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EDITORIAL

Biomarkers and inflammation in coronary artery disease: key insights

Coronary artery disease (CAD) remains one of the leading causes of morbidity and mortality worldwide, particularly in high-risk populations such as patients with diabetes and chronic kidney disease [1–5]. Recent research has focused on identifying novel biomarkers and understanding the role of inflammation in the progression of CAD, which could improve early diagnosis and treatment strategies. Additionally, the impact of renal dysfunction and inflammatory markers on major adverse cardiovascular events (MACE) and mortality post-percutaneous coronary intervention (PCI) has gathered significant attention [5–9]. This article explores key findings from recent studies, highlighting the role of circulating biomarkers, inflammation, and renal function in shaping cardiovascular outcomes in CAD patients.

Zhao et al. explored the association between the rs1333040 polymorphism and CAD in a Chinese population [10]. The study involved 500 CAD patients and 500 controls, with diagnoses confirmed by coronary angiography. Genotyping revealed a significant link between the T allele of rs1333040 and increased CAD risk. LDL-C levels and Gensini scores varied among different alleles, while those with the TC+CC genotype had higher HDL and ApoA levels in a recessive model. The TC+TT genotype was also identified as a CAD risk factor in a dominant model, establishing the T allele as a susceptibility marker.

The study by Seydel et al. investigated the relationship between SYNTAX scores and new inflammatory markers in ST-elevation myocardial infarction (STEMI) and Non-ST-elevation myocardial infarction (NSTEMI) patients [11]. It included 53 STEMI and 64 NSTEMI patients, analysing factors such as albumin-globulin ratio, fibrinogen-to-albumin ratio (FAR), and others. In NSTEMI patients, those with high SYNTAX scores had higher levels of age, glucose, fibrinogen, monocytes, and FAR, while lower levels of albumin and total protein were observed. FAR and monocyte levels were found to be independent predictors of a high SYNTAX score in NSTEMI patients. The study concluded that FAR was a significant marker for predicting disease severity in NSTEMI patients.

Li et al. investigated the role of TRPC5 in chronic intermittent hypoxia (CIH)-induced myocardial pyroptosis in a rat model of obstructive sleep apnoea-hypopnoea syndrome (OSAHS) [12]. CIH rats exhibited myocardial cell damage, including vesicular protrusions and pyroptotic bodies, with significantly elevated pyroptosis-related proteins like caspase-1, IL-1β, and IL-18. TRPC5 and its downstream proteins (NLRP3, p-CaMKIIβ/δ/γ, and HDAC4) were also upregulated, suggesting TRPC5 promotes inflammasome formation and pyroptosis through CaMKII phosphorylation and HDAC4 translocation (Figure 1). These results highlight TRPC5 as a potential therapeutic target for myocardial injury in OSAHS.

Sacubitril/Valsartan (Sac/Val) has demonstrated significant protective effects in myocardial infarction (MI) by targeting inflammation and fibrosis in the heart. In a mouse model of MI, Sac/Val treatment led to a reduction in myocardial infarct size and fibrosis, as well as a decrease in inflammation [13]. This was achieved primarily by promoting M2 macrophage polarisation, a process known for its anti-inflammatory and tissue-repairing properties. Additionally, Sac/Val activated the PI3K/Akt signalling pathway, which is essential for many of its cardioprotective effects. When the PI3K/Akt pathway was blocked, these beneficial outcomes were reversed, emphasising its critical role in mediating the drug's protective effects. These findings suggest that Sac/Val could mitigate MI-induced damage not only by reducing inflammation but also by enhancing key survival and repair mechanisms in the heart, positioning it as a promising therapy for managing MI-related damage.

Coronary artery calcium (CAC) is a key marker of subclinical atherosclerosis, influenced by various risk factors and statin use. In a study of 3484 patients undergoing CAC scoring and CT angiography, age was the most significant factor associated with a non-zero CAC score [14]. Male gender and statin use also accelerated the onset of CAC by 9–10 years. Other factors, such as diabetes, hypertension, and smoking, contributed to earlier CAC occurrence but had a lesser impact. These findings emphasise that statin use and male gender significantly hasten the development of CAC.

Circulating miRNAs have potential as biomarkers for early detection and management of CAD [15]. In a study assessing five candidate miRNAs (miR-21-5p, miR-133a-3p, miR-221-3p, miR-451a, and miR-584-5p) in 50 CAD patients and 50 controls, all were significantly upregulated in CAD patients. miR-133a-3p and miR-451a stood out as particularly strong biomarkers based on receiver operating characteristic analysis (Figure 2). These miRNAs, especially miR-133a-3p and miR-451a, show promise as valuable biomarkers for CAD diagnosis.

Crushed ticagrelor administered *via* nasogastric tube has been studied for effectiveness in acute coronary syndrome (ACS) patients, including those resuscitated or undergoing semi-urgent coronary artery bypass graft (CABG) surgery [16]. In both groups, over 85% of patients achieved platelet inhibition within 24 h, which was sustained through day 4. Pharmacokinetics showed a median peak plasma concentration (T_{max}) of 100 h, with consistent maximal concentrations (C_{max}). These findings demonstrate that crushed ticagrelor provides reliable platelet inhibition and consistent pharmacokinetics, making it a viable option when oral administration is not possible.

In STEMI patients, non-culprit lesions are common, and revascularization strategies can impact outcomes. A

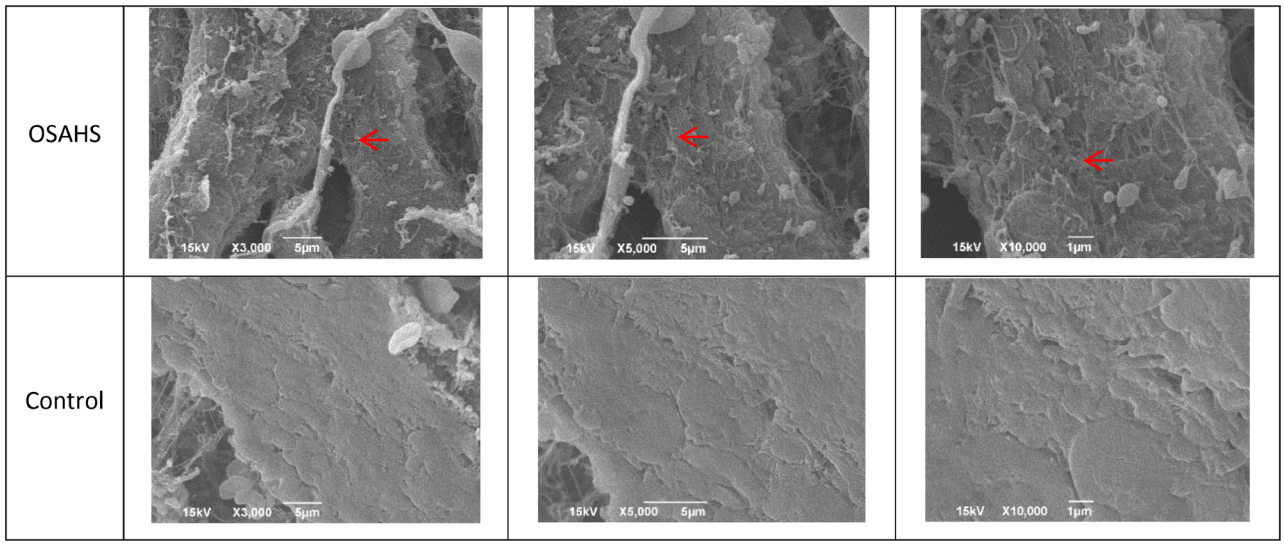

Figure 1. Changes in myocardial cell ultrastructure in control and OSAHS groups. Electron microscopy images showing that the morphology of myocardial cell changed after chronic intermittent hypoxia (CIH), as the organelles were severely damaged. Red arrows indicate formation of pyroptotic membrane pits and pores of varying size (from [12]).

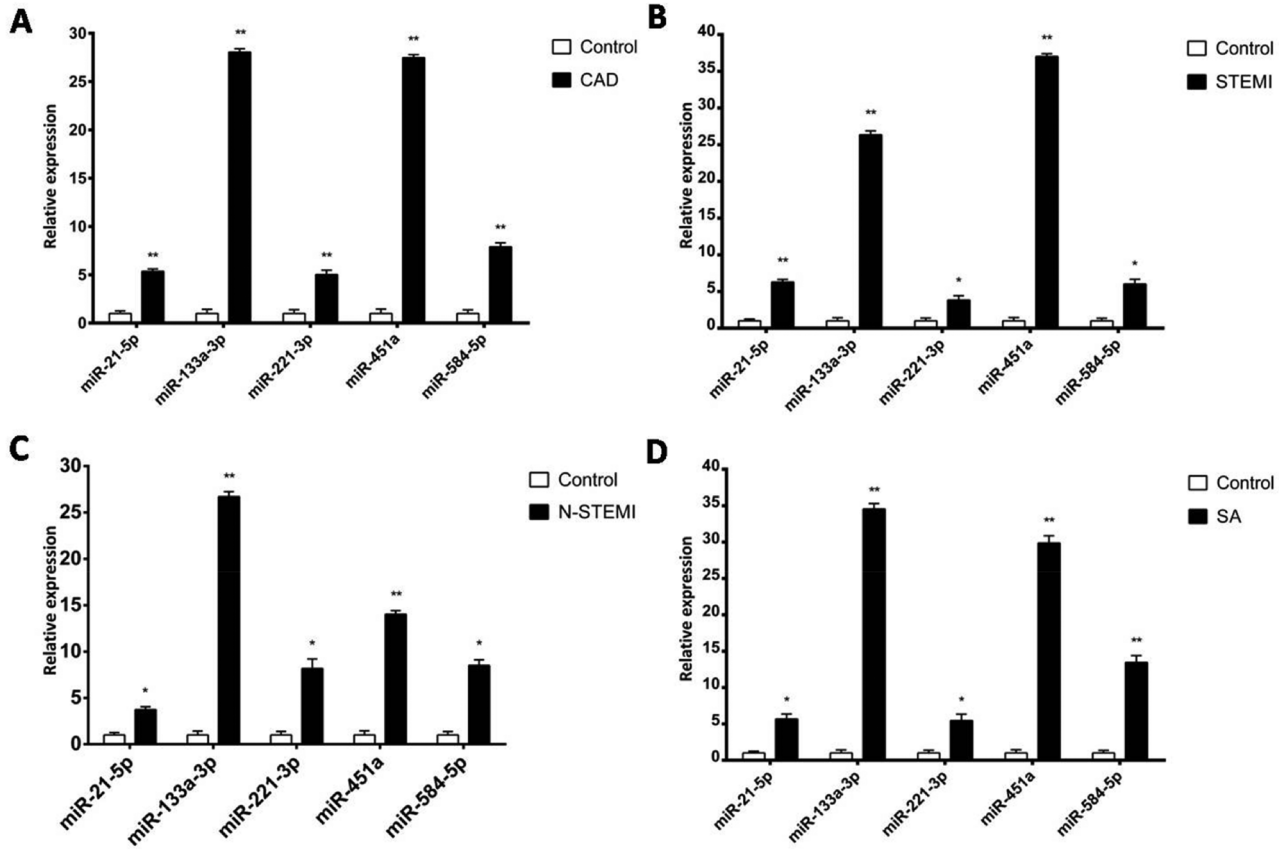

Figure 2. Relative expression (plasma levels) of candidate miRNAs. (A) Controls vs. CAD patients. (B) Controls vs. STEMI patients. (C) Controls vs. N-STEMI patients. (D) Controls vs SA (stable angina) patients. *$p < .005$, **$p < .0001$ [15].

study of 492 patients who underwent primary PCI assessed the handling of non-culprit lesions and calculated the residual SYNTAX score (rSS) at discharge [17]. Over 12 months, factors such as older age, higher Killip class (≥ II), lower eGFR (glomerular filtration rate), reduced left ventricular ejection fraction (LVEF), and higher rSS were linked to higher rates of recurrent MACE. Killip class ≥ II, LVEF, and rSS were independent predictors of

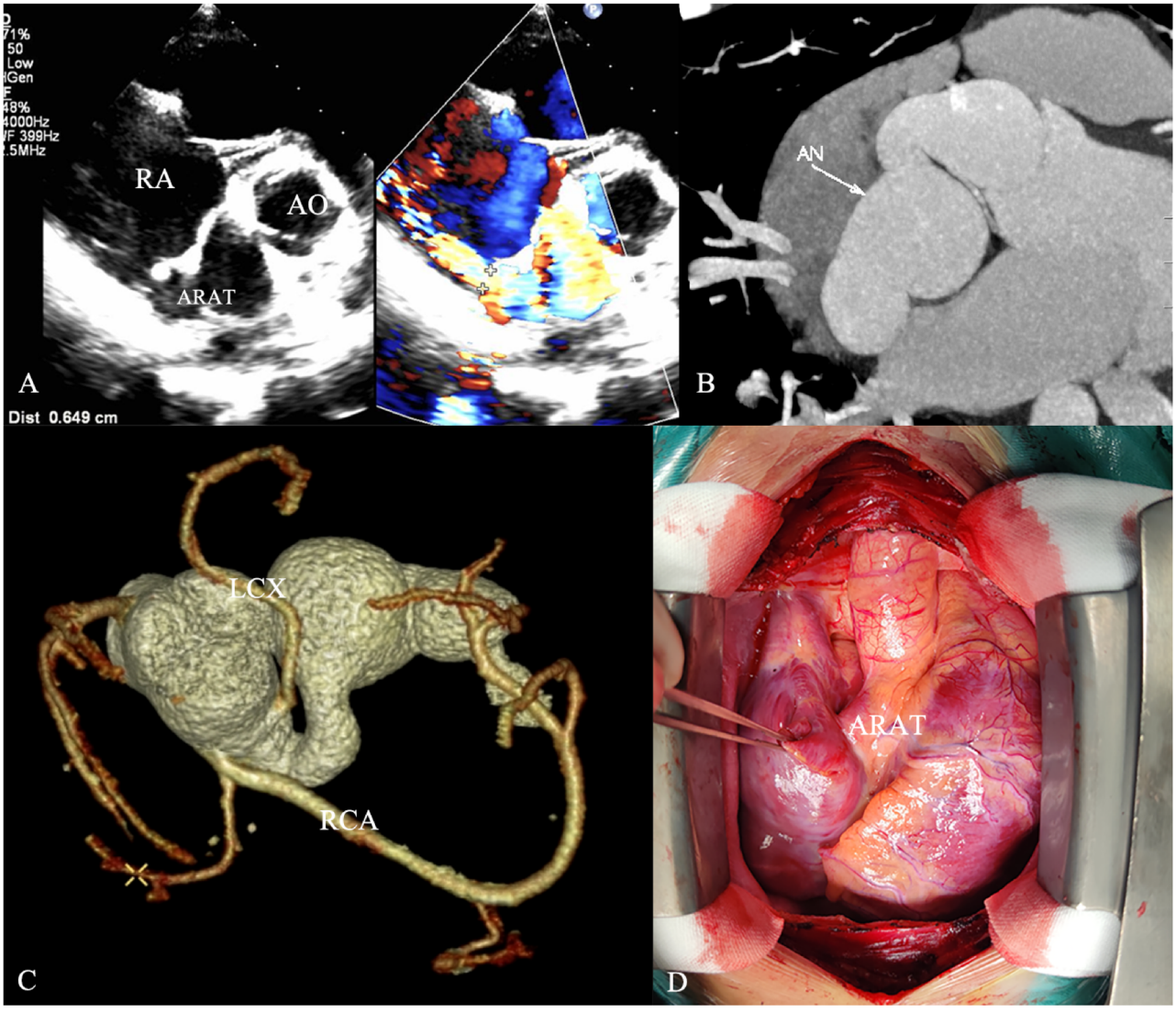

Figure 3. Transthoracic echocardiography (TTE) Doppler showing a continuous left-to-right shunt noted in the right atrium. (B,C) Computed tomography reconstruction showing a giant aneurysm (an) with an aorto-to-right atrium fistula and anomalous origin of left circumflex artery. (D) Intraoperative photograph clearly showing the aorto-right atrial tunnel (from [25]).

recurrent MACE, with an rSS above 8 showing strong predictive value for one-year MACE. High rSS patients may benefit from complete revascularization to reduce MACE risk.

Chronic kidney disease (CKD) significantly affects outcomes in diabetic patients undergoing PCI. In a study of 505 participants, those with severe CKD had much higher odds of one-month mortality, MACE, and triple vessel disease, with these risks persisting at six months [18]. Renal dysfunction, particularly severe CKD, was a strong predictor of poor post-PCI outcomes, and GFR showed good predictive accuracy for mortality. These findings highlight the importance of optimising renal function and tailoring cardiovascular management to improve outcomes in this high-risk population.

In this issue of *Acta Cardiologica*, alongside the original article mentioned, several focus images have also been featured (Figure 3) [19–29].

Disclosure statement

No potential conflict of interest was reported by the author(s).

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