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Original research

THE ROLE OF APO B, APO A1, AND THE APO B/APO A1 RATIO IN PREDICTING THE SEVERITY OF CORONARY ARTERY LESIONS IN PATIENTS WITH ACUTE CORONARY SYNDROME

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ABSTRACT

Background: *This study investigates the role of Apolipoprotein B (Apo B), Apolipoprotein A1 (Apo A1), and their ratio (Apo B/Apo A1) in predicting the severity of coronary artery lesions in Acute Coronary Syndrome (ACS). It aims to evaluate serum levels of these biomarkers and establish their cut-off values in predicting severe coronary stenosis using the Gensini score.*

Methods: *This single-center, cross-sectional study included 103 ACS patients who underwent coronary angiography between October 2024 and February 2025. Patients were categorized based on their Gensini scores into low (< 40 points, n = 64) and high (≥ 40 points, n = 39) groups. Serum levels of Apo B, Apo A1, and lipid parameters were measured. The diagnostic value of these biomarkers in identifying severe coronary artery lesions was assessed using receiver operating characteristic (ROC) curve analysis.*

Results: *The high Gensini group showed significantly lower Apo A1 levels (1.11 ± 0.19 vs. 1.29 ± 0.24 g/L, p < 0.001) and higher Apo B levels (1.13 ± 0.39 vs. 0.93 ± 0.28 g/L, p = 0.003) compared to the low Gensini group. The Apo B/Apo A1 ratio was significantly elevated in the high Gensini group (median 1.04 vs. 0.73, p < 0.001). The optimal cut-off value for the Apo B/Apo A1 ratio was 0.905, with 74.4% sensitivity and 82.8% specificity (AUC = 0.758). Conclusion: These results underscore the Apo B/Apo A1 ratio as a viable diagnostic for identifying individuals with significant coronary lesions and support the clinical relevance of apolipoprotein-based biomarkers in risk stratification of ACS.*

Keywords: *Apolipoprotein B, Apolipoprotein A1, Apo B/Apo A1 ratio, Acute coronary syndrome, Gensini score, Coronary artery disease*

I. INTRODUCTION

According to the World Health Organization, coronary artery disease (CAD) continued to be the leading cause of death worldwide in 2024 [1]. Among its clinical manifestations, acute coronary syndrome (ACS) represents the most severe form, associated with plaque instability and thrombus formation within the coronary arteries. Currently, the assessment of coronary artery disease risk is primarily based on traditional risk factors such as Total cholesterol, LDL-C, HDL-C, and Triglycerides. However, recent studies have indicated that these conventional lipid parameters do not fully reflect the burden of atherosclerosis [2].

Apolipoprotein B (Apo B), the main component of low-density lipoproteins (LDL) and very-low-density lipoproteins (VLDL), is closely associated with the formation of atherosclerotic plaques and the progression of coronary artery lesions [2]. In contrast, Apolipoprotein A1 (Apo A1), the principal component of high-density lipoproteins (HDL), is known for its cardioprotective effects through the transport of excess cholesterol out of blood vessels and prevention of plaque formation [3]. Therefore,

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the ApoB/ApoA1 ratio is considered an indicator that reflects the balance between atherogenic and anti-atherogenic factors. Epidemiological evidence has demonstrated a strong association between this ratio and cardiovascular risk, even surpassing traditional lipid markers in predictive value [4].

To date, there have been limited studies investigating the relationship between the Apo B/Apo A1 ratio and the severity of coronary artery stenosis in patients with CAD, particularly among those presenting with ACS. Therefore, we conducted this study to evaluate serum levels of Apo B, Apo A1, and the Apo B/Apo A1 ratio in patients with ACS; and to determine the cutoff values of Apo B, Apo A1, and the Apo B/Apo A1 ratio in predicting severe coronary artery lesions, as assessed by the Gensini score, in patients with ACS.

II. MATERIALS AND METHODS

2.1. Study Subjects

Inclusion criteria: Patients diagnosed with ACS, including ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), or unstable angina, based on the 2023 ESC guidelines [5], who underwent percutaneous coronary angiography.

Exclusion criteria [6]: Currently using medications that affect blood lipid levels, including statins, fibrates, ezetimibe, niacin, omega-3, or PCSK9 inhibitors within 4 weeks prior to hospital admission; Presence of primary cardiomyopathy, infective endocarditis, severe valvular heart disease, autoimmune diseases, or malignancy; Acute or chronic infectious diseases within 2 weeks prior to study enrollment; Hepatic failure (AST/ALT > 3 times the upper normal limit) or renal failure (eGFR < 30 ml/min/1.73m²); History of coronary stent implantation or coronary artery bypass grafting (CABG); Patients who do not consent to participate in the study.

Study period: From October 21, 2024, to February 11, 2025.

Study location: Department of Interventional Cardiology and Emergency Care - Cardiovascular Center, Hue Central Hospital.

2.2. Research methods

Study design: A cross-sectional descriptive study.

Sample size was calculated using the formula:

$$n = (Z_{1}\text{-}\alpha/_{2})^2 \cdot S^2 / (\varepsilon \cdot X)^2$$

Based on the study by Panayiotou in 2008, with $Z_{1}\text{-}\alpha/_{2} = 1.96$ and relative error $\varepsilon = 0.05$; $S = 0.22$; $X = 0.85$

The calculated sample size was n = 103 [7].

Coronary angiography and Gensini scoring: Coronary angiography was performed under fluoroscopy (Phillips Allura Xper system). The severity of coronary artery lesions was graded using the Gensini score [8]: Low Gensini score: < 40 points; High Gensini score: ≥ 40 points

2.3. Data processing and statistical analysis

Data were collected and coded using a standardized research form. Statistical analysis was performed using R software. Quantitative variables were expressed as mean ± standard deviation (SD) or median (interquartile range - IQR), while qualitative variables were presented as frequencies and percentages. Independent t-test (for normally distributed variables) or Mann-Whitney U test (for non-normally distributed variables) was used to compare quantitative variables. The Chi-square test was applied for qualitative variables. For comparisons involving more than two groups, one-way ANOVA was used if the data followed a normal distribution and homogeneity of variances. If these assumptions were not met, the Kruskal-Wallis test was used as an alternative. A p-value < 0.05 was considered statistically significant.

3.4. Ethical considerations

The study was approved by the Ethics Committee of the Undergraduate Training Office, University of Medicine and Pharmacy - Hue University, and Hue Central Hospital. All patients and/or their family members were fully informed and gave consent to participate in the study. The study procedures did not interfere with the diagnosis, treatment methods, or quality of care provided to the patients.

III. RESULTS

The mean age was 69.03 ± 10.88 years, with a male-to-female ratio of 51:52. Demographic factors including age, gender, BMI, and smoking status did not show statistically significant differences

between the low Gensini and high Gensini groups ($p > 0.05$). The high Gensini group had a markedly higher prevalence of hypertension (71.8%) compared to the low Gensini group (45.3%), and this difference was statistically significant ($p = 0.009$). The prevalence of type 2 diabetes was also higher in the high Gensini group (53.8% vs. 34.4%), although this difference did not reach statistical significance ($p = 0.052$) (Table 1). All four investigated variables-Apo A1, Apo B, the Apo B/Apo A1 ratio, and the non-HDL-C/HDL-C ratio showed statistically significant differences between the low and high Gensini score groups ($p < 0.05$) (Table 2)

Table 1: Demographic characteristics in two groups of coronary artery lesions classified by Gensini score

Variables		Low Gensini score (n=64)	High Gensini score (n=39)	Total	p-value
Age		69.30 ± 11.65	68.59 ± 9.61	69.03 ± 10.88	0,.51
Sex	Male	33 (32.04%)	18 (17.48%)	51	0.594
	Female	31 (30.09%)	21 (20.39%)	52	
BMI		21.60 ± 3.53	21.91 ± 4.44	21.72 ± 3.87	0.705
Smoking status	No	47 (45.63%)	23 (22.33%)	70	0.127
	Yes	17 (16.51%)	16 (15.53%)	33	
HTN	No	35 (54.7%)	11 (28.2%)	46	0.009
	Yes	29 (45.3%)	28 (71.8%)	57	
T2DM	Không	42 (65.6%)	18 (46.2%)	60	0.052
	Có	22 (34.4%)	21 (53.8%)	43	

Table 2: Comparison of Apo A1, Apo B, Apo B/Apo A1 Ratio, and Non-HDL-C/HDL-C ratio between the two Gensini score groups

Variables	Total (n=103)		p-value
	Low Gensini score (n=64)	High Gensini score (n=39)	
Apo A1			< 0.001
Mean ± SD	1.29 ± 0.24	1.11 ± 0.19	
Min - Max	0.79 - 1.80	0.72 - 1.46	
Apo B			0.003
Mean ± SD	0.93 ± 0.28	1.13 ± 0.39	
Min - Max	0.44 - 1,67	0.42 - 1.99	
Apo B/Apo A1 Ratio			< 0.001
Median (IQR)	0.73 (0.28)	1,04 (0.36)	
Min - Max	0.36 - 1.46	0.39 - 1.67	

Variables	Total (n=103)		p-value
	Low Gensini score (n=64)	High Gensini score (n=39)	
Non HDL-C/HDL-C Ratio			
Median (IQR)	3.19 (1.01)	4.25 (2.42)	p 0.001
Min - Max	1.52 - 6.42	1.11 - 7.87	

The optimal cut-off points for each index including Apo B/Apo A1 ratio, non HDL-C/HDL-C ratio, Apo B, and Apo A1 are 0.905, 3.39, 0.99 g/L, and 1.15 g/L respectively. At these optimal cut-off points, the Apo B/Apo A1 ratio has diagnostic value for severe coronary artery disease (Gensini score ≥ 40) with an area under the ROC curve (AUC) of 0.758 (Se: 74.4% and Sp: 82.8%) (Table 3 and Figure 1).

Table 3: Diagnostic value of ApoB, ApoA1, ApoB/ApoA1 ratio, and nonHDL-C/HDL-C ratio

Variables	Cut-off	Se (%)	Sp (%)	AUC	p-value
Apo B/ Apo A1 Ratio	0.905	74.4	82.8	0.758	< 0.001
Non HDL-C/ HDL-C Ratio	3.39	66.7	60.9	0.692	0.001
Apo B (g/L)	0.99	66.7	50	0.654	< 0.001
Apo A1 (g/L)	1.15	48.7	32.8	0.291	0.009

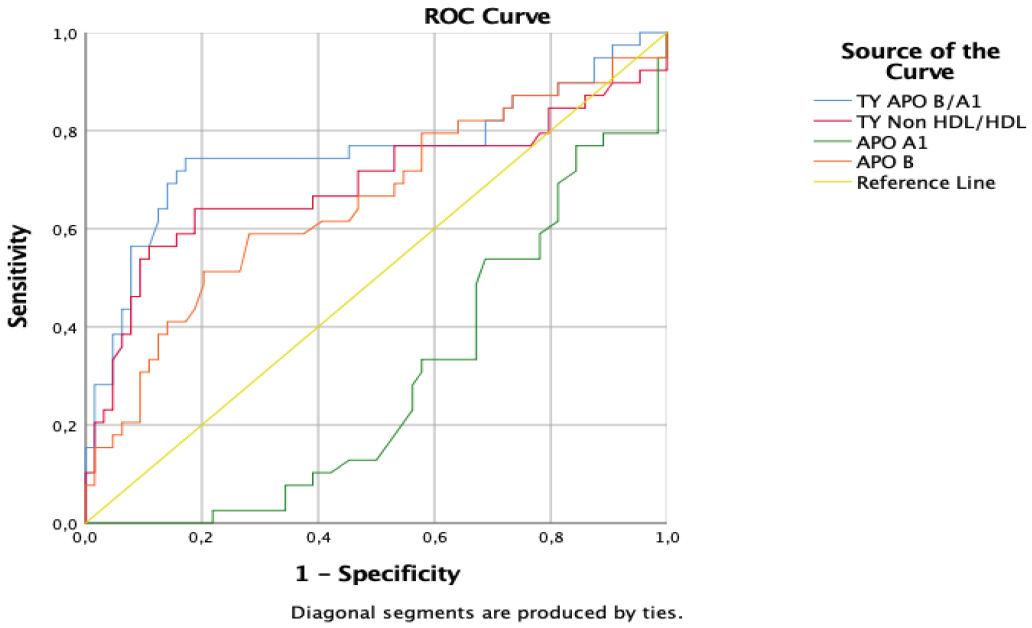

Figure 1: ROC curves of Apo B/Apo A1 ratio, nonHDL-C/HDL-C ratio, Apo A1, and Apo B in the high Gensini score group

IV. DISCUSSION

A total of 103 patients with ACS were enrolled, with a mean age of 69.03 ± 10.88 years and a nearly equal gender distribution (male-to-female ratio: 51:52). When comparing the low Gensini group (< 40 points, n = 64) and the high Gensini group (≥ 40 points, n = 39), no statistically significant differences were observed in age, sex, body mass index (BMI), smoking status, or the presence of type 2 diabetes mellitus (T2DM)

($p > 0.05$ for all). However, the prevalence of hypertension (HTN) was significantly higher in the high Gensini group (71.8%) compared to the low Gensini group (45.3%) with a p-value of 0.009. Although the proportion of patients with T2DM was higher in the high Gensini group (53.8%) than in the low Gensini group (34.4%), this difference did not reach statistical significance ($p = 0.052$).

In addition, there was a statistically significant difference in Apo A1, Apo B, Apo B/Apo A1 ratio, and non-HDL-C/HDL-C ratio levels between the two Gensini groups ($p < 0.005$). These results are consistent with the study by Yaseen et al., which also demonstrated significant differences in Apo B and the Apo B/Apo A1 ratio across the three Gensini groups ($p < 0.05$) [18]. Our study found that serum Apo A1 levels were inversely correlated with the severity of coronary artery lesions: Apo A1 levels decreased as Gensini scores increased ($p < 0.001$). This finding aligns with the results of Vu Anh Tuan et al.[8].

We identified optimal cut-off values for the Apo B/Apo A1 ratio, non-HDL-C/HDL-C ratio, Apo B, and Apo A1 as 0.905, 3.39, 0.99, and 1.15, respectively. Among these, the Apo B/Apo A1 ratio showed the highest diagnostic performance in identifying patients with high Gensini scores, with an AUC of 0.758 (Se 74.4% and Sp 82.8%). This finding is similar to that of Vu Anh Tuan et al., who reported a cut-off value of 0.725 for the Apo B/Apo A1 ratio (Se 86.7%, Sp 79.1%), with an AUC of 0.884[8]. Compared to our study, the cut-off value is higher, likely due to our specific focus on ACS patients. Similarly, the study by Yaseen et al. identified a cut-off value of 0.8 for the Apo B/Apo A1 ratio (Se 90%, Sp 70%). The clear difference in cut-off values between our study and Yaseen's may reflect different clinical priorities: Yaseen's higher sensitivity (with lower specificity) supports early detection, even at the cost of increased false positives[9].

In our study, the non-HDL-C/HDL-C ratio had an AUC of 0.692 (Se 66.7% and Sp 60.9%). Although the diagnostic value of the non-HDL-C/HDL-C ratio was lower than that of the Apo B/Apo A1 ratio (AUC = 0.758), the difference was not statistically significant ($p = 0.42$). Rahmani et al., in a study conducted in Iran on 251 patients with coronary artery disease, found that Apo B, Apo A1, and the Apo B/Apo A1 ratio had better diagnostic performance for atherosclerosis than traditional lipid and lipoprotein markers[10]. The AMORIS study, conducted on a large cohort of 175,000 individuals, also demonstrated that the Apo B/Apo A1 ratio better predicted cardiovascular risk than traditional lipid indices such as TC/HDL-C, LDL-C/HDL-C, and especially non-HDL-C/HDL-C[4]. Furthermore, a 2023 study by Yan Chen et al. concluded that the Apo B/Apo A1 ratio is associated with in-hospital mortality in elderly patients with acute myocardial infarction and outperformed other traditional lipid parameters[11]. These findings underscore the potential of the Apo B/Apo A1 ratio as a superior marker for cardiovascular risk assessment, compared with other lipid parameters such as Apo A1, Apo B, and non-HDL-C/HDL-C. Moreover, the INTERHEART study, conducted in over 30,000 individuals from 52 countries, demonstrated that the Apo B/Apo A1 ratio was a stronger predictor of myocardial infarction than traditional risk factors such as hypertension, smoking, and diabetes, regardless of gender, age, or ethnicity[12].

As the main apolipoprotein of atherogenic lipoproteins (LDL, VLDL), apo B is essential for the formation of lipid-rich plaques and the advancement of these plaques toward rupture in ACS. As seen in our high Gensini group, elevated Apo B levels indicate a higher burden of atherogenic particles. On the other hand, Apo A1, the main protein in HDL, possesses antioxidant and anti-inflammatory qualities and mediates reverse cholesterol transfer. Patients with significant coronary lesions may have less vascular protection, as indicated by their decreased Apo A1 levels. The imbalance between pro-atherogenic and anti-atherogenic forces is thus captured by the Apo B/Apo A1 ratio, which is particularly pertinent in the acute context of coronary instability.

Our study has several limitations: (1) The sample size is limited, which may affect the generalizability of results when applied to a broader population; (2) The study was conducted at a single medical center, thus we could not evaluate differences in population characteristics and environmental factors that might influence the relationship between the Apo B/Apo A1 ratio and the severity of coronary artery

disease; (3) Our study is cross-sectional, without long-term follow-up data to assess the prognostic value of the Apo B/Apo A1 ratio for future major cardiovascular events.

Despite these limitations, our findings provide important insights into the potential utility of the Apo B/Apo A1 ratio as a diagnostic marker for severe coronary artery disease, which could eventually lead to improved risk stratification in clinical practice. Even with a limited sample size, identifying a marker with good sensitivity and specificity (Se 74.4% and Sp 82.8%) is noteworthy and suggests this ratio merits further investigation.

V. CONCLUSION

Our study demonstrated that the Apo B/Apo A1 ratio is significantly associated with the severity of coronary artery disease in patients with ACS. Among the lipid-related indices evaluated, the Apo B/Apo A1 ratio exhibited the highest diagnostic performance in identifying patients with high Gensini scores, with a sensitivity of 74.4% and specificity of 82.8% at a cut-off value of 0.905. These results underscore the Apo B/Apo A1 ratio as a viable diagnostic for identifying individuals with significant coronary lesions and support the clinical relevance of apolipoprotein-based biomarkers in risk stratification of ACS.

Conflict of interest

The authors declare no conflict of interest.

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