First-in-Human Case of Transfemoral CardiAQ Mitral Valve Implantation

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Major advancements have been made in transcatheter aortic and pulmonary valve implantation during the past decade. However, transcatheter mitral valve implantation (TMVI) poses different challenges because of the complexity of the mitral valve apparatus. Although several companies are attempting to develop transcatheter approaches for mitral valve repair, these technologies may have limited applicability because of the heterogeneous nature of the disease and, to date, this strategy has had a difficult time demonstrating the efficacy that is equivalent to surgical approaches. In this report, we describe the first-in-human percutaneous transfemoral-TMVI, which was performed at Rigshospitalet in Copenhagen, Denmark on June 12, 2012 using a dedicated device.

Case

An 86-year-old male with symptomatic mitral regurgitation (MR) was referred for interventional treatment. Transesophageal echocardiography showed severe MR (grade, 3+ to 4) because of mitral annular dilatation and a severely restricted posterior mitral leaflet in a dilated left ventricle (LV) with ejection fraction 40%. The patient was declined for mitral valve surgery (Society of Thoracic Surgeons score, 31.9%) and for MitraClip treatment because of a too large systolic coaptation gap. An informed consent from the patient and approval from the Danish National Board of Health were obtained for this first-in-human TMVI procedure using the first-generation CardiAQ valve (CardiAQ Valve Technologies, Irvine, CA; Figure 1).

The procedure was performed under general anesthesia. In the right groin, access was obtained in the femoral vein (2 access sites—the highest for transseptal puncture and the delivery system and the lowest for a steering snare) and in the femoral artery (2 access sites—one for a triloop snare and one for a pigtail for LV angiograms; Figure 2A). Through the lower venous access, a steering snare was placed around the wire from the higher venous access; this snare was later used to steer the delivery system in the left atrium (Figure 2B). After standard transseptal puncture, a HiWire (Cook, Bloomington, IL) was maneuvered through the mitral annulus and LV cavity to the descending aorta. By means of a triloop snare introduced into the femoral artery, this HiWire was then captured to establish an arteriovenous loop. To ensure that the HiWire was not caught in the mitral apparatus, a 14-mm inflated Tyshak balloon (NuMED Inc, Hopkinton, MA) was tracked on the wire from the left atrium to the LV outflow tract and back, the so-called Copenhagen manoeuvre (Figure 2D). Once confirmed that the balloon could move freely, the HiWire was exchanged for a custom-made polytetrafluoroethylene-coated nitinol wire within a long 4-Fr catheter. The wire was snared and pulled out of the femoral arterial sheath to reestablish the arteriovenous loop.

The venous introducer sheath (30 Fr) was placed after gradual dilation of the highest venous access site, and the steering snare was positioned at the middle of the nose cone of the delivery system (Figure 2E). After smoothly advancing the delivery system through the atrial septum, pulling on the steering snare redirected the system toward the mitral valve. Once positioned into the LV (Figure 2F), the snare was released from the nose cone and pulled back to the shaft of the delivery system.

The landing zone between the mitral plane and the tip of papillary muscles was determined by transesophageal echocardiography and a left ventriculogram. By manipulating the arteriovenous loop and the delivery system, the CardiAQ valve could be positioned perpendicular to the mitral annular plane. A staged deployment allowed exposure of the ventricular anchors and careful positioning to capture the posterior mitral leaflet (Figure 2G). Finally, the anterior mitral leaflet was captured by pulling on the arteriovenous loop from the arterial side, before complete release of the TMV device (Figures 2H and 3). After angiographic and transesophageal echocardiographic confirmation of a well-positioned and well-functioning prosthesis, the delivery system was retracted and the resultant atrial septal defect was closed by a 16-mm Amplatzer Septal Occluder (St Jude Medical, St Paul, MN).

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As no previous experience with a TMVI procedure in man existed, extracorporeal circulation support was shortly used during valve deployment (15 minutes) to ensure hemodynamic stability. Considering the smooth valve deployment, this extracorporeal circulation support seemed post hoc not essential. Procedure and fluoroscopic times were 140 and 32 minutes, respectively, and 145 mL of contrast dye was used.

The patient made an uneventful recovery the first 24 to 48 hours, and a well-functioning TMV prosthesis was confirmed by echocardiography at 24 and 48 hours after TMVI (Figure 4). However, the patient died 68 hours post procedure because of a systemic inflammatory response syndrome, possibly triggered by the use of the extracorporeal assist device. Importantly, autopsy did not show significant pathology or malfunction of the TMV prosthesis and excluded perforation of adjacent structures.

Discussion

TMVI revolutionized the management of valvular aortic stenosis by providing a safe and efficacious alternative to surgical valve replacement in higher-risk patients. Similarly, the risk and uncertain benefit of mitral valve surgery in high-risk patients with severe MR have driven the search for new transcatheter mitral valve therapies.

The structure and function of the mitral valve, however, are far more complex than the aortic valve. This complexity poses many challenges in the development of TMVI systems: a larger and D-shaped annulus, the lack of a fibrous/calcified annular structure, a complex subvalvular apparatus, as well as the proximity of the mitral valve to the LV outflow tract, circumflex coronary artery, and coronary sinus. Interestingly, these challenges have been addressed in different ways, for example, by introducing a D-shaped stent design, annular versus apical anchoring, or a large inflow sealing area.[1–4] Also the CardiAQ prosthesis has been optimized since its first implant, as described in this report. The second-generation CardiAQ valve is built on the company's proprietary method for anchoring the implant through leaflet engagement, chordal preservation, and annular attachment, while offering improved flow properties and a novel feature for the prevention of paravalvular leaks. Moreover, the delivery system was optimized and made user-friendlier. In the first half of 2014, this second-generation CardiAQ valve has been successfully implanted at our center in 3 patients. In all cases, the TMVI procedures were performed by transapical approach (Figure I in the Data Supplement).[1]

The transapical approach seems to be more straightforward than the transfemoral approach as it demands less procedural steps. Moreover, obtaining axial alignment with the delivery system is much easier in the transapical procedure when compared with the transfemoral procedure. However, with this first-ever transfemoral-TMVI case described in this report, we demonstrate that TMVI is feasible by true percutaneous approach and with the use of standard interventional techniques. This approach could be of value when intending to treat even the frailest patients and could theoretically result in a shorter hospital length of stay. Moreover, this approach avoids inducement of further akinesia in LV wall function, which is a possible risk with a transapical approach, and avoids potential complications associated with the thin and friable tissue of the LV wall common among secondary MR patients with severely enlarged ventricles.

In April 2015, CardiAQ Valve Technologies received a Food and Drug Administration Investigational Device Exemption approval to conduct an early feasibility study. This study will enroll ≤20 patients and will involve both the transfemoral (n=10) and TA (n=10) TMVI systems. Also Neovasc Inc (Tiara valve),[2] Tendyne Inc (Tendyne valve),[3] and Edwards LifeSciences (Fortis valve)[4] performed their first-in-human TA-TMVI procedures in 2014 and recently received Food and Drug Administration approval for early feasibility trials, indicating that the TMVI technology has reached a new stage in its development.

Conclusions

Although major challenges remain before transforming TMVI into routine clinical practice, this procedure may become an important therapeutic alternative for patients with severe MR who are high-risk candidates for open mitral valve surgery. In this case report, we demonstrate that transfemoral-TMVI can be successfully achieved by the use of standard interventional techniques.

Disclosures

Dr Søndergaard is proctor for Medtronic (Minneapolis, MN) and received a research grant from St Jude Medical (St Paul, MN). Dr Franzen is proctor for and received speaker honoraria from Abbott Vascular (United States). Dr Quadri is the founder and co-owner of CardiAQ Valve Technologies (Irvine, IL). The other authors report no conflicts.

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KEY WORDS: mitral valve ■ mitral valve insufficiency ■ transcatheter aortic valve implantation

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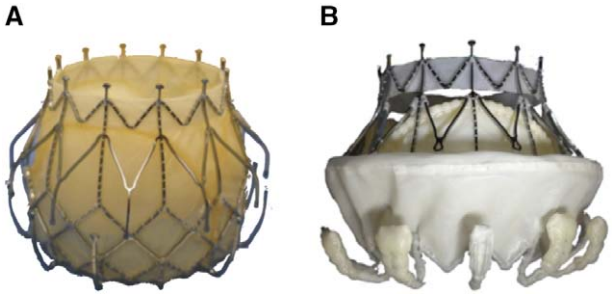

Figure 1. CardiAQ prosthesis consists of a self-expanding nitinol frame, which has 3 leaflets of bovine pericardial tissue and is covered with a polytetrafluoroethylene membrane to minimize paravalvular leakage. The frame design features 2 sets of opposing left ventricular anchors and allows for annular attachment without radial force. The frame engages and preserves the native subvalvular apparatus and features a 40-mm anchoring region and a 30-mm inflow region. **A**, First-generation device, as used in the first-in-human transfemoral CardiAQ case. **B**, Second-generation device, which offers improved load distribution, optimized flow properties in the left atrium, and better paravalvular leak prevention. Reproduced with permission from CardiAQ Valve Technologies. Copyright ©2015, CardiAQ Valve Technologies.

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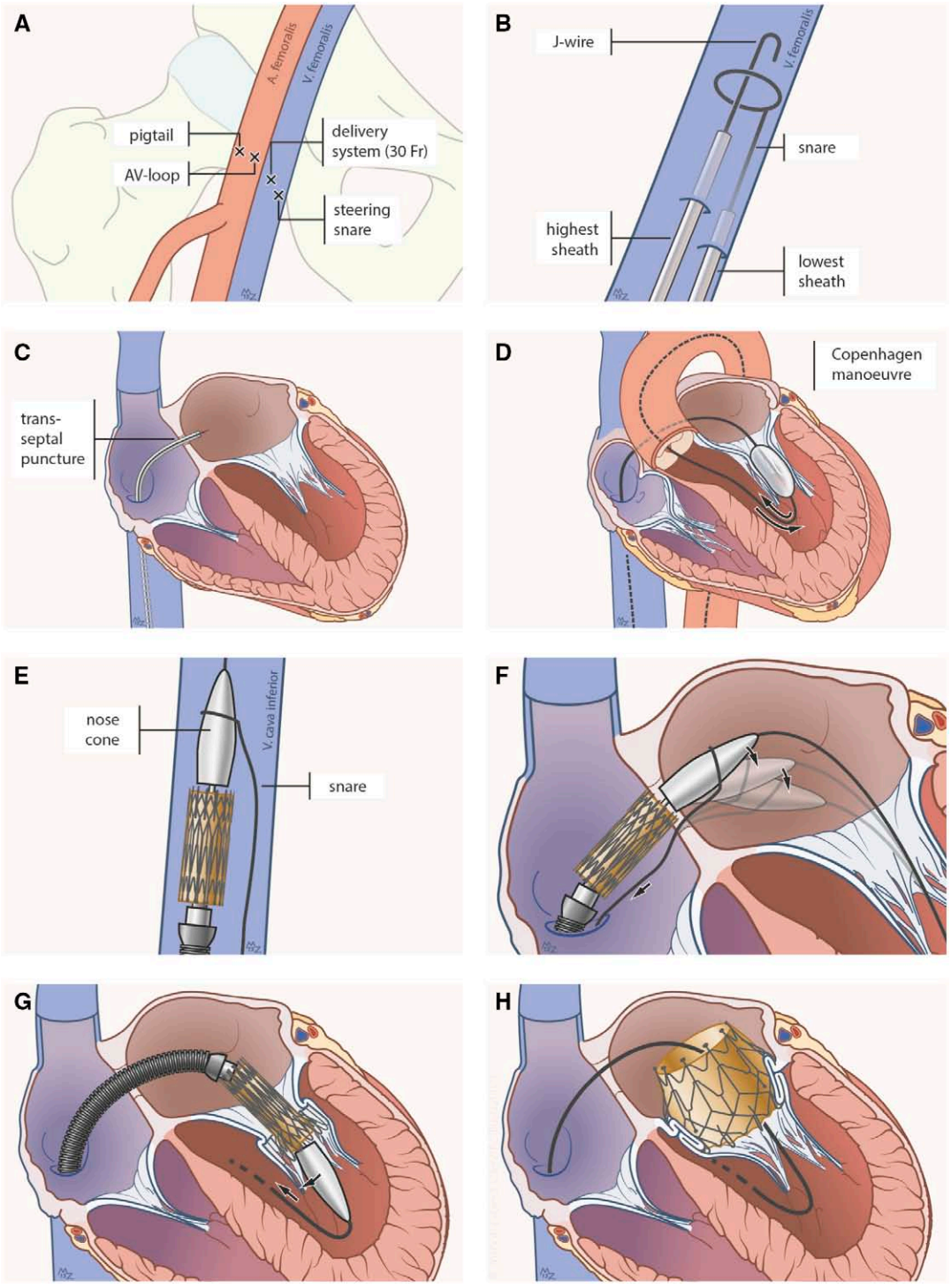

Figure 2. Essential steps of the transfemoral transcatheter mitral valve implantation procedure. **A**, Four accesses are obtained, 2 in the femoral artery and 2 in the femoral vein. **B**, Snaring technique in the iliofemoral vein. **C**, Standard transseptal puncture. **D**, Copenhagen manoeuvre with inflated 14-mm balloon to ensure that chordae are not caught. **E**, Positioning of the steering snare around the middle of the nose cone of the delivery system. **F**, Steering the delivery system toward the mitral valve by pulling the snare. **G**, Obtaining perpendicularity to the mitral annular plane by manipulating the arteriovenous (AV) loop and the delivery system. **H**, Final deployment of the CardiAQ valve with engagement of both mitral valve leaflets.

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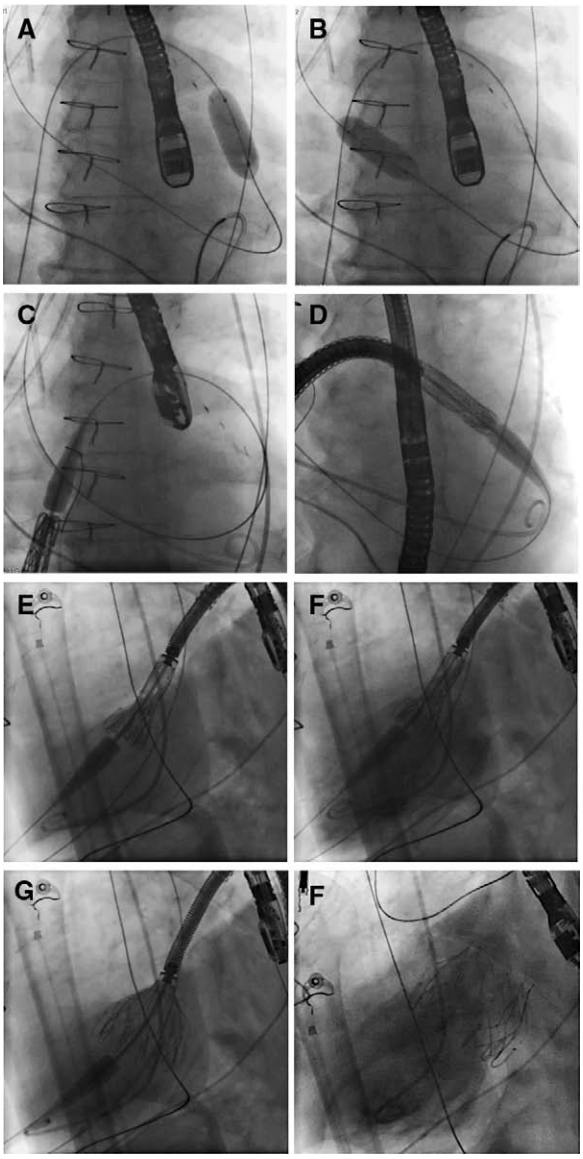

Figure 3. Implantation sequence. **A** and **B**, Copenhagen manoeuvre: an inflated 14-mm balloon is tracked from the left atrium to the left ventricular (LV) outflow tract to ensure that the wire is not caught in the chordae of the mitral valve. If resistance is experienced, the arteriovenous (AV) loop is reestablished. **C** and **D**, Advancement of the delivery system across the mitral annulus with the help of a steering snare, which is positioned around the middle of the nose cone. **E** and **F**, Coaxial alignment, which can be obtained by manipulating the AV loop and the delivery system, and opening of the LV anchors. **G**, Further staged deployment of the CardiAQ valve. **H**, Left ventriculogram showing good position of the CardiAQ valve and absence of significant mitral valve regurgitation.

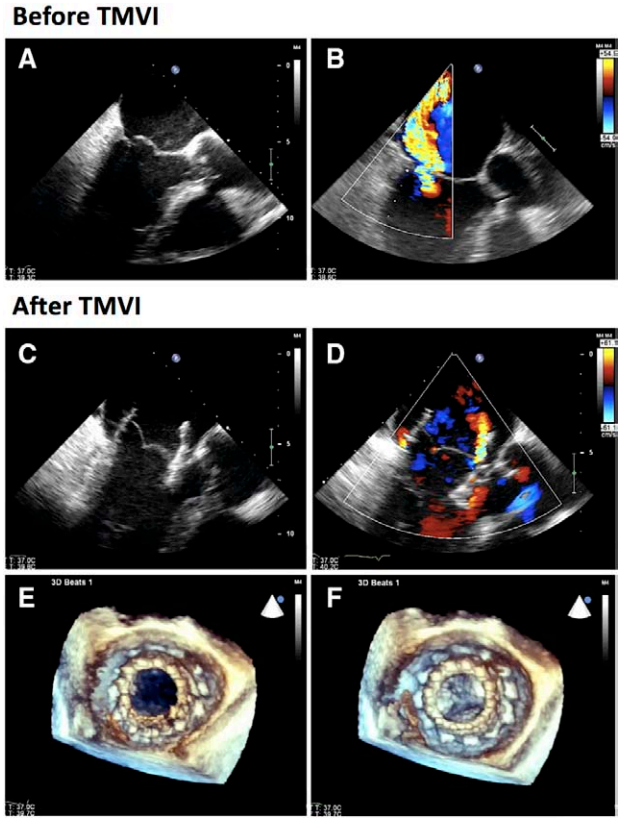

Figure 4. Echocardiographic images. **A** and **B**, Preprocedural severe mitral regurgitation because of mitral annular dilatation and a severely restricted posterior mitral leaflet with a large systolic coaptation gap. **C** and **D**, Evaluation 48 hours after transcatheter mitral valve implantation (TMVI) showing an accurate and stable position of the CardiAQ valve with a mean transvalvular pressure gradient of 2 mm Hg and only a mild paravalvular leakage. The left ventricular outflow tract (LVOT) peak gradient was 12 mm Hg and, thus, excluded LVOT obstruction. **E** and **F**, Three-dimensional images showing the bioprosthesis during diastole and systole.

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