**Background** There is limited evidence of the longitudinal impact of alcohol use and progression of structural cardiac changes amongst European populations at risk of heart failure (CV risk factors) or with pre-heart failure (asymptomatic but with cardiac changes, and no previous heart failure [HF]). Furthermore, the 2021 European guidelines describe beneficial effects in the general population of light alcohol (<140 g/week for men and <70g/week for women) usage on risk of HF, despite contrary emerging evidence.

**Aim** To understand the dose-response relationship between alcohol consumption and progression of pre-HF in a European population.

**Methods** This is a secondary analysis of the St Vincent’s Screening TO-Prevent Heart Failure (STOP-HF) trial amongst patients who are at risk of HF or with pre-HF, with documented alcohol intake and echocardiography at both baseline and follow up ≥18 months. Excluded were ex-drinkers and patients with symptomatic HF. The main outcome measure was the relationship between progression of cardiac functional changes (progression of pre-HF) or onset of symptomatic HF, stratified according to whether patients were classified as at risk of HF or with pre-HF at baseline, and 3 categories of alcohol dose: no alcohol usage; low alcohol use (up to 1 unit daily or 70g/week); moderate-high alcohol usage (>1 unit daily or >70g/week). Progression of pre-HF was defined as follow up left ventricular dysfunction (EF <50%) and a decline of at least 5% and/or lateral E/e was defined as follow up left ventricular dysfunction (EF <50%).

**Results** Of 744 patients included in the analysis (mean age 66.5 (9.8) years), 395 (53.1%) were female, 556 (74.7%) had hypertension, 145 (19.5%) had diabetes and 260 (34.9%) had pre-HF at baseline. Overall, a total of 201 (27.0%) patients reported no alcohol usage, 356 (47.8%) reported low (<70g/wk) alcohol intake and 187 (25.1%) reported moderate-high alcohol usage (>70g/wk) alcohol intake. There was no difference in reported alcohol usage between those at risk of HF and pre-HF patients. Those with moderate-high alcohol usage were younger, more likely to be male and had higher body mass index than patients with low alcohol usage. Over a median follow up period of 5.44 [IQR 4.33;6.73] years, 84 (11.3%) patients had progression of pre-HF or developed symptomatic HF. Moderate-high alcohol usage was associated with an adjusted 4.5 fold (95% CI 1.7- 15.9, p=0.004) increased risk of progression of pre-HF/HF amongst those with pre-HF at baseline compared to those who reported no alcohol intake. (Figure 1) Increased HF progression was also evident in moderate (70–140g/week) and high (>140g/week) alcohol use subgroups. Conversely, in patients at risk of HF, at baseline had no association of moderate-high alcohol usage with progression of HF. Finally, there was no protective associations of low alcohol usage (<70g/week) and progression of HF in any patient group.

**Conclusion** Moderate alcohol (>70g/week; more than 1 bottle of 12.5% wine/week) usage appears to be associated with progression of pre-HF and HF in European patients in the STOP-HF study (figure 1) and we did not observe protective benefits of low alcohol usage. These data are in accordance with recent evidence from Asian populations. European HF guidelines should reconsider advice suggesting any protective effects of alcohol on risk of heart failure.

**Abstracts**

**18 IDENTIFICATION AND EVALUATION OF NOVEL PROTEIN BIOMARKERS FOR ATRIAL FIBRILLATION**

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**Background** There is a need for improved biomarkers to diagnose atrial fibrillation (AF) earlier and reduce risk of future serious comorbidities. Quantitative protein profiling of atrial appendage tissue from patients with atrial fibrillation (AF n=10) and age/sex matched controls with normal sinus rhythm (control, n=10) was performed using mass spectrometry. Similarly, serum samples, collected longitudinally from patients with and without AF (n=186), were analysed to establish a comprehensive dataset that depicts changes in both the atrial tissue and circulating proteome as result of AF.

**Methods** Sections of formalin fixed paraffin embedded (FFPE) tissue were mechanically homogenised in Preomics™ LYSE.
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.