

Original Research Article

Surgical stress markers for postoperative complications: a prospective prognostic factor study

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Received: 22 March 2023

Revised: 14 April 2023

Accepted: 18 April 2023

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ABSTRACT

Background: Postoperative complications have previously been defined as “deviation from the normal postoperative course”. Although surgical advancements have reduced the postoperative mortality over the last few decades, the postoperative morbidity has remained high. Multiple factors as well as the severity of the surgical procedure itself are associated with adverse postoperative outcomes. Having prognostic factors established and available to assist with prognosis would be helpful in treatment planning and decision-making in post-operative patients. Objective of the study was to assess surgical stress markers as potential prognostic factors for postoperative complications.

Methods: This is a prospective cohort study conducted in department of general surgery over a period of 4 months. A total of 120 patients were included in the study. Data entry and statistical analysis were done using statistical package for the social sciences (SPSS) version 23. Chi-square test was used. Area under curve (AUC) and logistic regression were applied and odd's ratio was calculated in 95% confidence interval.

Results: Serum C-reactive protein (CRP) levels done at 72 hours, ALB levels at 24 hours were most predictive postoperative levels compared to the other perioperative serum levels.

Conclusions: Elevated serum CRP, albumin were associated with infective and non-infective complications and longer length of hospital stay and duration of the procedure.

Keywords: Post-operative complications, CRP, Albumin, Lactate

INTRODUCTION

Postoperative complications (POCs) have previously been defined as “deviation from the normal postoperative course”.¹ Although surgical advancements have reduced the postoperative mortality over the last few decades, the postoperative morbidity has remained high. In addition to the morbidity that patients suffer from, severe postoperative complications negatively affect postoperative outcomes, quality of life, financial burden and long-term prognosis.² It has been demonstrated that the impairment of microvascular blood flow both before

and after major abdominal surgery results in a higher rate of POCs.³

Multiple patient-related factors as well as the severity of the surgical procedure itself are associated with adverse postoperative outcomes.⁴ Many studies have confirmed that C-reactive protein (CRP) can be used as an inflammatory index to reflect the degree of trauma and inflammatory state.⁵ The plasma level of ALB reflects not only the nutritional status of the body, but also inflammation from surgical trauma. Galata et al found that the preoperative ALB level was an independent predictor

of major postoperative complications in Crohn's disease patients after colorectal surgery.⁶ The rationale for lactate monitoring in critically ill patients is based on the fact that hyperlactatemia is most often caused by tissue hypoperfusion and increased anaerobic glycolysis.⁷ Elevated lactate might also be due to an increased aerobic glycolysis, i.e., pyruvate production is higher than the capacity of pyruvate dehydrogenases, which occurs as a response to cytokine release, increased circulating catecholamines, or the accumulation of leukocytes at the site of inflammation.⁸

Having prognostic factors established and available to assist with prognosis would be helpful in treatment planning and decision-making in post-operative patients. The aim of our study is to assess if the surgical stress marker levels can predict the postoperative complications and death as potential prognostic factors within 30 days in patients undergoing elective surgeries.

METHODS

A prospective cohort study was done in the department of general surgery, Alluri Sita Ramaraju Academy of Medical Sciences for a period of 4 months from July 2022 to October 2022 on the post-operative population. This is an observational study.

Inclusion criteria

Patients over 18 years old; patients undergoing esophagus, gastric, liver, pancreas, endocrine, retroperitoneal, or colorectal surgery, uro gynaecological surgeries; and with operation time more than 2 hours were included.

Exclusion criteria

The patients who were on immunosuppressive therapy, with cognitive impairment or language comprehension problems, absence of the consent form prior to first blood sample, and orthopaedic and neurological surgeries were excluded.

Sample size was calculated by taking confidence interval (CI) at: 95%. The allowable error (l): 20% and assumed prevalence (P) is 44% (prevalence according to a study conducted by Alexandru Munteanu).⁹ Using the formula given, final sample size was rounded off to 125.

$$n = (Z_{\alpha/2})^2 pq / l^2$$

The sample was achieved by adopting convenient sampling method. The Institutional Ethics Committee of Medical College, Eluru reviewed the proposal for ethical consideration and approval was obtained prior to the study. Written consent was taken from all the respondents before data collection process.

For every patient the following data was recorded: sex, age, hospital stay in days, the duration of the procedure,

complications (fistulas, abscesses, general complications such as cardiac, pulmonary, liver, wound dehiscence, wound infections), serum albumin, lactate and CRP levels before surgery, on the 1st and 3rd day after the operation. Deaths were also recorded in the patients that occurs during the postoperative hospital stay. Each and every surgeon is equally experienced and qualified in performing these surgical procedures.

Plan of analysis

The data collected was analysed using Microsoft excel and trial version of statistical package for the social sciences (SPSS) 23 statistical packages. The data was presented in proportions and percentages using bar charts and pie charts. Qualitative data were expressed as frequency and percentage. Chi-square (χ^2) test of significance was used in order to compare proportions between 2 qualitative parameters. A p value less than or equal to 0.05 was considered statistically significant. The diagnostic performance of surgical markers was determined by receiver operating characteristics (ROC) curve analysis and calculation of the area under the ROC (AUROC). Logistic regression analysis was done and results were described as odds ratio (OR) and 95% confidence intervals (CIs).

RESULTS

Among 125 patients, only 120 were included as 5 refused to give blood sample multiple times. Table 1 concludes that 40 (33.3%) out of 120 patients experienced complications. 24 patients (60%) suffered from infective complications that includes wound infection, abscess and respiratory complications. 16 patients (40%) suffered from non-infective complications which consists of wound dehiscence, urinary retention and ileus.

When classified using Clavein-Dindo scale, 31 (77.5% of all patients) were grade 1-2 (i.e. required minor intervention), 9 (32.5% of all patients) were grade 3-4 (i.e. required major intervention). No mortality was seen.

Table 1: Post-operative complications by severity.

Complication	n	%
No complication	80	66.66
Any complication	40	33.33
Complication type		
Infective	24	60
Non infective	16	40
Complications severity (Clavein dindo grade)		
0	80	66.66
1	11	27.5
2	20	50
3	6	15
4	3	7.5
5	0	0

Table 2 shows that longer hospital stay ($p<0.002$) and duration of the procedure ($p<0.02$) were significantly associated with postoperative complications while age and gender were not associated with the rise in post-operative complications.

The lack of significance of Chi-square test indicates that the model is a good fit.

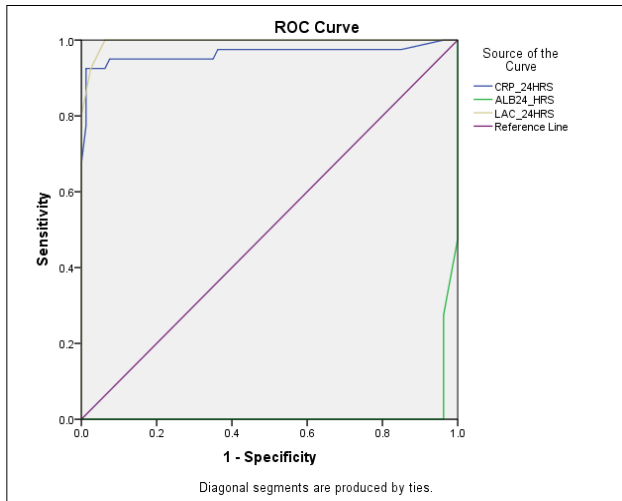


Figure 1: ROC curve analysis of markers post operatively at 24 hours.

Receiver operator characteristic ROC curve analysis for CRP levels 24 h postoperatively revealed an area under the curve (AUC) of 0.964 (95% confidence interval 0.917–1.000). ROC curve analysis for albumin 24 hours postoperatively as a marker for complications revealed an area under the curve (AUC) of 0.014 (95% confidence interval 0.000–0.031). ROC curve analysis for lactate 24 hours postoperatively revealed an area under the curve (AUC) of 0.995 (95% confidence interval 0.988–1.000).

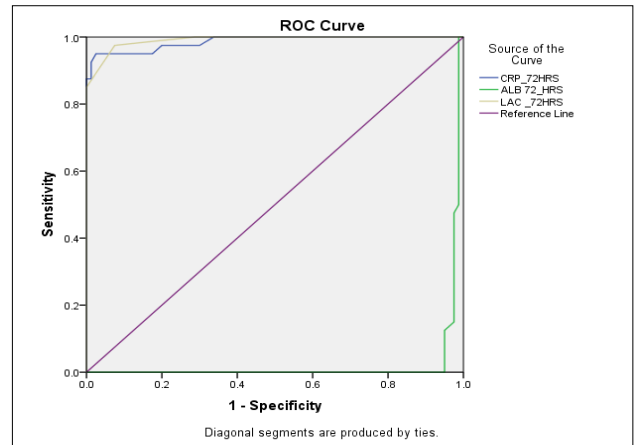


Fig 2: ROC curve analysis of markers post operatively at 72 hours.

Receiver operator characteristic ROC curve analysis revealed that CRP levels measured at 72 hours postoperatively had the highest predictive ability for post-operative complications with an AUC of 0.986 (95% confidence interval 0.968–1.000). ROC curve analysis for albumin levels 72 hours postoperatively revealed an AUC of 0.022 (95% confidence interval 0.000–0.050). ROC curve analysis for lactate levels 72 h postoperatively revealed an AUC of 0.991 (95% confidence interval 0.979–1.000).

Logistic regression analysis

Logistic regression analysis was performed to assess markers with highest predictive ability measured between 24 and 72 hours postoperatively for complications. It revealed CRP measured at 72 hours with highest predictive ability ($p=0.040$, $CI=1.006-1.314$). Albumin measured at 24 hours is found to be significant predictor for postoperative complications ($p=0.007$, $CI=0.00-0.288$). Lactate is not found to be significant predictor.

Table 2: Patients characteristics contributing to post-operative complications.

Characteristics	ALL	With complications		P value	Without complications	
		Interval	Frequency (%)		Interval	Frequency (%)
Age						
20-40	35	11	31.4	0.589	24	68.6
40-60	65	24	36.9		41	63.1
60-80	20	5	25		15	18.8
Gender						
Males	62	21	33.9	0.897	41	66.1
Females	58	19	32.8		39	67.2
Hospital stay (days)						
<8	69	15	21.7	0.002	54	78.3
>8	51	25	49		26	51
Duration of procedure (min)						
<180	66	16	24.2	0.020	50	75.8
>180	54	24	44.4		30	55.6

Table 3: Hosmer and Lemeshow Test.

Step	Chi-square	df	Sig.
1	0.313	8	1.000

Table 4: Logistic regression analysis.

Parameters	B	S.E.	Wald	df	Sig.	Exp (B)	95% C.I. for Exp (B)	
							Lower	Upper
CRP 72 hours	0.140	0.068	4.215	1	0.040	1.150	1.006	1.314
ALB 24 hours	-4.653	1.740	7.153	1	0.007	0.010	0.000	0.288
Constant	4.023	4.922	0.668	1	0.414	55.845		

Table 5: Complications seen in this study.

	Frequency (%)
Infective	
Wound infection	13(32.5)
Abscess	4 (1)
Wound leak	4 (1)
Respiratory complications	3 (7.5)
Non infective	
Wound dehiscence	8 (20)
Ileus	5 (12.5)
Urinary retention	3 (7.5)

Surgical stress markers like CRP levels at 72 hours predicted the post-operative infective complications and decrease in albumin levels i.e. albumin within 24 hours postoperatively was reliable to rule out the complications like wound infection, intra-abdominal abscess, wound leak, ileus, wound dehiscence, urinary retention and some respiratory complications like pneumonia.

DISCUSSION

The rate of postoperative complications in the current study was 33.3%. No deaths were recorded. Biological markers (CRP, albumin, and lactate) may play a significant role as independent predictors of mortality in critically ill patients. CRP is the most commonly available vector for detecting postoperative inflammation following major abdominal surgery and the most commonly used biomarker of infection in ICU patients which is similar to our study.¹⁰ The current study agrees with the study showing the CRP level on postoperative day (POD) 3 or 4 to be the best predictor of postoperative complications.¹¹ Meyer et al stated that an increase in CRP is a poor parameter for early detection of complications in critically ill surgical patients (odds ratio=0.983, 95% CI=0.932–1.036).¹² Present study can be validated by Örtqvist et al study on CRP and interleukin-6 on community-acquired pneumonia they support that CRP had diagnostic and prognostic importance to diagnose community-acquired pneumonia.¹³

Albumin is a negative acute phase protein with fast decline in case of inflammation. Study by Labgaa et al concluded that it is due to redistribution into the third space during

the first hours after various types of surgical procedures.¹⁴ They demonstrated in their cohort study of 138 patients after major abdominal surgery that a serum albumin drop greater than 2 g/l in the first postoperative days has an adverse outcome with [odds ratio: 6.89, 95% CI=2.96–16.14]. Ghoneima et al found that the preoperative CRP, haemoglobin (Hb), and ALB levels can act as predictors of septic complications in CD patients after surgery.¹⁵ Recently, some scholars have proposed that the CRP/ALB ratio (CAR) can predict postoperative complications in a timely manner in colorectal cancer, and its predictive value is better than that of CRP alone.¹⁶ This is consistent with Ranzani et al who examined CRP/albumin's ability to predict 90-day mortality in 334 patients.¹⁷ These authors found that the CRP/albumin ratio >2 in patients with sepsis/septic shock provided the highest sensitivity and responsiveness in predicting 90-days mortality. In our study we did not measure the CAR but proved that CRP and ALB independently were predictive.

In this study, higher serum CRP, albumin and lactate levels in the early postoperative period after the elective major surgeries were associated with an increased risk of POCs, a longer duration of hospital stay, despite similar postoperative care in all patients. We demonstrated that the lactate levels assessed at 12 hours following the operation had the highest predictive value of the adverse outcomes but on regression analysis, lactate was not found to be reliable. So we did not consider lactate levels as predictive marker of POCs. Bhat et al did a retrospective study among 207 patients and they revealed that ability to clear lactate is predictor for mortality among emergency admissions.¹⁸ Elevated serum lactate was associated with a longer length of hospital stay, with a p value of 0.043, consistent with other studies though their patients had a longer length of stay.^{19,20} CRP and albumin during the perioperative period had been studied, and the authors found that the antecedent CRP levels could predict hypoalbuminemia to some extent in the future, which reflected the close relationship between CRP and albumin.²¹

Limitations

The study was carried out at a tertiary health centre which could have caused random error especially at the time of sampling.

CONCLUSION

Elevated serum CRP, albumin was associated with infective and non-infective complications and longer length of hospital stay and duration of the procedure. Serum CRP levels done at 72 hours, albumin levels at 24 hours were most predictive postoperative levels compared to the other perioperative serum levels. Unlike other studies, lactate was not predictive in this study.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Bhupathi M, Mathi A, Sivakumar DCU. Surgical stress markers for postoperative complications: a prospective prognostic factor study. *Int Surg J* 2023;10:997-1001.