The role of JNK2 in triggered arrhythmic activities was assessed using a well-evaluated JNK2-specific inhibitor and our unique cardiac-specific MKK7D and MKK7D-JNK2dn mouse models with tamoxifen inducible overexpression of constitutively active MKK7 (a JNK upstream activator) or co-expression of MKK7D and inactive dominant negative JNK2 (JNK2dn).
Results: We found that binge alcohol exposure in aged mice (n=14) led to spontaneous PACs/PVCs (75% of the mice), and AT/VT episodes (50%) along with a 21% mortality rate. However, alcohol-exposed young (n=5) and non-alcohol-exposed aged mice (n=11) were absent of any spontaneous arrhythmic activities or premature death. Intriguingly, JNK2-specific inhibition *in vivo* abolished those alcohol-associated triggered activities and mortality in aged mice. The causative role of JNK2 in triggered arrhythmias and premature death was further supported by the high frequency of spontaneous PACs/PVCs and nonsustained AT/VT episodes along with a 50% mortality rate in MKK7D mice (n=10), which was strikingly alleviated in MKK7D-JNK2dn mice (n=5) with cardiac-specific JNK2 competitive inhibition.
Conclusion: Our findings are the first to reveal that stress kinase JNK2 underlies binge alcohol-evoked atrial and ventricular arrhythmia initiation in aged mice. Modulating JNK2 could be a novel therapeutic strategy to treat and/or prevent binge drinking-evoked cardiac arrhythmias.

PO-02-174

CHARACTERIZATION OF PAPILLARY MUSCLE ABLATION WITH OPTICAL MAPPING AT DIFFERENT TRANSMURAL PENETRATION DEPTHS IN LIVE HUMAN HEART

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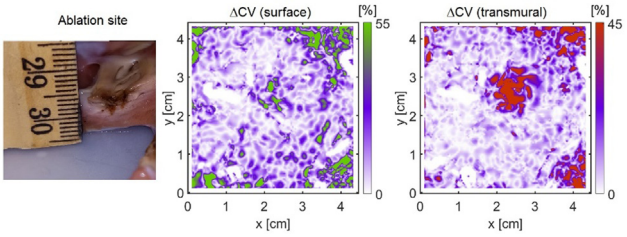
Background: Papillary muscles (PMs) are known triggers of ventricular arrhythmia, especially nonsustained ventricular tachycardia (VT) and sustained recurrent VT, and may play a role as triggers of ventricular fibrillation. Catheter ablation of PM is challenging and results in high VT recurrence rates.
Objective: Clinical characterization of PM electrophysiology is challenging due to the limited spatial resolution of electrode arrays, motion, and distal fields. Thus, ablation procedures are limited in two ways: inaccurate determination of target ablation zones and inaccurate characterization of lesion profiles. Characterization of PM before and after ablation can be accomplished with deep infrared optical mapping toward a better understanding of the role of the PM.
Methods: Using optical mapping and near-infrared voltage-sensitive fluorescent dyes, transmembrane potentials were recorded from the endocardial side of a live explanted human right ventricle free-wall (transplant recipient). We paced the myocardium at different cycle lengths (CLs) before and after ablation, and transmembrane potential maps were obtained using excitation light bands of different penetration depths to characterize the ablated zones transmurally.
Results: The PM exhibited alternans in action potential duration (APD) at longer CLs than wall tissue in non-ablated tissue, indicating a highly heterogeneous myocardium. The figure shows relative conduction velocity maps for subsequent beats before and after ablation. While dissection of the tissue appeared to show a transmural burn, optical mapping with different penetration depths, from green (surface) and near-infrared (NI, transmural) illumination, revealed that the transmural electrophysiology profile was ablated, only at the surface. The presence of conduction velocity alternans using NI light indicated incomplete ablation at the deeper subsurfaces, even though it appeared burnt during dissection.
Conclusion: Contemporary electro-mapping systems used in clinics often achieve limited electrophysiological characterization in the depth of ablated areas. Such measurements would yield results similar to optical mapping with the green light excitation band (surface only), suggesting successful ablation that may be incomplete and may result in recurrent VT. We demonstrate that optical mapping with NI light is a useful tool for quantitative characterization of ablation parameters.



PO-02-175

HUMAN EPICARDIAL ADIPOCYTE-DERIVED SPARCL1 PLAYS AN IMPORTANT ROLE IN SUPPRESSION OF POSTOPERATIVE ATRIAL FIBRILLATION IN PATIENTS UNDERGOING CARDIOVASCULAR SURGERY

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Background: Postoperative atrial fibrillation (POAF) occurs in 20-50% after cardiac surgery and exacerbates the short and long-term morbidity/mortality. Potential predisposing factors may exist in the epicardial adipose tissue (EAT) because of its anatomical position.
Objective: In order to explore a possible mechanistic link, we tried to identify the specific gene expression profile of secretome from the EAT in patients with POAF.
Methods: We prospectively evaluated 104 patients who underwent scheduled open-heart surgery between May 2020 and May 2022 without known AF (male 69 (66.3%); mean age 68.1 $\pm$ 12.3). They are allocated to two groups with (POAF group) or without (no-POAF group) POAF, which is defined as AF lasting over 30 seconds documented by monitor or 12-lead electrocardiogram after the operation. Human EAT samples were obtained from those patients during surgery and preadipocytes were isolated from them. Isolated preadipocytes were terminally differentiated to mature adipocytes and the mRNAs were extracted. Genome-wide expression profiling of 6 vs. 6 matched samples representing POAF or no-POAF group was done using Human Clariom S Assay-HT 16-Array Plate. The secreted protein levels in the adipocytes-cultured medium were also evaluated using enzyme-linked sorbent assay test to confirm the consistency of mRNA expression levels of adipocytes and its secreted protein levels.
Results: POAF was observed in 41 patients (39%). Patients in POAF group were significantly older than those in no-POAF group (71.3 $\pm$ 9.91 vs 66.0 $\pm$ 13.4, $p = 0.039$). Microarray analysis revealed that there were 132 down- or up-regulated genes (fold change >2.0 or <-2.0, $p < 0.05$) in epicardial adipocytes of no-POAF group compared to POAF group. Of these genes, 11 genes cording secretable molecules were validated by qPCR, showing that only SPARCL1 had significantly higher expression in no-POAF group than in POAF group ($p = 0.039$). The mRNA expression of SPARCL1 in adipocytes is significantly correlated with the concentration of SPARCL1 protein in the adipocyte-cultured medium ($p < 0.0001$, $r = 0.9068$). Patients aged >75 years had lower mRNA expression of SPARCL1 than patients aged ≤ 75 years ($p = 0.02$).
Conclusion: Our findings suggested that SPARCL1 expression in human epicardial adipocytes may play an important role in the