Slices of human neonatal and infantile myocardium: a novel experimental platform to study (patho)physiological properties at a cellular level

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Introduction: The current understanding of the neonatal and infantile human heart function at a cellular level has mainly been interpolated from experimental studies on animal and adult human heart tissue. This is mainly due to limited access to tissue and lack of suitable preparation techniques. For example, action potentials have not yet been recorded from neonatal and young patients’ myocardium. To gain deeper insight into the physiological and pharmacological properties of young myocardium, we established a technique for the preparation of vital tissue slices from biopsies of patients with hypoplastic left heart syndrome (HLHS) and Tetralogy of Fallot (TOF).

Methods: The study has been approved by the local ethics committee and consent was obtained from all patients’ parents. Tissue excised for implementation of a Sano shunt or during TOF correction was transferred into ice-cooled modified Tyrode’s solution, transferred to our laboratory and embedded into low-melting agarose. 300 µm thick slices were prepared using a vibratome. After induction of calcium tolerance and re-warming, slices were electrically stimulated and action potentials (AP) were recorded.

Results: Slices were obtained from 4 HLHS patients (mean age: 11.8±7.0 days) and 4 TOF patients (mean age 178.7±16.8 days). AP amplitude and maximal upstroke velocity (Vmax) were higher in TOF (Amplitude: 110.5±7.8 mV, n=24 vs. 79.2±19.3 mV, n=9, p=0.001, Vmax:79.2±12.4 V/s vs. 118.5±30 V/s, p<0.05). Action potential duration was longer in TOF (APD20: 137.0±23.0 ms vs. 105.0±36.3 ms, p = 0.01, APD50: 252.4±49.2 ms vs. 215.2±75.2 ms, n.s., APD90: 336.3±65.0 ms vs. 296.9±75.5 ms, n.s.). AP duration showed a strong frequency dependence in both groups (APD50 at 1 Hz: 296±865.4 ms, at 2 Hz: 252.4±49.2 ms, at 3 Hz: 197.4±39.8 ms, p<0.001).

Conclusions: Vital heart slices can be prepared from patient biopsies during surgery for congenital heart disease and are a suitable platform for physiological measurements at the cellular and multicellular level. This technique can be used for further physiological and pharmacological studies.