2. Cardiac Biology and Physiology

2.2 Oral presentations

OR05

Electrophysiological and immunohistological evaluation of SK channels from human ventricles: differential functional expression in valvular disease

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Background: SK channels are a family of potassium channels. They were initially described to be expressed in the atria with no significant role in the ventricles and, thus, proposed as a new therapeutic target to treat atrial arrhythmias. Protein expression in failing ventricles was later confirmed.
Aims: To determine the presence of SK2 and SK3 in ventricular biopsies from living donors with and without ventricular remodeling.
Methods: Left ventricular transmural biopsies (n=34) and papillary muscles (n=23) were obtained from patients, 44 of whom had valvular disease-related ventricular remodeling. As controls (non-remodelled), 13 biopsies were taken from a non-ischemic region in patients with ischemic cardiomyopathy. All patients gave written informed consent prior to surgery. The study complied with the principles of the declaration of Helsinki and was approved by local authorities. Immunohistological staining was performed for both SK2 and SK3. From a subset of patients, 350 µm-thick ventricular slices were produced and optically mapped to measure the Action Potential Duration (APD) at baseline and after the addition of SKA-31, a selective SK channel activator.
Results: SK2 was located in the membrane of cardiomyocytes in all patients. Expression levels of SK3 were higher in the epicardium than in the midmyocardium and endocardium and was expressed in the GAP junctions or in striations along the Z-lines. Non-remodelled myocardium had equal expression of SK3 in both locations while remodelled myocardium expressed SK3 in the Z-lines more than in GAP junctions. SK channels could only be activated in the remodelled ventricles, leading to a mean APD reduction of 11.3% in the midmyocardium and 12.3% in the endocardium.
Conclusions: SK channels are present in all human ventricular tissues, but can only be activated in remodelled tissue.