



PROGNOSTIC VALUE OF THE AST/ALT RATIO IN PREDICTING FUNCTIONAL SEVERITY AND SHORT-TERM OUTCOMES IN HFREF

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ABSTRACT

Background

Heart failure with reduced ejection fraction (HFrEF) is a systemic syndrome that is frequently accompanied by hepatic congestion and dysfunction. Although natriuretic peptides are established prognostic biomarkers, their availability may be limited in certain clinical settings. Inexpensive and routinely measured liver-derived parameters may provide additional prognostic information. The aspartate aminotransferase to alanine aminotransferase (AST/ALT) ratio has been proposed as a potential marker of disease severity in heart failure; however, evidence in HFrEF remains limited.

Objective

To evaluate the association between AST/ALT ratio and functional severity as well as short-term prognostic indicators in patients with HFrEF.

Methods

This hospital-based observational study included 75 consecutive patients with HFrEF (left ventricular ejection fraction, <40%). The AST/ALT ratio was calculated at admission and categorised as <1 or ≥1. Functional severity was assessed using the New York Heart Association (NYHA) functional class and left ventricular ejection fraction (LVEF). Group comparisons, trend analysis across NYHA classes, correlation analysis, ordinal logistic regression, and receiver operating characteristic (ROC) curve analyses were performed.

Results

Patients with an AST/ALT ratio ≥1 were older and had significantly higher transaminase levels. A greater proportion of these patients were classified as NYHA class II–III. The AST/ALT ratio increased significantly with worsening NYHA class (P = 0.04). Ordinal logistic regression showed

that the AST/ALT ratio independently predicted worse NYHA functional class (odds ratio 1.68, 95% confidence interval 1.02–2.78; $P = 0.04$). ROC analysis demonstrated moderate discriminatory ability for predicting NYHA $\geq$ II (AUC 0.66) and NYHA functional class $\geq$ III (AUC 0.69).

Conclusion

The AST/ALT ratio is associated with functional severity and short-term prognostic indicators in patients with HFrEF. Although not a standalone biomarker, it may serve as a practical adjunct for risk stratification when interpreted alongside conventional clinical assessments.

Keywords: heart failure, reduced ejection fraction, AST/ALT ratio, functional severity, prognosis

INTRODUCTION

Heart failure (HF) continues to be a significant contributor to morbidity and mortality on a global scale, despite advancements in pharmacological and device-based interventions.(1)

Heart failure with reduced ejection fraction (HFrEF) is associated with elevated rates of hospitalisation and adverse clinical outcomes. The aspartate aminotransferase (AST)/alanine aminotransferase (ALT) ratio serves as an indicator of hepatic congestion and hypoperfusion, which are frequently observed in patients with advanced heart failure. Elevated AST/ALT ratios are associated with poor clinical outcomes, including increased hospitalisation and mortality rates. This biomarker has the potential to augment existing risk models, thereby improving patient stratification and informing therapeutic decision-making.(2)

Heart failure is increasingly recognised as a multisystem disorder that extends beyond the scope of myocardial dysfunction. Reduced cardiac output and elevated venous pressure contribute to the dysfunction of peripheral organs, including the liver.(3) Hepatic congestion and hypoperfusion may lead to abnormal liver function tests, which are correlated with the severity and prognosis of HF.(4) Liver dysfunction in patients with HF is often indicated by elevated levels of bilirubin, transaminases, and alkaline phosphatase. These abnormalities are associated with worse clinical status and can serve as prognostic indicators. Consequently, monitoring liver function tests may provide valuable insights into disease progression and assist in tailoring patient management strategies.(5)

These liver function abnormalities may arise from both passive congestion due to elevated central venous pressure and reduced hepatic perfusion resulting from diminished cardiac output.(6) The extent of liver injury often parallels the severity of heart failure and exacerbates during episodes of acute decompensation. Therefore, integrating liver function assessment into routine clinical evaluation can enhance risk stratification and guide therapeutic decisions in HF patients.(7)

The AST/ALT ratio, commonly employed in hepatology to characterise liver injury patterns, provides insights into hepatocellular damage and congestion in the liver. Several studies have suggested an association between elevated AST/ALT ratios and adverse outcomes in cardiovascular disease. However, the role of this ratio in predicting functional severity and short-term outcomes in HFrEF remains unclear, particularly in contexts where access to advanced biomarkers is limited.(8–10)

This study aimed to evaluate the prognostic value of the AST/ALT ratio in patients with HFrEF, particularly in resource-limited settings. We hypothesised that an elevated AST/ALT ratio correlates with increased functional severity and poorer short-term outcomes in this population. Establishing this relationship could facilitate risk stratification and optimise management in cases where advanced biomarkers are not available.

METHODS

Study Design and Setting

This hospital-based observational study was conducted at the Government Thiruvapur Medical College over a one-year period.

Participants

Seventy-five consecutive adult patients diagnosed with heart failure were enrolled in the study.

Inclusion Criteria

- Diagnosis of heart failure based on Framingham criteria
- Left ventricular ejection fraction <40%
- Age ≥ 18 years

Exclusion Criteria

- Known primary liver disease
- Alcohol use disorder
- Sepsis or shock
- Malignancy
- Pregnancy
- Recent exposure to hepatotoxic medications

Data Collection

Demographic data, clinical history, heart failure aetiology, NYHA functional class, echocardiographic findings, and laboratory parameters were recorded upon admission. Serum AST and ALT levels were measured as part of routine evaluation, and the AST/ALT ratio was calculated.

Exposure Variable

The AST/ALT ratio was categorised as <1 or ≥ 1 , based on commonly used thresholds in the literature.

Outcome Measures

- Functional severity: NYHA functional class
- Short-term prognostic indicators: NYHA class at presentation and LVEF

Statistical Analysis

Continuous variables are expressed as mean $\pm$ standard deviation, and categorical variables are expressed as frequencies and percentages. Between-group comparisons were performed using independent t-tests or the Mann–Whitney U test, as appropriate. Categorical variables were analysed using the Chi-square or Fisher's exact test. Trends in the AST/ALT ratio across the NYHA classes were assessed using the Kruskal–Wallis test. Correlations were evaluated using Pearson or Spearman's coefficients. Ordinal logistic regression was used to identify the predictors of the NYHA functional class. ROC curve analysis was performed to assess the discriminatory performance. A two-sided p-value <0.05 was considered statistically significant.

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee. Written informed consent was obtained from all the participants.

RESULTS

The mean age of the study population was 66.1 ± 6.8 years old. Patients with an AST/ALT ratio ≥ 1 were older and had significantly higher AST and ALT levels. The mean LVEF was numerically lower in the higher ratio group, although this difference was not statistically significant. (Figure 1)

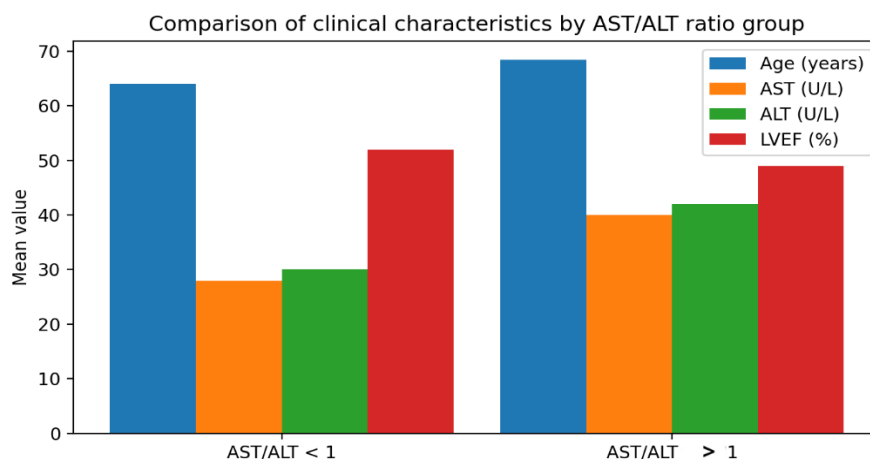


Figure 1 AST/ALT Ratio and Functional Severity

Patients with an AST/ALT ratio ≥ 1 were more frequently classified as NYHA class II and III. A significant increasing trend in the AST/ALT ratio was observed across the worsening NYHA functional class ($P = 0.04$).

Table 1 -Distribution of NYHA Functional Class According to AST/ALT Ratio

NYHA Class	AST/ALT < 1, n (%)	AST/ALT ≥ 1 , n (%)
Class I	29 (39%)	18 (24%)
Class II	30 (40%)	35 (47%)
Class III	16 (21%)	22 (29%)

Correlation Analysis

The AST/ALT ratio showed a weak inverse correlation with LVEF ($r = -0.11$, $P = 0.29$). A modest positive correlation was observed between the AST/ALT ratio and AST levels ($r = 0.30$, $P = 0.03$).

Table 2. Correlation of AST/ALT Ratio With Clinical and Laboratory Variables

Variable	Correlation Coefficient (r)	p value
AST/ALT ratio vs LVEF (%)	-0.11	0.29
AST/ALT ratio vs AST (U/L)	0.30	0.03
AST/ALT ratio vs ALT (U/L)	0.25	0.07

Regression Analysis

Ordinal logistic regression analysis showed that the AST/ALT ratio was independently associated with a worse NYHA functional class (odds ratio 1.68, 95% confidence interval 1.02–2.78; $P = 0.04$). (Figure 2)

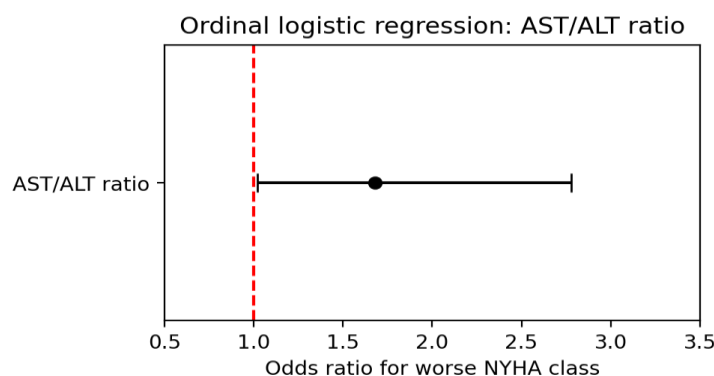


Figure 2 ROC Curve Analysis

ROC analysis demonstrated the moderate discriminatory ability of the AST/ALT ratio for predicting NYHA $\geq$ II (AUC 0.66) and NYHA $\geq$ III (AUC 0.69).

Table 3 - ROC Curve Performance of AST/ALT Ratio for Functional Severity

Outcome Predicted	AUC (95% CI)	Optimal Cut-off	Sensitivity (%)	Specificity (%)
NYHA $\geq$ II	0.66	≥ 1.0	64	62
NYHA $\geq$ III	0.69	≥ 1.1	67	65

DISCUSSION

This study clarifies the link between the AST/ALT ratio and both functional severity and short-term prognostic indicators in patients with heart failure with reduced ejection fraction (HFrEF). Notably, patients with a more severe New York Heart Association (NYHA) functional class exhibited elevated AST/ALT ratios, with the ratio progressively increasing as the functional categories worsened. Furthermore, the AST/ALT ratio maintained an independent association with functional severity, even after adjusting for relevant clinical variables, highlighting its potential as an additional marker of disease burden.

The correlation between a higher AST/ALT ratio and a more severe functional class is biologically plausible and aligns with the pathophysiology of advanced heart failure. (11) Hepatic dysfunction in heart failure primarily results from venous congestion and reduced hepatic perfusion, leading to hepatocellular injury and altered transaminase patterns. (12) Several studies have indicated that liver-derived parameters, including the AST/ALT ratio, are linked to adverse clinical profiles and poorer outcomes in heart failure. These findings support the idea that the AST/ALT ratio reflects systemic congestion and multisystem involvement rather than isolated myocardial dysfunction. (13)

However, not all studies have consistently shown a strong relationship between the AST/ALT ratio and heart failure severity or outcomes. (14) In the present study, the discriminatory performance of the AST/ALT ratio was moderate, as evidenced by ROC curve analysis. This observation aligns with reports suggesting that the AST/ALT ratio alone has limited sensitivity and specificity for prognostic classification of HCC.(15)

Additionally, the weak correlation observed between the AST/ALT ratio and left ventricular ejection fraction (LVEF) indicates that this ratio does not directly reflect systolic function. LVEF is an incomplete marker of disease severity because it does not account for systemic congestion, neurohormonal activation, or end-organ dysfunction. (16) In contrast, the stronger association with the NYHA functional class suggests that the AST/ALT ratio captures aspects of the global disease burden that are not fully reflected by echocardiographic measurements alone. (17)

Variations in study design, patient populations, and methods of assessing liver function may account for discrepancies in the literature. Studies including patients with preserved ejection fraction, mixed heart failure phenotypes, and unrecognised hepatic comorbidities may yield variable results. Furthermore, observational designs and modest sample sizes, including that of the present study, limit causal inference and generalisability. (9)

From a clinical perspective, the AST/ALT ratio should not be interpreted as a standalone prognostic biomarker. However, its value lies in its simplicity, low cost, and routine availability. In settings where access to natriuretic peptides or advanced biomarkers is limited, the AST/ALT ratio may provide incremental information when interpreted alongside clinical assessments and conventional investigations. Its association with functional severity suggests its potential utility in short-term risk stratification and clinical decision-making.(18)

Limitations

This study has several limitations. Its observational design precludes causal inference. The sample size was modest and derived from a single center, which may limit generalizability. Long-term outcomes, such as mortality and rehospitalisation, were not evaluated. Although the NYHA functional class is widely used in clinical practice, it is subject to inter-observer variability (IOV). These limitations should be considered when interpreting the findings.

Conclusion

In patients with HFREF, the AST/ALT ratio is associated with functional severity and short-term prognostic indicators. Although it should not replace established cardiac biomarkers, it may serve as a practical adjunct to conventional clinical assessments, particularly in resource-limited settings. Larger multicenter studies with longer follow-up periods are needed to further define its prognostic role and clinical utility.

References

1. Gui H, She R, Li J, Sabbah HN, Luzum J, Bryson TD, et al. Plasma Proteomic Profile Predicts Survival in Heart Failure With Reduced Ejection Fraction. *Circ: Genomic and Precision Medicine*. 2021 May 17;14(3).
2. Liu H, Zheng X, Zheng Y, Chen J, Huang Y, Yan H, et al. Association of AST/ALT ratio with 90-day outcomes in patients with acute exacerbation of chronic liver disease: a prospective multicenter cohort study in China. *Front Med*. 2024 Mar 21;11.
3. Shinagawa H, Ohsaka T, Nishii M, Naruke T, Takehana H, Koitabashi T, et al. Prognostic Significance of Increased Serum Bilirubin Levels Coincident With Cardiac Decompensation in Chronic Heart Failure. *Circ J*. 2008 Jan 1;72(3):364–369.
4. Alvarez A, Mukherjee D. Liver Abnormalities in Cardiac Diseases and Heart Failure. *Int J Angiol*. 2011 July 19;20(03):135–142.
5. Allen LA, Yusuf S, Pocock S, Wang D, Felker GM, Michelson EL, et al. Liver function abnormalities and outcome in patients with chronic heart failure: data from the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program. *European J of Heart Fail*. 2009 Jan 28;11(2):170–177.
6. Kubo SH. Liver Function Abnormalities in Chronic Heart Failure. *Arch Intern Med*. 1987 July 1;147(7):1227.
7. Omote K, Anzai T, Komoriyama H, Kamiya K, Kato Y, Noguchi K, et al. Impact of admission liver stiffness on long-term clinical outcomes in patients with acute decompensated heart failure. *Heart Vessels*. 2018 Dec 6;34(6):984–991.
8. Ewid M, Allihimy AS, Sherif H, Abazid R, Alkuraydis SA, Alharbi SA, et al. AST/ALT ratio predicts the functional severity of chronic heart failure with reduced left ventricular ejection fraction. *BMC Res Notes*. 2020 Mar 24;13(1).
9. Nyblom H, Aldenborg F, Olsson R, Björnsson E, Simrén M, Almer S. The AST/ALT ratio as an indicator of cirrhosis in patients with PBC. *Liver International*. 2006 Aug 3;26(7):840–845.
10. Chen SL, Li LF, Li JP, Zeng T, He X. Elevated Preoperative Serum Alanine Aminotransferase/Aspartate Aminotransferase (ALT/AST) Ratio Is Associated with Better Prognosis in Patients Undergoing Curative Treatment for Gastric Adenocarcinoma. *IJMS*. 2016 June 9;17(6):911.
11. Giannini E, Testa R, Malfatti F, Chiarbonello B, Romagnoli P, Risso D, et al. Validity and Clinical Utility of the Aspartate Aminotransferase–Alanine Aminotransferase Ratio in Assessing Disease Severity and Prognosis in Patients with Hepatitis C Virus–Related Chronic Liver Disease. *Arch Intern Med*. 2003 Jan 27;163(2):218.
12. Shen J, Li C, Zhang Y, Dai J, Wen T, Yu Y, et al. Baseline HBV-DNA load plus AST/ALT ratio predicts prognosis of HBV-related hepatocellular carcinoma after hepatectomy: A multicentre study. *Journal of Viral Hepatitis*. 2021 Sept 18;28(11):1587–1596.
13. Qin C, Wang W, Feng Y, Lyu X, Li T, Zhao B, et al. High aspartate aminotransferase to alanine aminotransferase ratio on admission as risk factor for poor prognosis in COVID-19 patients. *Sci Rep*. 2020 Oct 5;10(1).
14. Giannini E, Testa R, Botta F, Fasoli A, Lantieri PB, Ceppa P, et al. Progressive liver functional impairment is associated with an increase in AST/ALT ratio. *Dig Dis Sci*. 1999 June 1;44(6):1249–1253.
15. Cheng J, Zhao P, Liu J, Wu X, Liu X. Preoperative aspartate aminotransferase-to-platelet ratio index (APRI) is a predictor on postoperative outcomes of hepatocellular carcinoma. *Medicine*. 2016 Dec 1;95(48):e5486.

16. Fukino K, Higashitani M, Mizuno A, Murata N, Ueshima D, Kodama T, et al. Prognostic Impact of Reduced Left Ventricular Ejection Fraction After Endovascular Therapy for Lower Extremities. *Circ J*. 2024 Feb 22;88(3):341–350.
17. Blacher M, Grespan E, Danzmann LC, Zimmerman A, Beck-Da-Silva L, Rohde LE, et al. Revisiting heart failure assessment based on objective measures in NYHA functional classes I and II. *Heart*. 2021 Aug 25;107(18):1487–1492.
18. Chinnappan R, Yaqinuddin A, Alsalameh S, Al-Kattan K, Mir TA, Makhzoum T, et al. Low-Cost Point-of-Care Monitoring of ALT and AST Is Promising for Faster Decision Making and Diagnosis of Acute Liver Injury. *Diagnostics*. 2023 Sept 16;13(18):2967.