Abstract B55 Figure 1

triggered or reentrant mechanisms. Whilst these effects have been reported in animal and human stem cell-based models, to date there has been no investigation in more complex structures such as the human ventricular cardiac anisotropic sheet (hvCAS). Here, we investigated arrhythmogenicity, electrophysiological and calcium transient changes induced by hypokalaemia using this bioengineered platform.

Methods An optical mapping technique was applied on hvCAS derived from human pluripotent stem cells to visualize electrophysiological and calcium transient changes under normokalaemic (5mM KCl) and hypokalaemic (3mM KCl) conditions.

Results Hypokalaemia significantly increased the proportion of preparations showing spontaneous arrhythmias from 0/14 to 7/14 (Fisher's exact test, $P=0.003$) (figure 1D). Hypokalaemia reduced longitudinal conduction velocity (CV) from 7.81 to 7.18 cm s^{-1} ($n = 9-7$; $P=0.036$), transverse CV from 5.72 to 4.69 cm s^{-1} ($n = 12-11$; $P=0.030$), prolonged action potential at 90% repolarization (APD90) from 83.46 to 97.45 ms ($n = 13-15$; $P<0.001$), increased action potential amplitude from 0.888 to 1.195 ΔF ($n = 12-14$; $P<0.001$) and calcium transient amplitude from 0.76 to 1.37 ΔF ($n = 12-13$; $P<0.001$), and shortened effective refractory periods from 233 to 173 ms ($n = 16-14$; $P=0.038$). Figure 1 (A), (B) and (C) show the representative tracings and isochronal maps of normokalaemic and hypokalaemic samples.

Conclusions Hypokalaemia exerts pro-arrhythmic effects on hvCAS, which are associated with alterations in conduction velocity, repolarization, refractoriness and calcium handling. These preparations can provide a useful platform for investigating electrophysiological substrates and for arrhythmia screening.

Conflict of Interest None

BS6 COHERENT VORTEX FLOW IN THE ADULT RIGHT ATRIUM

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Brief introduction: In healthy adults, the right atrium (RA) serves as a reservoir for the systemic flow return from the superior vena cava (SVC) and inferior vena cava (IVC), preparing the two flows to be transferred to the right ventricle (RV) and pulmonary circulation. This study aims to quantify the haemodynamics of the RA and the associated SVC and IVC inflows, which have not been fully understood to date.

Basic Methods Eighteen adults with structurally normal hearts underwent 4D flow magnetic resonance imaging. The cardiac cycle was resolved to 20 temporal phases with a spatial resolution of $3 \times 3 \times 3$ mm cube. Analysis included objective visualisation of the flow structures in the RA identified by three different vortex identification criteria, kinetic energy (KE), enstrophy and dissipation. KE and helicity flux were also assessed in both caval veins.

Main Results Vortex identification methods confirmed that in the majority of participants the blood flow from the caval veins filling the RA during ventricular systole is not chaotic, but rather forms an organised pattern of a single coherent forward turning vortex structure. Thirteen participants displayed

a single vortex flow structure, four showed multiple vortices and one had a helical flow pattern without a clear vortex structure. A strong positive correlation exists between the flow KE and enstrophy density.

Conclusions and Implications This study suggests that flow energy in the RA is mainly rotational, part of which is connected by the highly helical SVC and IVC inflows. Multiple vortices tend to be associated with higher dissipation rates in the central RA region due to turbulence. The rotational nature of the flow in the RA maintains KE better than non-rotational flow. RA flow characteristics are highly related to the helicity content in the caval veins, as well as the KE flux intensity. Lower caval helicity or IVC KE flux dominance tends to favour single vortex formation while the opposite tends to lead to multiple vortices or the rare helical flow patterns. Atria lacking single vortex flow are inclined to have a larger energy input from atrial contraction.

Conflict of Interest n/a

BS7

PLASMA DESMOSINE AS A BIOMARKER IN ACUTE AORTIC SYNDROME

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Introduction Acute aortic syndromes (AAS) include aortic dissection, intramural haematoma and penetrating aortic ulcer, all of which are caused by aortic wall failure and associated with significant mortality. Although, treatment options currently include early surgical intervention or aggressive medical management, disease progression and devastating complications remain commonplace. Early diagnosis of AAS as well as ability to predict those at the highest risk of disease progression would represent significant progress in the care these patients receive. Desmosine is the cross-link component in the elastin molecule and is exclusively released from mature elastin breakdown, thus is a physiologically relevant biomarker of aortic elastin degradation. The aim of the study was to test the hypothesis that plasma desmosine (pDES) concentrations are elevated in AAS and has prognostic value in identifying those at risk of significant disease progression.

Method Patients over 25 years old with radiologically confirmed acute aortic syndrome were recruited as part of a prospective observational study (NCT03647566). Demographic details, AAS sub-category, time from index acute aortic syndrome event and pDES concentrations measured by stable isotope dilution LC-MS/MS were recorded at baseline. Baseline and follow up maximal aortic diameters were measured on contrast-enhanced computed tomography (CT) and change in aortic diameter over time was calculated. Control plasma desmosine samples were obtained at a 2:1 ratio control subjects participating in the United Kingdom Aneurysm Growth Study. Data presented as mean±standard deviation or median [interquartile range].

Results Plasma desmosine concentrations were measured in 53 patients (64 [53 to 71] years) with acute aortic syndromes and 106 control subjects (53 [44 to 60] years). In patients

with AAS, pDES concentrations were almost twice those of control subjects (0.58 ± 0.26 vs 0.27 ± 0.07 , $p < 0.001$). In those with AAS, plasma desmosine concentrations were seen to be highest at presentation, and reduced over time from the aortic syndrome event ($R = 0.51$, $p = 0.003$). Plasma desmosine concentration was the only variable associated with increasing aortic diameter over time ($R = 0.34$, $p = 0.014$).

Conclusion Plasma desmosine concentrations are elevated in patients with AAS, peak at the time of presentation and represents a promising biomarker for early identification and risk stratification in patients with AAS.

Conflict of Interest none to declare

BS8

GENETICALLY-DETERMINED SERUM CALCIUM LEVELS INFLUENCE MARKERS OF VENTRICULAR REPOLARISATION: A MENDELIAN RANDOMISATION STUDY

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Introduction Electrocardiographic (ECG) markers of ventricular depolarisation and repolarisation are associated with an increased risk of arrhythmia and sudden cardiac death. Our prior work indicated lower serum calcium concentrations are associated with longer QT and JT intervals in the general population. Here, we investigate whether serum calcium is a causal risk factor for changes in ECG measures using Mendelian Randomisation (MR).

Methods We performed a new genome-wide association study (GWAS) for serum calcium in >300,000 European-ancestry participants from UK-Biobank. Independent lead variants were extracted to be used as instrumental variables (figure 1). Two-sample MR analyses were performed to approximate the causal effect of serum calcium on QT, JT and QRS intervals using an inverse-weighted method in 76,226 UK-Biobank participants with ECG data, not contributing to the serum calcium GWAS. A secondary analysis was performed using lead variants from a calcium GWAS corrected for serum albumin. Sensitivity analyses were performed using contemporary methods to test for the presence of horizontal pleiotropy.

Results 205 independent lead calcium-associated variants were used as instrumental variables for Mendelian Randomisation. A decrease of 0.1 mmol/L genetically-determined serum calcium, was associated with longer QT (3.01ms (95% CI 2.03, 3.99)) and JT (2.89ms (1.91, 3.87)) intervals. A weak association was observed for QRS duration in secondary analyses only (0.39ms (0.08, 0.69)). Results were concordant in all sensitivity analyses.

Conclusion These analyses support a causal effect of serum calcium levels on ventricular repolarisation, in a middle-aged population of European-ancestry where serum calcium concentrations are likely stable and chronic. Modulation of calcium concentration may therefore directly influence cardiovascular disease risk. Further research into the effects of serum calcium concentration on arrhythmogenesis is warranted and calcium variants could be considered for inclusion in genetic risk score models for predictive testing.