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Original Article

Prognostic value of the CRP/albumin ratio and serum lactate level in aneurysmal subarachnoid hemorrhage: a comparative biomarker study

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Abstract: Objectives: Aneurysmal subarachnoid hemorrhage (aSAH) is a severe neurological emergency with high morbidity and mortality. This study evaluated the prognostic value of the C-reactive protein (CRP)/albumin ratio and serum lactate levels in patients with aSAH. Methods: A retrospective cohort of 186 patients was analyzed. CRP, albumin, and lactate were measured daily over the first 14 days. The primary outcome was functional status at discharge. Secondary outcomes included incidence of vasospasm and 14-day mortality. Results: A CRP/albumin ratio > 10 and lactate > 2.5 mmol/L were independently associated with poor outcomes, higher vasospasm rates, and increased mortality. Conclusion: Both the CRP/albumin ratio and serum lactate are independent, clinically useful biomarkers for predicting poor outcome following aSAH.

Keywords: Subarachnoid hemorrhage, aneurysmal subarachnoid hemorrhage, C-reactive protein, albumin, CRP/albumin ratio, serum lactate, biomarkers, prognosis, vasospasm, neurological outcome

Introduction

Subarachnoid hemorrhage (SAH) is a neurological emergency most commonly caused by a ruptured intracranial aneurysm, and despite advances in neurosurgical care and neurocritical management, it is associated with high morbidity and mortality [1, 2]. The current gold standard for predicting the outcome of patients with aneurysmal subarachnoid hemorrhage (aSAH) is the modified World Federation of Neurosurgical Societies' SAH grading scale [3]. Early prognostic assessment is essential for optimizing treatment strategies and resource allocation, and the use of reliable biomarkers can help identify high-risk patients and predict clinical outcome. Among the most studied biomarkers is C-reactive protein (CRP), a frequently elevated acute-phase reactant that reflects systemic inflammation [4, 5]. However, CRP levels alone may lack sufficient specificity, prompting the search for composite indices, such as the CRP/albumin ratio, that combine the effects of inflammation and nutritional status [6, 7]. High CRP/albumin ratios have been associated with worsened neurological recovery and a higher risk of secondary complications. Serum lactate, another candidate biomarker, reflects systemic hypoperfusion and anaerobic metabolism and has demonstrated prognostic importance in critical illness and acute brain injury [8, 9]. Recent studies have suggested that elevated lactate levels in the early stages of SAH are associated with cerebral vasospasm, delayed cerebral ischemia, and adverse neurological outcomes [10, 11]. The aim of this study was to evaluate comprehensively the prognostic significance of the CRP/albumin ratio and serum lactate levels in patients with aneurysmal subarachnoid hemorrhage (aSAH), focusing on their relationships to short-term functional outcome, vasospasm, and early mortality to support early predictions for clinical management.

Materials and methods

Study design and patient selection

This retrospective, observational cohort study included 186 patients hospitalized with a diagnosis of aSAH between January 2018 and

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December 2024. The diagnosis of SAH was confirmed in all patients using non-contrast computed tomography (CT), which was followed by digital subtraction angiography (DSA) or CT angiography (CTA) to determine the presence of an intracranial aneurysm.

Inclusion criteria were: (1) Age ≥ 18 years; (2) Diagnosis of aSAH confirmed radiologically; (3) Admission within 48 hours of hemorrhage onset; (4) Availability of complete laboratory and clinical outcome data.

Exclusion criteria included: (1) Chronic liver disease; (2) Active systemic infection at the time of admission; (3) Autoimmune or neoplastic diseases; (4) Use of immunosuppressive or anti-inflammatory medications; (5) Traumatic or non-aneurysmal SAH; (6) Death within the first 24 hours after admission.

The study was approved by the institutional ethics committee, and the requirement for informed consent was waived due to the retrospective nature of the research.

Data collection and biomarker assessment

Patients underwent routine laboratory testing upon admission and throughout the first 14 days following the hemorrhage. Serum samples were analyzed daily for CRP, albumin, and lactate using a fully automated biochemistry analyzer (e.g., Roche Cobas or equivalent system) in a single, certified laboratory to ensure consistency.

CRP levels were measured using a high-sensitivity immunoturbidimetric assay; Albumin levels were quantified using the bromocresol green dye-binding method; Serum lactate was determined enzymatically from peripheral venous blood samples.

The CRP/albumin ratio was calculated for each patient by dividing the CRP concentration (mg/L) by the serum albumin level (g/dL). Both individual values and the ratio were recorded daily. The analysis considered the highest CRP/albumin ratio and lactate value observed within the first 14 days.

Outcome measures

The primary outcome was functional status at discharge, assessed using the Modified Rankin Scale (mRS). Patients were classified into two outcome groups: (1) Favorable outcome: mRS 0-2; (2) Poor outcome: mRS 3-6.

Secondary outcomes included: (1) Incidence of symptomatic cerebral vasospasm, defined as the development of new neurological deficits not attributable to other causes and confirmed radiologically (CTA, DSA, or transcranial Doppler ultrasound); (2) 14-day all-cause mortality, defined as any death occurring within the first 14 days after onset.

Statistical analysis

All analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were first tested for normality using the Shapiro-Wilk test. Normally distributed continuous variables were expressed as mean ± standard deviation (SD) and compared using the independent samples t-test. Non-normally distributed variables were reported as medians and interquartile ranges (IQRs) and compared using the Mann-Whitney U test. Categorical variables were presented as frequencies and percentages, and group comparisons were performed with the Chi-square test or Fisher's exact test if appropriate. The association between biomarker levels and mRS scores was assessed using Spearman's rank correlation coefficient. Multivariate logistic regression analysis was applied to identify independent predictors of poor outcome, adjusting for age, Hunt-Hess grade, presence of vasospasm, CRP/albumin ratio, and lactate level. Model performance was evaluated by odds ratios (ORs) with 95% confidence intervals (CIs). Finally, a receiver operating characteristic (ROC) curve analysis was conducted to determine the predictive accuracy of the CRP/albumin ratio and lactate, and the area under the curve (AUC) was calculated.

Comparative analyses between groups (e.g., CRP/albumin ratio > 10 vs. ≤ 10; serum lactate > 2.5 mmol/L vs. ≤ 2.5 mmol/L) were conducted using the independent samples t-test or the Mann-Whitney U test, depending on the distribution of the data. The Chi-square test or Fisher's exact test was used for categorical comparisons.

To assess the strength and direction of associations between biomarker levels (CRP/albumin ratio and serum lactate) and clinical outcome

Table 1. Baseline demographic and clinical characteristics of patients with aneurysmal subarachnoid hemorrhage (aSAH)

Characteristic	Value (n = 186)
Age, median (IQR)	59 (48-67)
Female sex, n (%)	108 (58.1%)
Male sex, n (%)	78 (41.9%)
Hypertension, n (%)	92 (49.5%)
Diabetes mellitus, n (%)	38 (20.4%)
Smoking history, n (%)	64 (34.4%)
Hunt-Hess grade (I-II), n (%)	81 (43.5%)
Hunt-Hess grade (III-V), n (%)	105 (56.5%)
WFNS grade (I-III), n (%)	102 (54.8%)
WFNS grade (IV-V), n (%)	84 (45.2%)
Aneurysm location: anterior circulation, n (%)	142 (76.3%)
Aneurysm location: posterior circulation, n (%)	44 (23.7%)
Treatment: surgical clipping, n (%)	94 (50.5%)
Treatment: endovascular coiling, n (%)	92 (49.5%)

The table summarizes age distribution, sex ratio, comorbidities, clinical grades at admission (Hunt-Hess, WFNS), aneurysm location, and treatment modalities (clipping vs. coiling).

(mRS), Spearman's rank correlation coefficient was applied.

Multivariate logistic regression analysis was employed to identify independent predictors of poor functional outcome (defined as mRS 3-6 at discharge). Covariates included in the model were age, Hunt-Hess grade on admission, presence of symptomatic vasospasm, CRP/albumin ratio > 10, and serum lactate > 2.5 mmol/L. ORs with 95% CIs were reported.

An ROC curve analysis was used to evaluate the discriminative ability of the CRP/albumin ratio and serum lactate for predicting poor outcome. The area under the ROC curve was calculated for each biomarker, and the optimal cut-off value was determined based on the Youden index.

A two-tailed *p*-value < 0.05 was considered significant for all analyses.

Results

Demographic findings

The study included 186 patients with aSAH. The median age was 59 years (IQR: 48-67), and 58% of the cohort were female. Baseline demographic and clinical characteristics are summarized in **Table 1**. Based on biomarker stratification, 74 patients (39.8%) had an CRP/albumin ratio greater than 10, and 63 patients (33.9%) had serum lactate levels exceeding 2.5 mmol/L during the initial 14-day period (**Table 2**). In the multivariate logistic regression model adjusted for age, Hunt-Hess grade, and presence of vasospasm, both biomarkers remained independently associated with a poor functional outcome (defined as mRS 3-6 at discharge): (1) CRP/albumin ratio > 10: OR = 2.85 (95% CI: 1.76-4.59, P < 0.001); (2) Lactate > 2.5 mmol/L: OR = 1.92 (95% CI: 1.15-3.21, P = 0.012).

Comparison of groups according to serum level results

We can divide patient groups according to CRP/albumin ratio and serum lactate level as follows: (1) Poor prognosis group: CRP/albumin > 10 and serum lactate > 2.5 mmol/L; (2) Good prognosis group: CRP/albumin < 10 and serum lactate < 2.5 mmol/L.

Patients with a CRP/albumin ratio > 10 demonstrated significantly poorer neurological outcome than those with a ratio ≤ 10. The median mRS score at discharge was 4 (IQR: 3-5) in the high-ratio group versus 2 (IQR: 1-3) in the low-ratio group (P < 0.001). The incidence of symptomatic vasospasm was also markedly higher in the high-ratio group (45% vs. 22%, P = 0.001), as was 14-day mortality (18% vs. 6%, P = 0.002).

Similarly, elevated serum lactate levels (> 2.5 mmol/L) were associated with significantly worse clinical outcome. Patients in this group had a higher median mRS score (4 vs. 2, P < 0.001), increased vasospasm rate (43% vs. 25%, P = 0.003), and higher 14-day mortality rate (17% vs. 7%, P = 0.011) than those with lactate ≤ 2.5 mmol/L (**Table 3**).

The ROC curve analysis showed that the CRP/albumin ratio had an AUC of 0.82, indicating strong discriminatory ability for predicting a poor outcome. Serum lactate had an AUC of 0.78 (**Figure 1**). Daily trends of CRP/albumin

Table 2. Distribution of patients according to CRP/albumin ratio (> 10 vs. ≤ 10) and their corresponding outcomes

CRP/Albumin ratio	Patients (n)	Median mRS (IQR)	Vasospasm, n (%)	14-day mortality, n (%)
≤ 10	112	2 (1-3)	25 (22.3%)	7 (6.3%)
> 10	74	4 (3-5)	33 (44.6%)	13 (17.6%)
p-value	-	< 0.001	0.001	0.002

The table shows the relationship between CRP/albumin ratio categories and neurological outcomes (mRS scores), vasospasm incidence, and 14-day mortality rates.

Table 3. Distribution of patients according to serum lactate levels (> 2.5 mmol/L vs. ≤ 2.5 mmol/L) and their corresponding outcomes

Serum lactate level	Patients (n)	Median mRS (IQR)	Vasospasm, n (%)	14-day mortality, n (%)
≤ 2.5 mmol/L	123	2 (1-3)	31 (25.2%)	9 (7.3%)
> 2.5 mmol/L	63	4 (3-5)	27 (42.9%)	11 (17.5%)
p-value	-	< 0.001	0.003	0.011

The table presents the association between lactate level categories and clinical outcomes including mRS at discharge, vasospasm, and 14-day mortality.

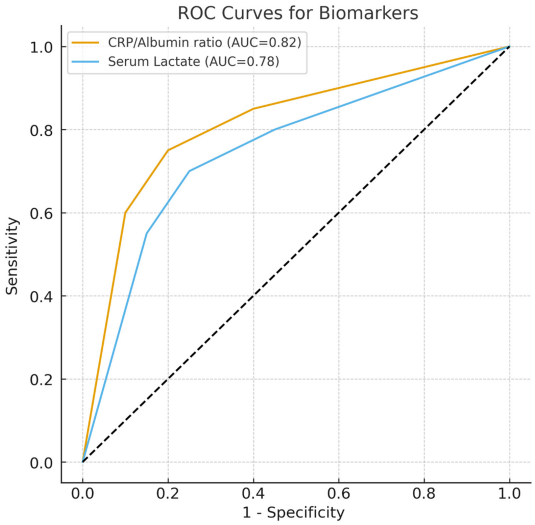

Figure 1. Receiver operating characteristic (ROC) curves for CRP/albumin ratio and serum lactate levels for predicting poor outcome (mRS 3-6) after aneurysmal subarachnoid hemorrhage. The CRP/albumin ratio demonstrated an AUC of 0.82 and serum lactate an AUC of 0.78. Both biomarkers showed strong discriminatory ability, with CRP/albumin ratio slightly superior in predictive accuracy.

ratios and lactate levels over the first 14 days, stratified by outcomes, are shown in **Figure 2**.

Discussion

This study clearly demonstrated that both the CRP/albumin ratio and the serum lactate level are independent and robust prognostic indicators in patients with aSAH. Elevated values of these biomarkers within the early acute phase - specifically, within the first 14 days post-ictus - were significantly associated with worse functional outcomes at discharge, higher incidence of symptomatic vasospasm, and increased 14-day mortality rate. These findings underscore the pathophysiologic importance of systemic inflammatory and metabolic responses in the early secondary brain injury cascade following SAH, complementing the existing literature on neuroinflammation and cerebral autoregulatory dysfunction [1-3].

The CRP/albumin ratio represents a novel and composite biomarker that integrates systemic inflammation and nutritional/metabolic status. While CRP alone is an established acute-phase reactant that rises in response to inflammation, albumin serves as a negative acute-phase protein whose levels generally decrease during critical illness due to increased capillary leakage and decreased hepatic synthesis. Therefore, the CRP/albumin ratio provides a more detailed assessment of patient status that accounts for both proinflammatory and catabolic processes [4, 5]. In the current study, patients with a CRP/albumin ratio > 10 had an approximately threefold increased likelihood of a poor neurological outcome (OR = 2.85), supporting the clinical importance of this measurement as an early prognostic tool.

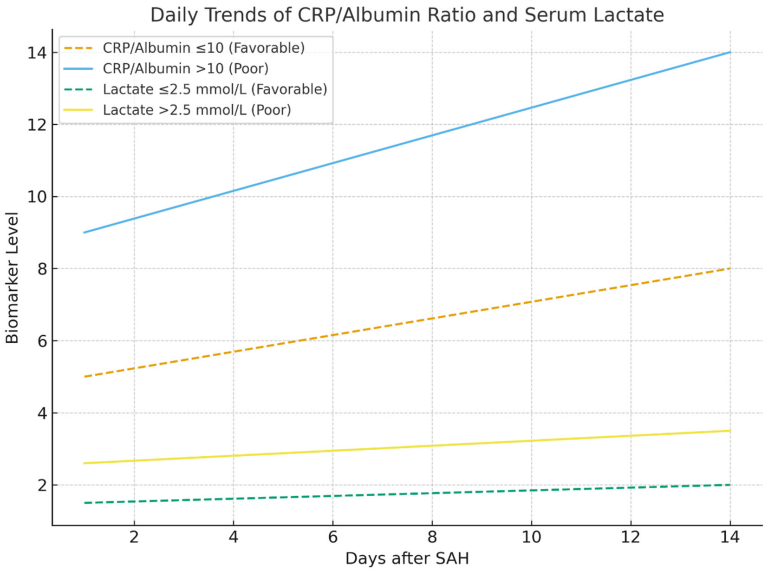

Figure 2. Daily trends of CRP/albumin ratio and serum lactate levels during the first 14 days following aneurysmal subarachnoid hemorrhage, stratified by outcome group. Patients with poor outcomes (mRS 3-6) exhibited consistently higher CRP/albumin ratios and lactate levels compared to those with favorable outcome (mRS 0-2).

Our results are consistent with previously published findings that high CRP/albumin ratios are associated with delayed cerebral ischemia (DCI), longer intensive care unit stays, and poor outcomes, as measured by the Glasgow Outcome Scale or the mRS [6-8]. Huang et al. noted that underlying mechanisms may include inflammatory cytokine cascades, endothelial dysfunction, oxidative stress, and blood-brain barrier disruption, all of which contribute to the progression of cerebral vasospasm and secondary injury [9].

Serum lactate, on the other hand, is a widely accepted marker of tissue hypoperfusion, anaerobic metabolism, and mitochondrial dysfunction. Oh et al. found that elevated serum lactate levels have been strongly associated with early brain injury, systemic hypoxia, and poor prognosis across multiple critical care populations [10]. We found the same results, with a serum lactate threshold of > 2.5 mmol/L independently predicting a poor outcome. These findings also align with the work of Barcoles et al., who demonstrated that elevated lactate is correlated with cerebral metabolic distress, neuroinflammation, cerebral glucose metabolism, and increased risk of early complications, such as sepsis or cardiopulmonary instability, in SAH patients [11].

Importantly, recent research suggests that, compared to isolated measurements, the temporal dynamics of lactate may provide greater prognostic accuracy. Poblete et al. reported that persistently elevated lactate or reduced lactate clearance is associated with ongoing cerebral and systemic metabolic stress, which may reflect treatment refractoriness or secondary insults, such as DCI or infection [12]. Although our study focused on peak values during the acute phase, future work may benefit from evaluating the prognostic value of lactate trends or clearance kinetics over time.

The ROC curve analysis in our study revealed strong predictive performance for both biomarkers, with AUCs of 0.82 for the CRP/albumin ratio and 0.78 for serum lactate, suggesting excellent discrimination between favorable and poor outcomes. The potential synergy between these two values may improve early clinical decision-making, allowing for more refined risk stratification and personalized treatment strategies. For example, high-risk patients may benefit from intensified hemodynamic management, early initiation of vasospasm prophylaxis, or timely surgical or endovascular interventions [13].

Despite these strengths, the study has several limitations. First, the retrospective design may have created an inherent selection bias and limited causal inference. Second, we did not assess serial trends or time-dependent changes in biomarker levels, which could provide additional prognostic granularity. Third, the data were obtained from two single-center cohorts, which may limit the generalizability of the cutoff values and predictive models. Future multicenter prospective studies with dynamic biomarker monitoring are needed to confirm and expand our findings. Ultimately, our results support the routine integration of the CRP/albumin ratio and serum lactate levels into the early treatment algorithm for patients with aSAH. These markers are cost-

effective, rapidly measurable, and clinically informative, providing a viable tool for early outcome prediction in a variety of care settings. Their incorporation into existing clinical grading systems, such as the Hunt-Hess or World Federation of Neurological Surgeons' grading scale for SAH, may further improve prognostic accuracy and support precision-based neurocritical care.

Conclusion

Both the CRP/albumin ratio and serum lactate levels serve as independent and significant prognostic biomarkers in aSAH. Elevated CRP/albumin ratios reflect a heightened systemic inflammatory state combined with nutritional compromise, while increased lactate levels indicate metabolic stress and impaired perfusion. Their predictive value is evident in their association with poor functional outcomes, increased risk of vasospasm, and early mortality. The integration of these biomarkers into clinical workflows may enhance early risk stratification, facilitate individualized treatment decisions, and ultimately improve outcomes in a SAH patients. Prospective multicenter studies and dynamic biomarker monitoring are warranted to optimize their utility in neurocritical care.

Disclosure of conflict of interest

None.

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