Background—Misplacement during percutaneous aortic valve implantation can be associated with severe complications. The direct flow medical (DFM) valve is repositionable and retrievable; however, the nonmetallic inflatable and conformable design of the valve results in less radial force, which may have an impact on stability and valve function over time. We, therefore, analyzed the midterm stability of the position, shape, and hemodynamic performance of the DFM percutaneous aortic valve.

Methods and Results—Sixteen symptomatic high-risk for surgery patients with aortic stenosis and a logistic EuroSCORE >20 underwent implantation and were the subject of this analysis. Clinical, echocardiographic, and dual-source multislice computed tomography data were obtained during 2-year follow-up. The 1- and 2-year survival rates were 81% and 69%, respectively. The dual-source multislice computed tomography follow-up indicated no changes in position, diameter, and orifice area of the DFM valve over time. Echocardiography revealed a significant decrease of the mean gradient from baseline (50.1±11.3 mm Hg) to 30 days (19.6±5.7 mm Hg, P<0.001), which remained stable over 2 years. The aortic valve area increased from 0.57±0.15 cm² at baseline to 1.47±0.35 cm² at 30 days (P<0.001) and did not significantly change during 2-year follow-up. Of the patients, 73% had no aortic regurgitation (AR) and 27% had minimal AR.

Conclusions—In this preliminary series, the 2-year follow-up data of patients, in whom the nonmetallic, repositionable, and retrievable DFM valve was successfully implanted, show stability of the position, shape, and hemodynamic performance, with no AR in most patients. (Circ Cardiovasc Interv. 2011;4:595-601.)

Key Words: percutaneous aortic valve implantation ■ aortic stenosis ■ retrievable aortic valve prosthesis
Valve detachment (n = 1). The 16 patients with permanent implantation had valve misplacement, which was only recognized after the procedure in 12 patients. As previously published,4 in 7 patients, the implantation of the prosthesis was not possible because of access problems (n = 1). The purpose of the present study was to analyze the midterm stability of the position, shape, and hemodynamic performance of the DFM valve.

**WHAT IS KNOWN**

- Misplacement during transcatheter aortic valve implantation can be associated with significant complications and severe aortic regurgitation. Percutaneous valves, which are repositionable and retrievable, may overcome these problems.

**WHAT THE STUDY ADDS**

- To our knowledge, this is the first report on the midterm performance of a catheter-based, repositionable, retrievable, nonmetallic aortic valve prosthesis for percutaneous implantation, evaluated by echocardiography and computed tomography.

**Methods**

**Patients**

Between September 2007 and March 2008, 25 patients with severe aortic stenosis and high surgical risk were enrolled at our center to evaluate the feasibility and safety of the transfemoral DFM aortic valve prosthesis. The device could be permanently implanted in 16 patients. As previously published,4 in 7 patients, the implantation of the prosthesis was not possible because of access problems (n = 2), a functionally bicuspid valve (n = 2), and excessive calcification of the aortic valve and/or left ventricular outflow tract (n = 3). Two other patients underwent surgical conversion because of undersizing (n = 1) and valve misplacement, which was only recognized after valve detachment (n = 1). The 16 patients with permanent implantation were included in the present study.

**Study Device and Implantation Procedure**

These 2 variables have been described elsewhere. In brief, the implant (Figure 1) is made of bovine pericardial tissue, which is fixed in a trileaflet configuration within a polyester fabric cuff. At the upper and lower margins of the valve, there are 2 independently inflatable rings, interconnected by a tubular bridging system. The upper (aortic) ring is connected to 3 position/fill lumens to steer the valve from the left ventricle to a position in the native aortic annulus and to inflate or deflate the device. The implant is loaded in a 22-F delivery catheter. The device was available in diameters of 23 and 25 mm and in heights of 16 and 17 mm, respectively.

After valvuloplasty, the delivery catheter is advanced into the left ventricle and the housing is retracted to expose the implant. The lower (ventricular) ring is filled with a 50:50 mixture of contrast and saline, and the implant is withdrawn up to the ventricular aspect of the aortic annulus. The aortic ring is then inflated, and the position and function of the valve is checked by transesophageal echo, fluoroscopic imaging, and angiography. If the position, orientation, or shape of the device is not acceptable, it can be deflated and the device can be repositioned or retrieved. Retrieval was performed in 7 patients for reasons previously described. Otherwise, the mixture of contrast and saline is replaced under constant pressure by a polymer, followed by the detachment of the position/fill lumens.

Dual-source multislice computed tomography (DSMCT) was performed with the SOMATOM Definition Flash (Siemens; Erlangen, Germany) before the procedure in 12 patients, between 1 week and 6 months after the procedure in 8 patients, and between 18 and 30 months in 12 patients. Therefore, 8 of 12 patients had DSMCT scans from at least 2 time points during follow-up (Table 1).

The raw DICOM DSMCT data were reconstructed and analyzed using a MedicView3D Graphic Station. The aortic valve plane is defined such that it passes through each of the 3 basal attachments of the native valve leaflets6,7 and was used as a positional reference for measurements of the implant rings. Mutually orthogonal multplanar reformatted and maximum intensity projection (MIP) views were oriented such that 1 plane was aligned parallel to the aortic valve plane in 3 dimensions. Position, diameter, shape, and orifice area were assessed over time for the aortic and ventricular ring balloons. Ring position was characterized by the mean average of the distance to the most distal and proximal ring positions of the center of the ring inflation channel (ie, the center of its range of positions relative to the aortic plane). All positional distances were measured from and perpendicular to the aortic valve plane. Ring diameter was represented by the mean average of the major and minor axes of the approximately elliptical perimeter, as viewed from an MIP slab oriented parallel to the aortic valve plane. In each case, the thickness of the MIP slab was set to include the complete ring. All diameter measurements were made to the center of the ring inflation channel. Ring shape was taken as the ratio of the major/minor elliptical axes. Orifice area was measured from the inner diameter of the ring, as viewed from the MIP slab oriented parallel to the aortic plane.

The uncertainty of each measurement was estimated to be ±1.5 mm (0.75 mm for each of the 2 distance line end points) based on the slice thickness of the raw scan data (typically 0.75 mm). By this estimation, a difference in diameter or position of <3.0 mm between 2 time points would not constitute a significant change.

**Echocardiographic Definition of AR**

AR was evaluated by color Doppler imaging and defined as follows: grade 1+, jet length less than one third of left ventricle (LV), LV normal size; grade 2+, jet length one half of LV length, vena contracta <10% of aortic valve annulus diameter; grade 3+, jet length to the apex of LV, vena contracta 10% to 20% of aortic valve annulus diameter; and grade 4+, broad jet to the LV length, vena contracta >20% of aortic valve annulus diameter.8

The Valve Academic Research Consortium (VARC) criteria for prosthetic aortic valve regurgitation (AR) were used as described by Leon et al.9
Accordingly, the definitions were as follows: mild AR, circumferential extent of paraprosthetic AR 10%, regurgitant volume 30 mL/beat, and regurgitant fraction 30%; moderate AR, circumferential extent of paraprosthetic AR 10% to 20%, regurgitant volume 30 to 59 mL/beat, and regurgitant fraction 30% to 50%; and severe AR, circumferential extent of paraprosthetic AR 20%, regurgitant volume 60 mL/beat, and regurgitant fraction >50%.

Statistics

Continuous variables were expressed as mean±SD.

Ordinal data were analyzed with the Wilcoxon signed rank test. For nonparametric paired binary data, the McNemar test was used. The stability of the gradient and the area after valve implantation was assessed by mixed linear modeling. An autoregressive heteroscedastic matrix of covariance was used. Random effects were added to the intercept of the model. Statistical analyses were performed with SPSS (version 19) and Graph Pad PRISM 3.0. *P*<0.05 was considered statistically significant.

Figure 2. Kaplan-Meier survival curve showing a survival rate of 83% after 1 year and 69% at the 2-year follow-up.
Results

Patients

From the cohort of 16 implanted patients, with an average logistic EuroSCORE of 29%, 1 patient died within 30 days because of a myocardial infarction (not device related); 15 patients were discharged, 2 died before the 1-year follow-up (respiratory failure and unknown cause in 1 each), and 1 died immediately before the 2-year follow-up (unknown cause). The 1-year survival rate was 81%, and the 2-year survival rate was 69% (Figure 2).

Clinical and Echocardiographic Follow-up

At 2 years, clinical and echocardiographic follow-up data were available in 11 patients. The baseline data of the patients are shown in Table 2, reflecting their high surgical risk. New York Heart Association class at the 2-year follow-up improved significantly in the 11 patients ($P<0.05$, Figure 3).

No conduction disturbances occurred during follow-up.

Echocardiography data at 2 years were available in 11 patients (Figure 4A through 4C, Table 3, and Table 4) and revealed a significant decrease of the mean gradient from baseline to 30 days ($50.1\pm11.3 \text{ mm Hg}$ at baseline versus...
Table 3. Mean Aortic Valve Gradient

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Baseline</th>
<th>30 d</th>
<th>90 d</th>
<th>180 d</th>
<th>365 d</th>
<th>720 d</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>53</td>
<td>15</td>
<td>17</td>
<td>13</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>66</td>
<td>17</td>
<td>28</td>
<td>21</td>
<td>28</td>
<td>17</td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>15</td>
<td>20</td>
<td>22</td>
<td>23</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>64</td>
<td>33</td>
<td>29</td>
<td>29</td>
<td>29</td>
<td>22</td>
</tr>
<tr>
<td>5</td>
<td>41</td>
<td>17</td>
<td>15</td>
<td>17</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>6</td>
<td>54</td>
<td>19</td>
<td>21</td>
<td>23</td>
<td>34</td>
<td>21</td>
</tr>
<tr>
<td>7</td>
<td>59</td>
<td>20</td>
<td>21</td>
<td>17</td>
<td>20</td>
<td>21</td>
</tr>
<tr>
<td>8</td>
<td>38</td>
<td>12</td>
<td>12</td>
<td>14</td>
<td>10</td>
<td>17</td>
</tr>
<tr>
<td>9</td>
<td>38</td>
<td>25</td>
<td>25</td>
<td>27</td>
<td>33</td>
<td>24</td>
</tr>
<tr>
<td>10</td>
<td>42</td>
<td>20</td>
<td>19</td>
<td>20</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>11</td>
<td>36</td>
<td>23</td>
<td>19</td>
<td>21</td>
<td>25</td>
<td>23</td>
</tr>
</tbody>
</table>

Individual data of the 11 patients during the 2-year follow-up are given.

Table 4. Mean Aortic Valve Area

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Baseline</th>
<th>30 d</th>
<th>90 d</th>
<th>180 d</th>
<th>365 d</th>
<th>720 d</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>c</td>
<td>1.87</td>
<td>2.5</td>
<td>2.1</td>
<td>1.93</td>
<td>1.98</td>
</tr>
<tr>
<td>2</td>
<td>0.41</td>
<td>1.5</td>
<td>1.3</td>
<td>0.91</td>
<td>1.14</td>
<td>1.06</td>
</tr>
<tr>
<td>3</td>
<td>0.34</td>
<td>1.35</td>
<td>1.4</td>
<td>1.34</td>
<td>1.21</td>
<td>1.1</td>
</tr>
<tr>
<td>4</td>
<td>0.42</td>
<td>1.2</td>
<td>1.25</td>
<td>1.19</td>
<td>1.02</td>
<td>1.6</td>
</tr>
<tr>
<td>5</td>
<td>0.79</td>
<td>1.8</td>
<td>1.55</td>
<td>1.43</td>
<td>1.51</td>
<td>2.84</td>
</tr>
<tr>
<td>6</td>
<td>0.6</td>
<td>1.6</td>
<td>1.39</td>
<td>1.26</td>
<td>1.05</td>
<td>ND</td>
</tr>
<tr>
<td>7</td>
<td>0.6</td>
<td>1.8</td>
<td>1.25</td>
<td>1.85</td>
<td>0.98</td>
<td>1.06</td>
</tr>
<tr>
<td>8</td>
<td>0.67</td>
<td>1.57</td>
<td>1.52</td>
<td>1.19</td>
<td>1.25</td>
<td>0.9</td>
</tr>
<tr>
<td>9</td>
<td>0.63</td>
<td>1.8</td>
<td>1.23</td>
<td>1.23</td>
<td>1.04</td>
<td>1.6</td>
</tr>
<tr>
<td>10</td>
<td>0.44</td>
<td>0.84</td>
<td>1.17</td>
<td>1.2</td>
<td>1.15</td>
<td>1.29</td>
</tr>
<tr>
<td>11</td>
<td>0.63</td>
<td>0.93</td>
<td>0.9</td>
<td>0.96</td>
<td>0.82</td>
<td>0.64</td>
</tr>
</tbody>
</table>

Individual data of the 11 patients during the 2-year follow-up are given. c indicates control; ND, not done.

19.6±5.7 mm Hg at 30 days; \( P<0.001 \), which remained stable over 2 years (18.8±4.5 mm Hg at 2-year follow-up) (Figure 4A). The stability levels of the mean aortic valve pressure gradient and the aortic valve area after implantation were assessed by mixed linear modeling. The time elapsed during follow-up was not significantly associated with a change in the pressure gradient \( (P=0.31 \text{ for time}) \). Thus, the gradient was essentially constant and was estimated at 20.3 mm Hg \( (95\% \text{ CI}, 16.8–23.9 \text{ mm Hg}) \). Based on the VARC criteria,\(^9\) the severity of prosthetic aortic valve stenosis is graded as normal \( (\text{mean gradient, } <20 \text{ mm Hg}) \), possible stenosis \( (20–35 \text{ mm Hg}) \), and significant stenosis \( (>35 \text{ mm Hg}) \). At 30 days, a mean gradient <20 mm Hg was found in 6 of 11 patients; 5 patients had a gradient between 20 and 35 mm Hg. At 2 years, in 5 of 11 patients, the gradient was <20 mm Hg; 6 patients had gradients between 20 and 35 mm Hg.

The aortic valve area increased from 0.57±0.15 cm\(^2\) at baseline to 1.47±0.35 cm\(^2\) at 30 days \( (P<0.001) \) and did not significantly change during the 2-year follow-up \( (1.41±0.74 \text{ cm}^2 \text{ at the 2-year follow-up}) \) (Figure 4B). During the first year after implantation, the aortic valve area, on average, decreased by 0.29 cm\(^2\). Overall, the decline in the aortic valve area during the first year after implantation resulted in a significant impact of the follow-up time on the aortic valve area \( (P=0.006) \). However, this change was not sustained at the 2-year follow-up. At 1 month after and at 2 years after implantation, the aortic valve areas were estimated at 1.49 cm\(^2\) \( (95\% \text{ CI, } 1.20–1.76 \text{ cm}^2) \) and 1.40 cm\(^2\) \( (95\% \text{ CI, } 0.99–1.80 \text{ cm}^2) \), respectively. According to the VARC criteria,\(^9\) an effective orifice area >1.2 cm\(^2\) is graded as “normal,” an effective orifice area of 1.2 to 0.8 cm\(^2\) is graded as “possible stenosis,” and an effective orifice area of <0.8 cm\(^2\) is graded as “significant stenosis.” The criterion for a normal effective orifice area was met at 30 days by 3 of 11 patients and at 2 years by 5 of 10 patients. The criterion for possible stenosis was met at 30 days by 7 of 11 patients and at 2 years by 5 of 10 patients.

AR was present as grade 1+ in all 11 patients before valve implantation. At the 2-year follow-up, AR was abolished in 73% of patients and detectable as grade 1+ in 27% of patients \( (P<0.001 \text{ compared with baseline, Figure 4C}) \). According to the VARC criteria, 73% of patients had no aortic valve regurgitation and 23% had mild AR.

Twelve patients underwent a DSMCT evaluation before the procedure, and 8 underwent at least 2 CT scans during follow-up (Table 1). The DSMCT data reconstruction and analysis indicated that no changes over time greater than the measurement uncertainty were present for position, diameter, and orifice area, and shape.

The positions of the aortic and ventricular rings during the follow-up period, ranging from 1 week to 28 months, are shown in Figure 5, indicating a stable position over time.

The mean ring diameters, the ratio of the maximal/minimal diameter, and the orifice areas of the prosthesis are shown in Table 1. The small deviations in the diameter and position values are all within the ±3.0-mm estimated uncertainty of the measurements and are, thus, not considered significant.
There was also no difference in ring position, ring diameters, and orifice areas, when measured during systole compared with diastole.

A representative case example of DSMCT follow-up of the direct-flow medical valve is shown in Figure 6.

Discussion

To our knowledge, this is the first report on the midterm valve performance of a repositionable, retrievable, nonmetallic aortic valve prosthesis for percutaneous implantation, evaluated by echocardiography and DSMCT.

The major findings of the present study are as follows: (1) a mortality at 1 and 2 years in the same order of magnitude of larger registries of the Edwards SAPIEN and the Medtronic CoreValve System (however, because of the few patients, this finding has to be viewed with caution); (2) a consistent improvement of the New York Heart Association class at 2 years; (3) a stable hemodynamic performance with no AR in 73% of patients and minimal AR in 27% of patients over 2 years; and (4) a stable position, diameter, orifice area, and shape of the direct-flow medical valve over time, with no evidence of recoil.

Despite being a first-in-humans study in a limited number of patients, the survival rate of the present patient cohort is well in agreement with those of larger registries. The 1- and 2-year mortality rates may be the consequence of the high comorbidity of the patients and their advanced age.

As a consequence of the valve design, which is more similar to a surgical biological prosthesis than to a stent-based percutaneous valve, the valve area increased to a mean value of 1.4 cm². This is smaller compared with the Edwards SAPIEN Valve prosthesis but similar to surgical valves and remained stable over 2 years. In 1 patient, after 2 years, the valve area was not different from baseline. Echocardiographic signs for valve degeneration were not present. The reason for the small valve area seems to be a mismatch in sizing, similar to that seen in some patients after bioprosthetic valve replacement. Also, the mean gradient that can be achieved with the DFM prosthesis more closely resembles gradients of surgical bioprostheses. For a fair comparison, however, these data have to be normalized by patient size. It remains to be determined in a larger trial, with longer follow-up, whether the somewhat higher gradient has any prognostic impact. The favorable hemodynamic changes (improvements) seen in this study, however, are accompanied by a consistent improvement in the New York Heart Association class of the patients over 2 years.

From observational studies, the presence of AR after TAVI has an impact on patient outcome. Significant AR (≥2+) values, after Edwards SAPIEN and Medtronic CoreValve, are found in 12% to 40% of the patients. In contrast, in the present study, AR was trivial, if present at all. This may be the result of more exact positioning, the possibility of repositioning the valve or exchanging it for a different size, or the possibility of a better sealing capability because of the ring balloon structure. Because of the small study population, these are preliminary findings that have to be proved in a larger trial.

Repositionability and retrievability are important features of the DFM valve, which distinguishes this valve from those presently commercially available. CoreValve misplacement has been described in 10% of the cases and is associated with a higher mortality and a higher incidence of coronary ischemia, stroke, and renal failure. Also, for the Edwards-SAPIEN prosthesis, dislocation has been reported in 4% to 11% of cases. In the present study, malpositioning of the valve could be avoided by the possibility of repositioning the device or retrieving it, which was done in 7 of 25 patients who were enrolled in the study.

In contrast to a metallic frame, which is attached to the aortic annulus and the aortic wall and is fixed by the calcified tissue, the DFM valve is stabilized by 2 rings, one is positioned in the left ventricular outflow tract and the other is positioned in the aortic sinus. The native valve is jailed by a polyester cuff with less opening force compared with the metal frame designs. Thus far, it was unknown whether such a valve design is stable in position over time and resistant to recoil. Therefore, sequential DSMCT was performed in all of our patients who survived 2 years after implantation. The ring
diameters, orifice area, and valve position did not change during 2 years of follow-up.

Clinical Implications

Because valve malposition during TAVI is associated with severe complications, the repositionability and retrievability of the DFM valve has the potential to increase the safety of the procedure. The excellent sealing capability minimizing AR may improve the patient’s long-term outcome after TAVI.

Limitations

The present study is a first-in-humans trial, with all its limitations. The number of patients is small, but echocardiographic and DSMCT follow-up data were complete; to our knowledge, the DSMCT study is the first systematic evaluation of percutaneous aortic valve prosthesis over 2 years.

Conclusions

In this preliminary series of patients, in whom the DFM valve was successfully implanted, the 2-year follow-up data show stability of the position, shape, and hemodynamic performance, with no AR in most patients.

Acknowledgments

Statistical support was provided by Dr Thomas Rau, MD.

Disclosures

J.H.H. received honoraria payment for CT analyses, and J.S. is the principle investigator of the DFM feasibility study.

References


Midterm Stability and Hemodynamic Performance of a Transfemorally Implantable Nonmetallic, Retrievable, and Repositionable Aortic Valve in Patients With Severe Aortic Stenosis: Up to 2-Year Follow-Up of the Direct-Flow Medical Valve: A Pilot Study
Klaudija Bijuklic, Thilo Tuebler, Hermann Reichenspurner, Hendrik Treede, Andreas Wandler, John H. Harreld, Reginald I. Low and Joachim Schofer

_Circ Cardiovasc Interv._ 2011;4:595-601; originally published online November 29, 2011; doi: 10.1161/CIRCINTERVENTIONS.111.964072

_Circulation: Cardiovascular Interventions_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2011 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-7640. Online ISSN: 1941-7632

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circinterventions.ahajournals.org/content/4/6/595

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation: Cardiovascular Interventions_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation: Cardiovascular Interventions_ is online at:
http://circinterventions.ahajournals.org//subscriptions/