

Diagnostic accuracy of the postoperative C - reactive protein to albumin ratio in prediction of complications after major abdominal surgery

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ABSTRACT

Introduction: postoperative complications are common after surgery for both benign and malignant disease, and results in infections, extended hospital stay, delayed return to normal status, increased financial burden and long-term morbidity hence early recognition of surgical complications and management is of utmost importance. **Aim:** To assess the predictive value of C-reactive protein to albumin ratio (CAR) and C-reactive protein (CRP) in determining the post-operative complications following major abdominal surgeries. **Methods:** this two-year prospective observational study was carried out at acharya vinoba bhav hospital and risk factors for post-operative complications in 100 eligible patients who were undergone major abdominal surgeries were identified using uni and multivariate analysis. Cut Off values, PPV, sensitivity and specificity of CAR and CRP was analysed by ROC curve. **Results:** in our study 62% patient developed post-operative complications and CAR on post-op. day three found to be independent risk factor for prediction of post-op. complication and has higher PPV than CRP. CAR cut-off value of 2.16 is associated with more post op complications. **Conclusion:** From our study it can be hypothesized that patients having CAR value of more than 2.16 on post op day 3 should be monitored carefully for development of complications. So that early intervention could reduce the unwanted sequelae associated with it.

Keywords: Clavien-Dindo classification, C - reactive protein, infections, major abdominal surgery postoperative complications

Introduction

Postoperative complications after major abdominal surgery are reported in up to 40% of patients and pose a major clinical problem due to their association with increased morbidity and mortality.^[1,2] Apart from increased morbidity and mortality rates it results in longer in-hospital stay, higher costs and even increased cancer recurrence rates.^[1] Early diagnosis and treatment are paramount to improve these outcomes.

Stress response to surgical intervention because of augmented immune, neuroendocrine and metabolic response leads to

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increased postoperative complications.^[3] Surgical intervention leads to activation of inflammatory response and release of Pro-inflammatory cytokines like IL-1, IL-6 and TNF- α upon which liver responds with increase or decrease of acute phase protein like CRP, albumin, fibrinogen and complement component of C3 and C4.^[3] CRP has been widely studied to predict postoperative complications and also as a guide for safe discharge following colorectal surgery.^[4] But major drawback associated with using CRP alone as a marker for post-operative complications is its slow kinetics peaking values on 2nd or 3rd day which could be too late for intervention, whereas albumin shows immediate response to surgical stress and also a reliable predictor of deranged protein metabolism which occurs in response to surgical stress.^[3,4]

Thus, ratio of CRP to albumin will precisely reflect the inflammatory and nutritional status and could serve as marker

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of negative outcome. Recently, Ishizuka and colleagues^[5] found a significant correlation between negative oncological outcomes in colorectal cancer patients and an elevated CRP to albumin ratio. Therefore, we theorize that CAR could be used as a simple and reliable predictor to identify patient at risk for postoperative complications. In the present study, we have evaluated the correlation between CAR and postoperative complications and compared the diagnostic accuracy between postoperative CAR and CRP in these patients.

Materials and Methods

The present study was conducted in department of general surgery at Acharya Vinoba Bhave rural hospital. After approval from institutional ethical committee data of the all the eligible patient undergoing elective major abdominal surgeries between August 2017 to September 2019 was collected. Those Patients who were reoperated prior to third postoperative day, albumin infusion prior to operation or during two postoperative days, ileostomy or colostomy closure, multivisceral resection, inflammatory bowel disease, or incomplete laboratory data were excluded. Baseline characteristic, surgical parameters and clinical outcome of the patient were recorded in preformed proforma. CRP and Albumin level were measured preoperatively on the day before surgery and on third post -op day. Post-operative complications that occurred during hospital stay or within 30 days of discharge were recorded and graded as per validated Clavien-Dindo scale^[6]; grades I-II were considered as minor and III-IV were considered as major complications, respectively. Categorical and continuous data was statistically analysed using Pearson's Chi-squared test and Student's t-test. For logistic regression analysis, a univariate analysis was performed and statistically significance value was set at $P < 0.05$ and then Binary logistic regression analysis done to identify the risk factor independently associated with post op complication.^[7] ROC curve was drawn for CAR and CRP, to compare cut-off values, diagnostic accuracy by calculating PPV, sensitivity and specificity.^[7] All of the data was analysed using SPSS statistical software version 22.0.

Results

In the present study out of 100 patients enrolled, 62 (62%) developed complications. there was no significant difference

in mean age of patient in complication and non-complication group (45.9 yr vs 46.5 yrs). majority of surgeries were hepatobiliary (48%) followed by lower G.I surgery (28%). But there was statistically significant difference in other Parameters like pre-op. CRP, serum albumin, haemoglobin, ASA grade and post-op. CRP on day3, CAR on day 3, duration of surgery, blood loss between two group. [Table 1]. In complication group 37 patient (60%) had major complications, (Clavien-Dindo grade III – IV). After univariate analysis, statistically significant ($p < 0.05$) factors were entered in to forward stepwise pattern in binomial logistic regression and CAR on post-op. day 3, pre op haemoglobin were found to be statistically significant independent risk factor for post op complications. (p value < 0.05). [Table 2] further diagnostic accuracy of CAR and CRP on post-op. day 3 was analysed using ROC curve and compared. [Table 3, Figure 1] CAR found to have more diagnostic accuracy with area under curve of .86 (CRP,.82) and PPV of 90.4%(CRP,89.5%), Since both had close PPV so, Youden's index was calculated which was higher for CAR (.57 vs .53). [Table 3] Thus, CAR appears to have better predictive value than CRP in predicting post-op. complications.

Discussion

Post-op. complications following major surgery not only brings psychological trauma but also increases hospital stay, treatment

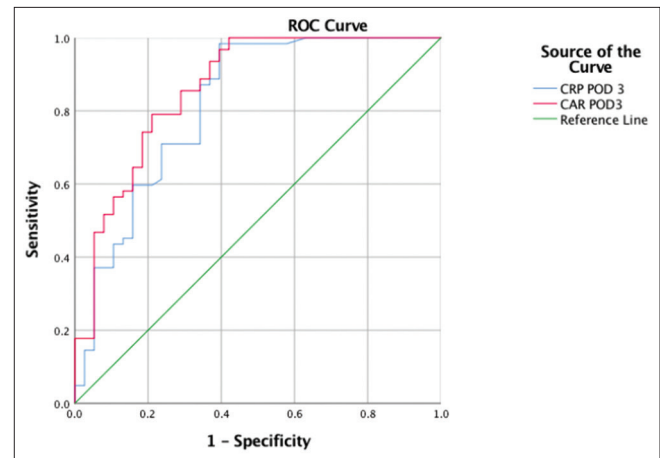


Figure 1: ROC curve showing postoperative CAR levels and CRP on POD 3 levels predictive of postoperative overall complications

Table 1: Baseline parameters of patients in both groups

Variables	Complication (n=62)	No Complication (n=38)	P
	Observations	Mean	
Age	45.9032±14.7667	46.4737±15.4373	0.854, NS
Pre- op Haemoglobin	10.8065±0.857	11.9750±0.9001	<0.001, S
Pre-operative CRP	7.52±3.62	4.97±2.81	<0.001, S
Pre-operative Albumin	23.63±3.24	31.53±4.81	0.001, S
Post-operative Day 3 CRP	101.92±41.14	56.67±38.04	<0.001, S
Post-operative Day 3 Albumin	24.6452±5.0864	30.9737±3.5601	<0.001, S
Post-operative Day 3 CAR	4.4921±2.4376	1.9347±1.5403	<0.001, S
Duration of Surgery	160.8065±40.9837	141.3158±35.9557	0.018, S
Blood Loss	214.1129±84.6280	153.4211±60.9065	0.015, S
ASA grade≥II	47	14	<0.001, S

Table 2: Binary logistic regression analysis of risk factors associated with postoperative complications

Coefficient	Estimate	Std. error	T	P
Intercept	6.6934946	2.2630287	2.958	0.00396
Albumin POD3	-0.0862492	0.0550732	-1.566	0.12084
ASA grade	-0.0996023	0.2641654	-0.377	0.70703
Blood loss	-0.0001767	0.0020803	-0.085	0.93248
CAR POD3	0.5892301	0.2152308	2.738	0.00746 (<0.05S)
CRP POD 3	-0.0127267	0.0089865	-1.416	0.16017
Duration of Surgery	-0.0007670	0.0043675	-0.176	0.86100
Preoperative CRP	0.0294987	0.0527538	0.559	0.57743
Pre-op Haemoglobin	-0.3763472	0.1335986	-2.817	0.00596(<0.05S)
Preoperative albumin	0.0273160	0.0400952	0.681	0.49744

Table 3: ROC curve analysis to compare the diagnostic accuracy of CAR and CRP on post-op. day 3 in predicting post-op. complications

Variable	CAR	CRP
Area under curve	0.862	0.818
Cut-off value	2.16	60.8
Sensitivity	87.10%	85.50%
Specificity	65.80%	71.1%
Positive Predictive Value	90.42%	89.54%
Negative Predictive Value	70.54%	78.46%
Youden's index	0.566	0.529

cost and delayed return to pre-morbid state. In the present stage of constrained medical resources and expensive medical treatment, we need a reliable and inexpensive marker which is easily available in general setting to identify impending post-op. complications for early and safe discharge. In our study, we found that CAR on day 3 with a cut-off value of 2.16 can be used as a reliable marker for predicting post-op. complications and it has a higher diagnostic accuracy than CRP alone (AUC of 0.862 vs 0.818). Any surgical intervention is associated with systemic inflammatory response which if increases or persists for longer time is associated with negative outcome therefore various inflammatory markers like modified Glasgow Prognostic Score (mGPS), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), postoperative Glasgow Prognostic Score (poGPS), and CRP to albumin ratio (CAR) have been studied to predict complications following surgery.^[8,9]

Watt *et al.*^[9] (2017) suggested prognostic role postoperative systemic inflammation score including postoperative C-reactive protein and albumin levels (C-reactive protein and albumin thresholds of >150 mg/L and <25 g/L, respectively) were associated with the development of infective complications ($p < 0.01$). Similar study conducted by Karayiannis *et al.*^[10] (2018); concluded that CAR on the post-op. day 3 has a better predictive value than CRP (AUC 0.721 vs 0.656). Patients with CAR > 2.0 suffered more complications following abdominal surgery (49.3% vs 22.1%, $P < 0.05$). Shibusani *et al.*^[4] (2016) found high preoperative CAR in colorectal cancer patients associated with worse relapse free ($p = 0.0015$) and tumour specific survival ($p = 0.0131$) and

may be superior modified Glasgow prognostic score (mGPS). Kim *et al.*^[11] reported that the CRP/albumin ratio at admission was positively correlated with prognosis in patients with severe sepsis or septic shock and also acts as a guide for early goal directed therapy.

In combination, CRP and albumin may be more valuable prognostic markers for outcomes across various diseases, providing both inflammatory and nutritional information.^[12] The combination of albumin and CRP into a single index has been suggested previously, and subsequent studies have shown that the CRP/albumin ratio is more consistent with prognosis than CRP or albumin alone.^[8] The CRP/albumin ratio has been extensively studied as an independent prognostic marker in patients with infection, malignancy, and other diseases.^[8,11] Results of our study were consistent with above mentioned study. the strength of our study was mix case load population of patients as most of other studies were conducted in single type of cases thus have a wider applicability but it has also limitation like single centre study, small sample size and Inclusion of cancer patients which usually have depleted nutritional status and an ongoing inflammation due malignancy. Despite of limitations, easy availability of test in general settings and consistent results of good diagnostic accuracy in various studies, CAR on third post-op. day can be used as a prognostic marker in predicting complications.

Conclusion

The current study established that an increased CRP/albumin ratio in post-operative period suggests ongoing deranged inflammatory and nutritional status and serves as a marker for likelihood of post-op. complications. Patients with CRP/albumin ratio greater than 2.16 should be intensively monitored for early detection of postoperative outcome to reduce postoperative complications, shorten hospital stay, and quickly return to pre-morbid functional activity. However further large center trials are needed to confirm the accuracy of this novel marker.

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Conflicts of interest

There are no conflicts of interest.

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