Percutaneous Mitral Valve Replacement Using a Transvenous, Transseptal Approach

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ABSTRACT

OBJECTIVES The aim of this paper is to describe the feasibility of a novel transcatheter approach for mitral valve replacement using only venous access.

BACKGROUND Failure of mitral valve prostheses necessitating reoperation can represent a high-risk clinical scenario. Although repeat cardiac surgery remains the standard of care for most failed mitral valve operations, nascent transcatheter options are under development for patients at high or extremely risk of surgery. Most often, this is performed via a transapical approach in the operating room, with associated risk of complications as well as extended length of hospital stay.

METHODS We describe a case series of 4 consecutive patients at high risk of reoperation with degenerative mitral prostheses (bioprosthetic valves or rings) who successfully underwent transvenous, transseptal mitral valve replacement with a commercially available transcatheter heart valve.

RESULTS From April to May 2014, 4 consecutive patients underwent transvenous, transseptal mitral valve replacement with a transcatheter heart valve. The mean age was 72 ± 9.9 years, and the average Society of Thoracic Surgeons risk score was 12.5 ± 7.2%. All patients had severe, life-limiting dyspnea. The 4 procedures were successful without intra- or post-procedural complications; echocardiography indicated a well-seated and functioning mitral valve-in-valve or valve-in-ring. Patients were discharged within 2 days after valve replacement with marked improvement in dyspnea.

CONCLUSIONS We describe an innovative technique of transcatheter mitral valve replacement. This case series demonstrates the feasibility of transcatheter mitral valve replacement using only femoral venous access, with a marked reduction in complications and length of hospital stay compared with transapical access or redo surgery.

The initial success of transcatheter aortic valve replacement has spurred the development of innovative approaches to other high-risk patient subsets (1-4). Although the current standard of care for patients with severe organic mitral valve disease is surgical mitral valve repair or replacement, subsequent degeneration of the repair or prosthetic valve can limit long-term success (5-7). Repeat valvular surgery is associated with in-hospital mortality rates as high as 12% and a length

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of stay of 2 to 3 weeks; thus, innovative ways to care for these patients are urgently needed (5,8).

Transapical access, an approach familiar to heart teams well versed in transcatheter aortic valve replacement, has been used for mitral valve in valve-in-ring implantation but is associated with major complications including bleeding in more than one-fourth of patients, and a minimum of 1-week length of hospital stay remains the rule (9–11). We, and others, have performed transvenous, transseptal mitral valve replacement with use of an apical rail via a small, percutaneously placed sheath in the ventricular apex or a venous-arterial loop exteriorized at the femoral artery (12–14). However, even with closure devices, percutaneous transapical access is associated with risk of hemothorax (15). Isolated case reports and small series describe mitral valve-in-valve or valve-in-ring procedures via a transseptal route (13,16).

To overcome these challenges, simplify access for transcatheter delivery, minimize procedural risk, and accelerate patient recovery, we developed a novel technique of valve-in-valve or valve-in-ring implantation that requires only venous access. We present a case series of patients at high risk of reoperation with degenerative mitral prostheses who successfully underwent transvenous, transseptal mitral valve replacement with commercially available transcatheter valves.

METHODS

This case series includes 4 consecutive patients who underwent a mitral valve-in-valve or valve-in-ring procedure via a transseptal approach without the use of left ventricular apical access or a venous-arterial rail for valve delivery. All procedures were performed in the Earl H. Wood Cardiac Catheterization Laboratory at Mayo Clinic in Rochester, Minnesota, from April to May 2014.

Procedural inclusion criteria included the presence of a mitral bioprosthesis or a complete ring amenable to placement of an appropriately sized SAPIEN prosthesis. Patients with incomplete rings were not considered. All patients were evaluated by a cardiothoracic surgeon at the referring hospital and at our institution and were deemed high or prohibitive risk for reoperation. Patients were engaged in a shared discussion of the therapeutic options including medical therapy, transcatheter valve replacement, or redo surgery. Patients were informed of the off-label use of the SAPIEN valve (Retroflex 3, Edwards Lifesciences, Irvine, California), and written informed consent was obtained. Institutional review board approval was obtained for this report.

PROCEDURE. The procedures were performed in a cardiac catheterization laboratory equipped with biplane fluoroscopic imaging. Procedures were planned and performed by clinicians from interventional cardiology, cardiovascular surgery, echocardiography, pediatric cardiology, and anesthesiology. Cardiac anatomy and valve sizing was performed using multimodality imaging, including transthoracic echocardiography, transesophageal echocardiography (TEE), and computed tomography (Figure 1, Online Video 1).

Detailed analysis of the anatomy of the ring or prosthetic valve, as well as confirmation of manufacturer-specified and measured internal diameters, was performed before the procedure (Figure 2). Procedures were performed with general anesthesia, and percutaneous femoral venous access was obtained after deployment of 1 Perclose ProGlide suture (Abbott Laboratories, Abbott Park, Illinois). Contralateral femoral venous and arterial access was obtained for ventricular pacing and emergency arterial access for left ventricular support if needed. Transseptal puncture was performed with a Brockenhour needle through a Mullins 7-French dilator (Medtronic, Inc., Minneapolis, Minnesota) under TEE and biplane fluoroscopic guidance. Care was taken to use fluoroscopic prosthetic valve landmarks to ensure a smooth curve into the mitral valve inflow with

**FIGURE 1 Pre-Procedural Planning With CT**

Computed tomography (CT) scan demonstrating traditional echocardiographic views of the heart in a patient with mitral stenosis after placement of 28-mm Carpentier–Edwards Physio ring (Edwards Lifesciences, Irvine, California) with an Alfieri stitch. See accompanying Online Video 1.
optimal coaxial alignment. Most often, this led to a posterior and subtly inferior transseptal puncture.

Unfractionated heparin was administered to maintain activated clotting time levels longer than 300 s. An Inoue guidewire (0.025 mm, 175 cm, Toray Industries, Inc., New York, New York) was placed through the transseptal dilator into the left atrium and the interatrial septum was dilated with a 14-F Inoue dilator. The venous sheath was then upsized to an Edwards 22- or 24-F Retroflex 3 delivery sheath (Edwards Lifesciences). A medium-curl Agilis steerable catheter (St. Jude Medical, Inc., St. Paul, Minnesota) was introduced into the left atrium and flexed and steered toward the mitral valve inflow, which was crossed with a 0.035-inch stiff Angled Glidewire (Terumo Medical Corp., Somerset, New Jersey) through a diagnostic 125-cm, 6-F multipurpose catheter. Once in the left ventricle, the glidewire was exchanged for a Lunderquist wire with a hand-formed, double left ventricular curve and a subtle secondary anterior deflection. If the Lunderquist would not track through the multipurpose catheter, the Agilis catheter was advanced through the mitral prosthesis into the left ventricle for greater support. The Agilis and multipurpose catheters were then removed, leaving the Lunderquist wire in place. The interatrial septum was dilated either with a 21-F TandemHeart kit dilator (Cardiac Assist, Inc., Pittsburgh, Pennsylvania) or an 8- to 10-mm diameter noncompliant balloon.

An Edwards SAPIEN transcatheter aortic valve (Edwards Lifesciences) was prepared and oriented for antegrade valve delivery. When introducing the delivery system, the marker “E” was placed down, so that clockwise rotation of the steering handle flexed the device to the patient’s left, aiding valve delivery. Balloon sizing or valvuloplasty was not performed. The transcatheter valve was advanced into the mitral prosthesis and carefully positioned straddling the sewing ring (Figure 3). Under rapid pacing, the transcatheter valve was slowly inflated and small push or pull movements on the stiff Lunderquist were used to make fine adjustments.

After prosthesis deployment, the degree of regurgitation and resultant gradients were measured, the delivery system removed and the resultant atrial septal defect assessed with TEE. All atrial septal defects in this series were small with slight left to right shunting, and none were closed. Heparin was reversed with protamine, and venous access was closed via Perclose ProGlide suture system (Abbott Laboratories) with light manual pressure applied for 5 min. Arterial access was closed with Perclose ProGlide sutures or manual pressure.
RESULTS

BASELINE CHARACTERISTICS. From April to May 2014, 4 patients underwent transseptal, transcatheter mitral valve replacement at our institution. Patient characteristics are summarized in Table 1. The mean age was 72 ± 9.9 years and the average Society of Thoracic Surgeons risk score was 12.5 ± 7.2%. All patients were women with multiple comorbidities, including the presence of severe pulmonary hypertension and some degree of right ventricular dysfunction. All patients had severe dyspnea on exertion.

### TABLE 1 Patient Characteristics

<table>
<thead>
<tr>
<th>Patient #1</th>
<th>Patient #2</th>
<th>Patient #3</th>
<th>Patient #4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>72</td>
<td>59</td>
<td>74</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Female</td>
<td>Female</td>
</tr>
<tr>
<td>STS score, %</td>
<td>11.2</td>
<td>23</td>
<td>7.8</td>
</tr>
<tr>
<td>History of CABG</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>68</td>
<td>57</td>
<td>64</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td>III</td>
<td>III-IV</td>
<td>III</td>
</tr>
<tr>
<td>Creatinine, mg/dl</td>
<td>0.9</td>
<td>Chronic dialysis</td>
<td>1.6</td>
</tr>
<tr>
<td>Other comorbidities (all patients have severe pulmonary hypertension)</td>
<td>PAD with previous left iliac stent, atrial fibrillation, COPD, frailty</td>
<td>Severe PAD, history aortofemoral bypass, renal failure on dialysis (5 yrs), diabetes type 2, oxygen requirement</td>
<td>Diabetes, history of pericarditis, atrial fibrillation, chronic renal insufficiency</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; NYHA = New York Heart Association; PAD = peripheral arterial disease; STS = Society of Thoracic Surgeons.
that limited quality of life. The indication for all patients’ initial valve procedures was mitral regurgitation due to degenerative mitral valve disease. Previously implanted prostheses varied by size (25 to 29 mm) and type (2 bioprosthetic valves and 2 annuloplasty rings). Concomitant procedures at the time of initial valve surgery included coronary artery bypass grafting (n = 2), left atrial appendage ligation (n = 2), and additional stitch placement (Alfieri stitch) in both of the repairs (Table 2). The mechanism of prosthetic dysfunction was mitral stenosis in the majority of patients (n = 3) with

![Table 2: Valve and Procedural Characteristics](image)

<table>
<thead>
<tr>
<th></th>
<th>Patient #1</th>
<th>Patient #2</th>
<th>Patient #3</th>
<th>Patient #4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
<td>Hancock bioprosthesis (Medtronic, Minneapolis, Minnesota)</td>
<td>Carbomedics Annuloflex ring (Sorin, Milan, Italy)</td>
<td>Carpentier-Edwards Physio ring (Edwards Lifesciences, Irvine, California)</td>
<td>Mosaic bioprosthesis (Medtronic, Minneapolis, Minnesota)</td>
</tr>
<tr>
<td><strong>Size, mm</strong></td>
<td>25</td>
<td>26</td>
<td>28</td>
<td>29</td>
</tr>
<tr>
<td><strong>Manufacturer ID, mm</strong></td>
<td>22.5</td>
<td>26</td>
<td>26.9</td>
<td>26</td>
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<tr>
<td><strong>TEE ID, mm</strong></td>
<td>21 × 21</td>
<td>19 × 18</td>
<td>15 × 24</td>
<td>20 × 22</td>
</tr>
<tr>
<td><strong>CT ID, mm</strong></td>
<td>22</td>
<td>18 × 17</td>
<td>17 × 27</td>
<td>19 × 23</td>
</tr>
<tr>
<td><strong>Mode of failure</strong></td>
<td>Stenosis</td>
<td>Stenosis</td>
<td>Stenosis</td>
<td>Prosthetic and periprosthetic regurgitation</td>
</tr>
<tr>
<td><strong>Transcatheter valve used</strong></td>
<td>23-mm SAPIEN</td>
<td>23-mm SAPIEN</td>
<td>26-mm SAPIEN</td>
<td>26-mm SAPIEN</td>
</tr>
<tr>
<td><strong>Pre-/post-TTE mitral gradient, mm Hg</strong></td>
<td>18/10</td>
<td>21/7</td>
<td>25/7</td>
<td>12/10</td>
</tr>
<tr>
<td><strong>Left atrial pressure, pre (A/V/mean mm Hg)</strong></td>
<td>21/31/20</td>
<td>21/39/23</td>
<td>23/40/26</td>
<td>20/50/26</td>
</tr>
<tr>
<td><strong>Left atrial pressure, post (A/V/mean mm Hg)</strong></td>
<td>25/43/27</td>
<td>20/32/20</td>
<td>18/23/20</td>
<td>21/38/23</td>
</tr>
<tr>
<td><strong>Pulmonary artery pressure, pre (systolic/diastolic) mm Hg</strong></td>
<td>Not measured</td>
<td>71/25</td>
<td>76/30</td>
<td>52/22</td>
</tr>
<tr>
<td><strong>Pulmonary artery pressure, post (systolic/diastolic) mm Hg</strong></td>
<td>Not measured</td>
<td>75/25</td>
<td>46/24</td>
<td>46/22</td>
</tr>
</tbody>
</table>

*Edwards Lifesciences, Irvine, California.
A = A wave; CT = computed tomography; ID = inner diameter; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography; V = V-wave.

**FIGURE 4**: Coaxial Valve-in-Ring Placement With Transseptal Access

(A) Final fluoroscopic appearance of a 26-mm Edwards SAPIEN valve in a 28-mm Carpentier-Edwards Physio ring (Edwards Lifesciences, Irvine, California) with a Lunderquist wire (Cook Medical, Bloomington, Indiana) shown. (B) Coaxial valve-in-ring alignment facilitated by careful selection of transseptal puncture location and curved stiff wire. See accompanying Online Video 2.
prosthetic and periprosthetic leak leading to severe mitral regurgitation in the fourth patient. Patients presented a mean of 6 ± 3.4 years after valve surgery (range, 4 to 11 years).

**PROCEDURAL OUTCOMES.** Coaxial alignment of the valve was obtained across the mitral annulus, aided by the flexion provided by the SAPIEN retroflex delivery system (Figure 4). In 3 of the 4 patients, the valve deployed predictably. In patient 3, with history of mitral valve repair including an Alfieri stitch, the valve was canted until the suture gave way, and then sat predictably for final deployment (Online Video 2). All patients had successful implantation of the valve without complications; there was no malpositioning, valve embolization, need for post-dilation, or need for subsequent surgery. Successful reduction in gradient and regurgitation was noted immediately by TEE (Figure 5, Online Videos 3 and 4).

**IN-HOSPITAL COURSE.** Patients were extubated in the cardiac catheterization laboratory and transferred to the general telemetry floor. The following morning, transthoracic echocardiography was performed, and patients were discharged to home shortly after. One patient with pre-existing dialysis stayed an additional day to undergo dialysis before traveling home. We tailored antiplatelet and anticoagulant therapy to each patient based on their comorbidities.

**FOLLOW-UP.** All patients were alive and symptomatically improved at the time of last follow-up (1 month post-procedure in 1 patient, 6 months post-procedure in 3 patients). None had had recurrent hospitalizations for heart failure. Systematic functional testing (e.g., 6-min walk test) was not performed.

**DISCUSSION**

Failure of mitral valve prostheses in patients with advanced age and multiple comorbidities is a high-risk clinical scenario with redo surgery associated with an increased risk of operative mortality and extended hospital stay (8). We previously developed a transseptal approach using the Melody valve (Medtronic) with an apical rail (14). We present a case series of

![Figure 5 Pre- and Post-Procedural Imaging of Mitral Valve-in-Ring](image_url)

(A) Three-dimensional transesophageal echocardiography demonstrates the geometric change in the annular shape after deployment of Edwards SAPIEN valve (Edwards Lifesciences, Irvine, California). (B) Continuous wave Doppler shows a reduction in mitral valve gradient from 16 mm Hg to 3 mm Hg after deployment. See accompanying Online Videos 3 and 4.
patients at high risk of reoperation with degenerated mitral bioprostheses who successfully underwent transvenous, transseptal mitral valve-in-prosthesis with minimal morbidity and mortality. The current technique both simplifies antegrade valve implantation and avoids the complications associated with transapical puncture. We believe that this technique represents an improvement over the apical rail technique and, with further refinement, may lead to a viable and generalizable technique for treating elderly high-risk patients with mitral bioprosthesis dysfunction. The steerable delivery system enabled coaxial geometry for successful antegrade valve delivery (17). We use the current technique in all cases as the primary delivery mode. Avoiding left ventricular apical access allowed for ambulation on the day of procedure and appropriateness for hospital discharge the following day, a striking difference compared with previous reports. In a series of 23 mitral valve-in-valve procedures performed via the transapical route, one-fourth of patients had a major bleeding complication, with a length of hospital stay of 6 days (interquartile range: 5 to 8 days) (17). In a mixed case series that included patients undergoing a transseptal approach (8 of 17 patients), the mean length of hospital stay was 10 ± 4 days (range: 3 to 26 days) (13). A venous-only approach provides a unique opportunity to avoid potential complications of bleeding, apical injury, and lung injury posed with thoracotomy, as well as increased length of hospital stay due to pain and recovery.

Important technical considerations include valve sizing. Careful study of valve geometry pre-procedure and of manufacturer’s specifications was critical to procedural execution. Similarly, surgical expertise with knowledge of various mitral valve repair techniques was critical to procedural success and reduced risk of embolization (18). We used the SAPIEN prosthesis, which is now no longer manufactured. The next generation SAPIEN XT and SAPIEN 3 prostheses have a longer delivery nose cone and require assembly in the inferior vena cava (with the balloon withdrawn against the valve leaflet direction of opening), potentially negative features for the antegrade technique. Crossing of the mitral valve with a wire may result in entanglement in chordae, a risk that we minimized with careful TEE visualization. Use of a balloon-tip catheter to cross the mitral valve may minimize this risk. If difficulty is encountered in antegrade crossing of the mitral valve, snaring the wire and exteriorizing out the femoral artery may be considered, although we did not have to do this in this small series. Care will need to be taken to ensure coaxiality of the prosthesis because the valve will tend to be canted toward the left ventricular outflow tract using this technique. This is particularly important with rings, in which the landing zone is shorter and precise placement more challenging. Two patients had had mitral valve repair with an Alfieri stitch. We did not select which orifice to cannulate, and the stitch yielded easily in both cases.

**STUDY LIMITATIONS.** This is a novel case series of transvenous mitral VIV implantation in 4 patients. While the technique herein has the potential to limit procedural morbidity, further study is needed in a larger patient cohort. This case series was limited to mitral bioprosthesis and repairs with complete rings.

**CONCLUSIONS**

Transcatheter mitral valve replacement using only femoral venous access can be safe and feasible. Patients at high or extreme risk of surgery may benefit from the approach with resultant decreases in complications and length of hospital stay compared with traditional surgery or a transapical approach.

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**PERSPECTIVES**

**WHAT IS KNOWN?** Mitral VIV implantation for a failing bioprosthesis is an emerging and promising therapy for patients at high surgical risk.

**WHAT IS NEW?** We describe a transseptal valve implantation technique that eliminates the need for transapical access or surgical incisions of any sort and uses only venous access.

**WHAT IS NEXT?** The technique has the potential to significantly reduce the morbidity and mortality of mitral VIV implantation; further clinical research and comparative outcome studies are needed.
REFERENCES


KEY WORDS degenerative mitral prosthesis, percutaneous mitral intervention, percutaneous mitral repair, transcatheter valve-in-ring procedure, transcatheter valve-in-valve procedure, transcatheter mitral valve replacement

APPENDIX For accompanying videos, please see the online version of this article.