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Arrhythmias and Device Therapy – Ventricular Arrhythmias and Sudden Cardiac Death (SCD), Pathophysiology and Mechanisms

Differentiating mechanisms of long duration ventricular fibrillation in acute ischemic myocardium vs. chronic infarct in an in-vivo porcine model

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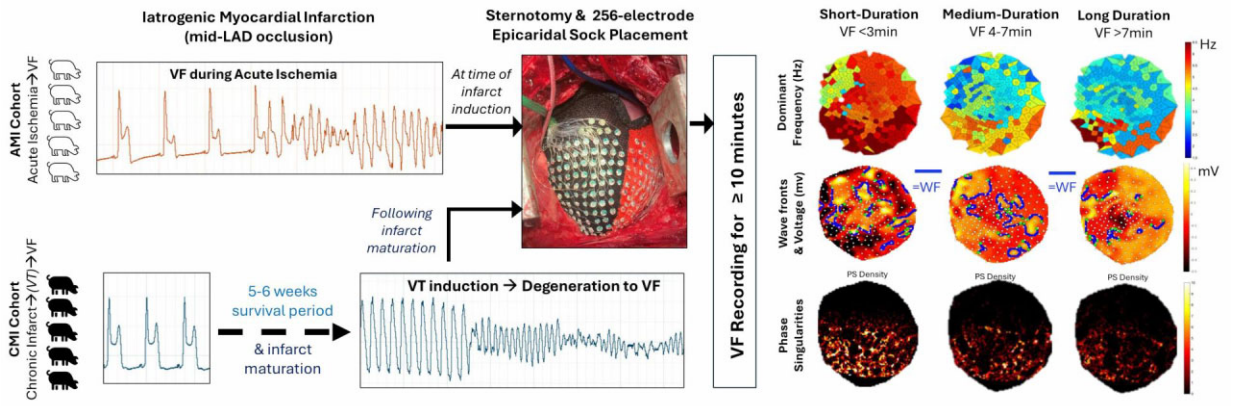
Background: The substrate-specific mechanism of long duration ventricular fibrillation (LDVF) is poorly characterized. Mechanisms of initiation as well as maintenance of VF may vary between underlying substrates and warrant individualised treatment.
Objective: Assess in an in-vivo porcine model if LDVF in acute ischemic myocardium compared to VF in chronic infarct is sustained by distinct substrate-specific mechanisms.
Method: 10 Danish Landrace pigs were studied (69.7±2.4kg) - 5 with VF during acute myocardial ischemia (AMI), 5 with VF and chronic infarct (CMI). Ischemia was induced by 45min percutaneous balloon-occlusion of the mid-LAD followed by reperfusion. For the AMI group a 256-electrode epicardial sock was placed on the heart and VF recorded following induction of acute ischemia/reperfusion. In the CMI group, pigs were recovered for 5-6 weeks enabling infarct maturation followed by epicardial sock mapping and VT induction via programmed stimulation with spontaneous degeneration to VF. In all pigs, VF was recorded for a minimum of 10 minutes sampled at 1kHz & low pass filtered at 40Hz. Dominant frequencies (DF) were calculated with a Fast Fourier transform and epicardial phase estimated at each electrode with Hilbert transform. Phase singularities (PS) and number of wavefronts (WF) were identified at 20ms intervals over 5sec in 60sec epochs. Rotors were defined as continuous PS (tracked at a resolution of 1ms) that persisted for >400ms (approx. 2 rotations) and stable rotors as those with lifetimes >1000ms.
Results: VF was recorded for 18.6±5.9min. Comparative analysis was undertaken for the first 10 minutes. All hearts continued to fibrillate until the end of the recording. Over the total recording, VF in context of acute ischemia manifested with significantly higher DFs (7.3±2.8 vs 5.8 ±1.7Hz, p<0.001), higher number of co-existing WFs (12.1±3.7 vs 8.7±4.6, p<0.001), number of co-existing phase singularities (27±9 vs 16 ±10, p<0.001) and total number of rotational drivers >400ms (3560 vs 3252, p <0.001). In turn PS lifespan, while generally short-lived, was significantly longer in chronic infarct pigs (45ms (IQR 99) vs 37ms (IQR 73), p <0.001).
Sub-analysis for short (0-3min), mid (4-7min) & long duration (8-10min) VF showed significant differences between AMI/CMI groups for all time-segments. In LDVF >7min, DF trends reversed and were significantly higher in CMI vs AMI (6.1±1.6 vs AMI 5.2±2.0Hz, p <0.001) and also number of stable epicardial rotational drivers persisting >1000ms were significantly higher in CMI in LDVF (57 vs 24, p<0.001).
Conclusion: There are significant differences and temporal changes in the dominant mechanisms between VF in acute ischemia vs chronic infarct. 1. Acute ischemic VF is characterised by higher DF, number of PS and WF in early stages of VF 2. More stable epicardial rotors exist in LDVF in chronic infarcts. These observations may inform more personalised pharmacological and electrical treatment of VF.

Experimental Setup and Analysis



Main results for VF-AMI vs VF-CMI