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Comprehensive and Integrative Experimentation Setup for Large Animals' Hybrid Valvular Heart Surgery

Mohamed Alaa, MD, PhD,[a,*] *Maria Tsopanomichalou Gklotsou, PhD,*[a]
Thang Duc Vu, MD, PhD,[a] *Lian Kah Ti, MBBS, MMed,*[b]
Chuen Neng Lee, MBBS, MMed, FRCS,[a,c]
and Theo Kofidis, MD, PD(Ger), FRCS, FAHA, FAMS[a,c]

[a] *Department of Cardiac, Thoracic and Vascular Surgery, Yong Loo Lin School of Medicine, National University of Singapore, Singapore*
[b] *Department of Anesthesia, National University of Singapore, Singapore*
[c] *National University Hospital, National University Health System, Singapore*

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ABSTRACT

Background: Experimental surgical procedures for atrioventricular valves present promising translational capabilities, and preclinical studies are necessary to assess their applicability and to train young enthusiastic heart teams. Here, we present a synopsis of experimental surgical procedures on porcine models for mitral valvular (MV) and tricuspid valvular (TV) interventions; mitral valve-in-valve implantation (MViV), transapical cardioscopic (TAC) MV replacement (MVR), TAC-MV annuloplasty, and tricuspid valve-in-a-ring (TViR) procedures.

Methods: Twenty-five ($n = 25$) female Yorkshire pigs of 55-65 kg is the total number used in the four approaches; seven animals underwent MViV, six TAC-MVR, six TAC-MV annuloplasty, and six TViR, respectively. All were subjected to a first conventional valvular surgery (bioprosthetic valve replacement and/or prosthetic ring repair). Then, after 4 wk, a less-invasive second surgery was performed using the transcatheter approaches under investigation. Except for the TAC-MVR and annuloplasty procedures, all animals were followed up for additional 4 wk.

Results: (1) MViV ($n = 7$): Standard MVR was successfully performed in all animals. Transvalvular pressure gradients and flow velocities were (P_{max} 3.77 ± 0.8 mmHg; P_{mean} 2.1 ± 0.6 mmHg, V_{max} 97 ± 13 cm/s; V_{mean} 68 ± 21 cm/s). Effective MViV followed (P_{max} 16.7 ± 1.8 mmHg; P_{mean} 6.2 ± 1.2 mmHg, V_{max} 216 ± 32 cm/s; V_{mean} 110 ± 24 cm/s). (2) TAC-MVR (n = 6): The overall bypass time was 177.2 ± 44.2 min. Transprosthetic P_{mean} was 4.6 ± 2.4 mmHg; no paravalvular leaks in all animals. (3) TAC-MV annuloplasty (n = 6): The implantation time was 47 ± 6 min. MV was competent, left ventricular ejection fraction (LV-EF%) was 63 ± 4%. (4) TViR (n = 6): Conventional TV ring repair was performed in all animals (P_{max} 2.42 ± 0.7 mmHg; P_{mean} 1.3 ± 0.6 mmHg, V_{max} 82 ± 10.4 cm/s; V_{mean} 65.4 ± 21 cm/s). All TViRs were implanted efficiently (P_{max} 4.7 ± 1.6 mmHg; P_{mean}

* Corresponding author. Department of Surgery, National University of Singapore, DSO (Kent Ridge), Building. 27 Medical Drive, # 03-01A, 117510 Singapore, Singapore. Tel./fax: +65 67758538.
E-mail address: surmaaao@nus.edu.sg (M. Alaa).
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2.7 ± 0.8 mmHg, V_{max} 105 ± 31 cm/s; V_{mean} 81 ± 16 cm/s). A mild paravalvular leak was observed in one animal (16%).

Conclusions: All studied experimental valvular interventions are feasible, within the context of well-trained cardiac surgery specialists, and all possibilities should be considered when treating a patient to determine which one suits best his individual challenges and scope.

Introduction

The National University of Singapore and the National University Health System (NUS–NUHS) have pioneered medical innovation and research in South East Asia, introducing novel techniques in clinical settings[1,2] and upgrading perioperative care for patients,[3] while simultaneously providing advanced training to aspiring young physicians through continuing medical and surgical education, hi-tech simulation centers, and participation in animal experiments and wet laboratories. For the last 8 y, the Cardiothoracic and Vascular Surgery Department has been applying diverse surgical procedures for atrioventricular (AV) valves, which present promising translational capabilities. Inherently, to facilitate the translational aspect, the use of large animal models (especially pigs) is a mandatory preclinical stage, in regard to the similarity of physiology and function, and to partial similarity of their cardiovascular system anatomy to humans.[4,5] Our extensive experience with the porcine model for cardiovascular disorders has produced prolific results and has given us a deep understanding of all the research challenges that may occur. Here we present an integrative overview of all gained animal experience as an approach toward clinically translated cardiothoracic surgical innovation, the scope of this study including all the surgical and the transcatheter interventions experimentally performed on AV valves divided into two distinct sections: (1) mitral valve (MV), (2) tricuspid valve (TV) interventions.

Mitral valve interventions

Concepts for the MV geometry, physiology, and function are currently established.[6-9] MV is undeniably the subsequent frontier after transcatheter aortic valve implantation success. With reasonable intermediate results, data on long-term outcomes are required. As with all new procedures, appropriate patient selection per each procedure will be needed for optimal results. Thus, better understanding of the anatomic and physiologic factors affecting the outcome, implantability of the currently used devices, and the need for device-specific anticoagulation will all be important to assure good outcomes. Anticoagulation strategy is still unclear and may play an important role in the success of transcatheter mitral valve replacement, as the devices are large, are covered with fabric, and most patients are in atrial fibrillation. Now, the transapical approach will likely remain the common access site, but developments in the delivery system and device profile will definitely move this technology toward the less-invasive approach. Transcatheter success will also depend on further trials from cardiac surgeons, cardiologists, sonographers, and bioengineers; to come up with new ideas to decipher the complexity of MV functions and to develop new approaches for repairing and/or replacing diseased valves for annually increasing number of patients with both rheumatic and degenerative MV etiologies.[10-13] Our surgical research goal was to perform state-of-the-art interventions to the MV either by repair or replacement,[1,14] namely, the transatrial valve-in-valve mitral valve replacement (MVR), the transapical cardioscopic (TAC) approach for MV annuloplasty,[14,15] and the TAC-MVR.[16]

The TAC approach has recently been proposed by our group as a proof-of-concept and a feasible method for providing concurrent surgical access to the MV.[14-16] Currently, the transapical approach is used primarily for transcatheter MV implantation.[13] It has also been used in a setting of simple valvular procedures on a beating heart.[17-21] However, these techniques are unable to address certain MV diseases such as degenerative or ischemic MV disease, or those involving multiple valves, and direct access for repair/replacement under cardiopulmonary bypass (CPB) may provide a more radical and long-term solution.[21] Video-assisted minimally invasive techniques are time tested for more than 2 decades with efficacy and well-established safety.[22,23] Adaptation of the well-established procedures to the transapical access may offer an alternative approach in selected patients, in whom current approaches carry excessive risk.[14-16] Our standard operating procedure (SOP) for CPB in porcine surgeries is provided in the supplementary materials (Appendix 1)

The TAC approach allows direct and full visualization of the subvalvular apparatus, where most of the mitral lesions locate, via a small apical and chest incision, and is, thereby, potentially less invasive than the conventional trans-sternal procedures. Nevertheless, technical optimization, the associated survival, and operative outcomes specific to this procedure have been addressed in our studies. As for MV repair and/or replacement, the main concerns for the TAC approach are (1) the injuries to valve leaflets, the chordae, and the ventricle, (2) changes in cardiac function due to the opening of the apex, and (3) completion of the procedure, especially when a bulky mitral ring/bioprosthesis is passed through the apex and anchored to the mitral annulus.[14-16]

Although some renowned centers worldwide are moving toward less-invasive MV interventions,[24,25] still large-scale applications on human patients are infrequent,[13] mainly because surgeons are not very familiar with the arsenal of techniques available and the pros and cons of each one in any given situation. Thus, a step back to the preclinical level is necessary to assess their applicability, to master the complex techniques, to overcome the challenges, to avoid the complications, and to pave the way for large clinical trials enabling the enthusiastic heart teams to acquire the cruising speed in favor of patients' safety and welfare.