Evaluating the reversibility potential of atrial cardiomyopathy on a clinical and cellular level

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Background: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is associated with various remodelling processes of the electrical and structural properties of the atrium, collectively referred to as atrial cardiomyopathy. Because these remodelling processes contribute significantly to the high recurrence rates and chronification of AF, the exact time course of their development and their reversion potential need to be further characterized.

Purpose: To investigate the time course and reversibility of atrial cardiomyopathy on a clinical, cellular and molecular level.

Methods: A clinically relevant porcine large animal model was used to study the structural and functional implications of atrial cardiomyopathy after different periods of burst pacing-induced AF (2, 4 and 8 weeks) and after a recovery period, following electrical cardioversion. The pigs were clinically characterized at each time point by echocardiography, cardiac MRI, and electrophysiological studies. After extraction of the heart, action potentials (APs) and ionic currents were measured on isolated atrial cardiomyocytes (CM) using the patch-clamp technique.

Results: After 4 weeks of AF induction, APD90 of isolated atrial cardiomyocytes was attenuated by 26%. Extending the AF induction period to 8 weeks caused an even stronger APD90 reduction by one-third, compared to SR controls. Accompanying, the TASK-1 current density was strongly upregulated in AF pigs. Those observations were in line with significant changes of the right atrial effective refractory period (AERP). At baseline, AERP_S1=400 ms yielded 186 ms, whereas it was reduced to 141 ms after eight weeks of AF. Addressing the reversibility of those changes, following cardioversion of AF and an 8 week long SR recovery period, AERP baseline values were almost restored. Likewise, APD90 shortening was partially reversed. Furthermore, indication of reversibility of AF-associated remodelling was also observed on a structural level. After eight weeks of AF induction, echocardiography revealed severe dilatation of both atria, whereas atrial diameters decreased significantly after restoration of SR.

Conclusion: Remodelling processes underlying atrial cardiomyopathy display a partial reversibility upon restoration and maintenance of SR.