

Original articles

Study of the serum apolipoprotein B/apolipoprotein A1 ratio in patients with chronic coronary syndrome

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Abstract

Background: Coronary artery disease is one of the leading causes of mortality and disease burden worldwide. Recently, Apolipoprotein B, Apolipoprotein A1, and particularly the ApoB/ApoA1 ratio have been recognized as valuable indicators for cardiovascular risk assessment.

Objectives: To investigate the clinical and paraclinical characteristics, serum levels of Apolipoprotein B, Apolipoprotein A1, and the Apolipoprotein B/Apolipoprotein A1 ratio in patients with chronic coronary syndrome. Additionally, to evaluate the associations and correlations between serum Apolipoprotein B, Apolipoprotein A1, the Apolipoprotein B/Apolipoprotein A1 ratio, and the SYNTAX II score in patients with chronic coronary syndrome.

Materials and Methods: Patients presenting with chest pain and admitted to the Cardiovascular Center of Hue Central Hospital were enrolled and classified into two groups according to the 2021 ACC/AHA guidelines: the obstructive chronic coronary syndrome group and the non-obstructive chronic coronary syndrome group.

Results: The study conducted on 110 patients with chronic coronary syndrome (CCS), multivessel disease predominated, with a mean SYNTAX II score of 28.8 ± 9.44 . Apo B, Apo A1, and notably the Apo B/Apo A1 ratio demonstrated significant value in predicting obstructive CCS. The Apo B/Apo A1 ratio yielded the highest diagnostic performance, with an optimal cut-off of 0.86 (AUC = 0.769, Se = 68.3%, Sp = 84.0%). Apo B correlated positively with total cholesterol, triglycerides, and non-HDL-C, whereas Apo A1 correlated positively with HDL-C and inversely with atherogenic lipids. As the SYNTAX II score increased, Apo B and the Apo B/Apo A1 ratio increased, while Apo A1 decreased. The strongest correlation with lesion severity and complexity was observed for the Apo B/Apo A1 ratio ($r = 0.745$, $p < 0.01$), clearly reflecting the severity and complexity of coronary artery lesions.

Conclusion: Apo B, Apo A1, and the Apo B/Apo A1 ratio demonstrated significant value in distinguishing patients with obstructive chronic coronary syndrome. Among them, the Apo B/Apo A1 ratio was the strongest indicator, clearly reflecting the severity and complexity of coronary artery lesions. These parameters were closely associated with the lipid profile and the SYNTAX II score. Their application may support more accurate risk stratification and guide more effective therapeutic decision-making.

Keywords: Apo B; Apo A1; Apo B/Apo A1 ratio; lipid profile; chronic coronary syndrome; coronary artery obstruction; SYNTAX II score.

1. INTRODUCTION

Coronary artery disease (CAD) remains the leading cause of mortality worldwide as of 2024 [1]. In the management of chronic coronary syndrome (CCS), accurate assessment of coronary lesion complexity is essential for selecting the optimal revascularization strategy. The SYNTAX II score (SSII) is currently considered a standard tool due to its ability to integrate angiographic characteristics with important clinical variables such as age, creatinine clearance, and left ventricular ejection fraction (LVEF), thereby enabling individualized prediction of

long-term mortality risk [2].

In addition to anatomical factors, dyslipidemia plays a central role in the development of atherosclerotic plaques. However, conventional lipid parameters often fail to fully reflect the true atherosclerotic burden. Recently, Apolipoprotein B (ApoB)-the main structural component of atherogenic lipoprotein particles and Apolipoprotein A1 (ApoA1) - the principal anti-atherogenic component of high-density lipoprotein (HDL)-have been recognized as more sensitive biomarkers [3]. In particular, the Apo B/Apo A1 ratio directly reflects the balance between

atherogenic and protective lipoproteins and has demonstrated superior predictive value compared with traditional lipid indices [4].

In Vietnam, studies investigating the association between this ratio and disease severity assessed by the SYNTAX II score in patients with CCS remain limited. Therefore, this study was conducted to achieve two objectives: evaluate the clinical and paraclinical characteristics, along with serum Apolipoprotein B, Apolipoprotein A1 levels, and the ApoB/ApoA1 ratio in patients with chronic coronary syndrome; and second, to determine the relationship and correlation between these biomarkers and the SYNTAX II score, thereby contributing to improved risk stratification and optimization of therapeutic strategies in patients with chronic coronary syndrome.

2. MATERIALS AND METHODS

2.1. Study Population

Patients presenting with chest pain and admitted to the Cardiovascular Center, Hue Central Hospital, from June 2024 to August 2025 were enrolled in the study. were classified into two groups according to the 2021 ACC/AHA Guideline [8]:

Obstructive chronic coronary syndrome (obstructive CCS): defined as $\geq 50\%$ stenosis of the left main coronary artery or at least one major epicardial coronary artery.

Non-obstructive chronic coronary syndrome (non-obstructive CCS): defined as the absence of $\geq 50\%$ stenosis in the left main coronary artery or any major epicardial coronary artery.

Inclusion criteria:

Patients diagnosed with Chronic Coronary Syndrome (CCS) according to the 2024 ESC guidelines[5]: stable angina and/or dyspnea; new-onset heart failure or newly reduced left ventricular systolic function suspected to be of ischemic origin; or chest pain suggestive of microvascular angina or coronary vasospasm. All patients provided informed consent to participate in the study.

Exclusion criteria:

Congenital coronary artery anomalies (e.g., coronary fistula, left coronary artery arising from the right coronary artery); Valvular heart disease, congenital heart disease; Current use of medications affecting serum lipid levels (including statins, fibrates, ezetimibe, niacin, omega-3 fatty acids, or PCSK9 inhibitors) within 4 weeks prior to admission; Severe chronic comorbid conditions, such as cirrhosis, chronic kidney disease, or long-term corticosteroid therapy (> 1 month); Life-threatening arrhythmias;

Patients who declined to participate in the study

2.2. Methods

Study design

A cross-sectional descriptive study was conducted from April 2024 to August 2025 at the Cardiovascular Center, Hue Central Hospital.

Sample size

A convenience sampling method was applied, and a total of 110 patients were enrolled.

Coronary angiography was performed under fluoroscopic guidance using the Philips Integris system. The severity of coronary artery disease was assessed using the SYNTAX II score:

The SYNTAX II score was calculated using the dedicated software available at: www.syntaxscore.com.

The SYNTAX II (SSII) score was obtained from the validated calculator that integrates both anatomical and clinical variables, including age, estimated glomerular filtration rate (eGFR), left ventricular ejection fraction (LVEF), left main disease, sex, COPD, and peripheral vascular disease.

Statistical analysis

Data were analyzed using SPSS software version 22.0. Qualitative variables were expressed as percentages (%) and compared using the Chi-square test (χ^2). Quantitative variables were presented as mean $\pm$ standard deviation (SD). The associations between variables were assessed using the Spearman correlation coefficient (r), interpreted as follows: Weak correlation: $r < 0.3$; Moderate correlation: $0.3 \leq r < 0.5$; Strong correlation: $0.5 \leq r < 0.7$; Very strong correlation: $r \geq 0.7$. The predictive value and the optimal cut-off points were determined using receiver operating characteristic (ROC) curve analysis and the area under the curve (AUC). A p-value < 0.05 was considered statistically significant.

3. Ethical considerations

The study was approved by the Institutional Ethics Committee of Hue University of Medicine and Pharmacy (approval code: H2024/509, dated June 10th, 2024). All participants were fully informed about the study's objectives and procedures and provided written informed consent prior to enrollment. Personal information was kept strictly confidential and used solely for scientific research purposes.

3. RESULTS

A total of 110 patients with chronic coronary syndrome (CCS) who were admitted to the Cardiovascular Center, Hue Central Hospital were included in this study. The main findings are presented as follows:

Table 1. Characteristics of major cardiovascular risk factors

Variables		Obstructive CCS (n = 60)	Non-obstructive CCS (n = 50)	Total	p-value
Age		64.67 ± 9.81	61.38 ± 11.09	63.17 ± 10.49	0.102
Sex	Male	34 (56.7%)	18 (36.0%)	52 (47.3%)	< 0,05
	Female	26 (43.3%)	32 (64.0%)	58 (52.7%)	
BMI (kg/m ²)	< 23	33 (55%)	36 (72%)	69 (62.7%)	0.066
	≥ 23	27 (45%)	14 (28%)	41 (37.3%)	
Comorbidities	Hypertension	45 (75%)	32 (64%)	77 (70%)	0.21
	T2DM	18 (30%)	12 (24%)	30 (27.3%)	0.482
	Smoking status	27 (45%)	15 (25%)	42 (38.2%)	0.107
	Dyslipidemia	34 (56.7%)	19 (38%)	53 (48.2%)	0.051

Table 2. Levels of Apo A1, Apo B, and the Apo B/Apo A1 ratio

Variables	Obstructive CCS (n = 60)	Non-obstructive CCS (n = 50)	p
	$\bar{X} \pm SD$ (g/l)	$\bar{X} \pm SD$ (g/l)	
Apo B	1.19 ± 0.41	0.85 ± 0.3	< 0.01
Apo A1	1.16 ± 0.26	1.36 ± 0.27	< 0.01
Apo B/Apo A1	1.11 ± 0.53	0.65 ± 0.27	< 0.01

The obstructive CCS group had markedly higher levels of Apo B and the Apo B/Apo A1 ratio compared with the non-obstructive CCS group. In contrast, Apo A1 was lower in the obstructive group than in the non-obstructive group, with all differences being statistically significant ($p < 0.01$).

Table 3. Levels of Apo B, Apo A1, and the Apo B/Apo A1 ratio according to the number of diseased coronary vessels

Number of diseased vessels	n	Apo B level	Apo A1 level	Apo B/Apo A1 Ratio
		$\bar{X} \pm SD$ (g/l)	$\bar{X} \pm SD$ (g/l)	$\bar{X} \pm SD$
1	22	1.04 ± 0.40	1.21 ± 0.30	0.94 ± 0.49
2	19	1.14 ± 0.40	1.16 ± 0.25	1.05 ± 0.45
3	19	1.41 ± 0.35	1.10 ± 0.23	1.38 ± 0.55
p		0.011	0.333	0.017

In our study, the 60 patients with obstructive CCS were stratified into tertiles according to the SYNTAXII score: low (0 to < 24.2), intermediate (24.2–31.4), and high (>31.4).

Table 4. Levels of Apo B, Apo A1, the Apo B/Apo A1 ratio, and SYNTAX II score

SYNTAX II Score	n	Apo B		Apo A1		Apo B/Apo A1 Ratio	
		$\bar{X} \pm SD$ (g/l)	p	$\bar{X} \pm SD$ (g/l)	p	$\bar{X} \pm SD$	p
Low SII	20	0.88 ± 0.29		1.33 ± 0.25		0.7 ± 0.28	
Intermediate SII	20	1.13 ± 0.4	< 0.05	1.17 ± 0.22	< 0.05	1 ± 0.35	< 0.05
High SII	20	1.55 ± 0.20		0.98 ± 0.19		1.64 ± 0.39	

Table 5. Correlation of Apo B, Apo A1, and Apo B/Apo A1 ratio with SYNTAX II score and the number of diseased vessels

	Apo B		Apo A1		Apo B/Apo A1 Ratio	
	r	p	r	p	r	p
SYNTAX II Score	0.619	< 0.01	-0.541	< 0.01	0.745	< 0.01
Number of diseased vessels	0.37	< 0.01	-0.19	0.139	0.35	< 0.01

Table 6. Cut-off values, sensitivity, specificity, and AUC of Apo B, Apo A1, and the Apo B/Apo A1 ratio in predicting the risk of obstructive CCS

Variables	Cut off	Se (%)	Sp (%)	AUC	p	95% KTC
Apo B (g/l)	1.01	68.3	74.0	0.737	< 0.01	0.645 - 0.829
Apo A1 (g/l)	1.18	53.3	80.0	0.704	< 0.01	0.607 - 0.801
Apo B/Apo A1 Ratio	0.86	68.3	84.0	0.769	< 0.01	0.680 - 0.858

Apo B had an optimal cut-off value of 1.01 g/L with an AUC of 0.737 (95% CI: 0.645–0.829), a sensitivity of 68.3% and a specificity of 74.0%. Apo A1 had a cut-off value of 1.18 g/L with an AUC of 0.704 (95% CI: 0.607–0.801), a sensitivity of 53.3% and a specificity of 80.0%. The Apo B/Apo A1 ratio showed the highest AUC, reaching 0.769 (95% CI: 0.680–0.858), with a cut-off value of 0.86, a sensitivity of 68.3%, and a specificity of 84.0%.

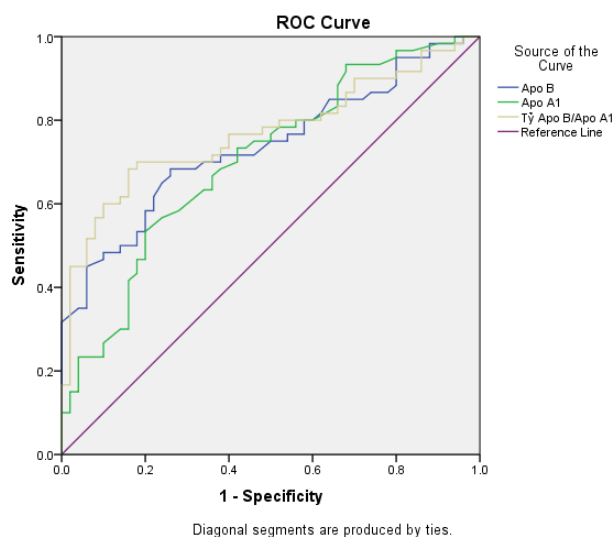


Figure 1. ROC curves of Apo B, Apo A1, and the Apo B/Apo A1 ratio in patients with obstructive chronic coronary syndrome

4. DISCUSSION

The mean age was 63.17 ± 10.49 years, with no significant difference between the obstructive and non-obstructive CCS groups ($p = 0.102$). Male patients were more common in the obstructive group, while females predominated in the non-obstructive group ($p < 0.05$). BMI and smoking status showed no significant differences between groups ($p > 0.05$). Hypertension, diabetes, and smoking were more frequent in the obstructive group, although the differences were not statistically significant. The

prevalence of dyslipidemia was similar between the two groups (Table 1).

The results of our study demonstrated that all three biomarkers-Apo B, Apo A1, and the Apo B/Apo A1 ratio had significant predictive value for identifying obstructive chronic coronary syndrome (CCS) ($p < 0.01$). Among them, the Apo B/Apo A1 ratio exhibited the highest diagnostic performance (AUC = 0.769; sensitivity = 68.3%; specificity = 84%), outperforming Apo B (AUC = 0.737) and Apo A1 (AUC = 0.704) when analyzed individually. This superiority

is attributable to its ability to simultaneously capture the two opposing components of atherosclerotic pathology: the burden of atherogenic lipoproteins (Apo B) and the protective reverse cholesterol transport mediated by Apo A1.

When compared with representative domestic studies, our optimal cut-off value of 0.86 lies between that reported by Vu Anh Tuan in patients with stable coronary artery disease (0.725) and the higher threshold of Ho Anh Binh in acute coronary syndrome (0.905) [6, 7]. This intermediate position aligns well with the pathophysiologic characteristics of CCS, in which acute inflammatory activity has subsided, yet lipid metabolic disturbances and atherosclerotic risk remain persistently elevated.

Dyslipidemia has been recognized as one of the major risk factors for coronary artery disease. As structural molecules of the lipoproteins that transport lipids in the bloodstream, Apo A-I and Apo B have been shown to have a close association with the pathogenesis and risk of coronary artery disease. In our study, Apo B and the Apo B/Apo A1 ratio increased markedly according to the number of stenotic vessels, from 1.04 ± 0.40 to 1.41 ± 0.35 g/L ($p = 0.011$) and from 0.94 ± 0.49 to 1.38 ± 0.55 ($p = 0.017$), respectively. Both were positively correlated with the extent of the lesions (Apo B: $r = 0.37$; Apo B/Apo A1: $r = 0.35$; $p < 0.01$). In contrast, Apo A1 decreased slightly but did not reach statistical significance. These results suggest a prominent role of atherogenic lipoproteins in the progression of multivessel disease. This trend is consistent with the data of Vu Anh Tuan (2021) and Lam Hung Hanh (2025), and is further supported by international studies by Yongyan Song and especially Min Tian ($n = 2,256$), in which the highest quartile of the Apo B/Apo A1 ratio increased the risk of three-vessel disease by 2.36 times (95% CI: 1.65 - 3.38) [6, 8, 9]. Taken together, the evidence shows that Apo B and the Apo B/Apo A1 ratio are strong markers reflecting the atherosclerotic burden and the extent of disease, outperforming traditional lipid parameters in risk stratification of chronic coronary artery disease.

Our study demonstrated significant differences in apolipoprotein levels when stratified according to the SYNTAX II score. Specifically, as the complexity of coronary lesions increased from the low to high group, Apo B levels and the Apo B/Apo A1 ratio increased markedly (from 0.88 ± 0.29 to 1.55 ± 0.20 g/L and from 0.70 ± 0.28 to 1.64 ± 0.39 , respectively; $p < 0.05$), while Apo A1 decreased significantly. Spearman correlation analysis confirmed that the Apo B/Apo A1 ratio had the strongest association

with the SYNTAX II score ($r = 0.745$; $p < 0.05$), outperforming individual parameters.

The positive association between the Apo B/Apo A1 ratio and the severity of coronary artery lesions is strongly supported when compared with other studies. Domestic studies by Lam Hung Hanh (2025), Vu Anh Tuan (2021), and Ho Anh Binh (2025) consistently reported that the Apo B/Apo A1 ratio increases in parallel with the degree of stenosis and the extent of coronary lesions [6, 7, 12]. Specifically, Vu Anh Tuan demonstrated an Apo B/Apo A1 AUC of 0.884 at a cut-off value of 0.725 in patients with stable and unstable coronary artery disease. Ho Anh Binh identified a cut-off value of 0.905 for predicting severe lesions with an AUC of 0.758, which is consistent with the trend observed in our study. Notably, our cut-off value (0.86) sits precisely between those of Vu Anh Tuan (0.725) and Ho Anh Binh (0.905). This pattern accurately reflects the intermediate position of CCS within the evolutionary spectrum of coronary artery disease, where acute vascular inflammation is partially controlled, yet underlying lipid dysregulation and atherogenic risk persist. International studies by Song et al. (2015), Min Tian (2019), and Rui Hui (2020), conducted on large cohorts of up to several thousand patients, have confirmed that the Apo B/Apo A1 ratio is an independent predictor of multivessel coronary artery disease (OR ranging from 1.92 to 2.93) [9, 10, 11].

Our study has several limitations: (1) The sample size is relatively small, which may limit the generalizability of the findings to broader and more diverse populations; (2) The study was conducted at a single medical center, preventing us from evaluating variations in demographic characteristics, disease patterns, and environmental factors that may influence the relationship between the Apo B/Apo A1 ratio and the severity of chronic coronary artery disease; (3) The cross-sectional design does not allow long-term follow-up to assess the prognostic value of the Apo B/Apo A1 ratio for future major cardiovascular events.

Despite these limitations, our findings provide important evidence supporting the potential utility of the Apo B/Apo A1 ratio as a useful marker for identifying patients with more severe coronary artery disease. With an area under the ROC curve of 0.769, along with a sensitivity of 68.3% and specificity of 84% at the optimal cut-off value of 0.86, this ratio demonstrates promising diagnostic performance and may contribute to improved clinical risk stratification. These results suggest that the Apo B/Apo A1 ratio warrants further investigation in larger cohorts and

longitudinal study designs to more comprehensively evaluate its prognostic significance.

5. CONCLUSION

Our study demonstrated that the Apo B/Apo A1 ratio is significantly associated with the severity of coronary artery disease in patients with chronic coronary syndrome. Among the lipid parameters evaluated, the Apo B/Apo A1 ratio showed the highest diagnostic performance in identifying patients with more severe coronary lesions, with an area under the ROC curve of 0.769, a sensitivity of 68.3%, and a specificity of 84% at the optimal cut-off value. These findings highlight that the Apo B/Apo A1 ratio is a useful biomarker for detecting patients with significant coronary artery involvement and reinforce the clinical relevance of apolipoprotein-based biomarkers in risk stratification for chronic coronary artery disease.

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