JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 68, NO. 10, 2016
ISSN 0735-1097
http://dx.doi.org/10.1016/j.jacc.2016.06.022

Transcatheter Edge-to-Edge Treatment of Functional Tricuspid Regurgitation in an Ex Vivo Pulsatile Heart Model

Riccardo Vismara, PhD,[a,b] Guido Gelpi, MD,[b,c] Santosh Prabhu, PhD,[d] Paolo Romitelli, MS,[e] Lauren G. Troxler, BS,[d] Andrea Mangini, MD,[a,b,c] Claudia Romagnoni, MD,[b,c] Monica Contino, MD,[b,c] Dylan T. Van Hoven, BS,[d] Federico Lucherini, MS,[a,b] Michal Jaworek, MS,[a,b] Alberto Redaelli, PhD,[a,b] Gianfranco B. Fiore, PhD,[a,b] Carlo Antona, MD[b,c,f]

ABSTRACT

BACKGROUND Although associated with left heart pathologies, functional tricuspid regurgitation (FTR) is often left untreated during left heart surgery. Hence, owing to its degenerative character, reoperation is often needed, encompassing an impressive (25% to 35%) mortality rate. Thus transcatheter approaches to FTR are raising great interest.

OBJECTIVES The authors evaluated the post-treatment effectiveness of the edge-to-edge technique using the percutaneous mitral valve repair device in an ex vivo pulsatile model of FTR.

METHODS The devices were implanted in 11 porcine hearts simulating FTR. In each heart, single-clip treatments involved grasping leaflet pairs in the medial or commissural position (6 combinations). Two-clip treatments were then performed considering all possible 15 combinations of leaflet pairs and medial/commissural grasping. Cardiac output, mean pulmonary pressure, and mean diastolic valve pressure gradient were evaluated in physiological and simulated pathological conditions (FTR), and post-treatments.

RESULTS Grasping the septal and anterior leaflets allowed for the best post-procedural outcome, ensuring a complete re-establishment of physiological-like hemodynamics. Septal and posterior grasping induced a significant recovery from FTR, although less marked. Conversely, grasping the anterior and posterior leaflets did not reduce FTR, and was detrimental in some specific cases.

CONCLUSIONS This experimental work demonstrated that the transcatheter edge-to-edge repair technique is a feasible approach for FTR. The study investigated this approach to develop a selective, specific structural intervention methodology for treating FTR, considering the several biomechanical factors that alter proper functionality of valvular substructures. These results can be used to guide the development of edge-to-edge repair techniques in treatment of FTR. (J Am Coll Cardiol 2016;68:1024–33) © 2016 by the American College of Cardiology Foundation. Published by Elsevier. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Mild to severe tricuspid valve (TV) regurgitation affects 1.6 million patients in the United States (1). It is associated with comorbidities such as peripheral edema, reduced cardiac output (CO), and heart failure, and can lead to premature death (2–4). This pathology can be secondary to damage of the TV structures (degenerative tricuspid regurgitation) or to structural changes in the

Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

From the [a]Dipartimento di Elettronica, Informazione e Bioingegneria, Politecnico di Milano, Milan, Italy; [b]ForcardioLab-Fondazione per la Ricerca in Cardiochirurgia ONLUS, Milan, Italy; [c]Cardiovascular Department, 'Luigi Sacco' General Hospital, Milan, Italy; [d]Abbott Vascular, Menlo Park, California; [e]Abbott Vascular International, Brussels, Belgium; and the [f]Università degli Studi di Milano, Milan, Italy. This study was supported in part by Abbott Laboratories, Abbott Park, Illinois, by Fondazione per la Ricerca in Cardiochirurgia ONLUS, Milan, Italy, and by the European Commission within the Horizon 2020 framework through the MSCA-ITN-ETN European Training Networks (project number 642458). Dr. Prabhu is an employee and shareholder in Abbott Vascular, Menlo Park, California. Mr. Romitelli is an employee of Abbott Vascular International, Brussels, Belgium. Ms. Troxler and Mr. Van Hoven are employees of Abbott Vascular, Menlo Park, California. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received May 29, 2016; revised manuscript received June 14, 2016, accepted June 16, 2016.

right heart (annular dilation and ventricular enlargement) that lead to improper TV leaflet coaptation, such as functional tricuspid regurgitation (FTR). Approximately 90% of all severe TV regurgitation is related to FTR (5,6).

FTR is often secondary to left heart pathologies, such as mitral valve regurgitation and stenosis (1,4). These pathologies can induce pressure and volume overload in the right ventricle (RV), which in turn can induce ventricle enlargement and tricuspid annular dilation. In this phase, TV regurgitation is typically mild. However, annular dilation is progressive and asymmetric, mostly involving the anterior and posterior leaflets that pull away from the coaptation lines with the septal leaflet (**Central Illustration**, panel A). FTR becomes more severe with increased RV dilation, which induces papillary muscle displacement and leaflet tethering, further worsening the FTR (1,4,7,8).

FTR is seldom treated during left heart surgery. Despite being well accepted that FTR is a deteriorating pathology, tricuspid treatment is usually only performed concomitantly to left heart surgery in cases of severe regurgitation. Consequently, the rate of FTR recurrence or worsening after surgical treatment of the left heart remains high, especially given the aging population (1,2,7,9). This leads to a potentially high frequency of reoperations, with in-hospital mortality as high as 25% to 35% (1,2). Thus, transcatheter approaches to FTR are considered an attractive strategy (1,2,7,10).

SEE PAGE 1034

Among the few transcatheter devices exploitable for FTR treatment, a percutaneous mitral valve repair system (MitraClip System, Abbott Vascular, Santa Clara, California), developed for mitral valve regurgitation, is a promising option (1,2,10). It allows replicating, in a less invasive manner, the edge-to-edge surgical approach that has provided good results in addressing FTR when combined with other therapies (11).

Several published clinical applications (12–15) of the percutaneous mitral valve repair system for treating TV regurgitation suggest the potential of this approach, particularly when septal and anterior leaflets are grasped (12,14). Open issues in this approach include the 3-leaflet anatomy, gaps between the leaflets, and the high density of tricuspid chordae, particularly in the commissural (Com) position.

This paper presents a systematic experimental study of the transcatheter edge-to-edge repair technique applied to an ex vivo model of FTR. Our aim was to evaluate the feasibility and efficacy of this technique in the 3-leaflet TV, focusing on assessing immediate post-operative outcomes in relation to: 1) which pair of leaflets is grasped; 2) where the pair of leaflets are grasped; and 3) if a 2-clip implantation improves results.

METHODS

Derived from a mock loop extensively used to simulate human circulation, the experimental system consisted of a pulsatile pump connected to a porcine heart obtained from the abattoir. The system accurately replicated the pulse flow and heart valve function in a beating heart (16–19). (More details are in the Online Appendix.) The right heart CO, mean pulmonary pressure (P_{pul}), and mean diastolic pressure gradient across the TV (Δp) were obtained from acquired data. Direct visualization of the valvular apparatus was recorded with a fiberscope (Olympus Europe, Hamburg, Germany) inserted in the right atrium. Echocardiographic views of the TV were acquired using an Epiq7 equipped with an X7-2t probe (Philips, Eindhoven, the Netherlands). The mock loop was set to simulate physiological rest conditions (heart rate 60 beats/min; stroke volume 70 ml; P_{pul} 10 to 15 mm Hg). Saline solution was used as working fluid.

EXPERIMENTAL MODEL OF FTR. We used porcine hearts from pigs weighing 170 ± 8 kg. Similar to published literature (20,21), the model exploited the tendency of the TV annulus and RV to dilate in order to achieve an experimental model of FTR. In the experimental apparatus, these extremely compliant structures started to dilate at physiological pulmonary pressure values. More specifically, the anterior and posterior portions of the TV annulus dilated, thus pulling the anterior and posterior leaflets away from the septal leaflet. Moreover, due to RV dilation, the papillary muscles anchored to the free ventricular wall were displaced, thus inducing leaflet tethering and in turn further TV incontinence. In the ex vivo model, both of these biomechanical determinants were controlled by means of 2 adjustable bands placed around the heart: 1 around the valvular plane, the other at the level of the papillary muscles. The first band was used to regulate annular diameter; the second to confine and control the RV dilation, thus adjusting papillary muscle displacement and associated leaflet tethering. To obtain physiological TV behavior, the 2 bands were adjusted until experienced surgeons visually verified proper coaptation of the leaflets. CO evaluation, direct fiberscope views, and echocardiographic images were used to support this decision. When the bands were released,

ABBREVIATIONS AND ACRONYMS

ANOVA = analysis of variance
A-P = anterior-posterior
CO = cardiac output
Com = commissural
Δp = diastolic pressure gradient across the tricuspid valve
FTR = functional tricuspid regurgitation
Med = medial
P_{pul} = pulmonary pressure
RV = right ventricle/ventricular
S-A = septal-anterior
S-P = septal-posterior
TV = tricuspid valve