



Role of the C-reactive protein/albumin ratio as a predictor of new-onset atrial fibrillation in critically ill patients

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Abstract:

Background: New-onset atrial fibrillation (NOAF) is a prevalent arrhythmia in critically ill cases. Serious mortality and morbidity are associated with it. The objective of this study was to assess the predictive value of the C-reactive protein (CRP)/albumin ratio (CAR) in critically ill patients admitted to the intensive care unit (ICU) regarding the occurrence of NOAF. **Results:** The participants in this observational research comprised 360 critically ill cases who were divided into two categories according to the onset of AF. Albumin and CRP levels in the serum were determined. CRP level divided by albumin level yielded the CAR ratio. NOAF predictors were identified utilizing multiple logistic regression analysis (MLRA). NOAF was found in 18 (5%) of the patients. The CAR was greater in cases with NOAF than in cases without NOAF ($p < 0.001$). The CAR was an independent predictor of NOAF according to MLRA (95% confidence interval (CI): 1.219-1.836; odds ratio (OR) = 1.496; $p < 0.001$). CAR exhibited a significantly larger area under the receiver operating characteristic (ROC) curves (AUC) in AF prediction compared to CRP (0.878 vs. 0.869; $p < 0.001$). The CAR cut-off point for AF prediction was 3.1. Additionally, a statistically significant predictor of ICU mortality was identified in CAR (95% CI: 0.848-0.929; AUC: 0.889; $p < 0.001$).

Conclusion: Patients who are critically ill with a high CAR at the time of admission have an increased risk of developing NOAF and worse clinical outcomes during hospitalization.

Keywords: C-reactive protein /albumin ratio; critical illness; new-onset atrial fibrillation

1. Background

NOAF is a prevalent arrhythmia in critically ill cases. NOAF varies in prevalence from 5% to 46% [1, 2]. Serious mortality and morbidity are associated with it [3, 4]. Existing evidence suggests that NOAF, while hospitalized, may elevate the likelihood of developing subsequent episodes of atrial fibrillation (AF), stroke [5], and readmission to the hospital [6]. The recognition of those who have the risk of acquiring NOAF and the implementation of the required precautions may reduce death and morbidity rates.

During a critical illness, atrial fibrillation is induced and maintained by many variables, including comorbidities and the intensity of the acute illness [7, 8]. Inflammation is vital to initiating and maintaining AF via inflammatory cell infiltration, fibrosis, and myocyte necrosis [9]. Numerous inflammatory biomarkers, most notably interleukin-6 (IL-6) and high-sensitive C-reactive protein (Hs-CRP), have been

identified as being elevated among individuals with different subgroups of atrial fibrillation (AF) in comparison to people with sinus rhythm [9].

A novel indicator linked to inflammation is the C-reactive protein (CRP)/albumin ratio (CAR). The CRP is a non-specific biomarker

of inflammation. Conversely, albumin is a vital peptide that functions as a blood carrier and regulates oncotic pressure within the body [10]. It has been shown that CAR is more precise than albumin or CRP levels alone for evaluating the inflammatory status in a number of cardiovascular [11, 12], cerebrovascular [13], and infectious diseases [14]. However, no prior research has been published regarding the correlation between CAR and NOAF in critically ill cases. This research sought to evaluate the utility of the CAR as a prognostic indicator for the occurrence of NOAF in intensive care unit-admitted critically ill individuals (the primary outcome) and its association with ICU mortality (the secondary outcome).

2. Methods:

Exclusion and inclusion criteria

From January to September 2023, this prospective investigation was carried out in the Critical Care Unit of Kasr Al-Ainy Hospital, Cairo University. The 360 critically ill individuals above 18 years of age who had been transferred to the ICU and possessed sinus rhythm as determined by a 12-lead ECG were recruited for the research.

The research project excluded individuals who satisfied any of the subsequent criteria: previous episodes of AF, a diagnosis of permanent or persistent AF, pregnancy, or

breastfeeding. Additionally, individuals who had end-stage kidney or hepatic diseases were ineligible.

Demographic data and clinical characteristics

Patient demographic information, including gender, age, comorbidities, and a primary reason for ICU admission, was gathered upon admission to the ICU. The patient's medical records (body temperature, breathing rate, pulse rate, and blood pressure) were evaluated upon admission. Furthermore, to assess the disease severity, the acute physiology and chronic health evaluation II (APACHE II) score was computed.

Laboratory findings and echocardiographic imaging

Initial serum concentrations of albumin and CRP were determined by drawing blood samples from patients upon admission into the ICU. Utilizing Roche Diagnostics Kits and a chemistry auto-analyzer (Hitachi 917), albumin concentrations were ascertained. The test kits provided by Teco Diagnostics (1268 N. Lakeview Ave., Anaheim, CA 92807, USA) were utilized to measure serum CRP. Normal albumin and CRP concentrations ranged from 3.5 to 5.2 g/dL and 0 to 5 mg/L, respectively.

In previous investigations, the CAR was computed by multiplying the CRP (mg/L) to

albumin (mg/L) ratio by 100 in order to ease comprehension [15]. Additionally, complete blood count, renal function, electrolytes, and arterial blood gas measurements were performed on blood specimens.

Echocardiography was conducted traditionally, utilizing a Philips Epiq 7 ultrasound system (Philips, MA, USA). Echocardiographic photos were obtained from the parasternal (long and short axis), apical (four and two chambers), as well as subcostal and suprasternal. The modified Simpsons methods assessed left ventricular volumes and systolic function.

Outcomes

The occurrence of any episode of NOAF throughout hospitalization, as detected by ECGs and rhythm strips, constituted the main result of the investigation. All individuals presented to the intensive care unit with a baseline ECG. Then, they were monitored with a rhythm recording during their ICU stay. NOAF had been established as AF attacks lasting 30 seconds or more, according to the European Cardiology Guidelines [16]. On the basis of the evolution of AF, cases were divided into two groups: group 1 (patients with NOAF) and group 2 (patients without NOAF). The correlation between CAR and ICU mortality among these patients constituted the secondary outcome.

Statistical methods

IBM SPSS version 28 (Armonk, New York, United States) was utilized to manage data and statistical analysis. Normality assessments were conducted on quantitative data utilizing the Shapiro-Wilk test, the Kolmogorov-Smirnov test, and direct data visualization techniques. Quantitative data were summarized using means and standard deviations, medians, and ranges in accordance with the principle of normality. Numerical and percentage summaries were compiled for the categorical data. In accordance with AF, quantitative data were compared employing the Mann-Whitney U test for non-normally distributed quantitative variables and the independent t-test for normally distributed quantitative variables. ROC analyses were performed to predict AF and mortality using CRP, albumin, and CAR. The diagnostic indices, areas under the curves with 95% confidence intervals, and optimal cut-off points were computed. Predictions of AF were made utilizing multivariate and univariate logistic regression analyses. Confidence intervals of 95% were computed for the odds ratios. Each statistical measure utilized a two-sided approach. *p* values below 0.05 were deemed to be statistically significant.

3. Results:

General and clinical characteristics

The baseline demographic, laboratory, and clinical results of the study population are detailed in Tables 1 and 2. Eighteen of the 360 patients (5%) acquired NOAF. Mortality was reported at 34.4%. The ICU length of stay was median at 5 days, with a range of 3 to 25 days; mechanical ventilation lasted median at 6 days, with a range of 3 to 25 days.

General characteristics according to AF

Those with AF demonstrated significantly higher AKI (38.9% vs. 17%, $p = 0.018$) than those without AF. The age and other parameters did not exhibit any statistically significant variations. (Table 3)

Clinical and laboratory findings according to AF

Cases with AF experienced considerably greater APACHE score (median = 25 vs. 12; $p < 0.001$), TLC (median = 17.5 vs. 8; $p < 0.001$), CRP (median = 200 vs. 50; $p < 0.001$), CAR (median = 6.8 vs. 1.5; $p < 0.001$), ICU stay (median = 12 vs. 4; $p < 0.001$), and mechanical ventilation duration (median = 10 vs. 6; $p = 0.007$) but lower hemoglobin (9.7 ± 1.6 vs. 11.1 ± 1.9 ; $p = 0.004$) and albumin (3 ± 0.5 vs. 3.2 ± 0.4 ; $p = 0.007$) compared to cases without AF. Additional laboratory and clinical variables did not differ statistically significantly (Table 4).

Those with AF had a greater mortality rate than those without (55.6% vs. 33.3%, respectively), but with borderline statistical significance ($p = 0.053$) (Table 4).

ROC analysis for CRP, albumin, and CAR to predict AF

ROC analysis was done for CRP, albumin, and CAR to indicate atrial fibrillation. Albumin demonstrated the lowest AUC of 0.641, with a 95% CI ranging from 0.493 to 0.790 ($p = 0.067$). The optimal cut-off point was ≤ 2.9 , at which specificity, sensitivity, NPV, and PPV were 86.8%, 44.4%, 96.7%, and 15.1%, respectively (Figure 1).

For CRP, the AUC was 0.869, with a 95% CI between 0.798 and 0.940 and a p -value less than 0.001, indicating excellent performance. The best cut-off point was >80 , at which specificity, sensitivity, NPV, and PPV were 70.5%, 94.4%, 99.6%, and 14.4%, respectively (Figure 1).

CAR had the highest AUC of 0.878, with a 95% CI between 0.811 and 0.945 and a p -value less than 0.001, indicating excellent performance. The optimal cut-off was > 3.1 , at which specificity, sensitivity, NPV, and PPV were 72.2%, 94.4%, 99.6%, and 15.2%, respectively (Figure 1).

ROC analysis for CRP, albumin, and CAR to indicate mortality

To predict mortality, ROC analysis was done for CRP, albumin, and CAR. Albumin had the lowest AUC of 0.629, with a 95% CI ranging from 0.568 to 0.690 ($p < 0.001$), indicating fair performance. The best cut-off point was ≤ 2.9 , at which specificity, sensitivity, PPV, and NPV were 92.4%, 28.2%, 66%, and 71%, respectively (Figure 2).

For CRP, the AUC was 0.885, with a 95% CI ranging from 0.843 to 0.926 ($p < 0.001$), indicating excellent performance of CRP. The ideal cut-off was > 67 , at which specificity, sensitivity, PPV, and NPV were 87.7%, 83.9%, 78.2%, and 91.2%, respectively (Figure 2).

CAR had the highest AUC of 0.889, with a 95% CI ranging from 0.848 to 0.929 ($p < 0.001$), indicating excellent performance. The ideal cut-off was > 2.2 , at which specificity, sensitivity, PPV, and NPV were 89.8%, 83.9%, 81.3%, and 91.4%, respectively (Figure 2).

Univariate and multivariate analysis to predict AF

All significant variables were included in multivariate and univariate logistic regression analyses to predict AF. Univariate regression analysis demonstrated that AKI (95% CI = 1.159-8.376; OR = 3.116; $p = 0.024$), hemoglobin (95% CI = 0.534-0.888; OR = 0.689, $p = 0.004$), albumin, (OR =

0.167, 95% CI = 0.046-0.604, $P = 0.006$), APACHE, (95% CI = 1.047-1.146; OR = 1.096; $p < 0.001$), TLC (95% CI = 1.034-1.175; OR = 1.102; $p = 0.003$), CRP (95% CI = 1.008-1.018; OR = 1.013; $p < 0.001$), and CAR (95% CI = 1.306-1.729; OR = 1.502; $p < 0.001$) were all predictors of AF (Table 5). In multivariate analysis, the sole primary indicator of AF was CAR. A rise of one unit was linked to a 50% greater incidence of AF (OR = 1.496, 95% CI = 1.219-1.836, $p < 0.001$) (Table 5).

4. Discussion:

This research evaluated the link between NOAF development and CAR value in critically ill ICU patients. It is worth mentioning that individuals who acquired NOAF during ICU hospitalization were more likely to have AKI than those who did not. CAR, WBC count, and CRP were significantly elevated in cases who acquired NOAF compared to those who did not. Meanwhile, patients who had NOAF exhibited decreased hemoglobin and albumin. Among the mentioned variables, the CAR emerged as a highly reliable predictor of NOAF occurrence in these patients.

In the current research, the observed incidence rate was determined to be 5%. Similarly, a retrospective study performed by Jacobs MS et al. explored that 6.4% of the

study group who were hospitalized in the ICU encountered NOAF during their stay [17]. While M. Wetterslev et al. established that 13.3% of ICU patients developed NOAF [18].

Although the precise mechanisms underlying the occurrence and progress of NOAF remain unknown, acute events during critical illness, particularly those of greater intensity, can increase the likelihood of developing arrhythmias as a result of the enhanced secretion of catecholamines, progressive impairment of autonomic function, and cardiac structural and electrical remodeling [19]. Inflammation, which is common during critical illness, can further raise the risk of arrhythmia formation as a consequence of atrial myocyte oxidative damage and direct infiltration of inflammatory cells [20]. Raised inflammatory markers in postoperative and sepsis cases are associated with a greater likelihood of AF development. [19]. Additionally, Meierhenrich et al. [21] stated that CRP concentrations in septic shock cases are significantly elevated prior to AF onset. Cases with NOAF had substantially elevated CRP levels compared to individuals without NOAF in the current study (median: 200 mg/L, IQR: 45-437 versus median: 50 mg/L, IQR: 10 - 358, respectively; $P < .001$). Similarly, in a research

investigation involving 782 individuals infected with SARS-CoV-2 [22], the authors observed that CRP levels were considerably elevated among those who acquired atrial fibrillation (AF) in comparison with individuals who had never acquired AF (median: 94.4 mg/dL; range: 51-148 and median: 20.65 mg/dL; range: 6.5-50.4, respectively; $p < 0.0001$).

Albumin concentrations were markedly lower among individuals with NOAF compared to those without NOAF in the current study (3 ± 0.5 mg/L versus 3.2 ± 0.4 mg/L; $p = 0.007$). This result is corroborated by the findings of van Beek et al. [23], who propose that in 97 ICU-admitted patients, low SA values were linked to NOAF development. Additionally, low concentrations of serum albumin upon admission to the ICU were identified by others [24] as a distinct predictor of ICU death rates *via* a multivariable approach (95% confidence interval 1.87 - 4.48; OR 3.74).

The present study demonstrated that people with NOAF exhibited notably elevated levels of CAR in comparison with individuals who maintained a typical sinus rhythm (median 6.8, IQR: 1.4-14.5 versus median: 1.5, IQR: 1-13.2, respectively; $p < 0.001$). In addition, the AUC for CAR was the highest at 0.878,

with a 95% CI of 0.811 to 0.945 ($p < 0.001$), showing excellent performance. The optimal cut-off was greater than 3.1%, with a specificity of 72.2% and a sensitivity of 94.4%.

Additionally, NOAF development can only be predicted independently by CAR (OR = 1.496, 95% CI = 1.219-1.836, $p < 0.001$). This implies that CAR may detect NOAF development more effectively than CRP. Consequently, a rising incidence of systemic inflammation among these patients lends credence to the notion that an underlying nutritional and/or inflammatory condition may contribute to the appearance of NOAF.

To date, no study has assessed the correlation between CAR and the occurrence of NOAF in critically ill cases. The prior investigations focused solely on individuals with sepsis or recovered from coronary artery bypass grafting (CABG) operations [11, 22] rather than encompassing a diverse population of cases transferred to the ICU.

In research by Karabacak et al. [11], the authors conducted an analysis of 830 individuals who underwent CABG. They observed that people who acquired postoperative atrial fibrillation following CABG had elevated levels of preoperative CAR compared to patients who maintained a typical sinus rhythm over the time following

surgery. Additionally, an elevated CAR value (CI: 1.598-2.142; OR: 1.854; $p < 0.001$) was identified as an independent predictor of postoperative atrial fibrillation.

Additionally, Pala et al. [25] found that CAR emerged as a reliable indicator of postoperative atrial fibrillation occurrence in a cohort of 336 patients who underwent CABG. (OR:19.164, 95% CI: 8.281-44.352, $p < 0.001$). Kelesoglu et al. [22] found in a separate investigation that SARS-CoV-2 patients who had NOAF possessed a higher CAR ($p < 0.001$) than those who did not have NOAF. CAR independently predicted NOAF, as determined by multivariate logistic regression (95% CI: 1.063-7.793; OR = 2.879; $p = 0.037$).

The present work identified the CAR at admission as an important indicator of higher death rates in critically ill cases, as determined by the ROC curve (95% CI 0.848 - 0.929; AUC 0.889; cut-off 2.2; $p < 0.001$). This discovery contributes to the existing literature on the prognostic significance of the CAR in these people. The potential correlation between CAR and death could be attributed to the involvement of inflammation. A retrospective cohort study was undertaken by Park et al. [26] involving 875 cases. Their investigation focused on assessing the prognostic significance of the

CRP/albumin ratio in order to predict mortality occurring 28 days subsequent to ICU admission. They demonstrated that the CRP/albumin ratio had a greater AUC for death than CRP ($p < 0.001$; 0.594 vs. 0.567). In 2,147 intensive care unit patients, a rise in CAR was found to be strongly linked with death risk, according to a separate study (27).

5. Conclusions:

In summary, this is the first research within the existing body of literature to evaluate the CAR as a predictor of NOAF occurrence among critically ill individuals confined to the ICU. The CAR value was discovered to be a highly accurate indicator of NOAF occurrence. In addition, CAR is potentially beneficial as a prognostic tool for predicting death in these individuals. Hence, the CAR, which is a rapid, cost-effective, and reproducible biomarker, could be employed for early treatment strategies to reduce ICU morbidity and mortality among these patients.

This study has some limitations. The CAR levels were only measured at the ICU admission. Follow-up with CAR could potentially enhance the validity of the findings. The study utilized a single center and involved a comparatively limited number of participants.

In the future, there is a need for larger and multicenter studies to fully investigate all potential AF factors. Notwithstanding these constraints, the findings of this research contribute valuable insights to the existing body of literature regarding the incidence of NOAF and hazards linked to its occurrence among critically ill cases.

List of abbreviations

NOAF: New onset atrial fibrillation

CAR: C-reactive protein /albumin ratio

ICU: Intensive Care Unit

APACHE II: Acute physiology and chronic health evaluation

CHF: Congestive heart failure

CAD: Coronary artery disease

LAD: left atrial diameter

LVEDD: left ventricular end-diastolic diameter

LVESD: left ventricular end-systolic diameter

IVSD: interventricular septal thickness at end-diastole

PWD: posterior wall thickness at end-diastole

TLC: total leucocyte count

MV: mechanical ventilation.

AKI: Acute kidney injury

CABG: Coronary artery bypass grafting

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6. References:

1. Kanji, S., D.R. Williamson, B.M. Yaghchi, M. Albert, and L. McIntyre (2012) *Epidemiology and management of atrial fibrillation in medical and noncardiac surgical adult intensive care unit patients.* Journal of Critical Care. 27(3): 326.e1-326.e8.DOI: 10.1016/j.jcrc.2011.10.011.
2. Seguin, P. and Y. Launey (2010) *Atrial fibrillation is not just an artefact in the ICU.* Critical care (London, England). 14(4): 182-182.DOI: 10.1186/cc9093.
3. Chen, A.Y., S.S. Sokol, J.P. Kress, and I. Lat (2015) *New-Onset Atrial Fibrillation Is an Independent Predictor of Mortality in Medical Intensive Care Unit Patients.* Annals of Pharmacotherapy. 49(5): 523-527.DOI: 10.1177/1060028015574726.
4. Rivero-Ayerza, M., W. Scholte op Reimer, M. Lenzen, DAMJ Theuns, L. Jordaens, M. Komajda, F. Follath, K. Swedberg, and J.G.F. Cleland (2008) *New-onset atrial fibrillation is an independent predictor of in-hospital mortality in hospitalized heart failure patients: results of the EuroHeart Failure Survey.* European Heart Journal. 29(13): 1618-1624.DOI: 10.1093/eurheartj/ehn217.
5. Frost, L., G. Engholm, S. Johnsen, H. Møller, and S. Husted (2000) *Incident stroke after discharge from the hospital with*

- a diagnosis of atrial fibrillation. The American Journal of Medicine. 108(1): 36-40.DOI: 10.1016/s0002-9343(99)00415-5.*
6. Walkey, A.J., B.G. Hammill, L.H. Curtis, and E.J. Benjamin (2014) *Long-term outcomes following development of new-onset atrial fibrillation during sepsis. Chest. 146(5): 1187-1195.DOI: 10.1378/chest.14-0003.*
 7. Bedford, J.P., J. Ede, and P.J. Watkinson (2021) *Triggers for new-onset atrial fibrillation in critically ill patients. Intensive and critical care nursing. 67: 103114-103114.DOI: 10.1016/j.iccn.2021.103114.*
 8. Bosch, N.A., J. Cimini, and A.J. Walkey (2018) *Atrial Fibrillation in the ICU. Chest. 154(6): 1424-1434.DOI: 10.1016/j.chest.2018.03.040.*
 9. Ren, Y., R.-X. Zeng, J.-J. Li, L.-H. Guo, D.-Y. He, Y. Li, P.-D. Liao, and M.-Z. Zhang (2015) *Relation of C-reactive protein and new-onset atrial fibrillation in patients with acute myocardial infarction: A systematic review and meta-analysis. International Journal of Cardiology. 190: 268-270.DOI: 10.1016/j.ijcard.2015.04.152.*
 10. Arques, S. (2020) *Serum albumin and cardiovascular disease: State-of-the-art review. Annales de Cardiologie et d'Angéiologie. 69(4): 192-200.DOI: 10.1016/j.ancard.2020.07.012.*
 11. Karabacak, K., E. Kubat, F.B. Akyol, M. Kadan, G. Erol, S. Doğancı, V. Yıldırım, and C. Bolcal (2020) *The C-reactive protein/albumin ratio as a new predictor for postoperative atrial fibrillation after coronary artery bypass graft surgery. Journal of Cardiac Surgery. 35(10): 2747-2753.DOI: 10.1111/jocs.14898.*
 12. Kalyoncuoglu, M. and G. Durmus (2020) *Relationship between C-reactive protein-to-albumin ratio and the extent of coronary artery disease in patients with non-ST-elevated myocardial infarction. Coronary Artery Disease. 31(2): 130-136.DOI: 10.1097/mca.0000000000000768.*
 13. Zhang, D., H. Yan, Y. Wei, X. Liu, Z. Zhuang, W. Dai, J. Li, W. Li, and C. Hang (2019) *C-Reactive Protein/Albumin Ratio Correlates With Disease Severity and Predicts Outcome in Patients With Aneurysmal Subarachnoid Hemorrhage. Frontiers in neurology. 10: 1186-1186.DOI: 10.3389/fneur.2019.01186.*
 14. Luo, B., M. Sun, X. Huo, and Y. Wang (2021) *Two new inflammatory markers related to the CURB-65 score for disease severity in patients with community-acquired pneumonia: The hypersensitive C-reactive protein to albumin ratio and*

- fibrinogen to albumin ratio*. *Open life sciences*. 16(1): 84-91.DOI: 10.1515/biol-2021-0011.
15. Kahraman, S., A.C. Dogan, G. Demirci, A.R. Demir, E. Yilmaz, H.Z. Agus, AK Kalkan, F. Uzun, and M. Erturk (2020) *The Prognostic Value of C-reactive Protein to Albumin Ratio in Patients with Isolated Degenerative Aortic Valve Stenosis Undergoing Surgical Aortic Valve Replacement*. *Brazilian journal of cardiovascular surgery*. 35(3): 299-306.DOI: 10.21470/1678-9741-2019-0114.
16. Potpara, T., N. Dagres, E. Arbelo, J. Bax, and C. Blomstrom-Lundqvist (2021) *2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the european Association of Cardio-Thoracic Surgery (EACTS)*. *Eur. Heart J*. 42: 373-498.
17. Jacobs, M.S., B. Loeff, A.C. Reidinga, M.J. Postma, M. Van Hulst, and RG Tieleman (2020) *Incidence, treatment and mortality of new-onset atrial fibrillation patients at the intensive care unit*. *Open heart*. 7(1): e001226-e001226.DOI: 10.1136/openhrt-2019-001226.
18. Wetterslev, M., et al. (2023) *Atrial Fibrillation (AFIB) in the ICU: Incidence, Risk Factors, and Outcomes: The International AFIB-ICU Cohort Study**. *Critical Care Medicine*. 51(9): 1124-1137.DOI: 10.1097/ccm.0000000000005883.
19. Klein Klouwenberg, P.M.C., et al. (2017) *Incidence, Predictors, and Outcomes of New-Onset Atrial Fibrillation in Critically Ill Patients with Sepsis. A Cohort Study*. *American Journal of Respiratory and Critical Care Medicine*. 195(2): 205-211.DOI: 10.1164/rccm.201603-0618oc.
20. Mihm, M.J., F. Yu, C.A. Carnes, P.J. Reiser, P.M. McCarthy, D.R. Van Wagoner, and J.A. Bauer (2001) *Impaired Myofibrillar Energetics and Oxidative Injury During Human Atrial Fibrillation*. *Circulation*. 104(2): 174-180.DOI: 10.1161/01.cir.104.2.174.
21. Meierhenrich, R., E. Steinhilber, C. Eggermann, M. Weiss, S. Voglic, D. Bögelein, A. Gauss, M. Georgieff, and W. Stahl (2010) *Incidence and prognostic impact of new-onset atrial fibrillation in patients with septic shock: a prospective observational study*. *Critical care (London, England)*. 14(3): R108-R108.DOI: 10.1186/cc9057.
22. Kelesoglu, S., Y. Yilmaz, E. Ozkan, B. Calapkorur, Z.B. Dursun, A. Ulu-Kilic, and D. Elcik (2021) *Usefulness of C-reactive protein/albumin ratio as a predictor of new-onset atrial fibrillation in SARS-COV-2*.

- Biomarkers in medicine. 15(13): 1167-1175.DOI: 10.2217/bmm-2020-0866.
23. van Beek, D.E.C., Y.A.M. Kuijpers, M.H.H. Königs, I.C.C. van der Horst, and T.W.L. Scheeren (2020) *Low serum albumin levels and new-onset atrial fibrillation in the ICU: a prospective cohort study*. Journal of Critical Care. 56: 26-30.DOI: 10.1016/j.jcrc.2019.11.011.
24. Atrash, A.K. and K. de Vasconcellos (2020) *Low albumin levels are associated with mortality in the critically ill: A retrospective observational study in a multidisciplinary intensive care unit*. The Southern African journal of critical care : the official journal of the Critical Care Society. 36(2): 10.7196/SAJCC.2020.v36i2.422.DOI: 10.7196/SAJCC.2020.v36i2.422.
25. Pala, A.A., A.K. As, Y.S. Urcun, M. Engin, Ş. Yavuz, and A.F. Özyazıcıoğlu (2022) *C-reactive protein/albumin ratio in predicting atrial fibrillation after coronary artery bypass grafting*. Cardiovascular Surgery and Interventions. 9(2): 066-072.
26. Park, J.E., et al. (2018) *The C-Reactive Protein/Albumin Ratio as a Predictor of Mortality in Critically Ill Patients*. Journal of clinical medicine. 7(10): 333.DOI: 10.3390/jcm7100333.
27. Deniz, M., P. Ozgun, and E. Ozdemir (2022) *Relationships between RDW, NLR, CAR, and APACHE II scores in the context of predicting the prognosis and mortality in ICU patients*. European Review for Medical and Pharmacological Sciences. 26(12).

Table 1: General characteristics of the patients under investigation

General characteristics		
Age (years)	Mean±SD	57±16
Sex		
Males	n (%)	182 (50.6)
Females	n (%)	178 (49.4)
Body mass index	Mean±SD	24±2
Diabetes	n (%)	129 (35.8)
Hypertension	n (%)	106 (29.4)
Smoking	n (%)	47 (13.1)
Sepsis	n (%)	64 (17.8)
Respiratory disease	n (%)	38 (10.6)
Neurological disease	n (%)	57 (15.8)
CHF	n (%)	44 (12.2)
CAD	n (%)	54 (15)
Acute kidney injury	n (%)	65 (18.1)
Cancer	n (%)	33 (9.2)

CHF: congestive heart failure; CAD: coronary artery disease.

Table 2: Laboratory results and clinical manifestations of the patients

The findings		
Mean arterial pressure	Mean±SD	66±7
Respiratory rate	Mean±SD	24±4
Heart rate	Mean±SD	100±7
Ejection fraction	Mean±SD	63±7
LAD	Mean±SD	3.8±0.4
LVESD	Mean±SD	3.3±0.5
LVEDD	Mean±SD	4.9±0.6
IVSD	Mean±SD	1±0.1
PWD	Mean±SD	1±0.1
APACHE	Median (range)	12 (6-45)
Hemoglobin	Mean±SD	11±1.9
TLC	Median (range)	8.1 (4-64)
Creatinine	Median (range)	1 (0.3-9)
CRP	Median (range)	50 (10-437)
Albumin	Mean±SD	3.2±0.4
CAR	Median (range)	1.6 (1-14.5)
Atrial fibrillation	n (%)	18 (5%)
Mortality	n (%)	124 (34.4)
ICU stay (days)	Median (range)	5 (3-25)
MV duration (days)	Median (range)	6 (3-25)

LAD: left atrial diameter; IVSD: interventricular septal thickness at end diastole; LVESD: left ventricular end-systolic diameter; LVEDD: left ventricular end-diastolic diameter; PWD: posterior wall thickness at end-diastole; APACHE: acute physiology and chronic health evaluation; TLC: total leucocyte count; CAR: CRP-Albumin ratio; MV: mechanical ventilation.

Table 3: General characteristics of the individuals under investigation according to AF

		AF		<i>p</i> -value
		Yes (n = 18)	No (n = 342)	
Age (years)	Mean±SD	61±11	57±16	0.345
Sex				
Males	n (%)	9 (50)	173 (50.6)	0.961
Females	n (%)	9 (50)	169 (49.4)	
Body mass index	Mean±SD	24±1	24±2	0.693
Diabetes	n (%)	5 (27.8)	124 (36.3)	0.465
Hypertension	n (%)	6 (33.3)	100 (29.2)	0.710
Smoking	n (%)	2 (11.1)	45 (13.2)	0.802
Sepsis	n (%)	3 (16.7)	61 (17.8)	0.899
Respiratory disease	n (%)	2 (11.1)	36 (10.5)	0.937
Neurological disease	n (%)	3 (16.7)	54 (15.8)	0.921
CAD	n (%)	2 (11.1)	52 (15.2)	0.635
CHF	n (%)	2 (11.1)	42 (12.3)	0.883
Acute kidney injury	n (%)	7 (38.9)	58 (17)	0.018*
Cancer	n (%)	1 (5.6)	32 (9.4)	0.586

**Significant p-value; CAD: coronary artery disease; CHF: congestive heart failure.*

Table 4: Laboratory and clinical findings of the studied patients according to AF

		AF		p-value
		Yes (n = 18)	No (n = 342)	
Mean arterial pressure	Mean±SD	65±6	66±7	0.429
Respiratory rate	Mean±SD	24±3	24±4	0.597
Heart rate	Mean±SD	102±5	99±7	0.09
Ejection fraction	Mean±SD	61±8	63±7	0.361
LAD	Mean±SD	3.9±0.4	3.8±0.4	0.153
LVESD	Mean±SD	3.2±0.6	3.3±0.5	0.554
LVEDD	Mean±SD	4.9±0.6	4.9±0.6	0.781
IVSD	Mean±SD	1±0.1	1±0.1	0.658
PWD	Mean±SD	1±0.1	1±0.1	0.606
APACHE	Median (range)	25 (10-33)	12 (6 - 45)	<0.001*
Hemoglobin	Mean±SD	9.7±1.6	11.1±1.9	0.004*
TLC	Median (range)	17.5 (6-30)	8 (4-64)	<0.001*
Creatinine	Median (range)	1.35 (0.5-7)	1 (0.3-9)	0.108
CRP	Median (range)	200 (45-437)	50 (10-358)	<0.001*
Albumin	Mean±SD	3±0.5	3.2±0.4	0.007*
CAR	Median (range)	6.8 (1.4-14.5)	1.5 (1-13.2)	<0.001*
ICU stay (days)	Median (range)	12 (4-25)	4 (3-25)	<0.001*
MV duration (days)	Median (range)	10 (3-20)	6 (3-25)	0.007*
Mortality	n (%)	10 (55.6)	114 (33.3)	0.053*

**Significant p-value; LAD: left atrial diameter; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; IVSD: interventricular septal thickness at end-diastole; PWD: posterior wall thickness at end-diastole; APACHE: acute physiology and chronic health evaluation; TLC: total leucocyte count; CAR: CRP-albumin ratio; MV: mechanical ventilation.*

Table 5: Univariate and multivariate logistic regression analysis to predict AF

	Univariate		Multivariate	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Acute kidney injury	3.116 (1.159-8.376)	0.024*	1.685 (0.479-5.931)	0.416
Hemoglobin	0.689 (0.534-0.888)	0.004*	1.119 (0.792-1.581)	0.523
Albumin †	0.167 (0.046-0.604)	0.006*	-	-
APACHE	1.096 (1.047-1.146)	<0.001*	0.979 (0.902-1.062)	0.608
TLC	1.102 (1.034-1.175)	0.003*	1.061 (0.988-1.14)	0.104
CRP †	1.013 (1.008-1.018)	<0.001*	-	-
CAR	1.502 (1.306-1.729)	<0.001*	1.496 (1.219-1.836)	<0.001*

**Significant p-value; 95% CI: 95% confidence interval; OR: odds ratio; APACHE: acute physiology and chronic health evaluation; TLC: total leucocyte count; CAR: CRP-albumin ratio; † Albumin and CRP were not included in the multivariate as they are part of the CAR.*

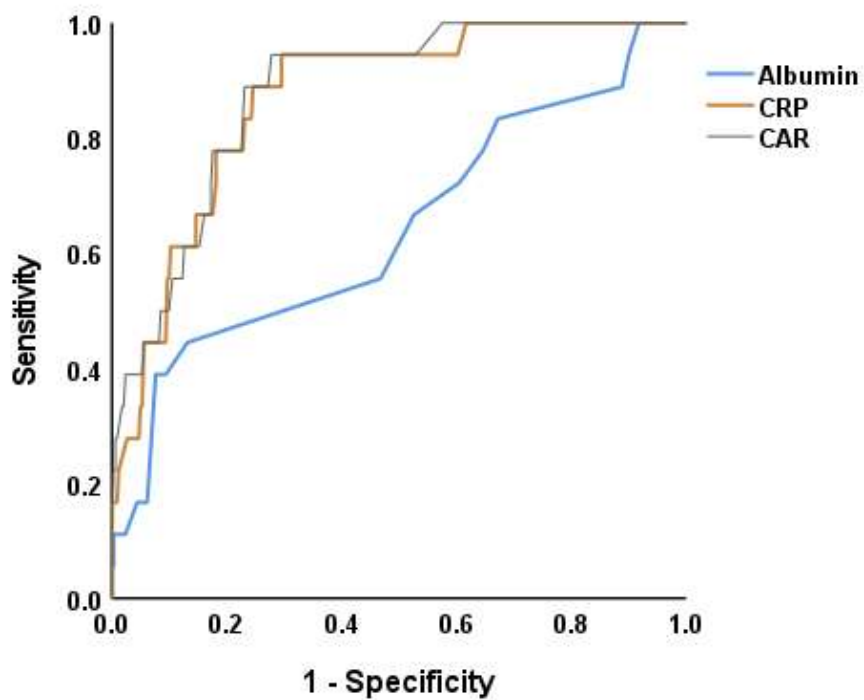


Figure1: ROC analysis for albumin, CRP, and CAR to predict AF.

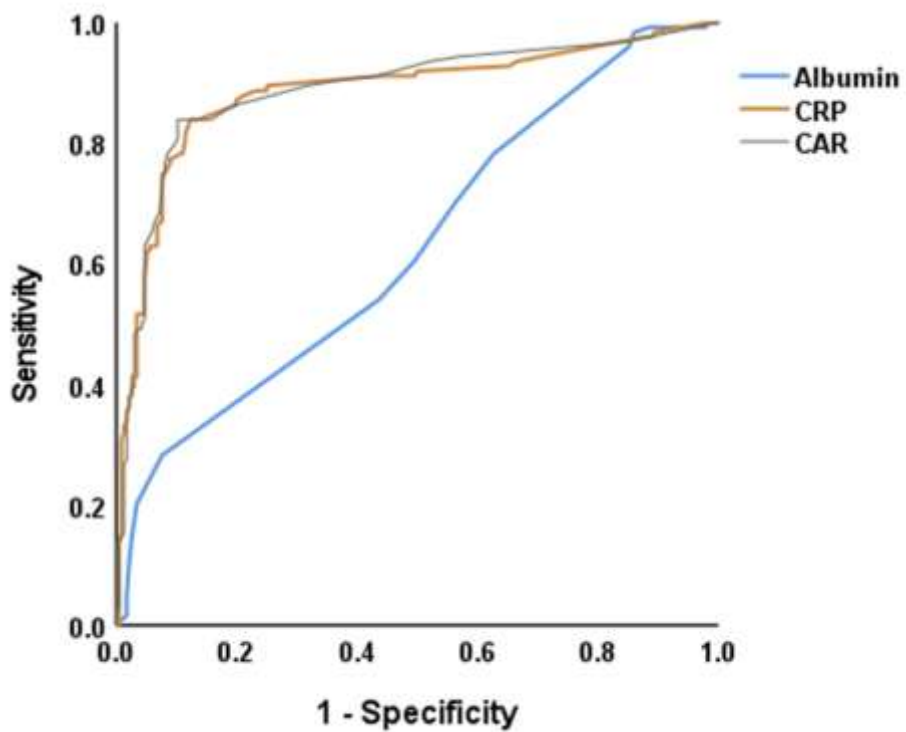


Figure2: ROC analysis for albumin, CRP, and CAR to predict mortality.