Acute and chronic anti-arrhythmogenic effect of liposome-encapsulated hemoglobin (HbV) on the Myocardium through improving myocardial electrical remodeling and the arrhythmogenic substrate in hemorrhagic shock-induced heart

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Introduction: Prolonged blood pressure < 40 mmHg in hemorrhagic shock (HS) causes irreversible heart dysfunction, “Shock Heart Syndrome” (SHS), which is associated with lethal arrhythmias (VT/VF).

Methods: To investigate whether liposome-encapsulated human hemoglobin (HbV) is comparable to washed red blood cells (wRBCs) for improving arrhythmogenesis in SHS in either acute or chronic phase, optical mapping analysis (OMP), electrophysiological study (EPS) and pathological examinations were performed in Sprague-Dawley rat hearts, being obtained from both acute and chronic phase when each rat survived. The first, they were subjected to acute HS by withdrawing 30% of total blood volume. After HS, rats were immediately resuscitated by transfusing exactly same amount of 5% albumin (5%ALB, n=13), HbV (n=13), or wRBCs (n=13). All rats in chronic phase survived at least several weeks. After excising heart, OMP and EPS were performed in Langendorf-perfused hearts.

Result: In both acute and chronic phase, OMP showed tendency for abnormal conduction and significantly impaired action potential duration dispersion (APDd) in left ventricle with 5%ALB (25±9 / 24±10 ms, Acute / Chronic phase). In contrast, myocardial conduction and APDd were substantially preserved with HbV (14±3 / 13±5 ms) and wRBCs (14±3 / 15±3 ms) as shown in Figure. Sustained VT/VF was easily provoked by burst pacing stimulus to left ventricle with 5%ALB. No VT/VF was induced with HbV and wRBCs. Pathology showed myocardial structural damage characterized by worse myocardial cell damage and Connexin43 with 5%ALB, whereas it was attenuated with HbV and wRBCs in both acute and chronic phase.

Conclusion: Ventricular structural remodeling after HS causes VT/VF in the presence of APDd. Transfusion of HbV prevents acutely and chronically VT/VF, similarly to transfusion of wRBCs, by preventing chronic electrical remodeling of APDd and preserving myocardial structures in HS-induced SHS.