Transapical Transcatheter Aortic Valve Implantation in Humans
Initial Clinical Experience

Samuel V. Lichtenstein, MD, PhD; Anson Cheung, MD; Jian Ye, MD; Christopher R. Thompson, MD; Ronald G. Carere, MD; Sanjeevan Pasupati, MD; John G. Webb, MD

Background—Aortic valve replacement with cardiopulmonary bypass is currently the treatment of choice for symptomatic aortic stenosis but carries a significant risk of morbidity and mortality, particularly in patients with comorbidities. Recently, percutaneous trans femoral aortic valve implantation has been proposed as a viable alternative in selected patients. We describe our experience with a new, minimally invasive, catheter-based approach to aortic valve implantation via left ventricular apical puncture without cardiopulmonary bypass or sternotomy.

Methods and Results—A left anterolateral intercostal incision is used to expose the left ventricular apex. Direct needle puncture of the apex allows introduction of a hemostatic sheath into the left ventricle. The valve prosthesis, constructed from a stainless steel stent with an attached trileaflet equine pericardial valve, is crimped onto a valvuloplasty balloon. The prosthetic valve and balloon catheter are passed over a wire into the left ventricle. Positioning within the aortic annulus is confirmed by fluoroscopy, aortography, and echocardiography. Rapid ventricular pacing is used to reduce cardiac output while the balloon is inflated, deploying the prosthesis within the annulus. Transapical aortic valve implantation was successfully performed in 7 patients in whom surgical risk was deemed excessive because of comorbidities. Echocardiographic median aortic valve area increased from 0.7 ± 0.1 cm² (interquartile range) to 1.8 ± 0.8 cm² (interquartile range). There were no intraprocedural deaths. At a follow up of 56 ± 56 days, 6 of 7 patients remain alive and well.

Conclusions—This initial experience suggests that transapical aortic valve implantation without cardiopulmonary bypass is feasible in selected patients with aortic stenosis. (Circulation. 2006;114:591-596.)

Key Words: aorta ▪ catheters ▪ stenosis ▪ valves ▪ valvuloplasty

Aortic valve replacement is the treatment of choice for patients with severe symptomatic degenerative aortic stenosis and is the only modality that offers both symptomatic relief and the potential for improved long-term survival. Symptomatic patients managed medically have a poor prognosis, and the hope of durable benefit with balloon aortic valvuloplasty has not been realized. However, many potential surgical candidates have significant comorbidities; as a result, open heart surgery with cardiopulmonary bypass may be associated with unacceptable mortality and morbidity.

Several groups have pursued the development of transcatheter valves.7-13 Percutaneous aortic valve implantation in humans was first performed as a femoral transvenous procedure with antegrade access to the aortic valve.14-16 Subsequently, we reported a femoral transarterial procedure.17,18 Our group’s initial animal developmental work used direct balloon catheter implantation from the left ventricular apex.12 Recently, we reported a case in which the transarterial delivery system was used to implant an aortic valve via the apex of the left ventricle.19,20 The present study describes our clinical experience and technique of prosthetic aortic valve implantation by direct left ventricular access using a beating-heart, catheter-based approach in humans.

Methods
The procedure was approved by the Therapeutic Products Directorate, Department of Health and Welfare, Ottawa, Canada, for compassionate clinical use in patients deemed not to be candidates for routine surgery and unsuitable for percutaneous transfemoral arterial valve implantation.

Prosthetic Valve System
The Cribier-Edwards valve (Edwards Lifesciences Inc, Irvine, Calif) is constructed from a tubular slotted stainless steel stent with an attached equine pericardial trileaflet valve (Figure 1). A sewn fabric cuff covers the left ventricular portion of the prosthesis. In vitro durability of the prosthetic valve has repeatedly been demonstrated to be >200 million cardiac cycles, corresponding to >5 years of life. Valves are supplied sterile in glutaraldehyde. At the time of this
experience, only a 26-mm-external-diameter prosthesis was available for transapical use. On the basis of our percutaneous implantation experience, the 26-mm prosthesis was considered appropriate for an echocardiographic annulus diameter of 20 to 25 mm. Valve sizing in this situation differs from that during traditional open surgery because variable expansion of the native calcified valve will accommodate a single size quite well (ie, 26 mm) despite a large range of annular sizes.

A mechanical crimping device is used to attach the prosthesis onto a specially constructed balloon deployment catheter. For the transapical approach, the occlusive fabric skirt must be mounted proximally on the balloon catheter. In these initial apical access cases, we used the identical valve and catheter delivery system designed for percutaneous femoral arterial access. In this system, the balloon delivery catheter shaft is contained within a steerable guiding catheter that can be actively flexed by rotation of an external handle.

**Procedure**

Patients were premedicated with aspirin, clopidogrel, and vancomycin. Procedures were performed by a combined team of cardiologists and cardiac surgeons in an operating room setting equipped with fluoroscopy. General anesthesia with double-lumen intubation was used. The apex of the left ventricle was identified by palpation and fluoroscopy. The pleural space overlying the apex (usually the sixth intercostal space) was entered via a 5- to 8-cm anterolateral thoracotomy. The pericardium over the apex of the left ventricle was identified and opened. Temporary epicardial ventricular pacing wires were placed on the left ventricle. Reliable capture was ensured at a rate of between 160 and 220 bpm with a reduction in systemic systolic arterial pressure to $\frac{1}{60} \text{mm Hg}$. During subsequent valvuloplasty and prosthesis deployment, rapid pacing was used to minimize transaortic flow and cardiac motion (Figure 2).

The thin portion of the left ventricular apex was identified by finger palpation and confirmed by simultaneous transesophageal echocardiographic imaging (TEE). Two paired orthogonal U-shaped sutures with pledgets were placed into the myocardium and passed through tensioning tourniquets. An arterial needle puncture allowed placement of a 7F sheath through the apex into the left ventricular cavity using a standard over-the-wire technique (Figure 3). Positive ventricular pressure and care to bleed all sheaths through appropriate ports prevented air entry into the ventricle. Heparin was administered to achieve an activated clotting time of $>250$ seconds. A wire (0.035-in J-curve Amplatz extra-stiff, Cook, Inc, Bloomington, Ind) was advanced through the aortic valve, around the arch, and into the descending aorta for stability. If necessary, a balloon catheter (Berman catheter, Arrow International Inc, Reading, Pa) was used to direct the wire in the direction of arterial flow past mitral chordae and around the aortic arch. The previously placed sheath was then exchanged for a larger 14F sheath. A valvuloplasty balloon (20 to 22 mm, Z-Med, Numed Inc, Hopkington, NY) was advanced over the wire to the level of the ascending aorta, evacuated of air, and test inflated with dilute contrast. The balloon was withdrawn to the level of the valve as determined by fluoroscopy and TEE. Rapid pacing was initiated, and when an adequate reduction in systemic arterial pressure was observed, the balloon was rapidly inflated and deflated.

The previously placed 14F sheath was exchanged over the wire for a larger 24F sheath. The prosthesis, balloon, and steerable catheter were passed over the previously placed wire and introduced as a unit through the sheath. The prosthesis balloon was advanced to the level of fluoroscopically visible valvular calcium. Aortic root angiography via a pigtail catheter introduced from the femoral artery and TEE were used to aid positioning. Rapid pacing was again used to reduce transvalvular flow and cardiac motion during valve deployment. After deployment, valve function was assessed by echocardiography and angiography. If paravalvular insufficiency was excessive, dilation of the prosthesis was repeated. After removal of the left ventricular sheath, hemostasis was secured with the previously placed pledgeted sutures. The pericardium was approximated to prevent myocardial herniation but allow drainage. A left chest tube was placed. Patients were maintained on aspirin indefinitely and

![Figure 1. A, The prosthesis is constructed of a stainless steel stent incorporating an equine pericardial trileaflet valve and fabric cuff. B, The prosthesis is crimped onto a valvuloplasty balloon catheter.](http://circ.ahajournals.org/)

![Figure 2. Rapid pacing with 2:1 capture followed by 1:1 capture and hypotension. Cessation of pacing is associated with rapid normalization of systemic arterial pressure.](http://circ.ahajournals.org/)
clopidogrel for 1 month. Transthoracic echocardiography was performed before discharge and at 1 month.

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

**Results**

**Patients**
Transapical left ventricular aortic valve implantation without cardiopulmonary bypass was performed in 7 patients with severe symptomatic aortic stenosis. All patients were judged to be at unacceptably high risk for routine open aortic valve replacement with cardiopulmonary bypass because of comorbidities. Age was 77 ± 9 years; 5 patients were male, and 2 were female; and their New York Heart Association functional class was 3 ± 1. Surgical mortality risk as estimated by logistic Euroscore was 35 ± 26%. Two patients were found to have porcelain aortas at previous thoracotomy. Patients were assessed for percutaneous transfemoral arterial valve implantation by an operator experienced in this technique but were judged unsuitable because of the presence of iliofemoral atherosclerosis in 5, iliac tortuosity in 1, and aortic tortuosity in 1. Echocardiographic mean aortic valve area 0.7 ± 0.1 cm².

**Table 1. Patient Demographics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
<th>Patient 6</th>
<th>Patient 7</th>
</tr>
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<tbody>
<tr>
<td>Age, y</td>
<td>76</td>
<td>77</td>
<td>76</td>
<td>70</td>
<td>63</td>
<td>90</td>
<td>91</td>
</tr>
<tr>
<td>Sex, female</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Limiting lung disease</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Coronary artery disease</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Cerebrovascular disease</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Peripheral vascular disease</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>GFR &lt; 60 mL/min</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>MR grade 3 or 4</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
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<td>Pulmonary hypertension</td>
<td>Yes</td>
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<td>No</td>
<td>No</td>
<td>No</td>
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<td>Yes</td>
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<td>Prior thoracotomy</td>
<td>No</td>
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<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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<td>Chest radiation</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Porcelain aorta</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Severe immobility</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>35%</td>
<td>60%</td>
<td>50%</td>
<td>50%</td>
<td>60%</td>
<td>50%</td>
<td>40%</td>
</tr>
<tr>
<td>Aortic valve area, cm²</td>
<td>0.7</td>
<td>0.6</td>
<td>0.6</td>
<td>0.8</td>
<td>1.2</td>
<td>0.4</td>
<td>0.7</td>
</tr>
<tr>
<td>Predicted surgical mortality,*</td>
<td>%</td>
<td>41</td>
<td>7</td>
<td>66</td>
<td>10</td>
<td>8</td>
<td>57</td>
</tr>
</tbody>
</table>

GFR indicates glomerular filtration rate; MR, mitral regurgitation; and LV, left ventricular.

*Logistic Euroscore estimation.21

**Procedure**
Prosthetic valve implantation was successful in all cases (Figure 4). Procedural characteristics are shown in Table 2. Fluoroscopic assessment of valvular calcium was used for initial positioning of the prosthesis. However, the amount and location of calcification were variable, requiring further assessment with repeated injections of radiographic contrast within the aortic root and online TEE (Figure 5). Integration of all 3 modalities by the implanting physician facilitated optimal positioning.

Rapid ventricular pacing was an effective and reproducible means of reducing transvalvular flow during balloon inflation.
Some degree of paravalvular insufficiency after initial deployment was evident in all patients. Paravalvular insufficiency was slightly high within the annulus but adequate in 2 patients. Positioning was judged optimal in 5 patients. Positioning was generally positioned slightly toward the ventricle before deployment so that if slight movement did occur, final positioning would be adequate.

All patients received 26-mm-diameter prostheses. Final positioning was judged optimal in 5 patients. Positioning was slightly high within the annulus but adequate in 2 patients. Some degree of paravalvular insufficiency after initial deployment was evident in all patients. Paravalvular insufficiency was judged excessive by TEE in 2 patients in whom redilation resulted in further expansion of the prosthesis and a satisfactory reduction in paravalvular regurgitation. At the completion of the procedure, aortic insufficiency grade was 1.0±0.8 by TEE.

### Follow-Up

Postprocedural transthoracic echocardiography reported a median transaortic gradient of 9±6 mm Hg (interquartile range) and an aortic valve area of 1.8±0.8 cm² (interquartile range). Echocardiography documented no change in valve function at 1 month (Table 3). In no patient did paravalvular insufficiency appear clinically significant. One patient died at day 12 of pneumonia despite echocardiographically normal prosthetic valve function. Thirty-day mortality rate was 14%. At a mean follow up of 87±56 days, 6 of 7 patients remained alive and well.

### Discussion

Aortic valve replacement is the treatment of choice in patients with severe symptomatic acquired aortic stenosis, offering both symptomatic relief and the potential of improved long-term survival. Symptomatic patients managed medically have a poor prognosis. Balloon valvuloplasty is palliative, and although it may result in temporary relief of symptoms, benefit is modest and restenosis is certain.

Unfortunately, many potential surgical candidates have significant comorbidities, and open heart surgery with cardiopulmonary bypass may pose risks that are unacceptable to them or their physicians. According to the Society of Thoracic Surgery Database (1998 to 2001), surgical aortic valve replacement carries a rate of serious complication or mortality of 16.8%. Operative risk is increased in the setting of comorbidities such as advanced age and others. In our patients, judged poor candidates for routine surgery with an estimated logistic Euroscore mortality of 35±26%, a 30-day mortality rate of 14% is encouraging.

The feasibility of percutaneous valve implantation was first demonstrated in an animal model by Anderson et al. Subsequently, several groups, including our own, pursued the development of percutaneous heart valves. Percutaneous aortic valve implantation in humans was first performed as a transvenous transseptal procedure with antegrade access to the aortic valve by Cribier et al. The technical complexity and risks associated with this procedure appear likely to limit its widespread application, however.

We reported the development of a transarterial retrograde technique that has had favorable initial results. Evaluation of this procedure is ongoing and remains encouraging. Although the transfemoral arterial procedure has proved successful, some patients are poorly suited to this approach because of femoral, iliac, or aortic size; tortuosity; or atheroma. Our initial percutaneous valve development had used direct balloon catheter implantation from the left ventricular apex in a porcine model. It was anticipated that in such individuals aortic valve implantation using a left ventricular apical approach would have advantages.

Obviously, optimal positioning of the prosthetic valve is critical. In our early percutaneous implantation experience, we sought to position the midpoint of the prosthesis adjacent to the aortic valve by Cribier et al. Subsequently, several groups, including our own, pursued the development of percutaneous heart valves. Percutaneous aortic valve implantation in humans was first performed as a transvenous transseptal procedure with antegrade access to the aortic valve by Cribier et al. The technical complexity and risks associated with this procedure appear likely to limit its widespread application, however.

### Table 2: Procedural Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic annulus diameter, mm</td>
<td>22±1</td>
<td>100</td>
</tr>
<tr>
<td>Prosthesis diameter 26 mm, n</td>
<td>7</td>
<td>100</td>
</tr>
<tr>
<td>Valve implantation successful, n</td>
<td>7</td>
<td>100</td>
</tr>
<tr>
<td>Postdeployment dilatation, n</td>
<td>2</td>
<td>33</td>
</tr>
<tr>
<td>Procedure time, min</td>
<td>218±18</td>
<td></td>
</tr>
<tr>
<td>Fluoroscopy time, min</td>
<td>16±4</td>
<td></td>
</tr>
<tr>
<td>Ventilator time, min</td>
<td>434±283</td>
<td></td>
</tr>
<tr>
<td>Chest tube removal, days</td>
<td>2.2±2.0</td>
<td></td>
</tr>
<tr>
<td>Blood loss, mL</td>
<td>285±157</td>
<td></td>
</tr>
<tr>
<td>Blood transfusion, n</td>
<td>2</td>
<td>29</td>
</tr>
<tr>
<td>Mortality at 30 days, n</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td>Median hospital stay, days*</td>
<td>8</td>
<td></td>
</tr>
</tbody>
</table>

*Before discharge or transfer.
to the major leaflet calcification. However, aortography and TEE often further clarify the relative positions of the prosthesis, annulus, and leaflets. Both native valve and native annulus appear to play a role in secure valve seating. The supra-annular aorta appears to play a less important role in valve securement. Ideal positioning appears to be dependent on prosthesis apposition with the annulus and outflow tract while extending just above the native leaflets. Device embolization was an unpredictable concern during early percutaneous implantation experience. However, with accurate positioning, sizing, and deployment techniques, prosthesis embolization appears likely to be rare, as reflected in this initial apical access experience.

Some degree of paravalvular insufficiency was common. In these patients with primarily aortic stenosis, however, the degree of native valve insufficiency before the procedure was comparable to the degree of paravalvular insufficiency after valve implantation. In no patient did the residual paravalvular leak appear clinically significant.

TEE demonstrates that paravalvular insufficiency is commonly due to inadequate apposition of the fabric cuff of the prosthesis and the aortic annulus. Our percutaneous implantation experience demonstrated that relative oversizing of the prosthesis is useful for reducing concerns about paravalvular insufficiency. Aggressive overdilation of a prosthesis would be expected to result in poor leaflet apposition, valvular insufficiency, and potentially impaired leaflet durability. Modest overdilation appears safe and was used commonly to ensure full prosthesis expansion in this series. An additional mechanism of paravalvular insufficiency is positioning the prosthesis either too high or too low in relation to the native annulus so that the fabric cuff is nonocclusive. The lack of clinically important paravalvular insufficiency in this series likely reflects routine prosthesis oversizing, modest postdilatation when necessary, and increasingly accurate positioning.

Coronary obstruction or stroke could conceivably occur as a result of embolization of friable valvular debris, although we have not observed this outcome with percutaneous valve implantation.17 Although positioning a prosthesis above the annulus could result in placement of the fabric cuff at the level of the coronary ostia, any resulting obstruction seems unlikely because the diameter of the stent is less than that of the sinus of Valsalva. However, the prosthesis can displace a bulky native coronary leaflet over a coronary ostium.17 An unusually bulky leaflet may represent a relative contraindication to implantation of a valved stent. Because the native calcified leaflets were removed from the hemodynamic stresses of the bloodstream, it is likely that further growth of the native leaflets will cease. Indeed, the calcium may possibly be reabsorbed and affect long-term valve fixation. Assessment of coronary patency seems prudent after implantation; in some cases, however, overlying stent struts may interfere with selective coronary intubation.

Valvuloplasty data suggest that stroke is a surprisingly infrequent occurrence despite heavy aortic valve calcification.6,22 It is likely that the calcific debris familiar to surgeons replacing the aortic valve results from violation of the aortic valve endothelium when the valve is resected. If this covering is kept intact during valvuloplasty and valve deployment, embolization does not occur, despite displacement or even crumbling of the calcium within this covering.

Potential complications unique to this procedure include a significant incidence of perivalvular leak. Myocardial perforation or mitral or aortic trauma could occur from misdirected stiff catheters. Extensive surgical experience with venting of the left ventricle and commissurotomy of the mitral valve via the apex would suggest that apical access can be managed safely without excessive blood loss or subsequent arrhythmogenic potential.

As currently conceived, this procedure crosses the traditional boundaries of the catheterization laboratory and operating room. The skills required for apical exposure and repair

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**TABLE 3. Echocardiographic Characteristics**

<table>
<thead>
<tr>
<th>Echocardiographic Parameter*</th>
<th>Before the Procedure†</th>
<th>After the Procedure†</th>
<th>At 1 Month‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic valve area, mm</td>
<td>0.7±0.1</td>
<td>1.8±0.8</td>
<td>1.6±0.7</td>
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<tr>
<td>Mean aortic gradient</td>
<td>31±10</td>
<td>9±6</td>
<td>7±10</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>50±10</td>
<td>50±20</td>
<td>50±20</td>
</tr>
<tr>
<td>Aortic regurgitation (grade 1–4)</td>
<td>1±1</td>
<td>1±1</td>
<td>2±1</td>
</tr>
<tr>
<td>Mitral regurgitation (grade 1–4)</td>
<td>3±2</td>
<td>2±3</td>
<td>2±1</td>
</tr>
</tbody>
</table>

*Median±interquartile range.
†Number of patients=7.
‡Number of patients=6. (One patient died before the 1-month follow-up.)
are those of the surgeon, and the skills required for transcatheter implantation and angiography are those of the interventional cardiologist. Although patients in this report were not considered candidates for, and did not require, cardiopulmonary bypass, it is possible to envision a situation in which conversion to traditional surgery might be required to deal with unforeseen complications. Similarly, should valve embolization or coronary compromise occur at the time of deployment, interventional management may be required.17 Successful replication of this favorable experience will likely require a practiced team approach to implementation.

Conclusions

Catheter-based aortic valve implantation is feasible through a minimally invasive apical approach without the need for cardiopulmonary bypass. This technique represents a new alternative for patients in whom open heart surgery or percutaneous procedures are not feasible or for patients who pose unacceptable risks.

Disclosures

Drs Webb, Carere, and Thompson have acted as consultants to and received honoraria from Edwards Lifesciences, Irvine, Calif. Dr Webb received funding from Edwards Lifesciences for the REVIVE trial. The other authors report no conflicts.

References


CLINICAL PERSPECTIVE

Aortic valve replacement with cardiopulmonary bypass carries a significant risk of morbidity and mortality, particularly in patients with comorbidities. Percutaneous transcatheter valve implantation via the femoral artery has been shown to be a viable alternative. The present study describes our initial experience with another catheter-based approach to aortic valve implantation using direct left ventricular apical puncture. Transapical transcatheter valve implantation without cardiopulmonary bypass or sternotomy was successfully performed in 7 patients in whom surgical risk was prohibitive. At 1 month, 6 of 7 patients remain alive with good prosthetic valve function. Transapical transcatheter valve implantation is a potential alternative for patients with aortic stenosis.
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