buffer. Protein lysates were digested with trypsin and Lys-C using the Preomics™ iST kit. Serum samples were enriched for low abundant serum proteins using High Select™ Top Abundant Protein Depletion Resin (Thermo). Unbiased, deep proteomic profiling of individual tissue and serum samples was performed using the diaPASEF workflow on a timsTOF Pro mass spectrometer. Nonparametric statistical tests were applied for subsequent data analysis in R and SPSS (version 27). Pathway analysis was performed using Ingenuity Pathway Analysis (IPA) software.

Results Label-free MS analysis led to the identification of over 6,000 proteins in FFPE tissue and over 500 serum proteins. More than 300 proteins were found to be significantly differentially expressed between AF and control samples at tissue level, with stringent cut-off criteria applied (observed fold change of ≥ 1.5 or ≤ -1.5 and p-value ≤ 0.005). Pathway analysis revealed that significantly up and down-regulated proteins mapped to Epithelial Adherens Junction Signalling and Atherosclerosis Signalling canonical pathways. The most up-regulated protein in AF correlated with tissue BNP levels (r=1.0, p<0.0001) and markers of tissue ischaemia (r=1.0, p<0.0001). The most down-regulated protein was inversely correlated with tissue levels of TGFβ, the primary pro-fibrotic cytokine in the heart (r = -0.9, p=0.037). Thirty-one significantly changed tissue proteins were also identified in serum samples and were found to be associated with (i) new-onset AF, (ii) paroxysmal AF and (iii) risk of future stroke and/or heart failure in patients with AF.

Conclusions The dataset has highlighted significant proteins associated with AF. We have verified that circulating levels of a number of these proteins are significantly associated with AF and, importantly, may be predictive of future cardiovascular comorbidities in patients with AF.

Introduction Interleukin-10 (IL-10) is an anti-inflammatory cytokine with potent deactivating properties on macrophages and T cells and plays an important role in atherosclerotic plaque maturation and rupture. A guanine (G) to adenine (A) substitution in the IL-10 gene at -1082bp (rs1800896) has been associated with reduced IL-10 production in vitro. We aimed to test the association of IL-10 -1082G/A with early or severe presentation of coronary artery disease (CAD) using a systematic review and updated meta-analysis of published association studies.

Methods Relevant studies were identified following a comprehensive online search on PubMed, EMBASE, MEDLINE and Scopus databases and stratified into two groups based on mode of CAD presentation: early or severe and non-severe. Study level odds ratios (ORs) and their 95% confidence intervals (CI) were pooled using random effects employing a Z test.

Results A total of 24 studies were included for quantitative synthesis with a sample of 19,135 (11,143 cases/7,992 controls). A significant association was derived for IL-10 -1082G/A and early or severe CAD via dominant, recessive, and allelic genetic model comparisons [OR 1.24 (95% CI 1.12-1.37)].
1.02, 1.50), p= 0.03; OR 1.32 (95% CI 1.03, 1.69), p= 0.03 and OR 1.18 (95% CI 1.02, 1.36), p= 0.02 respectively. In contrast, no significant association was seen for the pooled group or non-severe CAD (p= NS). Sensitivity analysis was performed for both subgroups across all three genetic model comparisons. Sensitivity analysis was performed where studies were excluded one after another, and the analysis was repeated after each omission. In the early or severe CAD subgroup, lower bound of the 95% CI generally remained over 1.0, indicating no significant deviation from the main association. (Figure 1, Panel A) Similarly, we observed consistency for the non-severe CAD subgroup, which remained non-significant after each omission. (Figure 1, Panel B).

Conclusions IL-10 -1082G/A appears to be associated with early or severe presentation of CAD. Further studies are warranted to confirm this association.

### ROLE OF LIPOPROTEIN (A) IN THE DEVELOPMENT OF YOUNG (<45 YEARS) ST-ELEVATION MYOCARDIAL INFARCTION

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Introduction Lipoprotein (a) [Lipo (a)] is a low-density lipoprotein (LDL) with an additional apolipoprotein (a) moiety, which has been associated with increased risk of ischaemic heart disease (IHD). The role in the development of acute ST-Elevation Myocardial Infarction in ‘young’ (≤45 years) patients has not previously been studied. This novel observational study aims to determine the association between elevated levels of Lipo (a) and development of STEMI ≤ 45 years, using comparisons with both those presenting with STEMI >45 years and previously healthy controls undergoing computed tomography coronary angiography (CTCA).

Methods All STEMI presentations to a single tertiary centre over a 75-month period were retrospectively reviewed. Patients ≤ 45 years at time of presentation were invited to attend for a global cardiovascular risk assessment (medical history, Body Mass Index (BMI) and waist circumference (WC) measurement, repeat blood lipid analysis, lipo (a) level and Familial Hypercholesterolaemia (FH) screening). Consecutive patients >45 years presenting with STEMI were prospectively recruited, with clinical measurements obtained at index presentation. Patients with non-obstructed coronary arteries, coronary artery dissection, or coronary vasospasm without thrombosis at angiography were excluded.

Patients without a prior diagnosis of ischaemic heart disease (IHD) undergoing computed coronary angiography were prospectively recruited, with clinical characteristics and lipoprotein (a) levels obtained. Degree of stenosis was used to stratify patients with normal coronaries (<20%), non-obstructive coronary artery disease (CAD) (20–70%), or obstructive CAD (>70%).

Results Over a 75-month period 9% of STEMIs (244/2630) were young. The recruitment of patients <45 years with STEMI (n=58) is described in figure 1. In total, 51 consecutive patients >45 years who presented with STEMI and 91 patients who presented for CTCA were recruited. Baseline characteristics and Lipo (a) results for each cohort are summarised in table 1. Of patients undergoing CTCA, 47% (43/92) had normal coronaries, 32% (29/92) NOCA and 21% (19/92) had obstructive CAD. STEMI patients <45 years had a significantly higher rate of elevated Lipoprotein (a) (31/58; 53%) compared with >45 years (16/50; 32%; p=0.025) and those undergoing CTCA (26/91; 29%; p=0.002). Lipoprotein (a) level was significantly higher in those <45 years (184 (73–236.8); (Q1–Q3)) compared those >45 years (184 (73–236.8); p=0.025), and those presenting for CTCA (50 (24–198); p=0.007), (figure 2). There were no significant differences in rates of detectable (>20nmol/L) Lipoprotein (a) (p=0.667) or rates of markedly elevated Lipoprotein (a) (>Cohort Q3) between groups (p=0.064).

Conclusion Patients presenting with young (<45 years) STEMI have both higher rates of elevated Lipoprotein (a) and higher absolute levels of Lipoprotein (a), compared with those presenting at an older age and those with no history of IHD. These findings suggest that elevated levels of Lipoprotein (a)