

Investigation of Mechanisms Underlying Takotsubo Syndrome Using an Electromechanical Heart Model

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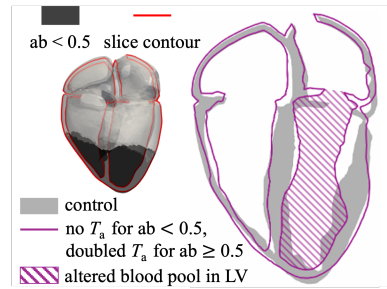
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Takotsubo syndrome (TTS) is a reversible form of heart failure typically affecting postmenopausal women after a stressful trigger. It is characterized by a transient ballooning of the left ventricle (LV) during systole and a rightward shift of the pressure-volume-loop (pV loop). The underlying pathophysiology of TTS remains unclear, with hypotheses ranging from a corruption of the Purkinje-muscle junctions (PMJs) or a change in active stress development (T_a) due to sympathetic overdrive.

We hypothesized four different mechanisms (A-D) to reproduce ballooning, by dividing the ventricles into an apical and a basal region. For scenario A, we deactivated PMJs in the apical region while preserving conduction and stress development in the myocardium. In scenario B, we disabled T_a in the apical region. We doubled T_a in the basal region in scenario C. For scenario D, we combined B and C. We compared all results to an unaltered control simulation.

Deactivation of the PMJs resulted in a slightly delayed onset of contraction in the apex without ballooning. There was no change in LV ejection fraction (LVEF) compared to the control simulation. Both scenarios B and D led to a visible ballooning effect (s. Fig), a lower LVEF (B: 36.1%, D: 43.4%) than in the control (56.6%) and a rightward shift of the pV loop. Scenario C, demonstrated a slightly stronger constriction in the basal region compared to the control and almost no change in LVEF (59.7%).

According to our findings, a corruption of the PMJs cannot be the sole cause for the TTS phenotype. Hypo-contractility in the apex appears to be the main factor driving apical ballooning, while basal hyper-contraction could be a contributing mechanism. The role of the sympathetic nervous system on T_a warrants exploration in follow-up work.



4-chamber slice of scenario D at systole. ab: apico-basal coordinate