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J. of Cardiovasc. Trans. Res. (2013) 6:660–661
DOI 10.1007/s12265-013-9480-1

Tissue-Engineered Heart Valves: Intra-operative Protocol

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Received: 7 May 2013 / Accepted: 31 May 2013 / Published online: 14 June 2013
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Abstract Tissue engineering of heart valves investigates the possibility to create a fully compatible and biomimetic graft able to provide host cell repopulation like the native living valve. Decellularized aortic and pulmonary valves and synthetic polymers have been used to promote the creation of a native-like scaffold suitable to be colonized by cells either in vitro, in dynamic bioreactors or in vivo using different animal models. The herein presented research provides the intra-operative protocol and details of surgical technique. Porcine aortic valve conduits were decellularized and implanted in the right ventricular outflow tract of Vietnamese pigs.

Keywords Tissue engineering · Surgical technique · Heart valves · Decellularization · Animal model

Associate Editor Jennifer L. Hall

Electronic supplementary material The online version of this article (doi:10.1007/s12265-013-9480-1) contains supplementary material, which is available to authorized users.

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Video Description

All animal experiments and surgical procedures were performed in compliance with standards ISO 10993-1, 10993-2 and UNI EN ISO 5840. Aortic valve conduits were isolated from young common breeding piglets (3–4 months old), decellularized according to TRICOL protocol [1, 2] and were implanted in the right ventricular outflow tract (RVOT) of Vietnamese pigs (VPs) using cardiopulmonary bypass.

The extracorporeal circulation (ECC) circuit was coupled with a paediatric oxygenator (Sorin Dideco D902 Lilliput 2), certified to provide blood flow up to 2,300 cc min^{-1} (100-cc filling volumes) which worked very well till 4,500 cc min^{-1} with maximal oxygen supply to the oxygenating chamber. VPs diuresis was stimulated with 18 % mannitol infusion in the ECC prime and with furosemide at an initial dosage of 1 to 2 mg kg^{-1}. The pump was a first-generation Stöckert HLM (Stöckert Instrumente, Schmitten, Germany). The prime formula and ECC weaning used were prepared as shown in Table 1.

The surgery began with a xypho-jugular incision followed by median longitudinal sternotomy and pericardiotomy. Screening of the total systemic ACT heparinization (ACT values >400 s) was determined as well. In order to activate the ECC, two Ticron 2-0 purse string sutures were trimmed on the ascending aorta, both internally and externally, eventually reinforced with pledgets. A paediatric aortic cannula (10–14 Fr, Medronic, Hopkinton, MA) was then inserted in the supra-aortic position, and the drainage of the cardiac chambers was performed with a double-vein cannulation for the superior and inferior venae cavae. Once all tubes were connected to the ECC circuit, the normothermic extracorporeal circulation (2.6 L min^{-1} m^{-1}) was turned on along with the ventilation suspension.

Table 1 Prime and ECC weaning formula

Prime	Quantity
Whole blood	500/600 cc
Electrolytic solution	50 cc
Sodium bicarbonate	10 mEq
Heparin	2,000 U.I.
Mannitol, 18 %	3 cc/kg
Furosemide	2 mg (0.2 cc)
Magnesium	2 g (20 cc)
Potassium	4 mEq (2 cc)
ECC weaning	
Magnesium	2 g (20 cc)
Potassium	5 mEq/L

The native pulmonary artery root was then removed from the beating heart, paying particular attention to avoiding damages to the coronary artery branches. The RVOT was then reconstructed using the decellularized aortic root with the coronary ostia trimmed and ligated [3, 4] (Fig. 1). With the procedure completed, the VP was weaned from ECC with restoration of mechanic lung ventilation. At the end, a retrosternal mediastinal drainage was positioned together with a pleural drainage.

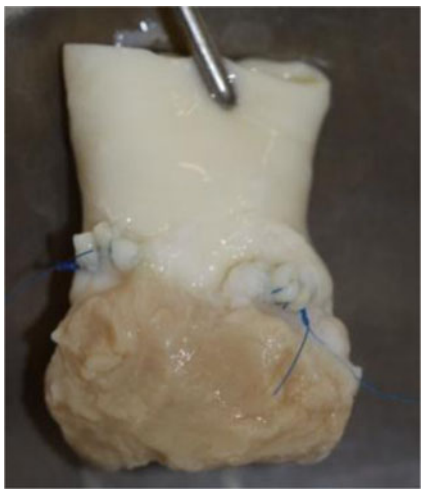

Fig. 1 Implantation of the prepared aortic decellularized root (coronary ostia trimmed)

After surgery, the animals were then weaned from the ventilator and allowed to breathe spontaneously. Post-operative anticoagulation therapy was maintained, providing the animals, two times daily, with 100 mg of lysine acetyl-salicylate administered IV. Antibiotic therapy (cefazolin 25-mg kg^{-1} bid) was also infused for 10 days after surgery to avoid endocarditis.

This translational research provides a complete methodological information for implantation of a tissue-engineered heart valve and animal handling during surgery and over the early post-operative time. Surgical feasibility has been demonstrated, and future studies have been initiated to assess long-term in vivo functionality as well as cell repopulation according to in vivo tissue-guided regeneration paradigm.

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