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IN THIS ISSUE

Dear Doctor,

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

Association between Urinary Uranium Concentrations and Cardiac Geometry and Left Ventricular Function

CARDIOVASCULAR DISEASE

INTRODUCTION- Uranium poisoning of soil and water is a global health hazard that has received insufficient attention, with significant regional variation in uranium concentrations attributed to both natural (geogenic) and man-made (anthropogenic) causes.[1] While uranium's nephrotoxicity is well-documented, its effects on cardiovascular health remain understudied. The Strong Heart Study (SHS) highlighted chronic exposure to environmental contaminants, such as arsenic and cadmium, as risk factors for cardiovascular disease (CVD). However, studies into how uranium affects these measures, and the progression of CVD is still crucial. This study aimed to assess whether uranium exposure, as measured by urinary uranium levels, is associated with cardiac geometry alterations and left ventricular (LV) function among young adults. These subclinical markers are crucial for understanding early cardiovascular risks associated with uranium exposure.[2]

METHODS- This prospective cohort study utilized data from the Strong Heart Family Study (SHFS), involving 1,332 participants aged below 50, free from diabetes and clinical CVD at baseline (2001-2003). Urinary uranium was measured using inductively coupled plasma-mass spectrometry, with results standardized to creatinine levels to account for dilution. Blood pressure and transthoracic echocardiography were measured at baseline and during a follow-up visit (2006-2009). To assess the relationship between baseline uranium and baseline and follow-up outcome measures, the study employed linear mixed-effects models for continuous variables and generalized estimating equations for binary measures. Continuous measurements of cardiac geometry and LV function, along with incident and prevalent LV hypertrophy, were the primary outcomes.

RESULTS- The study results showed that median urinary uranium concentration, adjusted for creatinine, was 0.029 mcg/g (interquartile range: 0.013–0.058 mcg/g). Participants with higher urinary uranium levels exhibited distinct patterns in cardiac geometry and left ventricular (LV) function (Figure 1). A log-doubling of urinary uranium was significantly associated with a 0.49 g/m², 95% CI: 0.07-0.92 g/m^2 increase in LV mass index and a 0.66 mL, 0.25-1.08 mL increase in stroke volume at baseline. Similarly, left atrial systolic diameter (0.01 cm/m^2, 0.01-0.02 cm/m^2) and LV internal diameter (0.08 cm/m^2, 0.02-0.13 cm/m^2; 0.11 cm, 0.05-0.17 cm/m^2) also demonstrated significant positive associations with urinary uranium levels. All individuals had a fully adjusted odds ratio for LVH of 1.09 (95% CI: 0.91-1.31) at baseline and 1.25 (95% CI: 1.06-1.48) at follow-up for a log-doubling of urine uranium. These associations were particularly pronounced among individuals with prehypertension or hypertension at baseline, where the odds ratio increased to 1.37 (95% CI: 1.16–1.63). In terms

of functional outcomes, urinary uranium was positively associated with an increase in pulse pressure over the follow-up period, particularly in participants with prehypertension or hypertension. At follow-up, a log-doubling of urinary uranium was linked to a 0.28 mm Hg increase in pulse pressure (95% CI: 0.05–0.52 mm Hg, $P < 0.05$), reflecting structural changes in arterial compliance and stiffness. However, there were no significant associations with other measures of systolic or diastolic function, such as ejection fraction, mitral E/A ratio, or deceleration time.

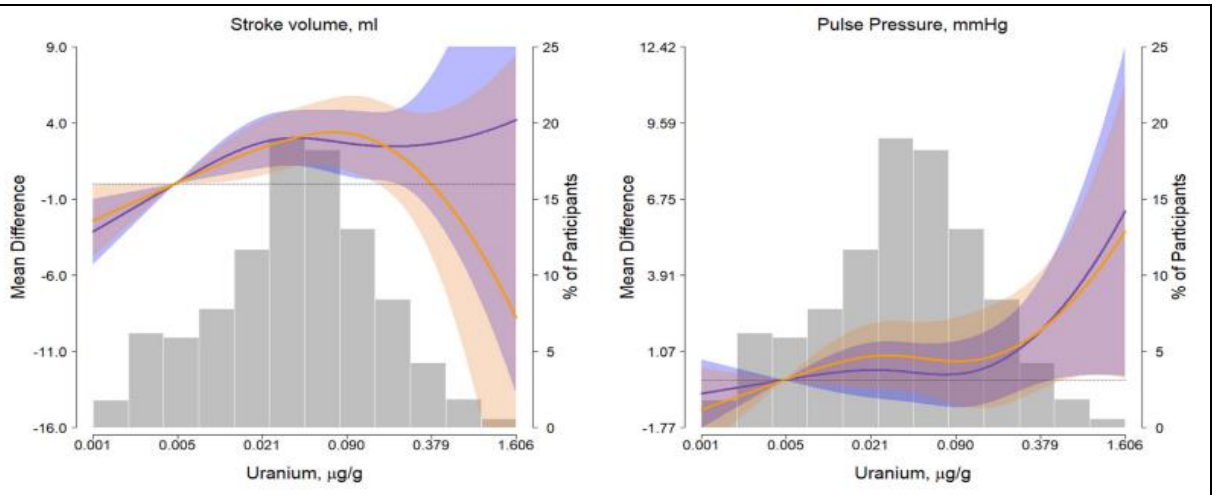

Figure 1. Prospective and Cross-Sectional Adjusted Mean Differences by Urine Uranium Levels for Selected Left Ventricular Function Measures

DISCUSSION- This study demonstrates a significant association between urinary uranium levels and changes in cardiac geometry and function, including increased LV mass index, left atrial diameter, and pulse pressure.[2] These findings align with Mendy A et al. (NHANES study) reported an increased risk of heart failure with higher urinary uranium levels, with an odds ratio (OR) of 5.20 (95% CI: 1.52–17.80) in the highest exposure groups. In addition, like current findings, the NHANES study highlighted uranium's role in exacerbating subclinical cardiac changes, particularly in populations with prolonged exposure to environmental contaminants.[3]

CONCLUSION- Urinary uranium levels are linked to significant alterations in cardiac geometry and function, including LV hypertrophy and increased pulse pressure, in a cohort of young adults. These findings highlight the importance of addressing environmental uranium exposure to mitigate long-term cardiovascular risks.

Adult cardiac geometry and LV function measurements, such as elevated pulse pressure and LV hypertrophy, were negatively correlated with urinary uranium levels.

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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

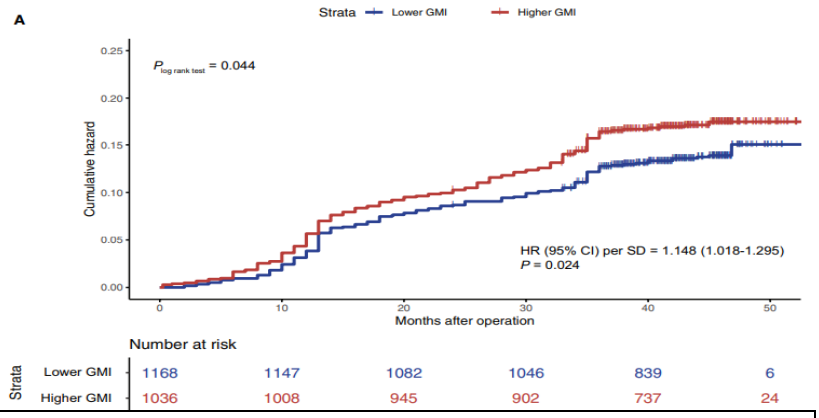

Figure 1. Associations of metabolomic indices of Gensini score with risk of major adverse cardiac events.

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.

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%.

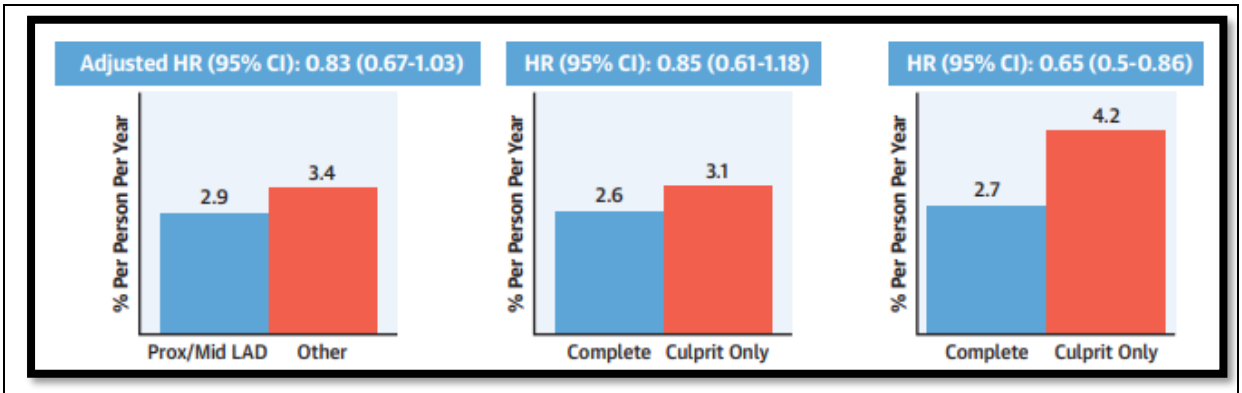

Figure 1. Proximal/mid-LAD NCL Vs other NCL Comparison

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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A rare case of acute decompensated heart failure due to transient left bundle branch block

INTRODUCTION- Transient left bundle branch block (LBBB) is a rare and unusual complication associated with acute coronary syndromes (ACS).[1] In the general population, 0.06–0.1% of people have LBBB. Nonetheless, LBBB is commonly observed in heart failure (HF) patients and is linked to increased rates of morbidity and death. By age 80, the prevalence has increased from less than 1% at age 50 to 6%.[2] LBBB significantly disrupts cardiac conduction, leading to dyssynchronous and inefficient left ventricular (LV) contraction, which can exacerbate or precipitate acute HF. Typically, the blood supply to the left bundle branch originates from the proximal left anterior descending artery (LAD) and, to a lesser extent, the right coronary artery (RCA). However, variations in coronary anatomy, such as involvement of the ramus intermedius (RI), can lead to atypical presentations. This study details an exceptional case of acute decompensated heart failure caused by transient LBBB due to critical stenosis of the RI artery, underscoring the importance of recognizing such presentations in clinical practice.[1]

CASE PRESENTATION- A 63-year-old woman with a history of hypertension and diabetes mellitus presented with acute onset of chest pain and shortness of breath. On admission, her blood pressure was 145/95 mmHg, and physical examination revealed pulmonary crackles, jugular vein distension, and a third heart sound. Electrocardiography showed sinus rhythm at 94 bpm and newly diagnosed complete LBBB. Chest radiography revealed diffuse bilateral pulmonary edema. A transthoracic echocardiogram (TTE) demonstrated significant intraventricular dyssynchrony, an ejection fraction (EF) of 35%, mild-to-moderate mitral regurgitation, and elevated pulmonary artery systolic pressure (45 mmHg). Laboratory tests showed elevated cardiac biomarkers, including a troponin I level of 0.049 ng/mL (normal <0.0156 ng/mL). After initial stabilization with oxygen, intravenous diuretics, and vasodilator therapy, the patient's symptoms improved. Given the clinical findings, an urgent coronary angiogram was performed, revealing 95% stenosis in the osteal segment of the bifid RI artery (Figure 1). The LAD, circumflex artery, and RCA were normal. Percutaneous coronary intervention (PCI) was successfully performed using balloon angioplasty, resulting in a 20% residual stenosis. Within 90 minutes post-PCI, repeat electrocardiography showed complete resolution of the LBBB. The patient's in-hospital recovery was uneventful. She was discharged after four days with no complaints. A follow-up TTE conducted 10 days later showed normalization of LV function (EF: 60%) and resolution of dyssynchrony and mitral regurgitation. Her two-year follow-up remained uneventful.

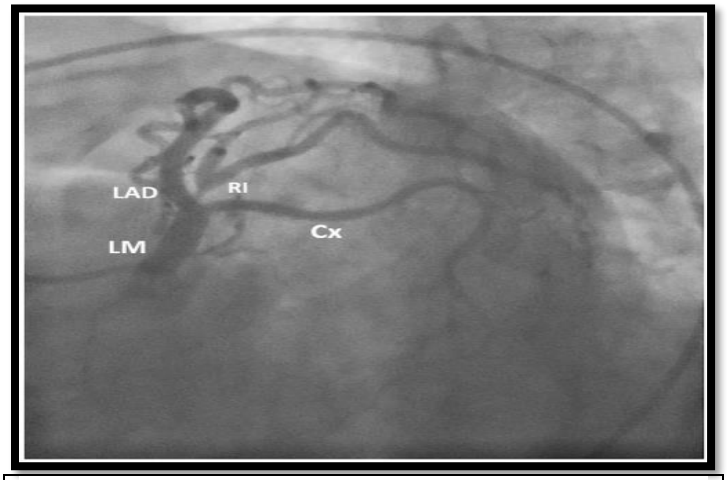

Figure 1. A bifid-shaped selective left coronary angiography reveals significant (95%) stenosis at the osteal portion of the ramus intermedius.

DISCUSSION- The current case demonstrates that transient left bundle branch block (LBBB), a rare consequence of ramus intermedius occlusion, can induce acute heart failure, a condition which was fully resolved following successful coronary revascularization.[1] This finding aligns with existing evidence suggesting that ischemia-induced conduction disturbances are reversible with appropriate intervention. For instance, Strauss DG et al. emphasized that the anatomical blood supply to the bundle branches plays a pivotal role in conduction abnormalities, correlating LBBB primarily with proximal LAD and RCA occlusions.[3] Similarly, this case highlights the RI as an alternative vascular contributor to LBBB, broadening the understanding of coronary circulation's role in electrical conduction. This case also reinforces the concept of the trifurcated left main (LM) coronary anatomy, as described by Kovacevic M et al.[4] By delineating the unique role of the RI in supplying areas traditionally attributed to the diagonal or obtuse marginal arteries, the current findings expand the anatomical framework critical for understanding complex coronary interventions.[1]

CONCLUSION- This case illustrates the potential for RI occlusion to cause transient ischemic LBBB and acute HF and it underscores the importance of considering atypical coronary anatomy in the evaluation of new-onset LBBB and HF. Successful revascularization not only resolved the LBBB but also restored normal cardiac function, emphasizing the reversibility of this condition when promptly managed. Clinicians should remain vigilant for such presentations to ensure accurate diagnosis and optimal treatment.

It is important to recognize ramus intermedius as a potential contributor to ischemic conduction disturbances.

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