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 natriuretic peptides, cardiac structural abnormalities and functional capacity in Diabetic Cardiomyopathy

INTRODUCTION- Diabetes mellitus is a global health concern, affecting over 415 million people, with an increasing prevalence projected in the coming decades. Cardiovascular complications are common in diabetes, and heart failure (HF) represents a significant source of morbidity and mortality in this population. Specifically, diabetic cardiomyopathy (DbCM), a condition characterized by heart muscle disease in the absence of other cardiovascular risk factors, has emerged as a critical contributor to HF. DbCM was associated with multiple pathophysiological mechanisms, including oxidative stress, altered metabolism, and calcium handling abnormalities. Identifying individuals at risk for HF, particularly in the asymptomatic stage (Stage B HF), is vital for early intervention.[1] The production of N-terminal pro-B-type natriuretic peptide (NT-proBNP) occurs in myocytes and is released into the bloodstream when atrial and ventricular pressures rise.[2] One approach to detect HF risk is measuring the biomarker NT-proBNP, which has been associated with worse outcomes in individuals with diabetes. However, the relationship between NT-proBNP levels, echocardiographic abnormalities, and functional status in patients with subclinical DbCM remains unclear. So, this study aimed to elucidate these associations using data from the ARISE-HF trial, which investigated the effects of aldose reductase inhibition in patients with DbCM.[1]

Cardiovascular Disease

METHODS- This was a subgroup analysis of the ongoing ARISE-HF trial, a phase 3, double-blinded, placebo-controlled clinical trial designed to evaluate the effects of the aldose reductase inhibitor AT-001 on exercise capacity in patients with DbCM. The inclusion criteria consisted of adults with type 2 diabetes (T2D), aged ≥60 years or ≥45 years with ≥10 years of diabetes or reduced renal function, who exhibited at least one of the following: structural cardiac abnormality, elevated cardiac biomarkers (NT-proBNP ≥50 ng/L), or impaired exercise tolerance (peak VO2 ≤75% predicted). Participants underwent baseline echocardiographic assessments and cardiopulmonary exercise testing (CPET). Health status was evaluated using the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the Physical Activity Scale for the Elderly (PASE). Echocardiographic parameters included measures of left ventricular mass, atrial volume, myocardial strain, and right ventricular systolic pressure. NT-proBNP concentrations were measured, and participants were stratified into quartiles.

RESULTS- A total of 685 participants with DbCM were included, with a mean age of 67 years, and 50% were female. The median NT-proBNP concentration was 71 ng/L. Participants in the lowest quartile of NT-proBNP (≤35 ng/L) were generally younger (mean age 64.1 years) and less likely to be female (31.6%) compared to those in the highest quartile (≥135 ng/L),

where the mean age was 69.8 years and 62.5% were female. The lowest quartile had higher heart rates (mean of 73 beats per minute) and better renal function, indicated by a higher estimated glomerular filtration rate (eGFR) of 84.8 mL/min/1.73 m², compared to the highest quartile, where the mean heart rate was 66 beats per minute and eGFR was 74.7 mL/min/1.73 m². Hemoglobin levels were also higher in the lowest quartile, suggesting better overall health compared to participants with higher NT-proBNP levels. Structural cardiac abnormalities were common, but there was no significant correlation between NT-proBNP levels and echocardiographic parameters. Participants in the higher NT-proBNP quartiles were generally older, had lower estimated glomerular filtration rates, and had worse functional capacity as indicated by CPET results, KCCQ scores, and PASE scores. In comparison to those with an NT-proBNP of <125 ng/L, those with an NT-proBNP of ≥125 ng/L showed lower KCCQ physical limits scores, lower KCCQ clinical summary scores (Figure 1), lower KCCQ overall summary scores, and lower physical activity scores. Higher NT-proBNP levels were associated with shorter CPET duration, lower peak VO2, and a higher ventilatory efficiency slope. Despite this, NT-proBNP concentrations did not correlate with structural measures such as left atrial volume index, left ventricular ejection fraction, or global longitudinal strain.

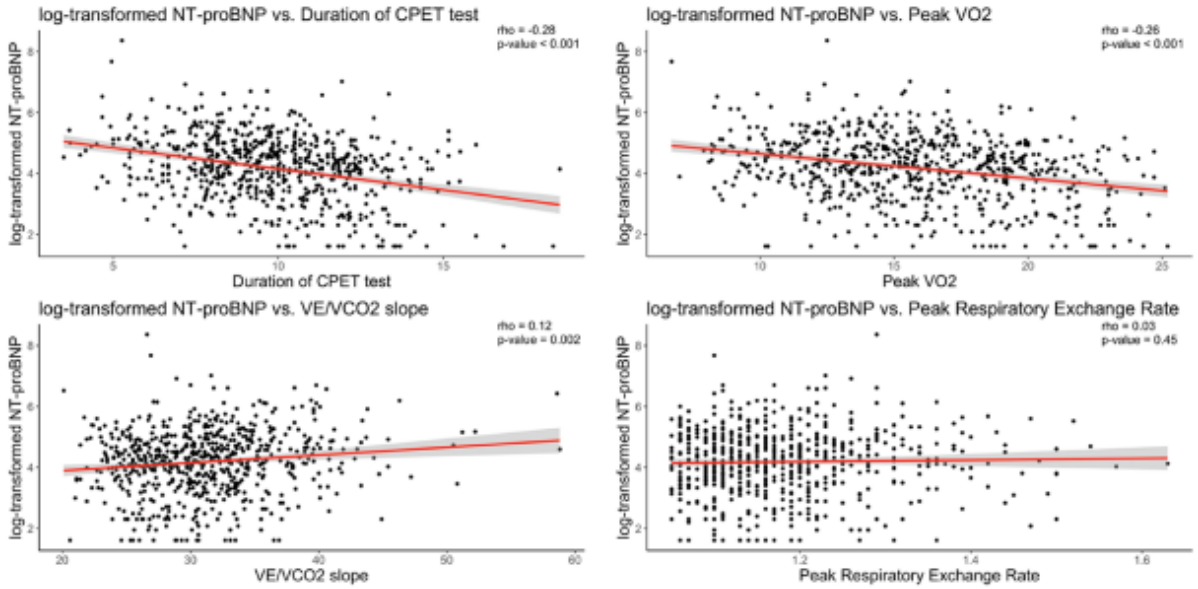

Figure 1. Association of NT-proBNP levels and cardiopulmonary exercise testing. Abbreviations NT-proBNP, N-terminal pro-B-type natriuretic peptide; CPET, cardiopulmonary exercise testing; VO2, maximal oxygen consumption; VE/VCO2, ventilatory efficiency.

DISCUSSION- This study indicated that in individuals with subclinical diabetic cardiomyopathy (DbCM), NT-proBNP levels were significantly associated with functional limitations, poorer health status, and lower physical activity but do not correlate with echocardiographic parameters of structural heart abnormalities.[1] Similarly, Wang et al. investigated patients with type 2 diabetes and non-ischemic Stage B heart failure, NT-proBNP levels were found to be correlated with exercise capacity but not with imaging markers of myocardial strain or left ventricular hypertrophy. Their results demonstrated that, while NT-proBNP could identify patients with reduced functional capacity, it was not an effective standalone indicator of underlying structural heart abnormalities.[3] This supported the

observation that NT-proBNP better reflects functional impairment rather than structural cardiac changes in patients with subclinical DbCM.[1]

CONCLUSION- This study concluded that in patients with subclinical DbCM, NT-proBNP concentrations correlate with functional impairments but not with cardiac structural abnormalities. This highlights the need for multimodality approaches in assessing HF risk in diabetic patients.

In patients with subclinical DbCM, NT-proBNP concentrations correlate with functional impairments but not with cardiac structural abnormalities.

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Impact of Obesity and Depressive Symptoms on Chest Pain in Patients with Nonobstructive Coronary Artery Disease

INTRODUCTION- Nonobstructive coronary artery disease (NOCAD) is a common condition that presents with chest pain (CP) despite the absence of significant blockages.[1] Also, it accounts for less than 50% of stenosis in coronary arteries. Understanding the risk factors for CP in NOCAD is crucial for developing targeted interventions to alleviate symptoms and improve outcomes. Obesity and depressive symptoms are two potential risk factors that may influence the prevalence and severity of CP in NOCAD. Obesity is a well-documented risk factor for cardiovascular disease, and studies have linked it to an increased risk of angina in the general population. However, its role in patients with NOCAD is not fully understood. Similarly, depression has been associated with more frequent and severe CP in various cardiac conditions. Obesity with angina in individuals with established NOCAD on angiography is unclear. So, this study aimed to investigate the relationships between obesity, depressive symptoms, and CP in patients with NOCAD, hypothesizing that both factors would be associated with a higher prevalence and frequency of CP.[2]

METHODS- This was a prospective study involving 814 participants from the Emory Cardiovascular Biobank, aged 20-90, who underwent left heart catheterization between 2003 and 2022. Eligible participants were aged 20-90 years and had angiographically confirmed NOCAD. Individuals with obstructive coronary artery disease (≥50% stenosis), heart failure, valvular disease, or other significant comorbidities were excluded. Data collection included demographic and clinical information, such as age, sex, race, medical history, and social

determinants of health. Obesity was defined using a body mass index (BMI) of 30 or higher, with further classification into obesity classes based on BMI ranges. Depressive symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9), a validated tool for screening depression, with scores indicating symptom severity. CP frequency was measured using the Seattle Angina Questionnaire (SAQ), a self-administered questionnaire that includes items on physical limitations, angina frequency, treatment satisfaction, and quality of life. The angina frequency domain score (AFCS), calculated from responses about the frequency of CP and nitroglycerin use, was used as the primary measure of CP. Statistical analyses involved logistic regression to determine factors associated with CP prevalence and linear regression to assess CP frequency. A mediation analysis was conducted to explore the role of depressive symptoms in the association between obesity and CP.

RESULTS- The average age of the study population was 58.8 years, with 52.6% of participants being female. Obesity was present in 42.7% of the sample, and CP was reported by 71.5%. The mean AFCS was 76.4, indicating varying degrees of angina frequency across the cohort. Compared to individuals without obesity, those with obesity had a higher prevalence of CP (77.6% vs. 67%, p<0.001) and reported more frequent CP (lower AFCS, p=0.02) (Figure 1). Multivariable analyses showed that obesity was independently associated with a 1.7 times higher likelihood of experiencing CP, even after adjusting for demographics, cardiovascular risk factors, and social determinants. Additionally, depressive symptoms, as indicated by higher PHQ-9 scores, were independently correlated with CP prevalence (OR 1.07, p=0.03). Interaction analyses revealed that the association between obesity and CP was more pronounced in men and individuals without depression, while women and those with depression showed higher baseline CP regardless of obesity status. Mediation analysis indicated that depressive symptoms partially mediated the association between obesity and CP, accounting for approximately 12.6% of the relationship. This suggests that addressing depressive symptoms may help alleviate CP in patients with NOCAD who are also obese.

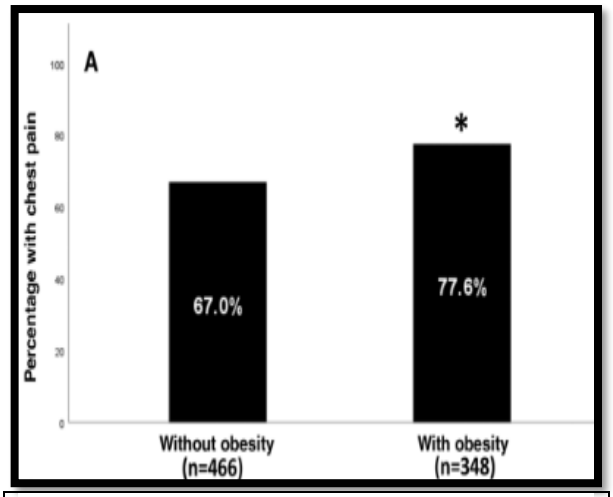

Figure 1. Prevalence of self-reported chest pain by obesity status

DISCUSSION- The association between depressive symptoms and CP observed in this study was also consistent with previous findings in cardiac populations.[2] A systematic review by Mommersteeg P et al. highlighted the higher prevalence of CP in individuals with NOCAD who also experienced anxiety and depression. Like the current results, they found that depressive symptoms were associated with a greater burden of CP. These findings suggest that the psychological state of patients plays a crucial role in the perception and severity of chest pain, potentially mediated by neurohormonal pathways and inflammatory processes that are affected by both depression and obesity.[3]

CONCLUSION- This study concluded that for individuals with NOCAD, obesity was linked to both the prevalence and frequency of self-reported chest pain, and this relationship was unaffected by demographics, medications, depressive symptoms, social determinants of health, or risk factors for CVD. Men and those without depression have a stronger correlation between self-reported chest pain and fat. In patients with NOCAD, the relationship between obesity and self-reported chest pain was partially mediated by depressive symptoms, and more severe depressive symptoms were independently linked to self-reported chest pain prevalence and burden.

In patients with nonobstructive coronary artery disease, obesity and depressive symptoms were independently linked to CP; in men, in particular, this association was partially mediated by depressive symptoms.

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Relationship between non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio and major adverse cardiovascular and cerebrovascular events in coronary artery disease

INTRODUCTION- Dyslipidemia is a significant contributor to adverse outcomes in patients with coronary artery disease (CAD), which remains a leading cause of mortality worldwide. Managing dyslipidemia traditionally focuses on reducing low-density lipoprotein cholesterol (LDL-C). However, residual cardiovascular risks persist even with aggressive LDL-C lowering, necessitating the identification of novel lipid indices that better predict adverse events.[1] The total cholesterol content of lipoproteins containing apolipoprotein B is known as non-high-density lipoprotein cholesterol (non-HDL-C). This comprises low-density lipoproteins (LDL), lipoprotein (a), intermediate-density lipoproteins (IDL), and very low-density lipoproteins (VLDL) and their metabolic remnants.[2] The non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) integrates both atherogenic and anti-atherogenic lipid parameters and has emerged as a potential risk marker. Nevertheless, there was a dearth of data regarding the association between the NHHR and the chance of adverse outcomes for CAD patients. So, this study aimed to evaluate the association between NHHR and the risk of major adverse cardiovascular and cerebrovascular events (MACCEs) in CAD patients undergoing percutaneous coronary intervention (PCI).[1]

METHODS- A retrospective analysis was conducted using data from 2251 patients who underwent PCI. Patients were included if they had complete data on total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) levels. The primary outcome was the incidence of MACCEs, which included cardiac mortality, acute myocardial infarction (AMI), stroke, and repeat revascularization. Patients were categorized into quintiles based on NHHR values: quintile 1 (<2.15), quintile 2 (2.15–2.77), quintile 3 (2.78–3.39), quintile 4 (3.40–4.22), and quintile 5 (>4.22). Data on demographics, clinical presentation, comorbidities, and treatment were collected. Logistic regression models were used to assess the relationship between NHHR and MACCEs, adjusting for confounders such as age, sex, smoking status, comorbidities (heart failure, atrial fibrillation, diabetes, hypertension), and medication use.

RESULTS- This study showed that over a median follow-up of 29.8 months, 270 patients experienced MACCEs. Patients in quintile 3 (NHHR 2.78–3.39) had the lowest adjusted odds of experiencing MACCEs (OR 0.64, 95% CI 0.42–0.99), while those in quintile 5 (>4.22) had an elevated risk (OR 1.17, 95% CI 0.74–1.64). Specifically, quintile 5 patients were more likely to be smokers and exhibited elevated levels of total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C). Furthermore, they had a higher prevalence of ST-segment elevation myocardial infarction (STEMI) and a greater history of diabetes. In contrast, patients in quintile 1 were typically older, more likely to be male, and presented with non-ST-segment elevation acute coronary syndrome (NSTE-ACS). They also had higher high-density lipoprotein cholesterol (HDL-C) levels and a greater percentage of bifurcation lesions. RCS analysis revealed a U-shaped association between NHHR and MACCEs, with the lowest risk observed at an NHHR of approximately 3.119 (Figure 1). Below this value, higher NHHR was associated with a decreased risk of MACCEs, while above this threshold, the risk increased significantly. Subgroup analysis demonstrated consistent U-shaped relationships across different patient demographics, except for younger patients (<65 years), where a linear association was observed.

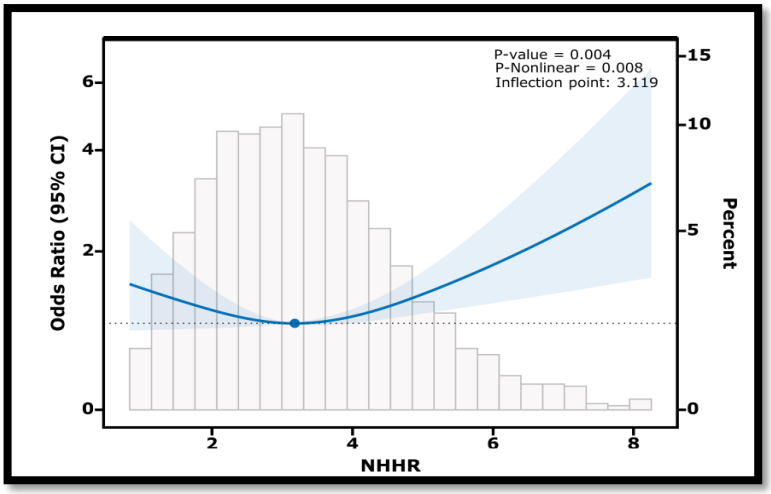

Figure 1. Association between NHHR and MACCEs in CAD patients with PCI

DISCUSSION- This study confirmed a U-shaped association between NHHR and the risk of MACCEs in CAD patients undergoing PCI, indicating that both very high and very low NHHR values were linked to increased adverse event risk. The findings suggested that NHHR was a more comprehensive lipid measure than individual lipid parameters like LDL-C, as it encompasses a balance of pro- and anti-atherogenic lipoproteins.[1] You J et al. reported similar associations between NHHR and adverse outcomes but did not completely explore non-linear

relationships or adjust for confounders. This study extends those findings by employing RCS analysis to better delineate the dose-response relationship and identify an optimal NHHR range for minimizing risk.[3]

CONCLUSION- This study concluded that the clinical utility of NHHR as a predictor of MACCEs in patients undergoing PCI, with an optimal range around 3.119 associated with the lowest risk. These findings suggested that NHHR could guide more personalized lipid management strategies in CAD patients.

In patients with CAD having PCI, this study shows a U-shaped relationship between the baseline NHHR and the incidence of MACCE.

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Case Report on Transcatheter Coil Embolization of a Coronary Cameral Fistula in a Young Male with a Structurally Normal Heart

INTRODUCTION- Coronary-cameral fistulas (CCF) are abnormal connections between one or more coronary arteries and a cardiac chamber, typically the right ventricle or atrium. The most common reasons for closure include a substantial left-to-right shunt, cardiac ischemia, and the avoidance of endoarteritis or rupture.[1] These connections can be congenital or acquired, with approximately 90% of cases being congenital due to the persistence of embryonic sinusoids. Although CCFs often remain asymptomatic, larger fistulas can lead to clinical symptoms such as angina, dyspnea, or heart failure due to the "coronary steal" phenomenon, where blood is diverted away from the coronary circulation. This case report presents a young male patient with a symptomatic CCF arising from the left coronary artery (LCA) to the right ventricle (RV), treated successfully using a transcatheter coil embolization approach.[2]

CASE PRESENTATION- A 20-year-old male was referred to a tertiary heart hospital for evaluation of persistent retrosternal chest pain and exertional dyspnea, classified as functional class III. The patient described the chest pain as a squeezing sensation that radiated to his left shoulder and worsened with physical activity, alleviating with rest. These symptoms had been occurring intermittently over the previous 6 months, but the patient had not sought medical attention until the symptoms became more severe and persistent. The patient had no

history of cardiac symptoms, chronic conditions, smoking, drug use, or family history of cardiovascular disease, and his lifestyle was unremarkable. On presentation, his vital signs were stable, and physical examination revealed no abnormalities in the heart, lungs, abdomen, or neurological system. The patient was admitted for diagnostic evaluation due to chest pain and dyspnea. Initial tests, including cardiac biomarkers, complete blood count (CBC), renal function, electrolytes, coagulation profiles, and Electrocardiography (ECG), were all normal. Transthoracic echocardiography (TTE) performed during the initial assessment showed a significantly dilated left coronary artery (LCA), measuring approximately 5 mm in diameter, with an aneurysmal enlargement reaching 2 cm. Additionally, a small orifice was noted connecting the aneurysm to the right ventricle (RV) body. The RV size and function were normal, with a preserved left ventricular ejection fraction (LVEF) of 60%. No other structural abnormalities were detected in the heart (Figure 1). A cardiac computed tomography angiography (CTA) confirmed the presence of a dilated LCA with a large aneurysm and a fistulous connection to the RV. Subsequent coronary angiography (CAG) corroborated these findings, showing a dilated LCA and a fistulous connection draining into the RV. Given the potential risks associated with untreated coronary-cameral fistula (CCF), including heart failure, arrhythmias, or aneurysm rupture, an interventional approach was chosen. The patient was prepped for a transcatheter coil embolization procedure. Under sterile conditions, femoral artery and vein access were obtained using the Seldinger technique, allowing for both diagnostic and interventional procedures. After successful catheterization and placement of an introducer sheath, anticoagulants were administered to reduce the risk of thromboembolism. A guiding catheter was then advanced to the coronary ostium through the femoral artery under fluoroscopic guidance. The aneurysmal segment of the LCA and the fistulous tract leading to the RV were navigated using a guidewire. Once the anatomy was fully assessed, coil embolization was performed to occlude the aneurysm and the fistula. A total of eight coils of varying sizes (ranging from 18 × 40 mm to 25 × 50 mm) were deployed sequentially into the aneurysmal sac, ensuring proper placement and cessation of blood flow within the aneurysm and fistula as confirmed by post-deployment angiography. The final CAG demonstrated no residual filling of the aneurysm, indicating successful occlusion. Post-procedure, the patient was closely monitored in the coronary care unit (CCU). He remained stable with no immediate complications, and his symptoms of chest pain and dyspnea resolved completely by the following day. A post-procedure chest X-ray was normal, and the femoral access sites were well-managed without signs of bleeding or other complications. The patient was discharged from the hospital in stable condition after 48 hours and scheduled for follow-up visits at 1, 3, and 6 months. During these follow-up appointments, the patient remained symptom-free, and follow-up imaging confirmed the sustained success of the intervention with no evidence of recurrence or complications.

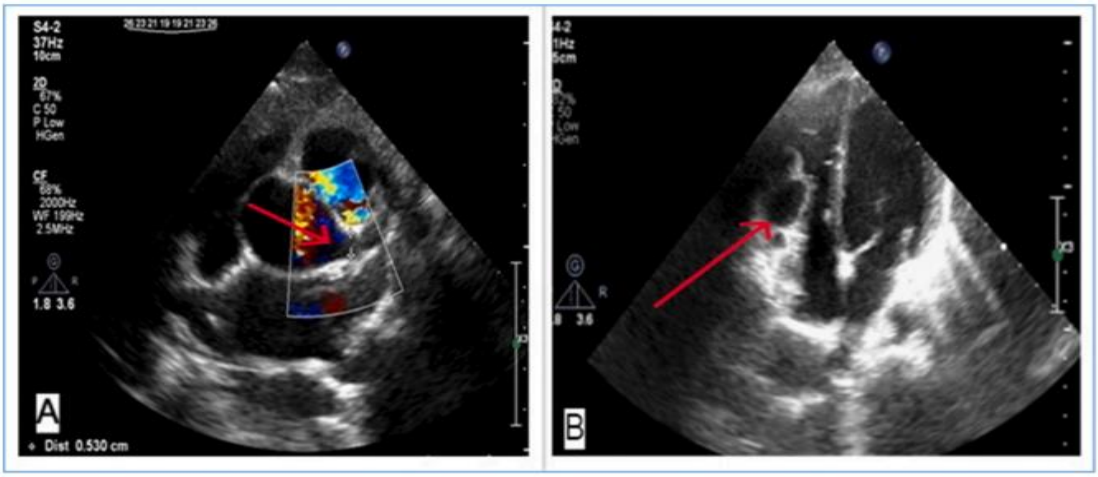

Figure 1. Transthoracic echocardiography (TTE) A) Left coronary artery dilatation (LCA) (red arrow); B) The red arrow indicates the coronary cameral fistula (CCF)

DISCUSSION- Coronary-cameral fistulas are rare, occurring in 0.002% of the general population and up to 0.25% during cardiac catheterization. Treatment typically involves surgical ligation or catheter-based closure to prevent complications like heart failure, myocardial infarction, or aneurysm rupture. In this patient, transcatheter coil embolization was successfully used as a minimally invasive option to occlude the fistula, leading to complete symptom resolution.[2] Like the current case, Trang PT et al. used a percutaneous transcatheter approach to occlude the fistula, leading to complete symptom resolution.[3] Both cases demonstrated that minimally invasive techniques can be effective for closing large symptomatic fistulas.

CONCLUSION- CCFs are a rare cardiac condition that can show a variety of anatomical and clinical features. Coronary angiography (CAG) is the most precise diagnostic procedure for figuring out the architecture of fistulas and potential treatment choices. Regardless of the severity of the symptoms, both small and big fistulas require surgical repair or a transcatheter treatment.

Coronary angiography (CAG) is the most precise diagnostic method for determining the structure of fistulas and potential treatment options.

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