ABSTRACT

Objectives

This study aimed to identify the practical applications of intravenous cell therapy for single-ventricle physiology (SVP) by establishing experimental SVP models.

Methods

An SVP with a three-stage palliation was constructed in an acute swine model without cardiopulmonary bypass. A modified Blalock–Taussig shunt (MBT) was created using an aortopulmonary shunt with the superior and inferior vena cava (SVC and IVC, respectively) connected to the left atrium (LA) (*n*=10). A bidirectional cavopulmonary shunt (BCPS) was constructed using a graft between the IVC and LA with an SVC cavopulmonary connection (*n*=10). The SVC and the IVC were connected to the pulmonary artery to establish a total cavopulmonary connection (TCPC, *n*=10). Half of the animal models were observed to examine their lifetimes. The other half and the biventricular sham control (n=5) were intravenously injected with cardiosphere-derived cells (CDCs), and the cardiac retention of CDCs was assessed after 2 h.

Results

All SVP models died within 20 h. Perioperative mortality was higher in the BCPS group because of lower oxygen saturation ($P<0.001$). Cardiac retention of intravenously delivered CDCs, as detected by magnetic resonance imaging and histology, was significantly higher in the MBT and BCPS groups than in the TCPC group ($P<0.01$).

Conclusions

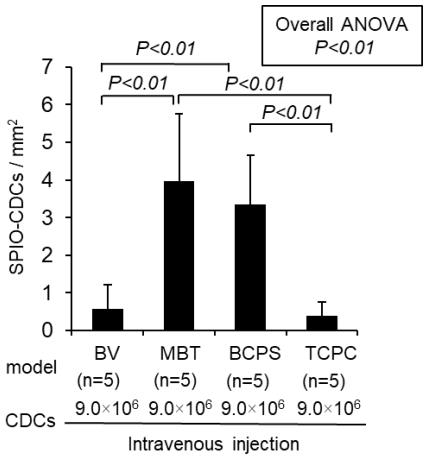
Without the total right heart exclusion, stage-specific SVP models can be functionally constructed in pigs with stable outcomes. Intravenous CDC injections may be applicable in patients with SVP before TCPC completion, given that the initial lung trafficking is efficiently bypassed and sufficient systemic blood flow is supplied from the single ventricle.

Graphical Abstract

Intravenously injected stem cells in stage-specific pig models were detected in the myocardium of stage 1 and 2 palliation models.

Summary

Three-stage right heart bypass model was established in pig to study early cardiac homing of the intravenously transplanted CDCs. Cardiac retention of delivered CDCs was significantly higher in the MBT and BCPS groups than in the TCPC group. Intravenous CDCs delivery through the lung bypass circuit is effective in targeting a single ventricle before TCPC completion.



Legend: BCPS: bidirectional cavopulmonary shunt; BV: biventricular; CDCs: cardiosphere-derived cells; MBT: modified Blalock–Taussig shunt; SPIO: superparamagnetic iron oxide; TCPC: total cavopulmonary connection