CARDIOLOGY UPDATES NEWSLETTER

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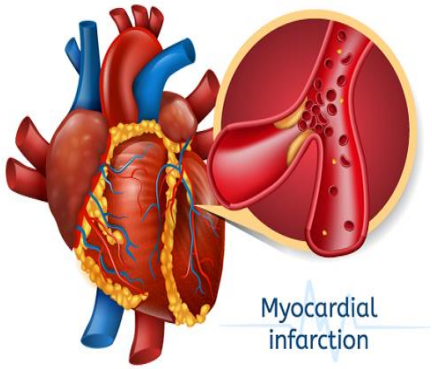
IN THIS ISSUE

Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you "Cardiology updates" which contains latest and interesting news in the field of Cardiology

Association between Lipoprotein(a) levels and the severity of significant multivessel coronary lesions in acute myocardial infarction

INTRODUCTION- Cardiovascular diseases particularly acute myocardial infarction (AMI), are the leading causes of global morbidity and mortality.[1] Biomarkers such as lipoprotein(a) [Lp(a)] are increasingly recognized as important predictors of cardiovascular risk. Elevated Lp(a) levels have been associated with the severity of coronary artery disease (CAD), especially multivessel disease (MVD), which carries worse outcomes than single-vessel disease.[2] The discovery of biomarkers uniquely predictive of multivessel disease (MVD) is still lacking, despite advancements in understanding biomarkers linked to AMI and single-vessel coronary disease.[1] This study aims to elucidate the relationship between Lp(a) levels and the prevalence of multivessel CAD in young patients with AMI.



METHODS- This was an observational study, involving 256 young adults diagnosed with AMI, divided based on Lp(a) levels (<30 mg/dL vs. ≥30 mg/dL). The study included young patients up to 55 years old for men and 60 years old for women. Participants underwent angiographic examination within 12 hours of AMI onset. Blood samples were analysed for lipid profiles, including Lp(a), using the COBAS INTEGRA 400 PLUS system. Coronary lesions were classified based on angiographic findings: significant stenosis (>50% for left main artery; >70% for other coronary arteries) and MVD if more than one artery was involved. Variables were compared using the Kruskal-Wallis and chi-square tests. Multivariate logistic regression identified independent predictors of MVD.

RESULTS- Baseline characteristics showed that most participants were male (79.69%) with a median age of 48.5 years. Cardiovascular risk factors, including smoking (66.02%) and dyslipidemia (88.67%), were prevalent. Patients with Lp(a) ≥30 mg/dL exhibited worse lipid profiles, including significantly lower HDL cholesterol (median: 40.19 mg/dL, $p<0.001$) and higher triglycerides (median: 130.5 mg/dL, $p<0.001$). Angiographic findings revealed a distinct difference in lesion distribution. MVD was more frequent in Group B, highlighting Lp(a)'s role in the severity of coronary artery disease. For the left main artery, patients with Lp(a) <30 mg/dL had slightly higher rates of no lesions (45.31% vs. 43.75%) and 70–99% stenosis (3.13% vs. 1.56%), while those with Lp(a) ≥30 mg/dL showed a greater prevalence of 1–69% stenosis (4.69% vs. 1.56%). In the left anterior descending artery (LAD), severe stenosis (70–99%) was more common in patients with elevated Lp(a) levels (20.31% vs. 12.50%). Similarly, in the circumflex artery, higher Lp(a) levels were associated with increased rates of 70–99% stenosis (12.50% vs. 9.38%) and >99% stenosis (6.25% vs. 4.69%). For the right coronary artery (RCA), patients with Lp(a) ≥30 mg/dL had fewer severe lesions (9.38% with >99% stenosis vs. 12.50%) but exhibited a higher proportion of no lesions (26.56% vs. 20.31%) (Figure 1). These findings suggest a trend toward more severe coronary lesions in patients with elevated Lp(a) levels, particularly in the LAD and circumflex arteries. Multivariate logistic regression confirmed Lp(a) ≥30 mg/dL as a strong independent predictor of MVD (odds ratio

[OR]: 5.472, p<0.001). Additionally, lower HDL levels were inversely correlated with MVD risk (OR: 0.926, p<0.001).

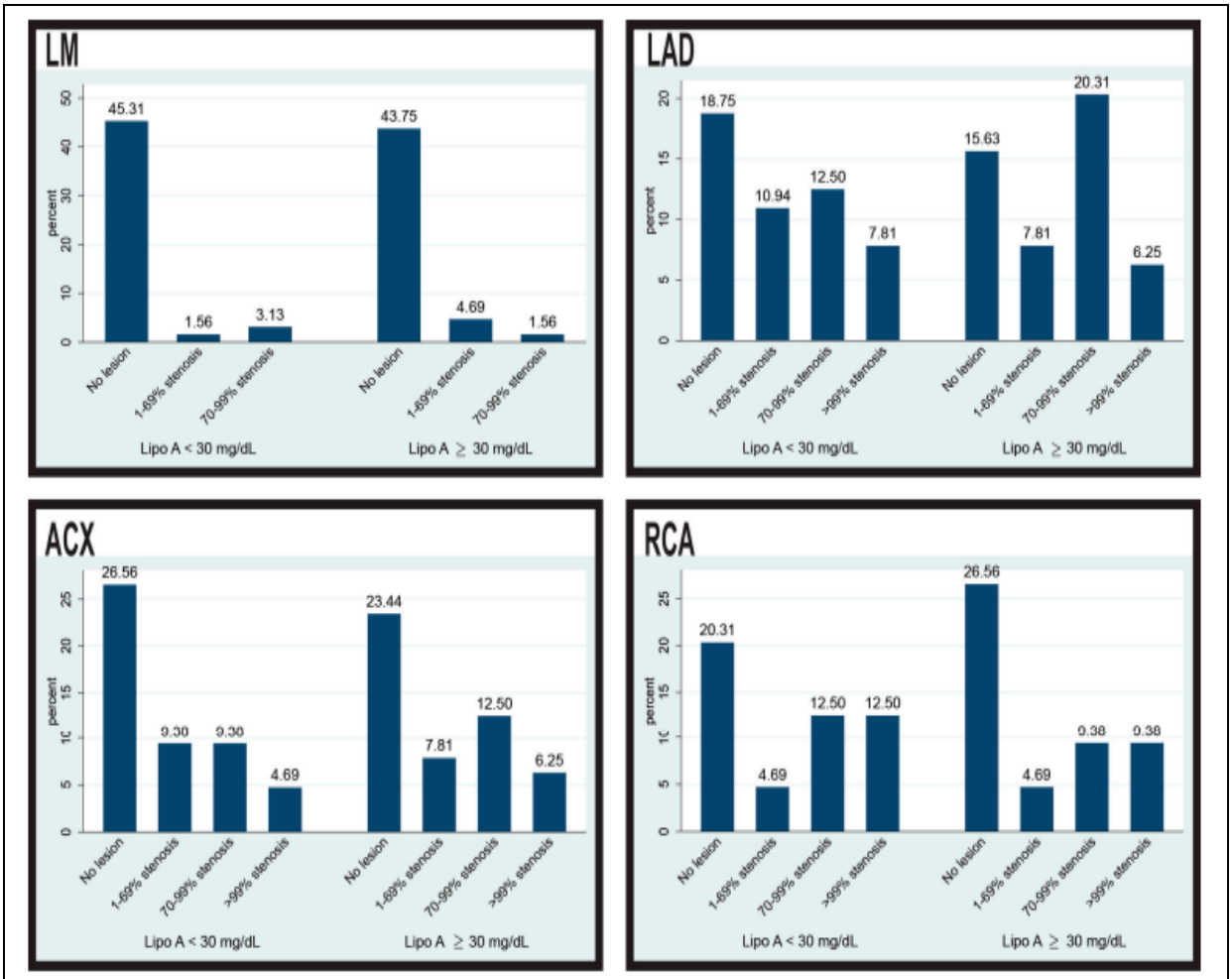


Figure 1. The severity of coronary lesions is determined by lipoprotein (a) levels in the major coronary arteries. LM: left main; LAD: left anterior descending artery; ACX: circumflex artery; and RCA: right coronary artery.

DISCUSSION- The current study reinforces the role of Lp(a) as a significant biomarker for CAD severity in young patients with AMI.[1] The findings align with Hoang V et al. which highlighted the association of elevated Lp(a) levels with multivessel disease and severe coronary involvement.[3] Additionally, the current study results demonstrate the relevance of aggressive lipid management strategies and suggest a lower Lp(a) cut-off (30 mg/dL) for risk stratification, as proposed in emerging literature.[1]

CONCLUSION- Elevated Lp(a) levels (≥30 mg/dL) significantly increase the risk of MVD in young AMI patients, emphasizing its role as a critical biomarker for CAD. Integrating Lp(a) assessments into clinical practice could enhance risk stratification and therapeutic targeting, particularly for high-risk populations. Further studies are warranted to refine these findings and explore targeted therapies addressing Lp(a)-mediated cardiovascular risks.

In the context of myocardial infarction, elevated plasma concentrations of lipoprotein (a) [Lp (a)] is a notable indicator for cardiovascular risk.

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Association of metabolomic biomarkers with plaque burden and instability in Coronary Atherosclerotic Disease

INTRODUCTION- Coronary atherosclerotic disease (CAD) is a major global health challenge, driven by risk factors such as hypertension, diabetes, and dyslipidemia.[1] The elevated levels of low-density lipoprotein cholesterol (LDL-C) are one of the primary risk factors for CAD. Nonetheless, CAD may develop in those without high LDL-C levels.[2] While lipid-lowering therapies form a cornerstone of CAD management, their effectiveness in mitigating cardiovascular risks remains incomplete. Recent advances in nuclear magnetic resonance (NMR)-based metabolomics offer promising insights into the role of metabolic disturbances, particularly dyslipidemia, in CAD progression. Even though metabolic markers have been examined in relation to the risk of cardiovascular disease in Western populations, there are few extensive studies that concentrate on the direct correlations between metabolite profiles and the degree of coronary atherosclerosis, as well as the metabonomic traits of Asian populations with CAD. Therefore, this study aims to investigate the associations between metabolomic biomarkers and plaque burden and instability in patients undergoing moderate lipid-lowering therapy.[1]

METHODS- This cohort study analysed 2560 newly diagnosed CAD patients from the GRAND cohort who received moderate lipid-lowering therapy. Serum samples were profiled using NMR spectroscopy, quantifying 175 metabolites, including lipoprotein subfractions and low-molecular-weight metabolites. The Gensini score evaluated plaque burden, while cardiac troponin T (cTnT) levels assessed plaque instability. Multivariate linear regression determined metabolite associations with CAD severity, and a Mendelian randomization approach explored potential causal relationships. Composite metabolomic indices were constructed to predict major adverse cardiac events (MACEs) during a median follow-up of 3.8 years.

RESULTS- LDL components, especially triglycerides and apolipoprotein B, exhibited a robust positive association with both the Gensini score (plaque burden) and cTnT levels (plaque instability). These markers displayed stronger correlations with CAD severity than traditional LDL cholesterol measurements. HDL components such as cholesterol esters, apolipoprotein A1, and apolipoprotein A2 were inversely associated with CAD severity. These finding highlights HDL's protective role, with larger HDL particles (HDL2, HDL3, and HDL4) showing stronger inverse associations compared to smaller HDL1 particles. Amino acids such as glycine and histidine were inversely associated with cTnT levels, while phenylalanine showed a positive correlation. Fatty acid composition revealed that a higher proportion of polyunsaturated fatty acids (PUFAs) was inversely associated with both plaque burden and instability, whereas mono-unsaturated fatty acids (MUFAs) showed a positive association with instability. The Gensini score–based metabolomic index was significantly associated with an increased risk of MACEs, including all-cause death, non-fatal myocardial infarction, stroke, ischemia-driven revascularization, and progression of coronary atherosclerosis. Per standard deviation increase in this index corresponded to a 14.8% higher risk of MACEs (HR, 1.148; 95% CI, 1.018–1.295) (Figure 1). Sensitivity analyses excluding patients with diabetes or reduced kidney function (eGFR <60 mL/min) confirmed consistent findings, supporting the robustness of the observed associations. A genetically higher level of apolipoprotein B was strongly associated with increased Gensini scores. In contrast, dihydrothymine was inversely associated with plaque burden.

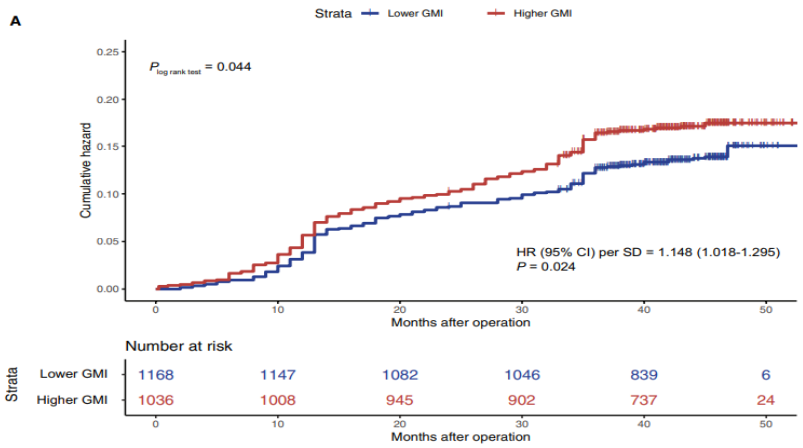

Figure 1. Associations of metabolomic indices of Gensini score with risk of major adverse cardiac events.

DISCUSSION- There was a positive association between LDL components, particularly apolipoprotein B and triglycerides within LDL, and plaque burden.[1] This finding aligns with Boekholdt SM et al. which demonstrated that apolipoprotein B outperformed LDL cholesterol as a predictor of CAD severity and cardiovascular events.[3] Similarly, Varbo A et al. highlighted that higher triglyceride-rich lipoproteins, rather than LDL cholesterol alone, were strongly associated with myocardial infarction risk. These findings support the notion that metabolomic profiling offers a more granular view of lipid abnormalities contributing to CAD progression.[4]

CONCLUSION- This study demonstrates the potential of metabolomic biomarkers in non-invasive risk assessment for CAD patients. Triglycerides and apolipoprotein B within LDL significantly predict plaque burden and instability, while HDL components exhibit protective associations. These biomarkers may serve as valuable tools in CAD prognosis and therapeutic targeting, reducing reliance on invasive diagnostic techniques.

Triglycerides and apolipoprotein B within LDL significantly predict plaque burden and instability, while HDL components exhibit protective associations.

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Impact of Nonculprit Lesions location on major clinical outcomes in ST-segment elevation myocardial infarction patients

INTRODUCTION- ST-segment elevation myocardial infarction (STEMI) is the most severe form of coronary artery disease (CAD), with significant morbidity and mortality. The most common cause of STEMI is a complete thrombotic blockage caused by an atherosclerotic plaque in an epicardial coronary artery.[1] Approximately 50% of STEMI patients have severe non-culprit lesions (NCLs) associated with worse outcomes. The COMPLETE (Complete vs Culprit-Only Revascularization to Treat Multi-Vessel Disease After Early PCI for STEMI) trial demonstrated that angiography-guided complete revascularization significantly reduced the risk of cardiovascular (CV) death or myocardial infarction (MI) compared to culprit-only PCI. Since LAD supplies up to 50% of the myocardium and is associated with high-risk features, such as lipid-rich plaques, but may cause less myocardial damage in non-culprit scenarios. Prior studies in stable CAD, including the recent ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) trial, showed no significant benefit of PCI over medical therapy for proximal LAD disease. However, the influence of NCL location, particularly in the left anterior descending (LAD) artery, on outcomes remains unclear. This sub-analysis of the COMPLETE trial aimed to evaluate the impact of NCL location and the benefit of complete revascularization versus culprit-only PCI on major outcomes, including CV death, MI, and ischemia-driven revascularization.[2]

METHODS- The COMPLETE trial was a multinational randomized study comparing culprit lesion-only PCI with complete revascularization in STEMI patients with multivessel disease (MVD). A total of 4,041 subjects were enrolled in this trial across 140 centers, with a median follow-up of 35.8 months. After successful primary PCI, eligible patients with at least one qualifying NCL were randomized to complete revascularization or culprit-only PCI. Randomization was stratified by the timing of NCL PCI (during hospitalization or within 45 days post-discharge). Qualifying NCLs had ≥70% stenosis (or 50%-69% with FFR <0.80), a diameter ≥2.5 mm, and were suitable for PCI. Outcomes included two coprimary endpoints:

(1) CV death or new MI, and (2) CV death, new MI, or ischemia-driven revascularization (IDR), with additional secondary outcomes such as MI, stroke, new onset NYHA functional class IV heart failure, and stent thrombosis.

RESULTS- The current study results showed that 1,666 patients had proximal or mid-LAD NCLs and 2,185 did not. Patients with proximal/mid-LAD NCLs were older, more likely female, and less likely to be current smokers. Procedural characteristics showed similar primary PCI rates, but those with proximal/mid-LAD NCLs had higher baseline left ventricular ejection fraction and SYNTAX scores, and more often had ≥2 vessels with NCLs. The first coprimary outcome (CV death or new MI) occurred in 8.5% of patients with proximal/mid-LAD NCLs compared to 9.9% with other NCL locations (HR: 0.83; 95% CI: 0.67-1.03). The second coprimary outcome (CV death, new MI, or IDR) occurred in 12.7% versus 13.2% respectively (HR: 0.95; 95% CI: 0.8-1.14). Similar patterns were observed for proximal LAD NCLs alone, with no significant differences compared to other NCL locations. Complete revascularization reduced the first coprimary outcome in patients without proximal/mid-LAD NCLs (HR: 0.65; 95% CI: 0.50-0.86) but showed no significant benefit in those with proximal/mid-LAD NCLs (HR: 0.85; 95% CI: 0.61-1.18; interaction P=0.235) (Figure 1). For the second coprimary outcome, complete revascularization reduced events in both groups with consistent benefit (interaction P=0.897). The secondary outcome (CV death, MI, IDR, unstable angina, or class IV heart failure) showed similar benefits with complete revascularization irrespective of NCL location (interaction P=0.909). Stratification by stenosis severity showed differential effects favoring complete revascularization in proximal/mid-LAD NCLs with stenosis ≥60%.

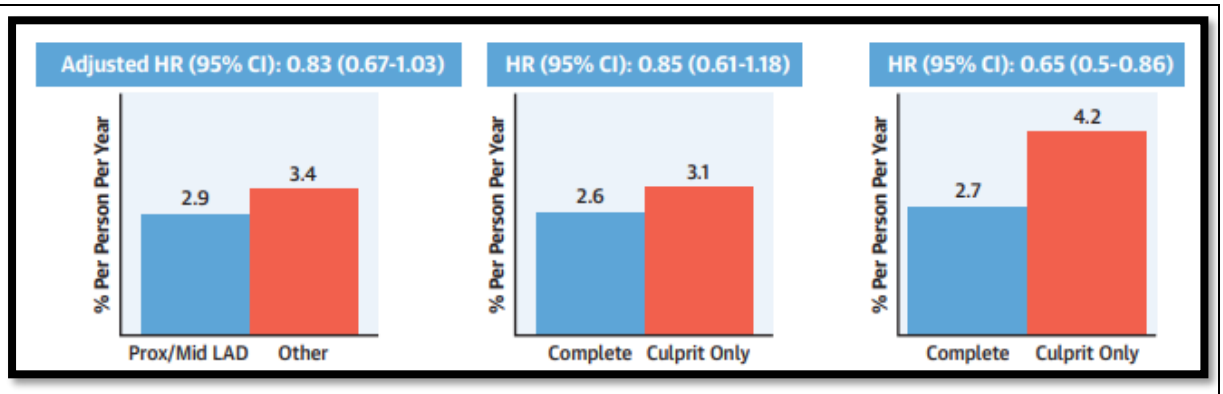

Figure 1. Proximal/mid-LAD NCL Vs other NCL Comparison

DISCUSSION- This sub-analysis demonstrated that complete revascularization provided consistent benefits in patients with and without proximal or mid-LAD NCLs, with no significant differences in major clinical outcomes between the two groups.[2] These findings are aligned with Lee JM et al., which showed that complete revascularization using physiology-guided strategies significantly reduced clinical events in patients with acute myocardial infarction (AMI), regardless of NCL location.[3] Both trials underline the importance of addressing nonculprit lesions to improve long-term outcomes.

CONCLUSION- Patients with/without proximal/mid-LAD NCLs exhibited comparable clinical outcomes when they presented with STEMI and multivessel CAD. Complete revascularization had a similar effect for patients with and without proximal/mid-LAD NCL

site, and there was no indication that coprimary and secondary outcomes differed. Regardless of the location of the NCL, the current findings support full revascularization.

Patients with a proximal/mid-LAD NCL had comparable event rates to those without among those who presented with STEMI and multivessel CAD.

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Case Report on Recurrent Syncope Linked to a Giant Right Coronary Artery Aneurysm

INTRODUCTION- Coronary artery aneurysm (CAA) is a clinical condition characterized by a localized expansion of the coronary artery that exceeds the 1.5-fold diameter of the neighbouring normal segment. Atherosclerosis is the leading cause in adults, and Kawasaki illness in children. CAA is a quite progressive condition that is identified by coronary angiography; however, it can result in deadly complications such as rupture, compression of surrounding cardiac tissues, thrombus formation, and distal embolization.[1] While CAAs are frequently asymptomatic and discovered incidentally, they can present with symptoms such as angina, myocardial infarction, or sudden cardiac death. Syncope as a presenting symptom is uncommon and has been reported in very few cases. This case details a 24-year-old woman who presented with recurrent syncope, later diagnosed with a giant right coronary artery aneurysm, highlighting the importance of multimodal imaging and the complexity of such cases.[2]

CASE PRESENTATION- A 24-year-old woman presented to the neurology department with a 2-month history of recurrent episodes of syncope. These episodes were described as sudden and transient losses of consciousness, with spontaneous recovery, occurring without any prodromal symptoms such as dizziness, chest pain, palpitations, shortness of breath, or visual disturbances. The patient denied experiencing associated symptoms like seizures, severe headaches, or confusion following the episodes. Her episodes were not triggered by physical activity, emotional stress, or positional changes. Neurological examination revealed no focal deficits or signs of seizure activity. Given the absence of neurological deficits or abnormalities in routine blood tests, the attending neurologist performed a brain MRI to exclude structural or functional brain pathology. The MRI findings were normal, ruling out central nervous system causes of syncope, such as stroke, tumor, or seizure disorder. The case was subsequently referred to the cardiology department for further evaluation. An electrocardiogram (ECG) revealed a normal sinus rhythm with no evidence of arrhythmias, conduction abnormalities, or

ischemic changes. Transthoracic echocardiography was performed, revealing a ring-like cystic lesion adjacent to the tricuspid valve in the right atrium. This structure measured approximately 2.39 × 1.90 cm and appeared solid at the periphery and cystic at the center. Color Doppler imaging showed no blood flow within the structure. To further evaluate the lesion, a computed tomography angiography (CTA) of the chest was performed. The CTA revealed a giant aneurysm arising from the right coronary artery (RCA), measuring 2.6 cm in diameter, with a 1.28 cm mural thrombus within the aneurysm (Figure 1). The aneurysm extended along the atrioventricular course of the RCA. Conventional coronary angiography confirmed the presence of the aneurysm and provided additional details regarding its location and size. The diagnosis of a giant right coronary artery aneurysm (CAA) was established. The likely cause of the patient's syncope was deemed to be intermittent mechanical obstruction of the right ventricular outflow tract (RVOT) caused by the aneurysm, leading to compromised cardiac output and transient cerebral hypoperfusion. Given the complexity of the condition, the patient was referred to a specialized cardiac center for further evaluation and definitive management. She was counseled on her condition and the potential need for surgical or catheter-based intervention to prevent complications such as rupture, thromboembolism, or persistent hemodynamic instability.

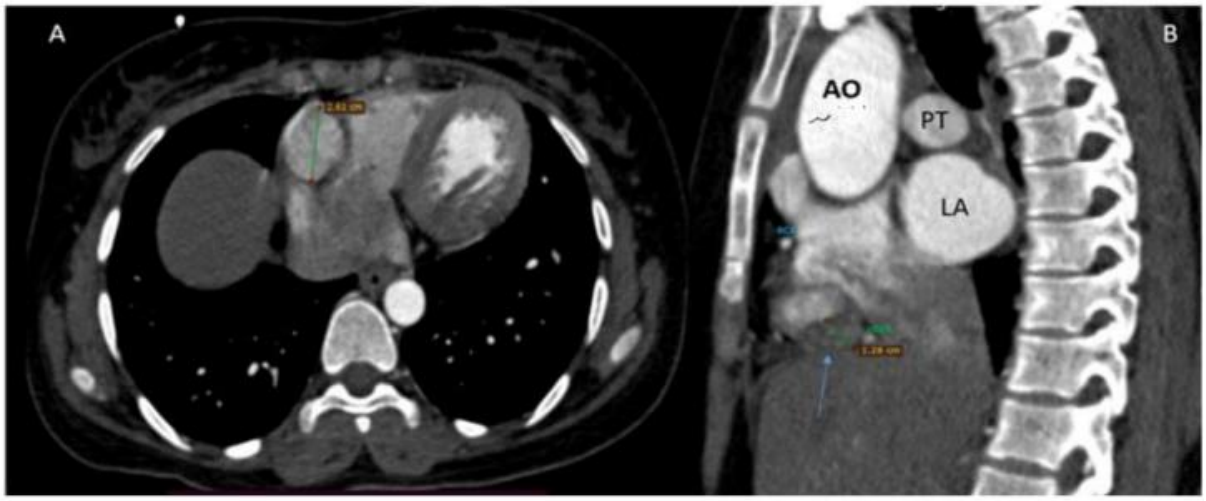

Figure 1. (A) The axial plane of CTA (B) The sagittal view of CTA Descended Aorta (AO), Pulmonary Trunk (PT), and Left Atrium (LA).

DISCUSSION- This case showed the uncommon occurrence of a large right coronary artery aneurysm with recurrent syncope, emphasizing the necessity of addressing CAA in patients with unexplained syncope.[2] For instance, Papadopoulos K et al. described a case of a giant left main coronary aneurysm causing ventricular arrhythmias and syncope due to mechanical compression of adjacent cardiac structures.[3] Similarly, Feng J et al. reported syncope linked to a Behçet's disease-related aneurysm, emphasizing the mechanical effects of aneurysm size and location.[4]

CONCLUSION- The rare presentation of a giant right coronary artery aneurysm with recurrent syncope highlights the importance of considering CAA in patients with unexplained syncope. Multimodal imaging is essential for accurate diagnosis and management. This case

contributes to the limited literature on CAAs and underscores the need for heightened clinical awareness and individualized treatment strategies to improve patient outcomes.

Multimodality imaging, comprising echocardiography, CTA, and coronary angiography, plays an important role in the correct diagnosis and therapy of CAA in unexplained syncope cases.

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