Regional Changes in Leaflet Coaptation Dynamics After Total Tricuspid Reconstruction

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Background. **Stentless porcine extracellular matrix tricuspid tube grafts were developed for tricuspid valve reconstruction. The purpose of this study was to conduct an echocardiographic assessment of the performance of native and tube graft leaflets in an acute porcine model.**

Methods. **Fourteen 65-kg pigs were randomly assigned to tube graft (n = 7) or control with native valve preservation (n = 7). Epicardial echocardiography was performed at baseline after sternotomy, after valve operation, and after hemodynamic stabilization.**

Results. **No baseline differences were found ($p > 0.05$). All valves were competent with only a mild central regurgitant jet in two tube grafts and two native valves. Tube graft valves were compared with native valves. Anterior-septal leaflet coaptation length (18 ± 6 mm versus 6 ± 1 mm, $p < 0.0005$), coaptation height (20 ± 9 mm versus 9 ± 4 mm, $p < 0.005$), and anterior leaflet length (31 ± 1 mm versus 22 ± 2 mm, $p < 0.00005$) were all significantly larger in the tube graft valves. The billowing index (0.8 ± 0.1 versus 0.9 ± 0.1, $p > 0.05$) and tenting height (5 ± 1 mm versus 4 ± 2 mm, $p > 0.1$) were not significantly different. Leaflet excursion angles for both leaflets were not significantly different between the native and tube graft valves ($p > 0.1$).**

Conclusions. **In a porcine experimental model, a competent tricuspid valve was constructed using extracellular matrix tube graft material. Coaptation geometry was significantly different from native valves with an increased coaptation zone because of excessive leaflet tissue in the tube graft valves. The tube graft tended to prolapse into the atrium, but it did not compromise the motion and competence of the leaflets.**

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The role of the tricuspid valve as an independent cause of congestive heart failure is an object of debate, although a general acceptance of a more aggressive surgical approach is being favored [1]. Earlier assumptions that tricuspid disease is rare and irrelevant to outcome after left-sided surgical procedures [2] have now been replaced by evidence of poor long-term outcome [3] if left untreated. This has led to an increase in tricuspid valve operations, both as concomitant and stand-alone procedures [4–7]. Tricuspid valve repair is uniformly favored over tricuspid valve replacement, which remains a problematic procedure due to risk of early prosthetic valve thrombosis and valve deterioration.

The concept of tissue engineering has led to the development of an acellular bioscaffold composed of porcine small intestinal submucosa extracellular matrix (ECM). This material possesses growth potential, low thrombogenicity, no scar tissue formation, no calcification, and the potential for integration with native tissue and repopulation with host cells [8, 9].

A tricuspid tube graft was developed for total valve reconstruction using ECM [10]. In previous studies, the tubular design has shown favorable flow dynamics and stress distribution [11]. Successful total valve reconstruction with ECM valves has also been shown for the pulmonary valve in pigs [12] and humans [13]. Total reconstruction of the tricuspid valve using this type of ECM has been described in sheep [10] with a postoperative competent valve and normal leaflet motion. Results from a retrospective study on 19 patients with tricuspid valve endocarditis, receiving an ECM tricuspid tube graft, showed good echocardiographic results with competent valves, although 3 patients needed reoperation due to papillary muscle detachment and 1 patient due to fungal infection of the tube graft. Follow-up was also limited to 18 months with several patients lost to follow-up [14]. The tube graft was constructed from one sheet of ECM (10 cm × 3.5 cm), which was folded once,

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allowing for construction of a tube by suturing the two shorter sides together using 6-0 Prolene (Ethicon, Somerville, NJ). The concept has to be definitively proved to be safe and durable in humans before implementation in clinical practice. An Early Feasibility Study is right now being performed in the United States using Cormatrix ECM as a tricuspid tube graft valve replacement in adults and children with tricuspid valve disease not amenable to repair (ClinicalTrials.gov identifier NCT02397668). The lack of complete understanding of physiologic and biomechanical behavior of the tube graft valve is still a limitation to the technology.

The aim of the present study was to evaluate leaflet motion, leaflet coaptation geometry, and valve competence in ECM tricuspid valves in comparison with the native tricuspid valves using echocardiography in pigs.

Material and Methods

Study Design

This study was designed as a randomized animal experimental study.

Animals

Twenty-two Danish Landrace pigs (65 kg) were randomly assigned to ECM valve (intervention) or no valve replacement (control). Two pigs were excluded because of pericarditis. Two pigs could not be weaned from bypass (one in each group) because of heart failure after a long cardioplegia time, and four pigs died of ventricular fibrillation before data collection (two in each group). No deaths were considered mechanically related to the operation, because the implanted valves showed no disruptions or dysfunction at necropsy. Fourteen animals comprised the study population with seven animals in each group. The experiment complied with the guidelines of the Danish Inspectorate of Animal Experimentation under the Department of Justice.

Surgical Procedure

Premedication, transportation, and anesthesia of the animals were described previously [15, 16]. A median sternotomy was performed, and heparin (40,000 IE) was given intravenously. A baseline epicardial echocardiography was performed. An aortic cannula was placed in the ascending aorta, followed by bicaval cannulation. Cold blood cardioplegia was administered in the aortic root (Harefield Hospital Formulation, 1:8 ratio). The tricuspid valve was exposed on the arrested heart through a right atriotomy. Miniature sonomicrometric crystals were implanted in the tricuspid annulus and papillary muscle, intended for another study [17].

In the ECM group, the native tricuspid valve was excised. ECM valves (CorMatrix; Cardiovascular Inc, Alpharetta, GA) were provided as tube grafts (height = 3.5 cm, circumference = 10.0 cm) and designed to fit the dimensions of the native valve in 65-kg animals based on previous measurements of the tricuspid porcine valve (unpublished data) and after personal communication with Dr R.G. Matheny. First, the distal end of the tube graft was sutured to each of the three papillary muscles using 5-0 Prolene (Ethicon) sutures (Figs 1A, 1B). The three tube graft leaflets were sized with 40% of the circumference for the anterior leaflet and 30% for the two remaining leaflets. The proximal circumference of the tube graft was sutured to the tricuspid annulus using three 5-0 Prolene (Ethicon) running sutures (Fig 1C), one for each of the three leaflet segments. Valve competence was confirmed using water testing (Fig 1D) before the insertion of measuring equipment and atrial closure. In the control group, the native tricuspid valve was preserved, but the valve was still exposed through an atriotomy. Cross-clamp time was kept just as long as in the intervention group before atrial closure and reperfusion.

After 40 minutes of reperfusion, the pig was weaned from cardiopulmonary bypass. After hemodynamic stabilization, the last epicardial echocardiography was performed. After data collection, the animals were euthanized. The heart was explanted, and proper position of the tube graft was confirmed.

Echocardiography

In reconstructive valve surgical procedures transesophageal echocardiography has shown a pivotal role in the evaluation of valve structure and function. In pigs, the presence of an extra left lung lobe situated inferior/diaphragmatic to the heart prevents transesophageal echocardiography. Transthoracic echocardiography in pigs is also a challenging task because of the shape of the porcine chest and the lung lobes. Accordingly, epicardial echocardiography was chosen to obtain an optimal acoustic window for the echocardiographic recordings.

All epicardial echocardiographic measurements were performed from an apical four-chamber view using conventional two-dimensional (2D) imaging. The diameter and measurements of the tricuspid annulus were shown to change significantly depending on view and transducer position [18]. Furthermore, the vena contracta of the tricuspid valve was typically imaged in the apical four-chamber view [7]. For these reasons, we chose one echocardiographic view and averaged measurements over two beats at specific time points in the heart cycle.

In all pigs, an apical right ventricular focused four-chamber imaging with stable electrocardiographic tracing was obtained over 10 cardiac cycles. The septum was used as reference to get a cross-sectional view of the septal and anterior leaflet and the coaptation between these leaflets. It was difficult to provide reproducible imaging of the smaller posterior leaflet, which also showed a high degree of variation in size and shape. Therefore, the posterior leaflet was not evaluated.

All echocardiographic recordings were performed with the animal in the supine position and using grayscale 2D imaging with adjustments of image contrast, frequency depth, and sector size for proper imaging. Color flow Doppler technique was used to confirm competence of the valves.

Data sets were stored digitally, and off-line analysis was performed in end systole (EchoPAC version 112.1.3;