# CHARACTERISTICS OF THE ANRIL rs2383207 POLYMORPHISM AND ITS ASSOCIATION WITH LIPID PARAMETERS AMONG PATIENTS WITH CHRONIC CORONARY SYNDROME IN CAN THO CITY

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*The rs2383207 polymorphism of the ANRIL gene has attracted considerable attention due to its association with coronary artery disease, but its effect on lipid metabolism remains unclear. In this cross-sectional study, 66 newly diagnosed patients with chronic coronary syndrome from three hospitals in Can Tho (June 2024 – May 2025) were analyzed for rs2383207 genotypes and lipid profiles. Most patients were ≥ 60 years (81.8%) and male (59.1%), with common risk factors including hypertension (90.9%), sedentary lifestyle (78.8%), and dyslipidemia (69.7%). The G allele was predominant at 65.9% and GA was the most frequent genotype at 68.2% while no AA genotype was observed. Carriers of the G allele had higher LDL-c (2.85 ± 1.28 vs. 2.20 ± 0.90 mmol/L; p < 0.001) and a higher risk of elevated LDL-c (OR = 2.6; 95% CI: 1.16 – 5.6; p = 0.024). At the genotype level, the GG group had higher total cholesterol (p = 0.021) and LDL-c (p < 0.001), as well as a higher risk of elevated total cholesterol (OR = 7.0; 95% CI: 1.6 – 30.8) and LDL-c (OR = 1.67; 95% CI: 1.31 – 2.12). No statistically significant differences were observed for triglycerides or HDL-c. These findings indicate that the G allele and GA genotype of the rs2383207 ANRIL polymorphism are common in patients with chronic coronary syndrome and are associated with elevated total cholesterol and LDL-c levels.*

**Keywords: rs2383207 polymorphism, *ANRIL* gene, lipid parameters, chronic coronary syndrome.**

## I. INTRODUCTION

Coronary artery disease (CAD) remains the leading cause of death worldwide, accounting for approximately 32% of annual mortality, equivalent to more than 17.9 million deaths according to the World Health Organization.[1] The primary pathophysiological mechanism of the disease is the formation of atherosclerotic plaques, driven by lipid accumulation in the arterial wall. Elevated low-density lipoprotein cholesterol (LDL-c) plays a central role, as LDL particles infiltrate the endothelium, trigger inflammation, and form the lipid core of atherosclerotic plaques.[2]

In addition to traditional risk factors such as hypertension, diabetes mellitus, smoking, and dyslipidemia, genetic factors also contribute significantly to the pathogenesis of CAD. Genome-wide association studies (GWAS) have identified more than 60 genetic loci associated with disease risk, among which the 9p21.3 locus is the most common and has the strongest effect. This locus contains the *ANRIL* (*CDKN2B-AS1*) gene, a long non-coding RNA (lncRNA), which has been shown to be closely associated with CAD in multiple populations. Mechanistically, ANRIL regulates the expression of neighboring

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genes such as *CDKN2A*, *CDKN2B*, and *MTAP*, thereby influencing vascular smooth muscle cell function, atherosclerosis progression, and plaque stability.[2,3]

Among the polymorphisms of the *ANRIL* gene, *rs2383207* has drawn considerable attention due to its association with the presence and severity of CAD. Recent meta-analyses have confirmed that this polymorphism is significantly associated with atherosclerotic risk in both Asian and European populations.[4] However, data regarding the impact of *rs2383207* on lipid parameters remain limited. Some evidence suggests that the 9p21 variant may affect lipid metabolism, with risk alleles associated with higher total cholesterol and lower HDL-c, although findings have not been consistent across studies.[2,3] In Vietnam, few studies have directly evaluated this association. Based on this gap in evidence, the present study was conducted to investigate the distribution characteristics of the *ANRIL rs2383207* polymorphism and its relationship with lipid parameters in patients with chronic coronary syndrome in Can Tho City.

## II. MATERIALS AND METHOD

### 1. Subjects

Individuals with chronic coronary syndrome who attended health examinations in Can Tho City from June 2024 to May 2025 were enrolled.

***Inclusion Criteria***

Patients with newly diagnosed chronic coronary syndrome, according to the 2019 ESC guidelines, were indicated for coronary angiography with or without intervention.[5] Patients provided informed consent to participate in the study.

***Exclusion criteria***

Patients with contraindications to coronary angiography according to the Ministry of Health, patients with a history of anaphylactic shock to contrast agents, patients with severe infection, terminal cancer, or coma, and patients with an estimated glomerular filtration rate < 30 ml/min/1.73 m² body surface area.[6]

### 2. Methods

***Study design***

Cross-sectional descriptive study.

***Sample size***

A convenient sampling method was applied in which patients with newly diagnosed chronic coronary syndrome at Can Tho University of Medicine and Pharmacy Hospital, Can Tho Central General Hospital, and Can Tho Cardiovascular Hospital who met both the inclusion and exclusion criteria were recruited. In practice, we enrolled 66 eligible subjects into the study.

***Study contents***

General characteristics included age (< 60 years and ≥ 60 years) and sex (male/female).

Cardiovascular risk factors included[5-7]:

- Obesity: Body mass index (BMI) ≥ 25 kg/m² according to the World Health Organization classification for adults in the Asia-Pacific region.

- Smoking:

+ Yes: currently smoking and having smoked at least 100 cigarettes in a lifetime.

+ No: never smoked, or former smoker who quit ≥ 5 years ago.

- Sedentary lifestyle:

+ Yes: physical activity < 5 days per week or < 15 minutes per day without sweating.

+ No: physical activity ≥ 5 days per week, each session lasting ≥ 15 minutes with sweating.

- Hypertension:

+ Yes: history of hypertension, current use of antihypertensive medication, or newly diagnosed hypertension according to the European Society of Cardiology guidelines,

defined as systolic blood pressure ≥ 140mmHg and/or diastolic blood pressure ≥ 90mmHg, measured in a clinic/hospital setting, confirmed on at least two separate visits with at least two readings per visit.

+ No: if the above criteria are not met.

- Diabetes mellitus:

+ Previously diagnosed diabetes or newly diagnosed according to the criteria of the American Diabetes Association (2022), when at least one of the following is present:

Fasting plasma glucose (after ≥ 8 hours of fasting) ≥ 126 mg/dl (7.0 mmol/L).

HbA1c ≥ 6.5% (48 mmol/mol).

Random plasma glucose ≥ 200 mg/dl (11.1 mmol/L) with classic symptoms of hyperglycemia.

In asymptomatic patients, the test should be repeated to confirm the diagnosis.

+ No diabetes: if none of the above criteria are met.

- Dyslipidemia: Dyslipidemia was defined as the presence of at least one of the following abnormalities: total cholesterol ≥ 200 mg/dL (5.2 mmol/L), LDL-c ≥ 70 mg/dL (1.8 mmol/L), HDL-c < 40 mg/dL (< 1.0 mmol/L), or triglycerides ≥ 150 mg/dL (1.7 mmol/L).

Allele types were G and A.

Genotypes of the *ANRIL rs2383207* polymorphism were GG, GA, and AA.

Lipid parameters included total cholesterol, triglycerides, HDL-cholesterol, and LDL-c measured in mmol/L.

***Data collection***

Study participants were fully recorded for personal information, medical history, and clinical characteristics. Fasting blood samples (after ≥ 12 hours of fasting) were collected, with a total of 4mL of peripheral venous blood: 2mL anticoagulated with EDTA and 2mL anticoagulated with heparin. The 2mL EDTA-anticoagulated blood sample was stored at 4°C until used for DNA extraction and analysis; the remaining sample was used for necessary biochemical investigations. All information and results were documented in a standardized data collection form.

DNA extraction procedure: DNA was extracted using the Qiagen kit. Cells were lysed with binding buffer and proteinase K, and the lysate was passed through a high-salt column. The silica membrane retained DNA while allowing other components to pass through. Purified DNA was eluted in a low-salt buffer and quantified by spectrophotometry at 260/280nm. Only samples with a purity ratio OD260/OD280 between 1.8 – 2.0 were used for PCR.

Identification of *rs2383207* polymorphism: The *rs2383207* genotype was determined by real-time polymerase chain reaction (Real-time PCR, RT-PCR) on the LightCycler 1.5® system (Roche) using hybridization probes labeled with 3′-fluorescein and 5′-LightCycler (TIB MOLBIOL GmbH, Berlin, Germany). The amplification protocol consisted of: initial denaturation at 95°C for 10 minutes; 45 cycles of denaturation at 95°C for 10 seconds, annealing at 60°C for 10 seconds, and extension at 72°C for 15 seconds; followed by melting at 95°C for 30 seconds, incubation at 40°C for 2 minutes, and cooling at 40°C for 30 seconds. Amplification products were identified based on the melting temperature (Tm) of each allele: allele A at 44.96°C and allele G at 55.43°C.

The reactions were performed in a volume of 20µL, including: 2.0µL LightCycler FastStart DNA Master HybProbe (Roche), 1.0µL reagent mix, 3.0mM $MgCl_2$, and 50ng genomic DNA. Genotyping quality was verified by independently replicating genotyping in randomly selected samples, with results showing 100% concordance with the initial

genotyping.

***Statistical analysis***

Data were cleaned and coded using Microsoft Excel and analyzed with SPSS version 26.0. Descriptive statistics included frequency, proportion, percentage, mean, and standard deviation.

**3. Research ethics**

The study was approved by the Ethics Committee in Biomedical Research of Can Tho University of Medicine and Pharmacy (No. 25.050.HV/PCT-HĐĐĐ) on June 28, 2024. All procedures were conducted in accordance with ethical standards in medical research.

## III. RESULTS

From June 2024 to May 2025, we collected 66 patients with chronic coronary syndrome and obtained the following results.

**Table 1. General characteristics of the study population**

| Characteristics | Frequency (n) | Percentage (%) |
|---|---|---|
| Age ≥60 years | 54 | 81.8 |
| Male sex | 39 | 59.1 |
| Obesity | 20 | 30.3 |
| Smoking | 36 | 54.5 |
| Sedentary lifestyle | 52 | 78.8 |
| Hypertension | 60 | 90.9 |
| Diabetes mellitus | 14 | 21.1 |
| Dyslipidemia | 46 | 69.7 |
| Total | 66 | 100 |

The majority of patients were aged 60 years or older (81.8%), and males predominated (59.1%). The prominent cardiovascular risk factors were hypertension (90.9%), sedentary lifestyle (78.8%), and dyslipidemia (69.7%).

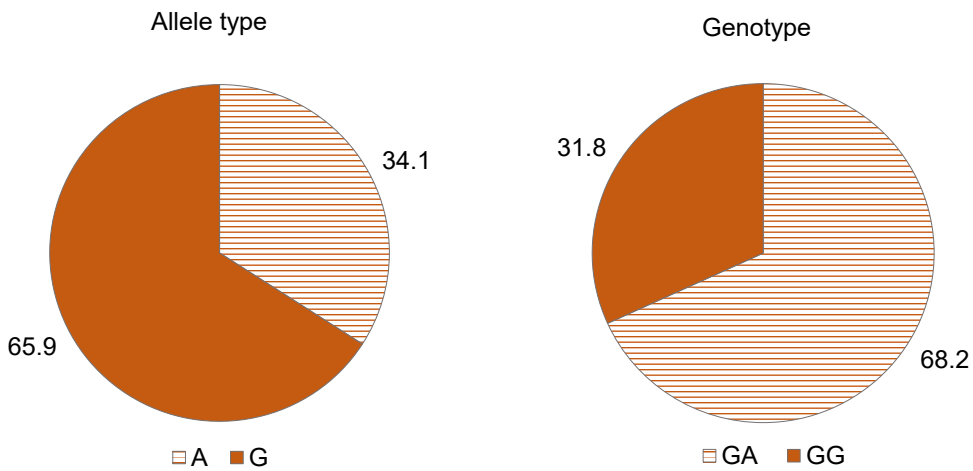


**Chart 1. Characteristics of the *ANRIL rs2383207* polymorphism**

The G allele predominated with a frequency of 65.9% while the A allele accounted for only 31.1%. Regarding genotype, GA was the most common at 68.2% and no cases with the homozygous AA genotype were observed.

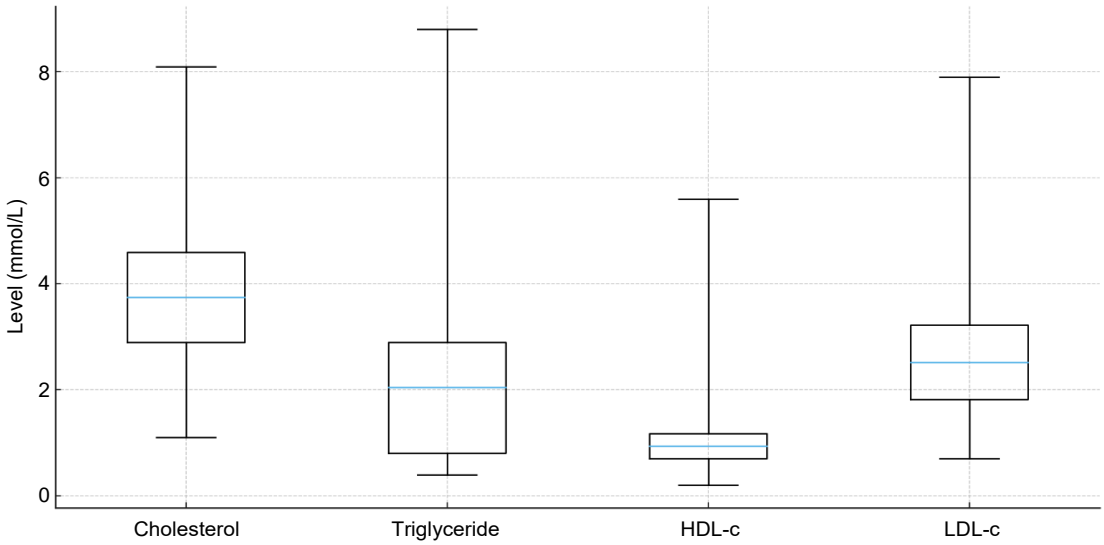


**Chart 2. Characteristics of dyslipidemia in the study population**

The mean total cholesterol concentration in the study population was 3.91 ± 1.48 mmol/L. The mean triglyceride concentration was 2.05 ± 1.44 mmol/L, which was higher than the normal threshold, indicating a tendency toward hypertriglyceridemia in the study group. The HDL-c concentration was relatively low at 1.11 ± 0.69 mmol/L. The mean LDL-c concentration was 2.63 ± 1.20 mmol/L.

**Table 2. Association between the ANRIL rs2383207 polymorphism and lipid parameters**

| Parameter (mmol/L) | rs2383207 polymorphism | | Mean ± SD | p* |
|---|---|---|---|---|
| *Total cholesterol* | Allele type | G | 4.07 ± 1.52 | 0.087 |
| | | A | 3.60 ± 1.36 | |
| | Genotype | GG | 4.57 ± 1.57 | *0.021* |
| | | GA | 3.60 ± 1.36 | |
| *Triglycerides* | Allele type | G | 2.14 ± 1.65 | 0.331 |
| | | A | 1.88 ± 0.90 | |
| | Genotype | GG | 2.41 ± 2.19 | 0.164 |
| | | GA | 1.88 ± 0.90 | |

| Parameter (mmol/L) | rs2383207 polymorphism | | Mean ± SD | p* |
|---|---|---|---|---|
| *HDL-c* | Allele type | G | 1.14 ± 0.78 | 0.503 |
| | | A | 1.06 ± 0.45 | |
| | Genotype | GG | 1.23 ± 1.03 | 0.339 |
| | | GA | 1.06 ± 0.45 | |
| *LDL-c* | Allele type | G | 2.85 ± 1.28 | *< 0.001* |
| | | A | 2.20 ± 0.90 | |
| | Genotype | GG | 3.55 ± 1.28 | *< 0.001* |
| | | GA | 2.20 ± 0.90 | |

**Independent Samples t-test*

No significant differences were observed between alleles of the rs2383207 polymorphism in relation to total cholesterol, triglycerides, or HDL-c. However, LDL-c concentrations were significantly higher in G allele carriers compared with A allele carriers ($p < 0.001$). At the genotype level, patients with the GG genotype had higher total cholesterol ($p = 0.021$) and LDL-c levels ($p < 0.001$) compared with the GA group, while no significant differences were found for triglycerides or HDL-c.

**Table 3. Association between the *ANRIL rs2383207* polymorphism and dyslipidemia characteristics**

| Characteristics of dyslipidemia | rs2383207 polymorphism | | Dyslipidemia | | OR (95% CI) | p |
|---|---|---|---|---|---|---|
| | | | Yes, n (%) | No, n (%) | | |
| *Increased total cholesterol* | Allele type | G | 17 (19.5) | 70 (80.5) | 3.4 (0.94 – 12.3) | 0.072* |
| | | A | 3 (6.7) | 42 (93.3) | | |
| | Genotype | GG | 7 (33.3) | 14 (66.7) | 7.0 (1.6 – 30.8) | *0.009** |
| | | GA | 3 (6.7) | 42 (93.3) | | |
| *Increased Triglycerides* | Allele type | G | 48 (55.2) | 39 (44.8) | 1.08 (0.52 – 2.21) | 0.856** |
| | | A | 24 (53.3) | 21 (46.7) | | |
| | Genotype | GG | 12 (57.1) | 9 (42.9) | 1.17 (0.41 – 3.31) | 0.797** |
| | | GA | 24 (53.3) | 21 (46.7) | | |
| *Decreased HDL-c* | Allele type | G | 45 (51.7) | 42 (48.3) | 0.86 (0.42 – 1.77) | 0.716** |
| | | A | 25 (55.6) | 20 (44.4) | | |
| | Genotype | GG | 10 (47.6) | 11 (52.4) | 0.73 (0.26 – 2.06) | 0.603** |
| | | GA | 25 (55.6) | 20 (44.4) | | |

| Characteristics of dyslipidemia | rs2383207 polymorphism | | Dyslipidemia | | OR (95% CI) | p |
|---|---|---|---|---|---|---|
| | | | Yes, n (%) | No, n (%) | | |
| *Increased LDL-c* | Allele type | G | 69 (79.3) | 18 (20.7) | 2.6 (1.16 – 5.6) | *0.024*** |
| | | A | 27 (60) | 18 (40) | | |
| | Genotype | GG | 21 (100) | 0 (0.0) | 1.67 (1.31 – 2.12) | *< 0.001** |
| | | GA | 27 (60) | 18 (40) | | |

**Fisher's Exact test, **Chi-square test*

Our study did not identify statistically significant associations between the rs2383207 polymorphism and increased triglycerides or decreased HDL-c. However, patients carrying the G allele had a higher likelihood of elevated LDL-c compared with the A allele (OR = 2.6, 95% CI: 1.16 – 5.6, p = 0.024). At the genotype level, the GG group showed significantly higher risks of increased total cholesterol (OR = 7.0, 95% CI: 1.6 – 30.8, p = 0.009) and increased LDL-c (OR = 1.67, 95% CI: 1.31 – 2.12, p < 0.001) compared with GA carriers.

## IV. DISCUSSION

Our study collected data from 66 newly diagnosed patients with chronic coronary syndrome in Can Tho City and examined the association between the *rs2383207* polymorphism of the *ANRIL* gene and lipid parameters. The results showed that LDL-c concentrations were higher in carriers of the G allele compared with the A allele, p < 0.001. In addition, patients with the GG genotype had higher total cholesterol compared with the GA genotype, p = 0.021, and LDL-c was also higher compared with the GA group, p < 0.001. These findings suggest that the rs2383207 polymorphism of ANRIL may be associated with changes in cholesterol and LDL-c levels in patients with chronic coronary syndrome.

Genetic analysis showed that the G allele of *rs2383207* was predominant (65.9%), whereas the A allele was less frequent (34.1%). In terms of genotype, the heterozygous GA was most common (68.2%), the homozygous GG accounted for 31.8%, and no cases with the AA genotype were detected. These results are consistent with some other studies in Asian populations where the risk allele at the 9p21 locus has been reported at a relatively high frequency, while the other allele is rare among patients with CAD.[4] For instance, Zhou et al. (2020) studied Chinese patients with CAD and found that the risk allele of *rs2383207* had a high frequency, and its presence, combined with family history, significantly increased the risk of CAD.[8] Our results were also consistent with the study by Tran Viet An et al. (2025) on 44 patients with chronic coronary syndrome. That study reported a predominance of the G allele (75%) compared with the A allele (25%), with GG accounting for 61.4% and GA for 34.1%.[9] Notably, the AA genotype appeared in 4.5% of cases in that study. This difference may be due to the small sample size and random variation within the population, although both studies agree that the G allele is the predominant allele at the *rs2383207* locus of *ANRIL* in Vietnamese patients with chronic coronary syndrome. Because our study sample size was limited to 66 patients, the absence of the AA genotype may reflect the low frequency of the A allele, and the distribution pattern requires confirmation in a larger cohort. Overall, the genotype and allele distribution of *rs2383207* in our study

were consistent with reports from other CAD populations.

A notable finding of this study was the significant differences in LDL-c and total cholesterol concentrations across genotype groups. Specifically, carriers of the G allele had markedly higher mean LDL-c compared with carriers of the A allele ($p < 0.001$). Genotype analysis showed that patients with the GG genotype had significantly higher total cholesterol compared with the GA group ($p = 0.021$), and similarly, LDL-c levels were higher in GG compared with GA ($p < 0.001$). Thus, carriers of two G alleles (GG), considered to have a higher genetic risk load, tended to have higher LDL-c concentrations compared with those with the GA genotype. This result suggests an association between the *rs2383207* polymorphism (G allele) and elevated LDL-c in patients with chronic coronary syndrome. Our findings are partially in line with the report by Temel et al. (2019) in Turkish patients with CAD. That study demonstrated that risk variants at 9p21 (*rs4977574* and *rs1333040*) were associated with higher total cholesterol in patients carrying the risk allele.[3] Temel et al. also reported reduced HDL-c concentrations in carriers of the 9p21 risk allele.[3] In our study, although mean HDL-c was lower in the GG group compared with GA (1.05 ± 0.30 versus 1.17 ± 0.32 mmol/L), the difference was not statistically significant ($p=0.339$). The difference in HDL-c between studies may reflect population characteristics or limited sample sizes. Nonetheless, both studies support the hypothesis that variants at the 9p21 locus are associated with lipid disturbances, particularly an increase in atherogenic cholesterol fractions (higher LDL-c and lower HDL-c).[10]

On the other hand, other lipid parameters such as triglycerides did not differ significantly between genotype groups in our study ($p > 0.05$). This is consistent with previous observations that the effect of the 9p21 locus is not primarily mediated through triglyceride variation. Indeed, large-scale GWAS have shown that the 9p21 locus increases CAD risk by approximately 30% per risk allele but is not directly linked to major lipid metabolism genes.[2] Approximately 20% of identified CAD risk loci are located near lipid-regulating genes (LDL, triglycerides, lipoprotein(a)), but 9p21 is not among them.[2]

In addition to these notable findings, several limitations should be considered. First, the sample size of 66 patients was relatively small, which reduced statistical power and may have overlooked small differences or rare genotypes such as AA. Second, the cross-sectional descriptive design does not allow conclusions on causality between genetic polymorphism and lipid levels, and potential confounders may not have been fully adjusted for. Third, the study focused on a single polymorphism, whereas cardiovascular risk results from complex gene-environment interactions. Fourth, we did not perform a detailed classification of chronic coronary syndrome subtypes, which may limit the interpretation of our findings. Therefore, the results should be interpreted with caution and not generalized as *rs2383207* alone determining lipid levels.

## V. CONCLUSION

The study showed that the G allele and GA genotype of the *ANRIL rs2383207* polymorphism predominated in patients with chronic coronary syndrome. Notably, patients carrying the GG genotype showed higher total cholesterol ($p = 0.021$) and significantly higher LDL-c ($p < 0.001$) compared with GA carriers. Carriers of the G allele also had higher LDL-c concentrations and an increased risk of elevated LDL-c ($p < 0.05$). In contrast, no statistically significant

differences were observed for triglycerides or HDL-c across alleles or genotypes.

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