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Evaluation of the C-Reactive Protein to Serum Albumin Ratio (CAR) as a Biomarker to Predict Prognosis in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease.

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Abstract

Background: Acute exacerbation of COPD (AECOPD) carries substantial in-hospital mortality. The CRP-to-serum-albumin ratio (CAR) integrates systemic inflammation (CRP) with the catabolic-nutritional state (albumin) and may be a simple, low-cost prognostic marker. We evaluated admission and serial CAR for in-hospital mortality in AECOPD. ***Methods:*** Prospective observational cohort of 102 consecutive adults with AECOPD (Anthonisen criteria) at Amaltas Institute of Medical Sciences, Dewas, over 18 months. CAR was measured at admission, day 3, day 5, and at discharge/death. Survivors (n = 92) were followed at 1, 3, and 6 months. Discrimination for in-hospital mortality used ROC analysis with bootstrap confidence intervals; optimal cut-offs by the Youden index. ***Results:*** In-hospital mortality was 9.8% (10/102). Admission CAR was higher in non-survivors than survivors (median 41.3 vs 9.8; p = 0.002) and discriminated in-hospital mortality (AUC 0.799; 95% CI 0.597–0.955). At the optimal admission cut-off (CAR ≥ 34.81): sensitivity 80%, specificity 85.9%, PPV 38.1%, NPV 97.5%. Discrimination improved with serial measurement (day-3 AUC 0.925; day-5 AUC 0.977). CAR fell significantly from admission to day 5 in survivors (p < 0.001) but not in non-survivors (p = 0.85). ***Conclusion:*** CRP and serum albumin are inexpensive, routine tests, and CAR needs only their ratio. Admission CAR is a useful risk-stratifier in AECOPD, and serial (day-5) CAR further improves identification of patients at risk of in-hospital death. External validation in larger multicentre cohorts is required.

Keywords: Chronic obstructive pulmonary disease; Acute exacerbation; C-reactive protein; Serum albumin; CRP-to-albumin ratio; Prognosis; In-hospital mortality.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterised by persistent respiratory symptoms and airflow limitation that is not fully reversible, arising from chronic airway inflammation and structural remodelling. It is among the leading causes of death worldwide. The COPD is by definition confirmed when the post-bronchodilator FEV1/FVC ratio is less than 0.70 [1]. The continuous exposure to harmful substances smoke, pollution, occupational dust, etc. sustains the chronic inflammatory process that does not entirely resolve. These patients go through episodes of relative stability with acute decompensation by exacerbations. Such occurrences are the most dreaded clinical outcome.

Exacerbation happens when breathing becomes significantly and quantifiably worse than the baseline of the patient in his or her day-to-day functioning, and necessitates a modification in treatment [2]. The secondary effects of such episodes are well-known and alarming: the lung functioning becomes reduced under an accelerated rate [3], the quality of life drops significantly in almost all possible spheres, the cost of hospital treatment grows significantly more than the stable disease management needs. The risk of mortality during the episodes is by far the most critical clinical outcome, especially when it comes to patients with advanced illnesses and low physiological reserve.

The pathophysiology of COPD is multifactorial as it is characterized by chronic airway inflammation that is accompanied by uncontrolled oxidative stress, imbalance between proteases and antiproteases, and remodelling of lung tissue. All these cascades dramatically increase when there is exacerbation. Systemic circulation is leaked with inflammatory mediators such as IL-6 and TNF-alpha [4]. The level of serum C-reactive protein increases dramatically, because the liver increases the production of this inflammatory protein in reaction to the pro-inflammatory signals [5]. The elevation of CRP does not determine the cause of the elevation; it may be infections, tissue damage, or general inflammation [6]. CRP is a stronger predictor of exacerbation and accelerated deterioration in COPD populations [7].

Albumin takes a quite different course in the acute illness. Albumin, the major circulating protein in the body, the concentration of which decreases in the case of inflammation, which is due to a decrease in inflammatory conditions, a process that is indicative of two parallel biological processes. On the one hand, the direct inhibitory effect of pro-inflammatory cytokines on the production of hepatic albumin; on the other, malnutrition of the protein and progressive wasting which is one of the signs of the further development of COPD gradually drain the stores [8]. Poor hospital outcomes and high mortality in a broad clinical context are predicted by low serum albumin, independent of other variables [9-11].

MATERIALS AND METHODS

Study Design

A Prospective Cohort Study.

Our study involved a prospective cohort study with a 18-month follow-up (January 2023 to June 2024) in Amaltas Institute of Medical Sciences, Dewas, Madhya Pradesh a 1200-bed teaching hospital. The Department of Respiratory Medicine has 30 specifically allocated beds and handles about 400 COPD-related admissions every year.

Study Population

We recruited 102 sequential adult patients who were admitted with acute COPD exacerbation. Inclusion criteria included (a) patients aged 18 years or older, (b) spirometry-confirmed COPD (FEV1/ FVC ratio less than 0.70 after bronchodilator inhalation), (c) patients with Anthonisen criteria of an exacerbation of COPD (increased purulence of sputum, increased sputum volume, or dyspnea).We excluded patients with (a) active malignancy, (b) recent surgery (within 30 days), (c) antibiotic use within 72 hours preceding admission, (d) documented immunocompromise (HIV, on immunosuppressants), (e) declined to participate.

Statistical Analysis

CAR was calculated as serum CRP (mg/L) divided by serum albumin (g/dL). Continuous variables are summarised as mean ± SD and, because CAR was right-skewed, also as median (IQR); categorical variables as n (%). CAR was compared between survivors and non-survivors using the Mann–Whitney U test. Discrimination for in-hospital mortality used ROC curves; AUC is reported with 95% bootstrap confidence intervals (2000 resamples).

The optimal cut-off at each time point was the Youden index; patients with CAR ≥ the threshold were classified high-risk. Sensitivity, specificity, PPV and NPV were computed from the 2 × 2 table. Within-subject change from admission to day 5 was tested with the Wilcoxon signed-rank test. ROC analysis was repeated excluding the outlier P-44. $p < 0.05$ (two-sided) was significant. Analyses used IBM SPSS Statistics v26.0 and GraphPad Prism 9.

The study was approved by the Institutional Ethics Committee, Amaltas Institute of Medical Sciences, Dewas. Written informed consent was obtained from all participants; the study followed the Declaration of Helsinki and ICMR guidelines.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics (N = 102)

Characteristic	Value
Total patients	102
Age (years), mean ± SD	60.0 ± 12.4
Age range (years)	40 – 90
Male, n (%)	89 (87.3%)
Female, n (%)	13 (12.7%)
Smoking history >10 years, n (%)	54 (52.9%)
Hypertension, n (%)	12 (11.8%)
Diabetes mellitus, n (%)	7 (6.9%)
In-hospital mortality, n (%)	10 (9.8%)

Our cohort of 102 patients (89 male, 13 female; 87.3% male) had mean age 60.0 years (SD 12.4, range 40–90 years).

Table 2: Documented Comorbidity Profile

Category	n	%
Hypertension only	10	9.8%
Diabetes mellitus only	5	4.9%
Hypertension + diabetes mellitus	2	2.0%
No significant comorbidity	85	83.3%
Total	102	100.0%

Table 3: Serial CRP, Albumin, and CAR Values During Hospitalisation (N = 102, mean ± SD)

Time point	CRP (mg/L) mean±SD	Albumin (g/dL) mean±SD	CAR mean±SD	CAR median (IQR)
Admission	52.5 ± 51.7	3.02 ± 0.52	19.4 ± 22.0	10.7 (4.3–27.4)
Day 3	39.0 ± 44.0	3.06 ± 0.50	14.4 ± 19.3	6.7 (2.5–18.7)
Day 5	29.5 ± 47.0	3.16 ± 0.53	11.9 ± 28.0	3.9 (1.4–11.4)
Discharge / death	22.4 ± 44.4	3.21 ± 0.55	10.2 ± 33.6	2.2 (0.5–7.7)

Table 4: CAR in Survivors vs deceased

Time point	Survivors (n=92)	Deceased (n=10)	p-value*
Admission CAR	9.8 (4.3–21.7)	41.3 (35.2–72.8)	0.002
Day 3 CAR	5.5 (2.2–14.5)	42.1 (36.0–56.3)	< 0.001
Day 5 CAR	3.6 (1.2–9.0)	40.8 (31.8–53.7)	< 0.001
Discharge / death CAR	1.5 (0.4–4.5)	40.7 (29.8–58.6)	< 0.001

Table 5: Summary of Deceased Patients (n = 10)

Patient ID	Age	Sex	GOLD	Admission CAR	Day-5 CAR	Pre-admission adherence
P-18	61	M	III	82.55	56.29	Poor
P-30	41	M	III	50.48	39.66	Poor
P-31	77	M	II	36.43	37.54	Poor
P-32	76	M	IV	34.81	29.92	Poor
P-42	73	M	IV	5.24	21.89	Poor
P-44	46	M	III	104.98	248.57	Poor
P-63	90	M	IV	3.75	11.80	Poor
P-71	57	M	IV	38.36	106.44	Poor
P-81	41	M	III	80.22	46.02	Poor
P-85	53	M	III	44.27	41.98	Poor

Table 6: ROC Analysis – Diagnostic Performance at Optimal Cutoff

Parameter	Admission CAR	Day-3 CAR	Day-5 CAR
AUC	0.799	0.925	0.977
95% CI	0.597–0.955	0.821–0.989	0.937–1.000
Optimal cut-off	34.81	21.22	11.80
Sensitivity	80.0%	90.0%	100.0%
Specificity	85.9%	87.0%	85.9%
PPV	38.1%	42.9%	43.5%
NPV	97.5%	98.8%	100.0%

DISCUSSION

Our findings add to the limited literature evaluating CAR as a prognostic marker in AECOPD. Admission CAR was significantly higher in non-survivors (median 41.3 vs 9.8 in survivors; p = 0.002) and provided acceptable discrimination for in-hospital mortality (AUC 0.799), consistent with the prognostic role of systemic inflammation and hypoalbuminaemia in COPD [7,10]. The wide 95% CI (0.597–0.955) reflects the small number of events (10 deaths) and warrants cautious interpretation. Serial measurement improved discrimination, with day-5 CAR showing the strongest association. Importantly, CAR fell significantly from admission to day 5 in survivors (p < 0.001) but not in those who died (p = 0.85), indicating that failure of CAR to fall — rather than the admission value alone — marks a poor trajectory. The very high day-5 AUC (0.977) from only ten events is likely optimistic and needs validation.

Mechanistically, CRP elevation reflects systemic inflammation while a fall in albumin reflects catabolism and nutritional depletion [11,13]. Combined as a ratio, CAR captures the inflammatory–nutritional state more comprehensively than either alone, an approach first described for inflammation-based prognostication in oncology [14].

All 10 decedents (100%) had poor pre-admission adherence versus 64/92 survivors (69.6%) adherent. This unadjusted association is hypothesis-generating only: it is confounded by disease severity, was not based on post-discharge adherence (all deaths occurred during the index admission), and must not be interpreted causally.

Limitations: single centre; few events (n = 10) producing wide CIs and risk of overfitting (especially the day-5 model); predominantly male cohort; CAR highly skewed (median/IQR and non-parametric tests used); two deaths had low admission CAR (CAR misses non-inflammatory deaths); spirometry during exacerbation is unreliable; pre-admission adherence assessed retrospectively; post-discharge follow-up not reported here. External validation in larger, multicentre, sex-balanced cohorts with predefined cut-offs is needed.

CONCLUSION

The CRP-to-albumin ratio is a simple, inexpensive prognostic indicator in AECOPD. Admission CAR (AUC 0.799) provides acceptable risk stratification, and serial particularly day-5 CAR adds discriminative value, helping identify patients who need more intensive treatment. Because CRP and albumin are routine and low-cost, a simple threshold (approximately CAR $\geq$ 35) could flag higher-risk patients for closer monitoring, earlier intervention, and structured adherence and nutritional support [15]. These findings are exploratory and require prospective external validation before routine use.

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