periodic skeletal muscle paralysis in several inheritable ion channel diseases.

B-011-03

SGK1 DEFICIENCY IS PROTECTIVE IN A MODEL OF SEPSIS-RELATED ATRIAL FIBRILLATION

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Background: Sepsis is associated with new onset atrial fibrillation (AF), and AF in septic patients is associated with worse outcomes. Serum glucocorticoid kinase 1 (SGK1), a serine/threonine kinase in the PI-3 kinase pathway, is involved in cardiac inflammation. Prior work has suggested a potential therapeutic role for SGK1 inhibition in cardiac arrhythmias, which we investigated in a model of bacterial sepsis-induced AF.
Objective: We sought to determine if 1) CLP, a well established model of polymicrobial sepsis leads to an increased risk of AF, and 2) whether SGK1 inhibition is protective in this model.
Methods: Cecal ligation and puncture was performed in male wild type C57/Bl6 (WT) and mice with cardiac specific knockdown of SGK1 (SGK1 DN). Approximately 7 (range 7-9) days after sepsis induction, the mice underwent terminal *in vivo* electrophysiology studies to determine AF inducibility and basic atrial/ventricular tissue parameters. Additional mice were used to perform optical mapping to determine EP properties and flow cytometry to determine cellular composition.
Results: CLP-induced sepsis in WT mice led to high AF inducibility (5 out of 7 mice), as well as AF frequency and burden during EP study. As compared with naïve controls, the AF phenotype was associated with significantly slowed right atrial conduction velocity (0.54±0.03 versus 0.62±0.08 m/s) along with a similar trend in the left atrium, as measured by optical mapping. Flow cytometry revealed that sepsis increased fibroblasts, macrophages, and neutrophils in the atrial wall when compared to control mice without CLP. When CLP was performed in WT and SGK1 DN littermates, SGK1 DN mice had significantly ($p<0.05$ by chi-squared) lower AF inducibility (3 out of 8) than the WT mice (7 out of 8). In addition, there was a significant decrease in AF frequency and a trend towards a decrease in total AF burden during the entirety of the EP study.
Conclusion: Bacterial sepsis in mice remodels the atrial cell composition and increases AF inducibility. Genetic SGK1 inhibition protected septic mice against AF. These data motivate further investigation into how inflammatory remodeling of atria contributes to sepsis-induced AF, and the potential of SGK1 inhibitors for treatment of this entity.

B-011-04

ABLATION SCAR IN A SINGLE PULMONARY VEIN CAUSES PROARRHYTHMIC MECHANICAL DESTABILIZATION IN HEALTHY SHEEP ATRIA

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Background: Atrial and pulmonary vein (PV) stretch is proarrhythmic, but the mechanical effect of PV ablation scar on atrial fibrillation (AF) arrhythmogenesis is unknown. We hypothesize that discontinuous PV ablation scars are proarrhythmic because they create heterogeneous stretch.
Objective: To measure local atrial strain and AF inducibility in healthy sheep hearts with and without PV ablation scar.
Methods: Functional cardiac MRIs acquired in vivo in sheep (n=12) before and 3 months after discontinuous PV ablation by radiofrequency in the right PV (RPV) were analyzed with a feature-tracking algorithm to obtain local strain in the left atrium (LA). Explanted hearts were perfused with 1:4 blood:Tyrode's solution in a dual-chamber working-heart set-up. Multi-electrode endocardial catheters were positioned in the RPV and left PV (LPV) for premature stimulation during low (~12mmHg) and high (~25mmHg) LA pressure. Control hearts (n=12) underwent similar ex vivo investigation.
Results: The maximum longitudinal strain of the myocardial wall between the RPV and LPV increased from 20±6 (mean±SD) to 34±16% (pre vs. post-ablation, respectively; p=0.032), whereas the maximum radial motion fraction of the LA septum close to the RPV decreased from 46±10 to 36±7% (pre vs. post, p=0.035). Sustained AF (>30s) was more often induced during stimulation in ablated than in control hearts (22% vs. 9% of induction attempts (n=73 vs. n=87), respectively, p=0.025). In ablated hearts, an increase in LA pressure augmented AF inducibility (11% vs. 34% of induction attempts, n=38 vs. n=35, low vs. high LA pressure, respectively, p=0.024), whereas this was not the case in control hearts (2% vs. 17% of induction attempts (n=45 vs. n=42), low vs. high, p=0.237). Moreover, the diastolic stimulation threshold was higher in ablated than control hearts (90 (60) (median (IQR)) and 75 (40) mA, p=0.007).
Conclusion: Local PV ablation scar caused localized disparate mechanical changes and increased inducibility of sustained AF, especially during increased LA pressure. This was associated with decreased tissue excitability. Therefore, ablation scar in a single PV causes an atrial arrhythmogenic substrate. Ablation lesion sets that homogenize atrial mechanics may improve the AF ablation success.

B-011-05

PANORAMIC OPTICAL MAPPING AND MICRO COMPUTED TOMOGRAPHY FOR IN-DEPTH 3D CHARACTERIZATION OF THE ARRHYTHMOGENIC SUBSTRATE IN MURINE HEARTS

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Background: Optical mapping of murine hearts is currently limited to the epicardium. Action potential duration (APD) heterogeneity is a key driver for initiation and persistence of reentry. When combined with micro CT, optical mapping can provide data on anatomical alterations and structural remodeling contributing to arrhythmogenesis.
Objective: In this study, we developed a 3D visualization tool combining panoramic optical mapping (POM) with a convolutional neural network automatically segmenting the heart anatomy on micro CT for improved