Retrograde Transarterial Implantation of a Nonmetallic Aortic Valve Prosthesis in High–Surgical-Risk Patients With Severe Aortic Stenosis
A First-in-Man Feasibility and Safety Study

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Background—To assess the feasibility and safety of retrograde transarterial implantation of a novel nonmetallic aortic valve prosthesis (Direct Flow Medical Inc, Santa Rosa, Calif), a prospective single-center study was performed in patients with severe aortic stenosis at high risk for open-heart surgery.

Methods and Results—Fifteen patients (intention-to-treat cohort) with an aortic valve area ≤0.8 cm², a ≥35-mm Hg mean transvalvular pressure gradient, and a logistic EuroSCORE ≥20% were enrolled. Percutaneous aortic valve replacement was performed with the patient under general anesthesia. Hemodynamic parameters were assessed before and after implantation by transesophageal echocardiography. Clinical follow-up and transthoracic echocardiographic assessment were obtained at 30 days. Procedural success was achieved in 12 patients (80%). Surgical conversion became necessary at day 2 in 1 patient; 11 patients (73%) were discharged with a permanent implant. In these patients, implantation resulted acutely in a significant increase in aortic valve area (median, 1.64 [interquartile range, 1.27 to 1.74] versus 0.60 [0.46 to 0.69] cm²; P=0.0033) and a concomitant reduction in the mean pressure gradient (14.0 [13.2 to 16.5] versus 54.0 [43.2 to 59.8] mm Hg; P=0.0033). At 30 days, 1 cardiac death (6.7%; 95% CI, 0.2% to 32.0%) and 1 major stroke were observed. The 10 surviving patients with a permanent implant showed marked hemodynamic and clinical improvement at this time point.

Conclusions—In this small series of patients, percutaneous implantation of the Direct Flow Medical aortic valve prosthesis in high–surgical-risk patients was feasible and associated with a reasonably low safety profile. (Circ Cardiovasc Intervent. 2008;1:126-133.)

Key Words: aorta ■ catheterization ■ prosthesis ■ stenosis ■ valves

Recent years have witnessed the emergence of percutaneous treatment of valvular aortic stenosis as a clinical entity.1-11 Initial experience in humans has focused on patients deemed at high risk or unsuitable for surgery2,3,5,8–10 or patients with end-stage aortic stenosis in whom the percutaneous treatment modality was attempted on a compassionate-use basis.1,4,6,7 To date, investigators have used bioprosthetic valves made of equine, bovine, or porcine pericardium attached to a balloon-expandable stainless-steel or self-expanding nitinol stent frame. Catheter-based implantation of these types of valve prosthesis has been achieved using an antegrade approach by way of a transseptal puncture,1-3 a retrograde transfemoral approach,3-5,8 or an antegrade transapical approach.5,9 As the failure to properly deploy a stent-based valve prosthesis may necessitate emergent cardiac surgery, a prosthesis that allows repeated attempts at the correct sizing and positioning in situ is desirable. We report our initial clinical experience with a novel nonmetallic aortic valve prosthesis that can be retrieved and repositioned or exchanged before permanent implantation.

Clinical Perspective see p 133

Methods

Study Protocol
All patients were treated under an investigational plan designed to assess the feasibility and safety of permanent percutaneous implantation of the Direct Flow Medical (Santa Rosa, Calif) aortic valve prosthesis (Direct Flow Medical Inc, Santa Rosa, Calif).
prosthesis in high–surgical-risk patients with severe aortic valve stenosis. Feasibility was defined as procedural success (ie, correct placement of the prosthesis in the subcoronary position with an associated absolute reduction in the mean transvalvular pressure gradient to <25 mm Hg in the absence of severe aortic regurgitation). Safety was defined as the absence at 30 days of major adverse cardiac and cerebrovascular events (death, myocardial infarction, emergent cardiac surgery, and minor or major stroke) or other valve-related adverse events. High surgical risk was determined by consensus of 2 experienced cardiac surgeons.

Patients were prospectively screened and enrolled if they met all of the following inclusion criteria: symptomatic valvular aortic stenosis with an aortic valve area ≤0.8 cm² and a ≥35–mm Hg mean valvular gradient; an aortic annular diameter between 19 and 23 mm; a contraindication to surgery because of concomitant comorbidities; a logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) ≥20%;12 valvular and peripheral anatomy appropriate to accommodate the study device and its delivery system; and an age ≥70 years. Major exclusion criteria were a life expectancy <1 year, contraindication to any study medication, serum creatinine >2.0 mg/dL, prior valve surgery, endocarditis in the last 18 months, myocardial infarction within the last 30 days, clinically significant (>2+) mitral insufficiency, cardiac decompensation, and stroke in the past 6 months. The study was approved by the Ethics Committee of the Hamburg Board of Physicians, and all patients gave written informed consent.

Screening

The screening of patients potentially suited for percutaneous aortic valve replacement comprised a physical examination to assess the clinical history and current clinical status; transthoracic echocardiography to assess aortic valve dimensions, the severity of aortic stenosis and, if present, aortic regurgitation; coronary angiography to exclude clinically relevant coronary stenoses; and multislice computed tomography to assess cross-sectional diameters of the entire aortic valve apparatus from 15 mm below to 30 mm above the annulus in 5-mm planar increments and determine the distance of the coronary ostia from the annulus. Multislice computed tomography was also used to assess valvular calcification and evaluate the delivery route for a 22-F catheter system (7.9-mm outer diameter) against the native aortic annulus is achieved by pulling or pushing at the proximal end of the delivery system; alignment of the implant in the aortic valvular plane as well as atraumatic passage through the aorta and the native aortic valve. The distal end of the implant housing during advancement to allow independent inflatable balloon rings. The rings are interconnected by a tubular bridging (Figure 2). Implant deployment and retrieval is controlled by handles incorporated into the delivery system is a nitinol mesh basket into which the delivery catheter system is advanced over a 0.035-in guidewire. Incorporated into the delivery system is a nitinol mesh basket into which the implant can be withdrawn and retrieved before final implantation (Figure 2). Implant deployment and retrieval is controlled by handles at the proximal end of the delivery system; alignment of the implant against the native aortic annulus is achieved by pulling or pushing at the proximal ends of the positioning/fill lumens.

Study Device

The implant (Figure 1) consists of a trileaflet valve made of bovine pericardial tissue that is encased in a slightly tapered, conformable, polyester fabric cuff.13,14 Both the upper (aortic) and the lower (ventricular) margin of the cuff consist of an independently inflatable balloon ring. The rings are interconnected by a tubular bridging system that is inflatable only via inflation of the aortic ring. To position and align the implant in the aortic valvular plane as well as separately inflate and deflate the balloon rings, 3 detachable positioning/fill lumens connect to the aortic ring of the implant at angular distances of 120° along its perimeter. For introduction, the implant is loaded into a flexible 22-F housing at the distal end of a 15-F multilumen delivery catheter. One of the lumens houses a catheter with an olive-shaped plastic “pearl” at its distal tip, which covers the distal end of the implant housing during advancement to allowatraumatic passage through the aorta and the native aortic valve. The delivery system is advanced over a 0.035-in guidewire. Incorporated into the delivery system is a nitinol mesh basket into which the implant can be withdrawn and retrieved before final implantation.
Implant is available in heights of 16 and 17 mm and diameters of 23 and 25 mm, corresponding to outer aortic ring diameters of 27 and 29 mm, respectively.

**Implantation Procedure**

All procedures were performed at the University Heart Center Hamburg, with the patient under general anesthesia but without extracorporeal circulation, in a hybrid suite equipped for both cardiac catheterization and cardiovascular surgery. The patients had to be premedicated with acetylsalicylic acid (aspirin, 100 mg/d) and clopidogrel (75 mg/d) for 5 days. Patients not on this regimen were given an intravenous bolus of 500 mg of aspirin and an oral loading dose of 600 mg of clopidogrel immediately before the intervention. Transesophageal echocardiography was performed throughout the procedure. A standard surgical cut-down gave access to the femoral artery with the wider dimension and the least calcification and tortuosity on preprocedural computed tomography (mostly the right femoral artery), while a 6-F pigtail catheter for fluoroscopic visualization of the ascending aorta was introduced into the contralateral femoral artery via a 6-F introducer sheath. A pacemaker lead was placed in the right ventricle by way of the jugular vein. The surgically exposed femoral artery was fitted with a 22-F introducer sheath. After sheath placement, an intravenous bolus of 5000 to 10 000 U of heparin (depending on the patient’s weight) was administered to achieve and maintain an activated clotting time of >300 seconds.

After multiple balloon valvuloplasties under rapid pacing (≈200/min) until leaflet mobility was markedly improved and a mean pressure gradient of ≈30 mm Hg was achieved, the delivery catheter was advanced during sinus rhythm (or atrial fibrillation in 3 patients) over a 0.035-in superstiff guidewire until the implant housing was fully contained in the left ventricle. Retraction of the housing then exposed the implant, which was subsequently expanded by injecting a 50:50 mix of saline and contrast agent into both balloon rings. Thereafter, both rings were deflated, the device aligned, and the ventricular ring inflated. At this point, the prosthetic valve was already functioning. The implant was then withdrawn such that the inflated ventricular ring fit against the ventricular aspect of the native annulus. The aortic ring was again inflated with the saline/contrast mix. Using fluoroscopy, transesophageal echocardiography, and aortography, the implant was checked for correct (subcoronary) position and paravalvular leaks and, if necessary, partially deflated, readvanced into the left ventricle, realigned and repositioned, or completely removed and exchanged for another implant. Once the position and function of the prosthesis was deemed satisfactory, the saline/contrast mix was replaced, while maintaining a pressure of 8 to 10 atmospheres, with a polymer that becomes solid in 10 minutes and cures completely within 24 hours to keep the implant permanently in place. Contrast media added to the polymer enhanced...
the fluoroscopic visibility of the prosthesis rings. The positioning/fill lumens were then detached and the delivery system removed. The intervention was concluded with final aortography and transesophageal echocardiography to assess coronary patency, central aortic regurgitation and pressure gradients, aortic orifice area, and paravalvular leaks. Vascular access sites in the groin were closed by purse string sutures in 11 of 13 patients; 2 patients needed open anastomosis after careful resection of vessel margins. Wounds were closed by running sutures and covered with compression bandages. A case example of an implantation procedure is provided in Figure 3.

The patients were transferred to the intensive care unit and general anesthesia was discontinued. On day 1 after the intervention, patients were started on a combination therapy of clopidogrel (75 mg/d for 6 months) and aspirin (100 mg/d indefinitely).

Follow-Up
Patients were asked to return after 30 days for an assessment of their clinical status and a transthoracic echocardiographic examination.

Statistics
Continuous variables are presented by their median and interquartile range (IQR). Categorical variables are presented as counts and percentages. Exact 95% CIs were calculated based on the binomial distribution. Changes in continuous variables between baseline and at 30 days were assessed using Wilcoxon signed rank test. Comparisons between categorical variables were performed using the continuity-corrected chi-square test. These analyses used the StatView 4.5 software package (Abacus Concepts Inc, Berkeley, Calif). A 2-tailed probability value <0.05 was considered statistically significant.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agreed to the manuscript as written.

Results

Procedural Outcomes
After a median of 7 (IQR, 6 to 11) balloon valvuloplasties with mostly 2 balloons of 25-mm diameter (for the 23-mm implant) or 28-mm diameter (for the 25-mm implant), procedural success was achieved in 12 patients (80%; 95% CI, 52 to 96%). In 2 patients, the introducer sheath could not be advanced through a severely calcified iliofemoral vasculature. In another patient who had a functionally bicuspid native valve secondary to fusion of 2 leaflets at the commissures, expansion of two 23-mm implants was judged inadequate both times and the procedure was terminated without implantation. The patient underwent surgical aortic valve replacement after 9 days because of clinical instability with severe dyspnea at rest; she recovered uneventfully. The other 2 patients were continued on medical treatment. In the 12 successfully treated patients, procedure duration ranged from...
315 minutes (first procedure) to 118 minutes (last procedure), with an average of 193 minutes. The actual implantation of the prosthesis (from insertion of the delivery catheter to the time the inflation media reached its cured state in the syringe) lasted for a median of 36 minutes, with an IQR of 33 to 45 minutes. Implantation time was markedly prolonged to 102 minutes in patient 12, in whom an occlusion of the left main coronary artery that was noted after successful deployment of the implant had to be dilated and stented. Fluoroscopy time amounted to a median of 34 minutes (IQR, 28.5 to 58.0 minutes).

After implantation, 4 patients had no evidence of transvalvular insufficiency. Minor paravalvular leaks were detected in 6 patients, and central aortic regurgitation of trivial and moderate (2+) severity was present in 1 patient each.

Surgical conversion after 48 hours became necessary in patient 5, in whom the native aortic annulus turned out to be too small for the implant. The aortic ring could not be fully deployed, which subsequently caused an increase in the peak transvalvular pressure gradient to 90 mm Hg. Thus, a total of 11 of 15 patients (73%; 95% CI, 45 to 92%) received a permanent implant. Device sizes were 23 mm in 8 patients and 25 mm in 3 patients.

Hospitalization
Of the 11 patients with a permanent implant, 10 were discharged after a median of 7 days (IQR, 6 to 7 days). One patient was still hospitalized at 30 days for stroke rehabilitation.

Device Recoveries
Device recoveries were performed in 3 of 12 successfully treated patients (25%). In the first patient of our series, calcification of the native annulus prevented complete inflation of the aortic ring of a 23-mm device. It was then exchanged for a (higher) 25-mm device of which the aortic ring could be fully inflated, sealing the calcific deposit that prevented adequate inflation of the 23-mm device. In another patient, the implant, after inflation of the ventricular ring, slipped back into the ascending aorta during alignment attempts in the native annulus; it was retrieved and exchanged for another implant of the same size, which could be successfully deployed. A third patient presented with subvalvular circumferential calcification of the native annulus that impeded complete inflation of the ventricular ring of the implant; on retrieval of the device and reintroduction with different angulation relative to the native annulus, correct positioning was eventually achieved. In addition, 2 devices were recovered in the patient with a functionally bicuspid native valve who did not receive a permanent implant. The 5 device recoveries took a median of 7.5 minutes (IQR, 7 to 8 minutes).

Adverse Events

Major adverse cardiac and cerebrovascular events occurred in 3 patients (20%; 95% CI, 4% to 48%; Table 3). The patient in whom intraprocedural stenting of the left main coronary artery was performed died at 36 hours after an inferior (ie, right coronary artery–related) myocardial infarction. Autopsy revealed a patent stent but a total occlusion of the distal right coronary artery at a site where a 70% stenosis had been identified preintervention that was adjudicated as being clinically not relevant. Another patient with chronic atrial fibrillation sustained a major stroke at 12 hours that resulted in dysarthria and motor weakness of the right arm and necessitated prolonged rehabilitation at an outside hospital. One patient required surgical conversion (see above).

A minor adverse event was the intraprocedural occurrence of a groin hematoma that required immediate surgical removal. Atroventricular conduction block was not induced in any patient.

Acute Hemodynamic Outcomes of Patients With a Permanent Implant

In the 11 patients who received a permanent implant, the mean transvalvular pressure gradient decreased significantly from a median of 54.0 (IQR, 43.2 to 59.8) to 14.0 (13.2 to 16.5) mm Hg ($P=0.0033$), secondary to a fully functioning implant with a significantly increased effective orifice area (median, 1.64 [1.27 to 1.74] versus 0.60 [0.46 to 0.69] cm$^2$; $P=0.0033$; Table 4 and Figure 4). Accordingly, the peak aortic pressure gradient measured after implantation was also significantly reduced (median, 29.0 [24.2 to 32.8] versus 64.0 [68.2 to 98.0] mm Hg; $P=0.0033$).

Follow-Up
Clinical and transthoracic echocardiographic follow-up was obtained at a median of 35 days (IQR, 29 to 36 days) from 10 patients with a permanent implant. A clinical improvement by 2 NYHA functional classes was observed in 4 patients and by 1 NYHA functional class in 5 patients; 1 patient remained in NYHA functional class I (Figure 5). The difference in the distribution of NYHA functional class between baseline and 30 days was statistically significant ($P=0.0029$ by continuity-corrected $\chi^2$ test).

Transthoracic echocardiography revealed adequate position and function of the implant in all 10 patients. The presence of paravalvular leaks and central aortic regurgitation was unchanged with respect to postimplantation except for 1 patient in whom 2+ aortic regurgitation on transesophageal echocardiography was now measured as 1+. Aortic orifice area was essentially unchanged, and the slight increase in mean aortic pressure gradient from a median of 14.0 mm Hg

<table>
<thead>
<tr>
<th>Table 3. Adverse Events Within 30 days</th>
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<tbody>
<tr>
<td>Major events</td>
</tr>
<tr>
<td>Death</td>
</tr>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Surgical conversion</td>
</tr>
<tr>
<td>Total (hierarchical)</td>
</tr>
<tr>
<td>Other events</td>
</tr>
<tr>
<td>Atrioventricular conduction block</td>
</tr>
<tr>
<td>Intraprocedural groin hematoma</td>
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</table>

Values are n (%), 95% CI.
to a median of 17.0 mm Hg did not reach statistical significance (Figure 4 and Table 4). Left ventricular ejection fraction increased relative to baseline in 8 patients but decreased in 2; the overall difference of 68% (54% to 74%) at 30 days versus 61% (46% to 67%) at baseline was statistically not significant (P=0.0829; Figure 6).

### Discussion

This report demonstrates the feasibility and safety of retrograde transfemoral implantation of a nonmetallic aortic valve prosthesis in a first-in-man series of 15 high-surgical-risk patients with severe aortic stenosis. Acute procedural success was achieved in 12 patients (80%) of whom 11 (73%) were discharged with a permanent implant. In the latter patients, successful implantation resulted in a significant reduction of the mean transvalvular pressure gradient secondary to a significant increase in effective aortic valve area. After implantation, no patient exhibited aortic insufficiency, neither central nor paravalvular, of hemodynamic relevance, attesting to adequate sealing of the native aortic annulus by the implant. Coronary compromise during the intervention occurred in only 1 patient in whom correct deployment of the implant in the subcoronary position caused the displacement of an aortic-wall plaque, impeding inflow into the left main coronary artery; the condition was remedied by ostial stenting. Major in-hospital cardiovascular and cerebral events occurred in 2 of the 15 patients (13%) and comprised 1 cardiac death after a myocardial infarction and 1 major stroke; this incidence seems not to be different from that reported in first-in-man studies of stent-based percutaneous valve prostheses.3–6 One patient of our

### Table 4. Echocardiography in Patients Who Received a Permanent Implant

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline* (n=11)</th>
<th>Post Procedure† (n=11)</th>
<th>Change vs Baseline (n=11)</th>
<th>30 days* (n=10)</th>
<th>Change vs Post Proc. (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean pressure gradient, mm Hg</td>
<td>54.0 (43.2–59.8)</td>
<td>14.0 (13.2–16.5)</td>
<td>−40 (−45−−30)</td>
<td>17.0 (15–20)</td>
<td>2.5 (0–9)</td>
</tr>
<tr>
<td>Peak pressure gradient, mm Hg</td>
<td>64.0 (68.2–98.0)</td>
<td>29.0 (24.2–32.8)</td>
<td>−52 (−68−−48)</td>
<td>34.5 (27–38)</td>
<td>4 (−3–10)</td>
</tr>
<tr>
<td>Aortic valve area, cm²</td>
<td>0.60 (0.46–0.69)</td>
<td>1.64 (1.27–1.74)</td>
<td>0.89 (0.81–1.07)</td>
<td>1.58 (1.5–1.8)</td>
<td>0.02 (−0.09–0.23)</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>61 (46–67)</td>
<td></td>
<td></td>
<td>68 (54–74)</td>
<td>8.5 (−1–15)</td>
</tr>
</tbody>
</table>

Values are medians and (in parentheses) interquartile ranges.
LVEF indicates left ventricular ejection fraction.
*By transthoracic echocardiography.
†By transesophageal echocardiography.

Figure 4. Box-and-whiskers plots of mean transvalvular aortic pressure gradient (A) and effective aortic orifice area (B) at baseline, postimplantation, and at 30-day follow-up in patients with a permanent implant. Horizontal bar within box represents median (numeric value next to it); top and bottom of box represent 75th and 25th percentile, respectively; ends of top and bottom whisker represent 90th and 10th percentile, respectively. Post measurements were taken with transesophageal echocardiography, whereas baseline and 30-day measurements were taken with transthoracic echocardiography. Probability values represent paired comparisons (n=11 patients for the comparison of baseline versus post; n=10 patients for the comparison of post versus 30 days).

Figure 5. Change in NYHA functional class from baseline to 30 days in 10 patients with a permanent implant. Improvements by at least 1 functional class were observed in all patients but 1. The difference in the distributions at baseline and 30 days was statistically highly significant (P=0.0029).
series required a surgical conversion; the total rate of major procedure-related adverse events was 20%. At 30 days, prosthesis performance was maintained in all surviving patients with a permanent implant. Left ventricular ejection fraction had an average increased and symptomatic relief, as reflected by an overall significant reduction in NYHA functional class in all but 1 patient, who was already in NYHA functional class I at baseline.

Advantages of the Nonmetallic Implant
The most obvious advantage of the nonmetallic aortic valve prosthesis is that it gives the operator unprecedented freedom of handling the device during implantation. It is nonmetallic and, in its unexpanded state, highly flexible and can be easily negotiated, even through a calcified aortic arch; it allows repeated advancement and retraction across the native annulus for proper positioning; it immediately functions on expansion and thus requires no rapid pacing during the actual implantation; and it can be checked for competent sealing of the annulus and adequate valve performance before permanent implantation. The implant can be readily retrieved and exchanged for another implant of the same or a different size should it slip back into the ascending aorta from its intended position or in cases where correct placement cannot be achieved. Thus, the characteristics of the nonmetallic implant render intraprocedural migration into the ascending or descending aorta almost impossible and reduce the likelihood of emergent surgical conversion.

The design of the implant allows fixation of the aortic ring in a subcoronary position without encroachment on the coronary ostia and fixation of the ventricular ring in a subannular position without impairing the mobility of the anterior mitral leaflet.

The atraumatic advancement of the implant delivery system, particularly through the aortic arch and the native aortic annulus, may account for the low incidence of cerebrovascular events observed in the present series. It cannot be determined if the stroke that occurred 12 hours after the intervention was related to the procedure or to the patient’s chronic atrial fibrillation.

Potential Disadvantages of the Nonmetallic Implant
Balloon-expandable as well as self-expanding stent-based aortic valve prostheses exert pronounced radial force on the surrounding tissue, thereby sealing the native aortic annulus and ensuring prosthesis function. With the nonmetallic implant, annular sealing is accomplished by the prosthesis rings, while the “passive” polymer-filled bridging system connecting the rings must withstand circumferential outer forces. It is therefore necessary to possibly reduce such forces and create an adequate, preferably circular, opening of the native annulus by multiple valvuloplasties (a median of 7 in our series) during rapid pacing before implantation is attempted. A circular opening and, subsequently, implantation could not be achieved in the patient with a functionally bicuspid native valve; in another patient, full expansion of the aortic prosthesis ring was prevented by a native annulus too small for the implant. Both patients underwent surgical valve replacement. Repeated rapid pacing in patients with severe aortic stenosis may result in global and irreversible myocardial ischemia. Also, it is not known if progression of sclerotic disease will eventually cause a reduction in effective aortic valve area in patients with a permanent percutaneous implant.

Impact of the Learning Curve
As is generally the case with new therapeutic technologies, increased operator experience will likely reduce the incidence of screening failures, avoid adverse events, and “streamline” the various procedural steps. In 2 patients of our series, the 22-F introducer sheath could not be advanced through severely calcified iliac arteries, and the intervention had to be aborted. More experience in the interpretation of the calcification status of the iliofemoral vasculature on the screening computed tomograms may have avoided these screening, and ultimately procedural, failures. It is expected that the development of an 18-F device will also help to reduce the number of screening failures. In patient 5, the intervention was concluded supposedly successful even though the aortic ring of the implant appeared indented and nonplanar on fluoroscopy (Figure 7) and the mean transvalvular pressure gradient was 30 mm Hg. Within 2 days, the gradient increased significantly and the patient underwent sur-

Figure 6. Left ventricular ejection fraction at baseline and 30 days in 10 patients with a permanent implant. Large dots indicate means; error bars indicate SD.

Figure 7. Fluoroscopic image of implant in patient 5 before exchange of inflation media. Ventricular ring appears circular, but aortic ring appears indented and nonplanar (arrow).
gical conversion. Thus, a perfectly circular and planar appearance of the prosthesis rings on fluoroscopy seems to be mandatory before an intervention can be concluded.

Limitations
The patients in this study represent a highly selected cohort. They were all elderly with a high–surgical-risk profile due to significant comorbidities. Therefore, our results may not be extrapolated to younger patients with severe aortic stenosis but less critical surgical risk conditions. The number of patients was small and, thus, all percentages were associated with wide 95% CIs. More confident estimates of success and complications rates will be gained with more patients. Follow-up in this study was restricted to 30 days. Thus, no statements can yet be made on the long-term durability of the implant and clinical outcome of the patients.

Conclusions
This single-center first-in-man study has shown that retrograde transarterial implantation of the Direct Flow Medical nonmetallic aortic valve prosthesis is feasible in the majority of patients. Patients discharged with a permanent implant showed marked hemodynamic and significant clinical improvement at 30 days. The incidence of major periprocedural events was reasonably low, with 1 death, 1 stroke, and 1 surgical conversion. A greater number of patients and longer follow-up are necessary for a more confident assessment of procedural success as well as long-term mortality and morbidity.

Sources of Funding
This study was sponsored by Direct Flow Medical Inc, Santa Rosa, Calif.

Disclosures
Drs Low and Bolling serve as consultants to Direct Flow Medical Inc, and Dr Bolling owns stock options in Direct Flow Medical Inc. Drs Schofer and Tübler have received reimbursement from Direct Flow Medical Inc for travels to scientific meetings. The other authors report no conflicts of interest.

References

CLINICAL PERSPECTIVE
We performed a first-in-man study of percutaneous implantation of a novel nonmetallic aortic valve prosthesis in a small series of 15 patients with severe aortic valve stenosis who were at high risk for open-heart surgery. Implantation was acutely successful in 12 patients (80%) in whom a significant increase in aortic valve area and a concomitant reduction in the mean transvalvular pressure gradient was achieved. One patient had to undergo surgical conversion at day 2, thus 13 patients (73%) were discharged with a permanent implant. At 30 days, 1 cardiac death (6.7%; 95% CI, 0.2% to 32.0%) and 1 major stroke were observed. The 10 patients surviving 30 days with a permanent implant showed marked hemodynamic and clinical improvement. The major advantage of the highly flexible prosthesis is that it gives the operator unprecedented freedom of handling the device during implantation; it can be easily negotiated even through a calcified aortic arch, allows repeated advancement and retraction across the native annulus for proper positioning, and functions immediately upon expansion. A greater number of patients and longer follow-up are necessary for a more confident assessment of procedural success as well as long-term mortality and morbidity.
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