection done for various pathological causes, require an anastomosis method for the restoration of continuity of the intestine.

This is associated with varied degree of morbidity and mortality. The breakdown of the suture line may result in peritonitis, fecal fistula formation and other fatal septic complications.

Safety in the gastrointestinal surgery may thus depend to a great extent on the factors that influence the healing of anastomosis, technical expertise of the operating surgeon in performing of the anastomosis and the type of anastamosis. However, with adequate supervision, there is little difference between the outcomes of anastomosis performed by trainees and those performed by established surgeons [1].

Colorectal cancer (CRC) is a formidable health problem worldwide. It is the third most common cancer in men (663000 cases, 10.0% of all cancer cases) and the second most common in women (571000 cases, 9.4% of all cancer cases) [2].

Almost 60% of cases are encountered in developed countries. The number of CRC-related deaths is estimated to be approximately 608000 worldwide, accounting for 8% of all cancer deaths and making CRC the fourth most common cause of death due to cancer. In India, the annual incidence rates (AARs) for colon cancer and rectal cancer in men are 4.4 and 4.1 per 100000, respectively. The AAR for colon cancer in women is 3.9 per 100000. Colon cancer ranks 8th and rectal cancer ranks 9th among men. For women, rectal cancer does not figure in the top 10 cancers, whereas colon cancer ranks 9th[3].

In the 2013 report, the highest AAR in men for CRCs was recorded in Thiruvananthapuram (4.1) followed by Bangalore (3.9) and Mumbai (3.7). The highest AAR in women for CRCs was recorded in Nagaland (5.2) followed by Aizwal (4.5) [3].

Objectives of the Study

1. To assess the changes occurring in the level of CRP with respect to the septic complications among patients undergoing elective colorectal surgery.
2. To assess the accuracy of C-reactive protein as an early predictor of septic complications after elective colorectal surgery.

Methodology

Materials and Methods

Source of Data

The source of data is from pre tested Performa. Which takes into account clinical history, general physical examination relevant investigations and imaging modalities and post-operative follow up samples of CRP protein were taken on days 2,4,6 and 9.

Patients admitted in JSS medical college and hospital in Mysore during October 2013 to October 2015. Who requires elective colorectal surgery in the form of resections and anastomosis.

Methods of Collection of Data

- Patients admitted in JSS Hospital who has undergone elective colorectal surgery.
- A standard Performa will be used during the initial evaluation of the patient to obtain the relevant information.

One Blood sample for CRP before surgery and other samples on postoperative days 2, 4, 6, and 9 will be taken.

All the measurements are done using SPSS version 21.0. The graphs were made using Microsoft Excel.

Mode of selection of cases and methods of analysis

Patients admitted in surgery ward of JSS hospital full filing inclusion criteria and exclusion criteria.

Study design

Prospective, observational study

Sampling

- Simple random sampling

Sample Size

30 samples

Inclusion Criteria

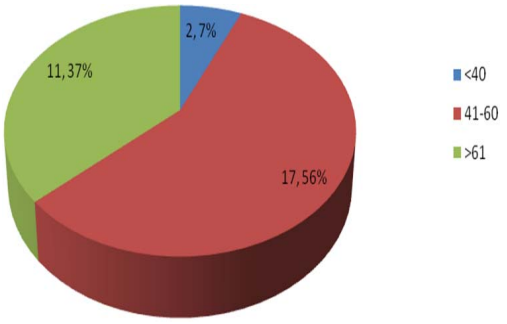
All patients requiring colorectal surgery in the form of resection and anastomosis.

Exclusion Criteria

1. Age<18years.
2. Pregnancy.
3. Emergency surgery.
4. Infection prior to surgery and
5. Hyperthermic intraperitoneal chemotherapy for carcinomatosis.

Results

1. Age Distribution



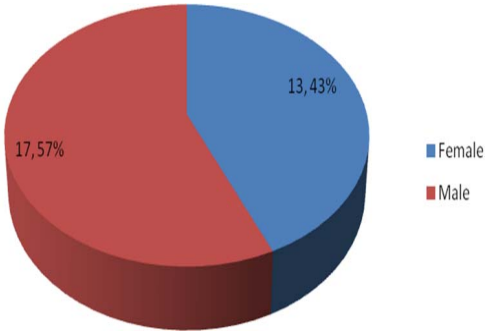
Graph 1: Age distribution

Table 1:

	Mean	Standard Deviation	Median	Minimum	Maximum
age	58.4	14.4	58.0	20.0	87.0

In our study mean age distribution 58 years. 56% belong to the age group 41 to 60 years. People aged 50-60 years are more prone to colorectal diseases.

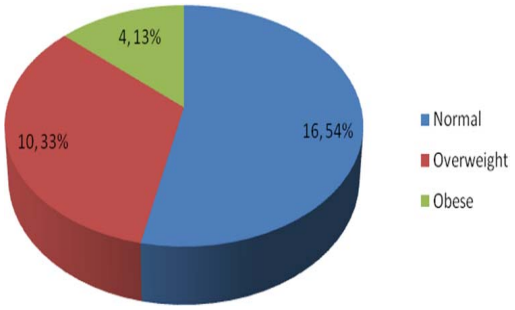
2. Sex distribution



Graph 2: Sex distribution

In our study male patients were more as compared to female. This is accordance with other studies.

3. Body mass index

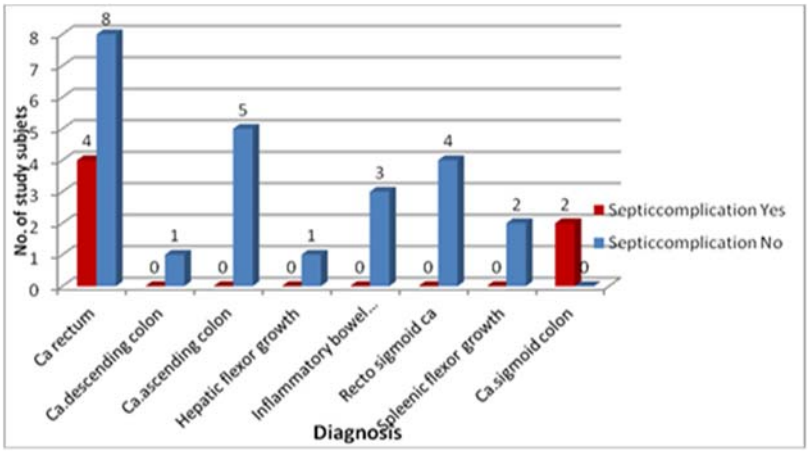


Graph 3: Body Mass Index

In our study patients with normal BMI were 16, i.e. 54% and obese patients were 4, i.e.13% and overweight were 10 patients i.e. 33%.

3. Distribution of colorectal Diseases

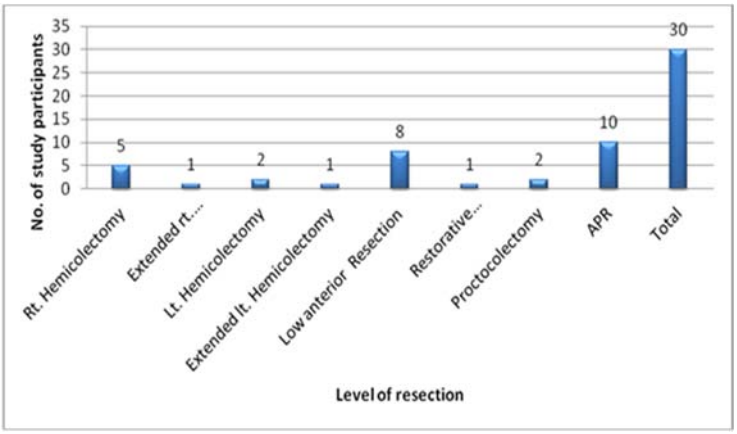
In our study carcinoma rectum was more common with 40% and least common was disease of descending colon. Incidence of carcinoma rectum is more common in other studies as well.



Graph 4: Distribution of colorectal Diseases

Level of Resection

As a site of resection anastomosis is a major predictor for post-operative septic complications. In our study majority were end colostomy, colo-colic anastomosis i.e. APR / LAR 60%



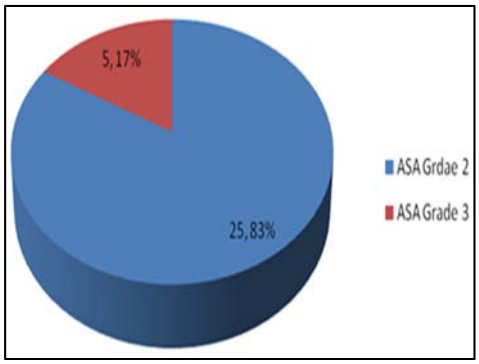
Graph 5: Level of Resection

Table 2: Variables affecting post-operative complications

	Mean	SD	Median	Minimum	Maximum
BMI	22.16	2.76	22.45	17.90	27.60
Preop albumin	4.01	.60	4.00	2.90	5.00
Preop TC	7475.30	1959.99	7827.00	1152.00	10600.00
Preop CRP	.57	.58	.35	.10	3.00
Duration of surgery	3.06	.42	3.10	2.30	4.00

Table 3: ASA Grade

ASA	n	%
2.00	25	83.3
3.00	5	16.7
Total	30	100

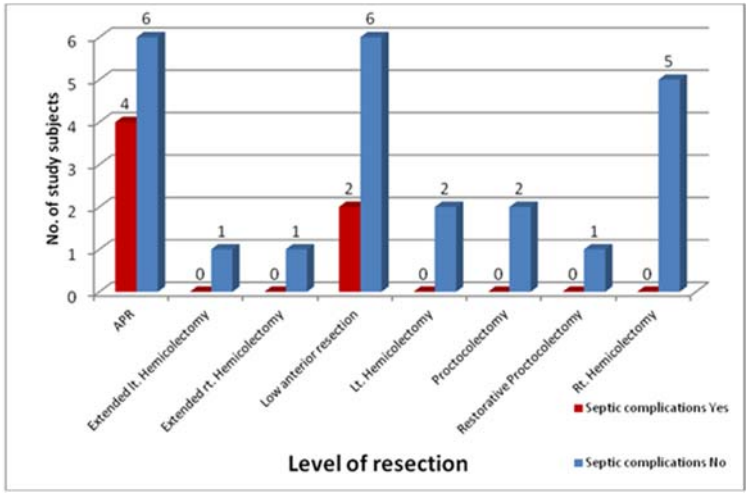


Graph 6: ASA Grade

Table 4: Level of resection anastomosis and septic complications

Level of resection	Septic complications			
	No		Yes	
	n	%	n	%
APR	6	60.0	4	40.0
Extended Lef.Hemicolectomy	1	100.0	0	.0
Extended Right Hemicolectomy	1	100.0	0	.0
Low anterior resection	6	75.0	2	25.0
Left. Hemicolectomy	2	100.0	0	.0
Proctocolectomy	2	100.0	0	.0
Restorative proctocolectomy	1	100.0	0	.0
Right Hemicolectomy	5	100.0	0	.0
Total	24	80.0	6	20.0

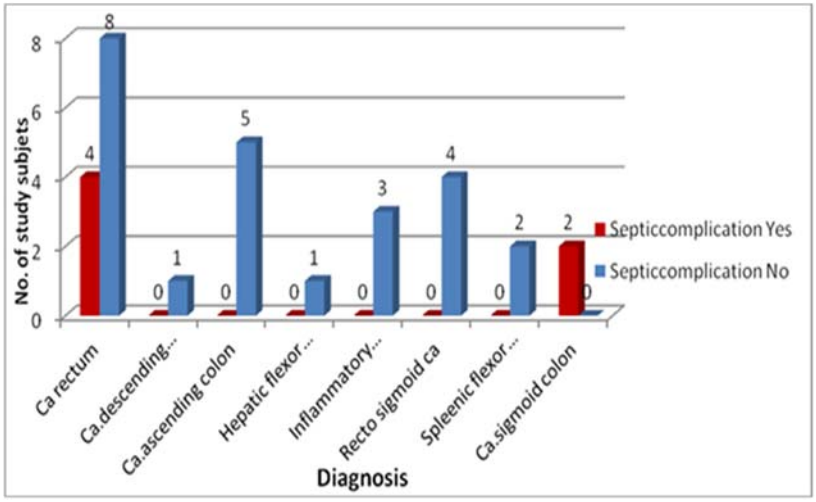
Chi-square test, p=0.4



Graph 7: Level of resection anastomosis and septic complications.

As incidence of carcinoma rectum is increasing, septic complication related to surgery arealso becoming more. In our study majority of complications are encountered in APR i.e. 40%, LAR 25% both are rectal disease procedure related complications, but are statistically less significant.

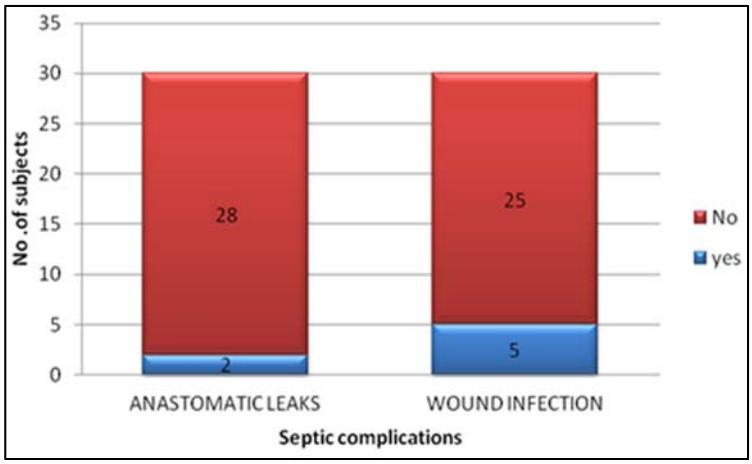
According to the literature procedure related complications are more in distal part of intestine, which coincides with our study involving disease of rectum, which is 66.7%.



Graph 8: Septic Complications

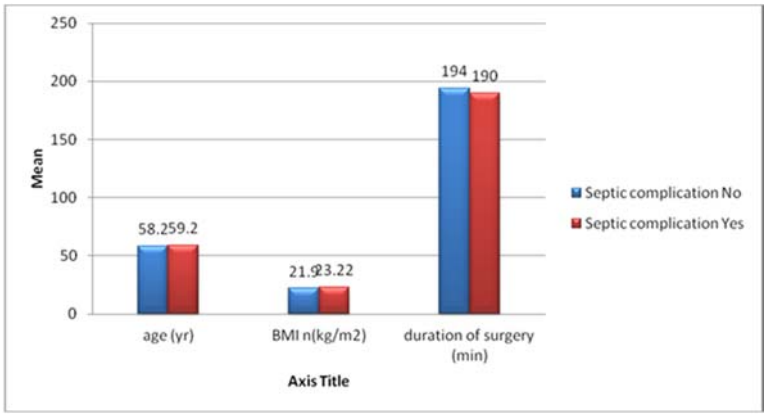
Table 5: Specific post-operative complications

Post op complications	n	%
Anastomatic_Leaks	2	6.7
Woundinfection- Ssi	5	16.7
Fistula /Sinus	0	.0
Pneumonia	0	.0
Post_Op_Adhesionstricture	0	.0



Graph 9: Specific post-operative complication

In our study after elective colorectal surgery surgical site infections was 16.7%, anastmotic leak was 6.7% and mortality occurred in one patient i.e., 3.33%.This is similar to the outcomes described in other studies.

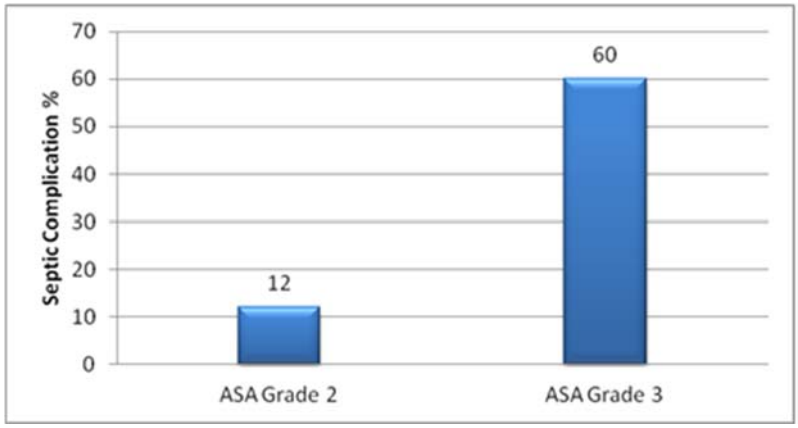


Graph 10: Variables affecting septic complications

Table 6: Variables affecting septic complications

		Septic complications				
		No		Yes		
		n	%	n	%	P
Age yrs	<40	2	100.0	0	.0	0.7
	41-60	13	76.5	4	23.5	
	>61	9	81.8	2	18.2	
BMI	Normal	14	87.5	2	12.5	0.3
	Overweight	8	80.0	2	20.0	
	Obese	2	50.0	2	50.0	
ASA	Grade 2	22	88.0	3	12.0	0.02
	Grade 3	2	40.0	3	60.0	

Chi-square test



Graph 11: ASA Grade affecting septic complications

ASA grade is considered one major risk factor for post-operative complication.

In our study patients with ASA grade 3 as associated with multiple complications ($P < 0.05$)

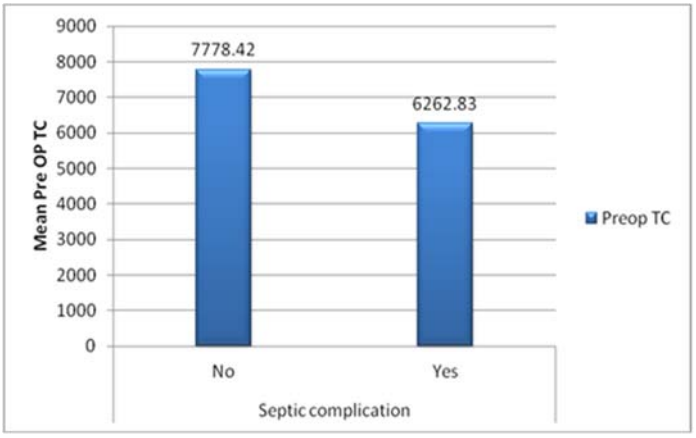
This is significant in our study. Apart from ASA grade other risk factor is pre- operative albumin level ($P<0.05$) which is significantly affect the outcome in our study.

Table 7: Variables affecting septic complications

	Septic complications						
	No			Yes			
	Mean	SD	Median	Mean	SD	Median	P
Preop Albumin	4.16	.55	4.15	3.43	.41	3.55	0.002
Preop TC	7778.42	1620.79	8002.00	6262.83	2827.00	7070.50	0.8
PreopCRP	.59	.62	.35	.50	.40	.45	0.9
DOS in min	194.0	24.1	195.0	190.0	36.2	175.0	0.7

Independent t test

Apart from ASA grade among other risk factor pre-operative albumin level ($P <0.05$) which is significantly affects out come in our study.



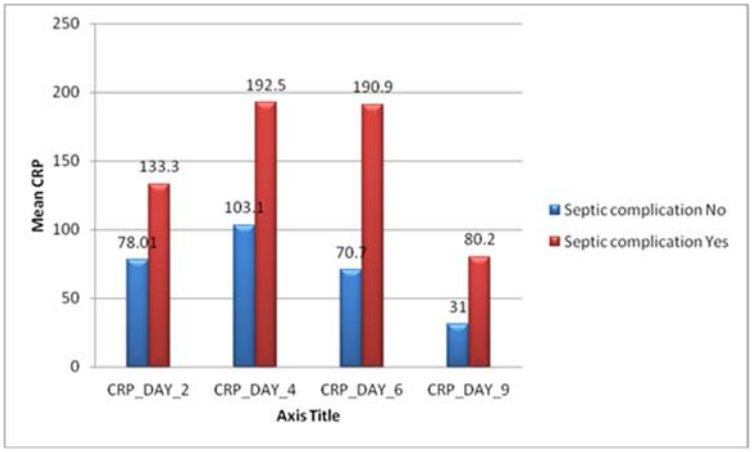
Graph 12: Total leukocyte count affecting post-operative complications

Table 8: CRP

	Septic complications						
	No			Yes			P
	Mean	SD	Median	Mean	SD	Median	
CRP_DAY_2	78.01	38.06	69.20	133.30	35.13	128.50	0.003
CRP_DAY_4	103.09	26.10	102.75	192.53	73.47	192.00	0.003
CRP_DAY_6	70.72	35.16	69.50	190.97	71.84	188.30	0.003
CRP_DAY_9	31.04	18.09	23.70	80.20	35.84	82.00	0.003

Mann Whitney test

In our study, CRP level at day 4 has maximum effect the outcome which was very significant compared at other day CRP level. Overall CRP level all the days have significant outcome in our study.

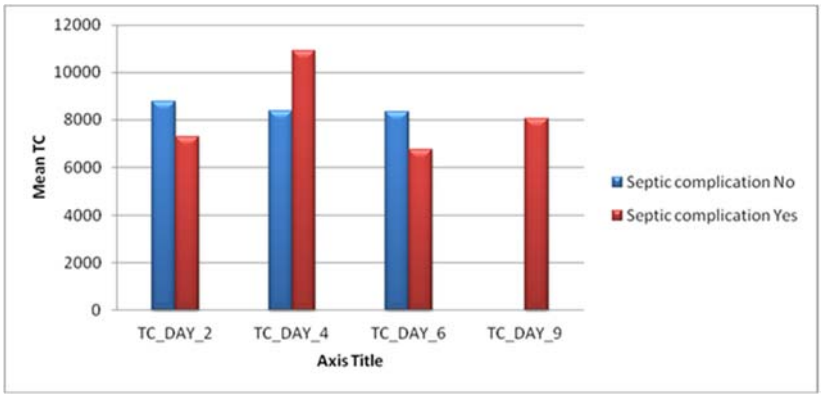


Graph 13: CRP

Table 9: Total leukocytescount affecting post-operative complications

	Septic complications						
	No (24)			Yes (6)			P
	Mean	SD	Median	Mean	SD	Median	
TC_DAY_2	8765.13	1000.75	8789.00	7291.42	5274.31	9530.00	0.5
TC_DAY_4	8376.92	1243.25	8140.00	10915.33	452.73	11000.00	<0.0001
TC_DAY_6	8353.00	1970.48	8136.00	6758.00	4634.81	8030.00	1
TC_DAY_9	.00	.	.00	8040.00	.	8040.00	NA

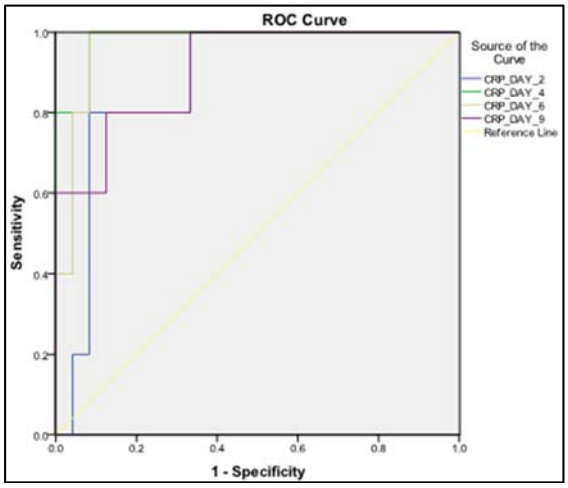
Mann Whitney test



Graph 14: Total leukocytes count affecting post-operative complications

Increased total leukocytes count predicts the ongoing septic complications. This is correlated with CRP level at day 4 in our study. Total WBC count and CRP level together has more sensitivity in predicting ongoing sepsis.

AUC, CRP



Graph 15: ROC curve

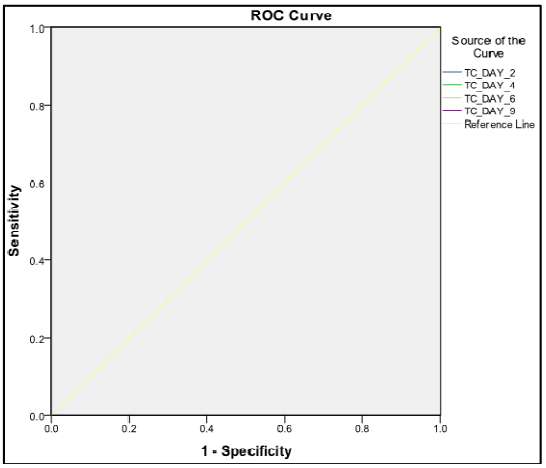
Area Under the Curve					
Test Result Variable(s)	Area	Std. Error[a]	p	Confidence Interval- 95%	
				Lower Bound	Upper Bound
CRP_DAY_2	.875	.072	.009	.735	1.000
CRP_DAY_4	.983	.021	.001	.942	1.000
CRP_DAY_6	.967	.031	.001	.906	1.000
CRP_DAY_9	.908	.068	.005	.775	1.000

In our study CRP level reached maximum at POD 4.Base on ROC curve, cut of value was 125 mg/l, so POD4 CRP level has maximum sensitivity and specificity in predicting septic complications.

		Septic complication		Total
		No	Yes	
CRP (>125)	No	22	1	23
	Yes	2	5	7
Total		24	6	30

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	83.33%	43.65, 96.99
Specificity	91.67%	74.15, 97.68
Positive Predictive Value	71.43%	35.89, 91.78
Negative Predictive Value	95.65%	79.01, 99.23
Diagnostic Accuracy	90%	74.38, 96.54

TC Area Under the Curve					
Test Result Variable (s)	Area	Std. Error[a]	p	Confidence Interval -95%	
				Lower Bound	Upper Bound
TC_DAY_2	1.000	.000	.317	1.000	1.000
TC_DAY_4	1.000	.000	.317	1.000	1.000
TC_DAY_6	1.000	.000	.317	1.000	1.000
TC_DAY_9	1.000	.000	.317	1.000	1.000



Graph 16: Diagnosis

Discussion

Despite many advances in surgery, the quest for uneventful healing of the intestinal anastomosis remains a challenge after colon and rectal resections. Anastomotic leak is the most serious complication of surgical treatment and a significant obstacle to the successful treatment of patients with colorectal resection. It is more common after rectal surgery, between 8% and 14%, [4-6] compared to the colon, ranging from 3% to 7%. [7, 8] It has been shown that about 40% of clinically significant leaks are diagnosed after discharge from hospital and require readmission for abdominal symptoms. [24, 25] This rate is certainly increasing in the era of fast track colorectal surgery with earlier discharges from the hospital (usually as early as the fourth postoperative day). In our study majority of patients between 41-60 years of age and mean age presentation is 58.4years, male: female ratio 4:3.

The anastamotic leakage is a serious complication which should be diagnosed as early as possible to reduce the associated morbidity and mortality. Thus the need for an early diagnosis of anastomotic leakage becomes clear. However, this diagnosis is not always easy in the early postoperative period because of the few clinical manifestations present at that time, which contributes to increased morbidity and mortality.

According to Alves *et al*. [9], the delayed diagnosis (after POD 5) of anastomotic leakage is associated with a mortality rate of 18%, but minimal morbidity if diagnosed and treated before POD 5. Early detection of this complication is essential for timely institution of treatment, making early distinctive markers useful.

CRP is the most popular and widely available marker of the acute inflammatory response, [23] the production of CRP occurs almost exclusively in the liver by hepatocytes as part of the acute-phase response upon stimulation by interleukin (IL)-6, tumour necrosis factor-α, and IL-1-β originating at the site of inflammation. It is a pentameric protein with various molecular functions including complement activation and opsonisation [10]. Within 6 h after stimulation, CRP serum levels exceed normal values and peak after about 48 h. CRP has a nearly constant serum half-life of about 19 hours. Therefore, the CRP serum concentration is determined by its synthesis rate and reflects the intensity of the stimulus for acute inflammatory responses [11]. In numerous studies, the significance of the serial measurement of CRP in serum in detecting infectious complications of surgical treatment and/or AL was shown [12-15].

In our study majority were rectal carcinoma which was around 33.2%. There were 12 patients with carcinoma rectum. All of them underwent elective surgery out of which 4 of them had septic complications i.e. 66.7%. Other major cases involved were carcinoma ascending colon which was 20% but none of them developed any complication. There were 2 cases of carcinoma sigmoid colon both developed septic complication. This suggests that more distal the pathology in intestines more chances of septic complication. This observation is similar to the other studies as well.

In our study, APR accounted for majority of the procedure, in which 4 out of 10 cases had septic complications, 8 patients underwent LAR and 2 of them had septic complication. In total 30 colonic procedures 6 developed complication i.e. 20% (*p*-0.4), which is statistically less significant, probably as they are all elective surgeries.

In our study after elective colorectal surgery, surgical site infections was 16.7%, anastomotic leak 6.7% and mortality occurred in one patient i.e., 3.33%.Similar results observed in other studies with elective surgeries in their study group.

Among various risk factors involved in post-operative complication, in our study we studies BMI, pre-albumin level, pre-op TC and pre-op CRP level. Pre-operative hypoalbumienia has significant impact on post-operative outcome which has similar observation in other studies.

In this series, we observed that from the second postoperative day onwards, mean serum CRP was significantly higher in the group who developed leakage, and this marker remained elevated until the diagnosis of the complication. These results are consistent with others recently published study series.

The diagnostic accuracy of CRP on POD 2 and 4 as a predictor of septic complications after elective colorectal surgery (areas under the curve of 0.875 and 0.983, respectively) were only slightly similar to those obtained by Welsch *et al*. [17] (0.80 and 0.88, respectively) and François Radais *et al* (0.706 and 0.804, respectively).

In patients undergoing anterior rectal resection, Welsh *et al*. concluded that serum CRP levels above 140 mg/L on POD 3 had a sensitivity of 80%, specificity of 81% and positive predictive value of 85.7% in the prediction of postoperative complications.

Our study showed CRP level, reached maximum on POD4. So POD4 CRP level has maximum sensitivity of (83.33%), specificity of (91.67%) and the positive predictive value of 71.43% in the prediction of postoperative septic complications.

The mean cut of value of CRP in our study was 125 mg/L. Korner *et al*. have published a work similar to the present one, the study material including all types of colorectal surgery. Their methods and results are similar to the present study. They showed that CRP at POD 3 had 82% accuracy (we obtained 90% at POD 4). They had a higher cut-off than the present studies (190 vs. 125 mg/l), obtaining a similar sensitivity (82%) for the detection of postoperative septic complications. It is well known that CRP peaks between POD 2 and 3 and then declines. This may explain the higher cut-off value obtained at POD 3 by Korner *et al*. Which we obtained at POD 4. They also obtained a similar accuracy in POD 5 and 7, as we did in POD 6 (91%). This tallying between both works is a strong argument in favour of the usefulness of the CRP in this setting [18].

This seems to suggest that the early and sustained elevation of postoperative serum CRP may be used as a predictor of anastomotic leakage in patients in whom other infectious complications (respiratory, urinary tract and surgical wound infections) have be excluded.

The changes observed in postoperative CRP levels in patients who developed leakage demonstrate the presence of an inflammatory process and the activation of hepatic synthesis of CRP immediately after the surgical procedure (and before the occurrence of clinical manifestations). As the synthesis of this inflammatory marker is dependent only on the liver function and not compromised by any other organ failure, the rate of CRP production actually reflects the intensity of the inflammatory process [16]. Tissue ischemia at the suture line of a leaking anastomosis seems to be responsible for the appearance of an intense and early inflammatory response, with subsequent increased synthesis of CRP [16]. The theory stating that poor tissue perfusion

increases the risk of anastomotic complications could be demonstrated in several studies [19-22].

Establishing a cut-off value for clinical decision making in general is often a trade-off. For safe early discharge (for example in the setting of fast track surgery), it is more important to detect most complications than to avoid unnecessary further investigation. The present work was done in order to define the conditions for a safe discharge prior to start a program of fast-track surgery. We would prefer to decrease morbidity and readmission rates, even at the cost of increasing the duration of hospital stay for a minority of patients due to false positive results. Thus, we preferred to obtain high sensitivity (83.33%) and a high negative predictive value (95.65%). This choice prompted the selection of the cut-off at 125 mg/l on POD 4, Welsch *et al.* chose a higher cut-off value (140 mg/l), thus obtaining lower sensitivity (54.3%) and a higher specificity, Warschkow *et al*. Demonstrated that CRP values exceeding 123 mg/l on POD 4 where associated a higher risk of septic complications. These authors found that CRP level above 143 mg/L had a good diagnostic accuracy to detect infectious complications with an AUC ROC 0.76.

The total leukocyte count on POD 4 was significantly higher in patients with septic complications but its accuracy was much lower than for CRP, so the total leukocyte count is not asuseful as the serum CRP which rises much earlier. Our findings are similar to those reported in several other studies. Combination of CRP and total leukocyte count is more accurate in detecting risk for anastomotic leak.

Our results show that the anastomotic leak was clinically significant on POD 4. CRP is a non-specific, systemic, manifestation of an active inflammatory process; but our results show that, in the elective colorectal surgery, its elevation on POD 4 should be considered as an alarm to avoid discharging those patients.

Our study has some limitations. It is a single centre study and the number of clinical events is small which limits the statistical power of our analysis. Despite these limitations our study provides support to the use of serial measurements of CRP after elective colorectal surgery for early identification of patients at risk of developing septic complications.

Conclusion

Septic complications are inevitable companion of colorectal surgery in certain number of patients, and hence, its detection is of paramount importance because it allows early implementation of therapeutic measures to reduce the morbidity and mortality.

Our study suggested that serial CRP measurements after elective colorectal surgery could be used as a diagnostic biomarker in the early prediction of postoperative septic complications.

The present study shows that measurement of CRP on 4th POD can be used as an indicator for safe discharge from hospital after colorectal surgery.

Patients with CRP values higher than 125 mg/l should undergo further imaging (namely CT scan) to search for septic complications.

Daily postoperative CRP measurements may therefore be useful in identifying those patients requiring careful clinical reassessment and possibly imaging to confirm or exclude anastomotic leakage, especially if other sources of infection (such as the wound, chest or urinary tract) can be excluded.

References

1. WJ Hawkins. With adequate supervision, the grade of the operating surgeon is not a determinant of outcome for patients undergoing urgent colorectal surgery. Ann R Coll Surg Engl 2007; 89:760-65.
2. Globocan 2008: (http://globocan.iarc.fr/factsheets/cancers/colorectal.asp) (2008).
3. NCRP. Three-year report of the population based cancer registries- 2009-2011. National cancer registry programme, Indian council of medical research (ICMR), Bangalore, India, 2013.
4. Trencheva K, Morrissey KP, Wells M, Mancuso CA, Lee SW, Sonoda T *et al*. Identifying important predictors for anastomoticleak after colon and rectal resection: prospective studyon 616 patients. Ann Surg 2013; 257(1):108-13.
5. Komen N, Dijk J, Lalmahomed Z, Klop K, Hop W, Kleinrensink G *et al*. After-hours colorectal surgery: a risk factor for anastomotic leakage, Int J Colorectal Dis. 2009; 24(7):789-95.
6. Shiomi A, Ito M, Saito N, Hirai T, Ohue M, Kubo Y *et al*. The indicationsfor a diverting stoma in low anterior resection forrectal cancer: a prospective multicentre study of 222 patientsfrom Japanese cancer centers. Colorectal Dis 2011; 13(12):1384-9.
7. Rickert A, Willeke F, Kienle P, Post S. Management and outcomeof anastomotic leakage after colonic surgery. Colorectal Dis 2009; 12(10):216-23.
8. Krarup PM, Jorgensen LN, Andreasen AH, Harling H. A nationwide study on anastomotic leakage after colonic cancer surgery. Colorectal Dis 2012; 14(10):661-7.
9. A. Alves, Y. Panis, D. Trancart, J.M. Regimbeau, M. Pocard, P. Valleur. Factors associated with clinically significant anastomotic leakage after large bowel resection: multivariate analysis of 707 patients, World J Surg. 2002; 26:499-502.
10. Gabay C, Kushner I. Acute-phase proteins and other systemicresponses to inflammation, N Engl J Med. 1999; 340:6.
11. Vigushin DM, Pepys MB, Hawkins PN. Metabolic and scintigraphicstudies of radioiodinated human C-reactive protein inhealth and disease, J Clin Invest. 1993; 91(4):1351-7.
12. Kørner H, Nielsen HJ, Søreide JA, Nedrebø BS, Søreide K, Knapp JC. Diagnostic accuracy of C-reactive protein for intraabdominalinfections after colorectal resections, J Gastrointest Surg. 2009; 13(9):1599-606.
13. Woeste G, Müller C, Bechstein WO, Wullstein C. Increased serumlevels of C-reactive protein precede anastomotic leakage in colorectalsurgery, World J Surg. 2010; 34(1):140-6.
14. MacKay GJ, Molloy RG, O'Dwyer PJ. C-reactive protein as a predictorof postoperative infective complications following electivecolorectal resection. Colorectal Dis 2011; 13(5):583-7.
15. Ortega-Deballon P, Radais F, Facy O, D'Athis P, Masson D, Charles PE *et al*. C-reactive protein is an early predictor of septic complications after elective colorectal surgery, World J Surg. 2010; 34(4):808-14.
16. T. Welsch, S.A. Müller, A. Ulrich, A. Kischlat, U. Hinz, P. Kienle *et al*. C-Reactive protein as early predictor for infectious postoperative complications in rectal surgery, Int J Colorectal Dis. 2007; 22:1499-1507.

17. Welsch T, Müller SA, Ulrich A, Kischlat A, Hinz U, Kienle P *et al*. C-reactive protein as early predictor for infectious postoperative complications in rectal surgery, Int J Colorectal Dis. 2007; 22:1499-507.
18. Korner H, Nielsen HJ, Soreide JA, Nedrebo BS, Soreide K, Knapp JC. Diagnostic accuracy of C-reactive protein for intraabdominal infections after colorectal resections, J Gastrointest Surg. 2009; 13:1599-1606.
19. J.A. Attard, M.J. Raval, G.R. Martin, J. Kolb, M. Afrouzian, WD. Buie *et al*. The effects of systemic hipoxia on colon anastomotic healing: an animal model. Dis Colon Rectum 2005; 48:1460-1470.
20. A. Shandall, R. Lowndes, H.L. Young. Colonic anastomotic healing and oxigen tension, Br J Surg. 1985; 72:606-609.
21. W.G. Sheridan, R.H. Lowndes, H.L. Young. Tissue oxygen tension as a predictor of colonic anastomotic healing. Dis Colon Rectum 1987; 30:867-871.
22. A. Vignali, L. Gianotti, M. Braga, G. Radaelli, L. Malvezzi, V. Di CarloAltered microperfusion at the rectal stump is predictive for rectal anastomotic leakDis Colon Rectum 2000; 43:76-82.
23. Simon L, Gauvin F, Amre DK, Saint-Louis P, Lacroix J. Serumprocalcitonin and C-reactive protein levels as markers of bacterialinfection: a systematic review and meta-analysis. Clin Infect Dis 2004; 39(2):206-17.
24. Hyman N, Manchester TL, Osler T, Burns B, Cataldo PA. Anastomotic leaks after intestinal anastomosis: it's later than you think. Ann Surg. 2007; 245:254-8.
25. Alves A, Panis Y, Trancart D *et al*. Factor associated with clinically significant anastomotic leakage after large bowel resection: multivariate analysis of 707 patients, World J Surg. 2002; 26:499-52.