Acute Improvement in Global and Regional Left Ventricular Systolic Function After Percutaneous Heart Valve Implantation in Patients With Symptomatic Aortic Stenosis

Fabrice Bauer, MD; Hélène Eltchaninoff, MD; Christophe Tron, MD; Pierre-François Lesault, MD; Carla Agatiello, MD; Deborah Nercolini, MD; Geneviève Derumeaux, MD; Alain Cribier, MD

Background—The newly developed percutaneous heart valve (PHV) implantation technique decreases transaortic pressure gradient in patients with aortic stenosis. PHV replacement effects on left ventricular (LV) global and regional systolic function are currently unknown.

Methods and Results—Eight patients with severe aortic stenosis had 2D echocardiography at baseline and 24 hours after PHV implantation to evaluate changes in LV volume and LV ejection fraction. Regional function, ie, both peak systolic anterior and posterior wall tissue velocity, as well as strain and strain rate imaging, were measured by tissue Doppler imaging from a short-axis view. At 24 hours, a significant reduction in transaortic mean pressure gradient (from 46±15 to 8±3 mm Hg; P<0.0001) was accompanied by an increase in aortic valve area (from 0.59±0.11 to 1.69±0.11 cm²; P<0.0001). LV end-diastolic volume remained unchanged (102±36 to 101±12 mL; P=NS), whereas LV ejection fraction increased (48±18% to 57±12%; P<0.01). Improvement in posterior wall displacement (posterior wall tissue velocity increased from 2.2±0.5 to 4.4±1.0 cm/s; P=0.0003) and deformation (strain rate imaging increased from 1.0±0.3 to 1.9±0.7 s⁻¹; P=0.009, and strain increased from 11±5% to 17±9%; P=0.02) were observed.

Conclusions—Immediately after PHV replacement, improvement of LV global and regional systolic function was evidenced by tissue Doppler imaging. (Circulation. 2004;110:1473-1476.)

Key Words: systole ■ aorta ■ stenosis ■ echocardiography ■ valves

In patients with severe aortic stenosis (AS), subclinical systolic abnormalities are underestimated and may contribute to symptoms despite normal ejection fraction. Abnormal left ventricular (LV) systolic function starts at early stage of the disease, with reduction of regional deformation secondary to extensive remodeling of the extracellular matrix leading to hypertrophy and ultimately to depressed LV ejection fraction. This is related to the critical afterload imposed by the aortic valve stenosis. Tissue Doppler imaging is one of the most appropriate ultrasound technologies capable of detecting any clinical and subclinical regional LV dysfunction in numerous diseases using displacement and deformation indices.¹³

By reducing transaortic pressure gradient, percutaneous heart valve (PHV) implantation successfully cures LV elevated afterload in patients with AS.¹ However, its effects on LV systolic function are unknown. We therefore applied tissue Doppler imaging to detect subtle improvement in global and regional LV systolic function immediately after PHV implantation.

Methods

The protocol was approved by a local, national, and international board. All patients gave written informed consent before participation. Subjects had an aortic valve area <0.7 cm².

Eight consecutive AS patients who were symptomatic despite maximal medical therapy underwent PHV implantation after being declined by 2 independent surgeons due to hemodynamic instability and associated severe comorbidities. Twenty-four hours before PHV implantation, transhotoracic 2D and Doppler echocardiography was performed. The day of aortic valve implantation, aortic catheterization was carried out simultaneously with LV catheterization. On the pressure tracings, aortic systolic pressure, aortic diastolic pressure, peak systolic LV pressure, and LV end-diastolic pressure were measured. Peak-to-peak and mean systolic transaortic pressure were determined. Nonsurgical aortic valve replacement procedure has been described elsewhere.⁵⁻⁶ In 6 cases, the anterograde transseptal approach was used, whereas in 2 cases, the retrograde arterial method was used. Briefly, a stiff 0.035-inch guide wire was engaged through the native aortic valve, and then the PHV was advanced over the wire within the stenotic native valve. After optimal positioning, the prosthetic heart valve was delivered by maximal balloon inflation, 23 mm in diameter, under fast cardiac pacing (220 bpm) to decrease the blood flow and help stabilize the balloon/PHV assembly during inflation. Hemodynamic parameters and transhotoracic echocardiography were reiterated immediately after PHV implantation. Transhotoracic echocardiography was repeated 24 hours after the procedure.

Echocardiographic Studies

Parasternal and apical views were obtained by use of a VingMed ultrasound system. For echocardiographic acquisition, parameters...
were averaged during 3 to 5 cardiac cycles. LV outflow tract pulsed-Doppler spectrum as well as transaortic Doppler spectrum in the 5-chamber view were acquired for velocity recording. Posterior and anterior wall velocities (3 cycles) were recorded with 2D color tissue Doppler imaging at a frame rate averaging 110 frames per second.

**Echocardiographic Analysis**

A single observer performed the analysis online for conventional echocardiographic parameters and offline for tissue Doppler measurements using a workstation (EchoPac software). Measurements included LV end-systolic and end-diastolic volumes and LV ejection fraction. LV outflow tract cross-sectional area (CSA) was determined from the parasternal long-axis view. Aortic valve was analyzed for velocity time integral (TVIAo), mean pressure gradient, and peak pressure gradient derived from the modified Bernoulli equation; peak pressure gradient=$4v^2$, where $v$ (m/s) is transaortic peak velocity. LV outflow tract was interrogated for velocity time integral (TVIlvot). Aortic valve area by echocardiography (AVA) was calculated from the continuity equation: AVA=$(CSA\times TVIlvot)/TVIAo$.

For tissue Doppler velocity measurement, sample volumes were placed at the posterior and the anterior wall from the parasternal short-axis views. Strain rate imaging and strain were determined as described previously. An offset of 10.8 mm was used for both strain studies. Tissue velocity, strain rate imaging, and strain curves were calculated from exactly the same sample volume. We therefore measured peak systolic tissue velocity, peak systolic strain rate imaging (SRIps), and peak systolic strain (Sps) (Figure 1).

**Statistics**

Preimplantation and postimplantation data were compared by paired t test. Significance was set at $P<0.05$.

**Results**

Mean age was 82.6±3.3 years (range, 77 to 88 years; 6 women). All patients were in NYHA class IV, with 2 patients in cardiogenic shock. By echocardiography, all patients had severe AS, with AVA averaging 0.59±0.11 cm². Peak pressure gradient and mean pressure gradient were 78±19 and 46±15 mm Hg, respectively. LV ejection fraction averaged 48±18% (range, 22% to 73%), and LV ejection fraction was lower than 45% in 3 patients. Nonsurgical aortic valve replacement was successfully achieved in all patients.

**Changes in Hemodynamics and Aortic Valve Properties After PHV Implantation**

All data are summarized in the Table. There were no changes in aortic systolic and diastolic pressures or in heart rate, whereas LV systolic and LV end-diastolic pressures significantly decreased after PHV implantation. Immediately after

**Acute Changes in Aortic Pressure, LV Hemodynamics, and Echocardiographic Parameters Before and After PHV Implantation**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>24 Hours After PHV Implantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, bpm</td>
<td>73±11</td>
<td>91±24</td>
</tr>
<tr>
<td>Invasive data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic systolic pressure, mm Hg</td>
<td>112±10</td>
<td>124±11</td>
</tr>
<tr>
<td>Aortic diastolic pressure, mm Hg</td>
<td>64±9</td>
<td>64±13</td>
</tr>
<tr>
<td>LV systolic pressure, mm Hg</td>
<td>165±27</td>
<td>131±30*</td>
</tr>
<tr>
<td>LV end-diastolic pressure, mm Hg</td>
<td>9±5</td>
<td>7±4*</td>
</tr>
<tr>
<td>Peak-to-peak pressure gradient, mm Hg</td>
<td>49±6</td>
<td>5±3*</td>
</tr>
<tr>
<td>Mean pressure gradient, mm Hg</td>
<td>45±12</td>
<td>3±2*</td>
</tr>
<tr>
<td>Echocardiographic data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak pressure gradient, mm Hg</td>
<td>78±19</td>
<td>20±7*</td>
</tr>
<tr>
<td>Mean pressure gradient, mm Hg</td>
<td>46±15</td>
<td>8±3*</td>
</tr>
<tr>
<td>LV end-systolic volume, mm Hg</td>
<td>102±36</td>
<td>101±12</td>
</tr>
<tr>
<td>LV end-diastolic volume, mm Hg</td>
<td>49±25</td>
<td>45±17</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>48±18</td>
<td>57±12*</td>
</tr>
<tr>
<td>&lt;45% (n=3), %</td>
<td>29±5</td>
<td>43±4*</td>
</tr>
<tr>
<td>&gt;45% (n=5), %</td>
<td>60±11</td>
<td>65±7</td>
</tr>
<tr>
<td>Aortic valve area, cm²</td>
<td>0.59±0.11</td>
<td>1.69±0.11*</td>
</tr>
</tbody>
</table>

*$P<0.05$. 

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**Figure 1.** Top, Baseline; bottom, 24 hours. Peak systolic velocity (A), peak systolic strain rate imaging (B), and peak systolic strain (C) increase (arrows). Top, Before PHV implantation. Bottom, After PHV implantation.
the procedure, transaortic peak pressure gradient by echocardiography was significantly reduced (20±7 mm Hg; P<0.01), as was mean pressure gradient (8±3 mm Hg; P<0.0001) with concomitant increase in AVA (1.69±0.11 cm$^2$, P<0.0001).

Changes in Global and Regional Systolic Function
LV end-diastolic and end-systolic volumes were unchanged, but LV ejection fraction increased from 48±18% to 57±12% (P<0.01) at follow-up (Table). Improvement in LV ejection fraction was obvious in patients with low ejection fraction.

Peak systolic tissue velocity was significantly improved at LV posterior wall, whereas it was relatively unchanged at LV anterior wall (2.2±0.5 before versus 4.4±1.0 cm/s$^{-1}$ after procedure, P=0.0003, and 2.1±1.1 before versus 2.8±1.5 cm/s$^{-1}$ after procedure, P=0.29, respectively; Figures 1A and 2A).

SRPs was significantly enhanced in all patients both at LV posterior and anterior wall (1.0±0.3 before versus 1.9±0.7 cm/s$^{-1}$ after procedure, P=0.009; 0.8±0.5 before versus 1.5±0.3 cm/s$^{-1}$ after procedure, P=0.002, respectively; Figures 1B and 2B). Similarly, improvement of Sps was evidenced in all patients but 1 at both LV posterior and anterior wall (11±5% before versus 17±9% after procedure, P=0.02; 11±9% before versus 18±7% after procedure, P=0.02, respectively; Figures 1C and 2C).

Five patients were alive at 1-month follow-up. By ANOVA, they had persistent improvement in SRPs and Sps at LV posterior wall (1.7±0.5 s$^{-1}$ and 17±3%, P<0.05, respectively) and anterior wall (1.6±0.3 s$^{-1}$ and 19±5%, P<0.05, respectively).

Discussion
Systolic Function in Patients With Aortic Stenosis
In the evolving course of AS, patients frequently have global LV dysfunction, evidenced by echocardiographic low ejection fraction. Recently, subclinical LV systolic dysfunction by tissue Doppler imaging was found in patients with AS despite good ejection fraction. Displacement and deformation of some LV regional portions were significantly decreased compared with baseline. The progressive accumulation of interstitial collagen fibers in hypertrophied left ventricle, in parallel to an increase in heart weight, contributes to a spectrum of regional ventricular dysfunction involving either the diastolic or systolic phase of the cardiac cycle. This phenomenon precedes the global LV dysfunction.

Conventional echocardiography is appropriate to detect global LV dysfunction but not subclinical systolic abnormalities. Sensitivity of tissue Doppler imaging is superior and is now being used to evidence regional systolic dysfunction at early stages of pressure-overloaded left ventricle before ejection fraction deteriorates. Patients with essential hypertension and normal ejection fraction have reduced LV longitudinal function. In patients with AS, the degree of abnormality in regional deformation correlates with aortic valve area.

Reversibility of Systolic Dysfunction After PHV Implantation
Surgical aortic valve replacement favorably modifies LV remodeling by immediate fall in afterload at early stage and later on corrects the neurohormonal imbalance. Improvement in LV ejection fraction is apparent in patients with low LV ejection fraction before surgery exhibiting a contractile
reserve under dobutamine test but less remarkable in patients with normal ejection fraction based on conventional 2D echocardiography study. Tissue Doppler imaging is preferable to analyzes subtle changes in systolic function at a time when ejection fraction remains normal. In pressure-overloaded rats with normal usual indices of systolic function, Derumeaux et al demonstrated early abnormal regional LV systolic function, i.e., deformation. Recovery in regional deformation was apparent at early but not late debanding. Such findings have never been reported in humans.

Percutaneous valve replacement is a new promising technique introduced as an alternative to surgical aortic valve replacement in a subset of nonsurgical patients with AS. We demonstrated in the present study significant improvement in global and regional LV function as soon as PHV implantation, even in patients with low ejection fraction. This improvement 24 hours after the procedure suggests the main influence of afterload on regional systolic function. Although our population was not compared with age-matched controls, strain rate imaging and strain did not normalized after valve implantation. Improvement in regional deformation is limited by the collagen content that correlates directly to the severity and the duration of the disease, which makes the regional systolic function partially reversible at short-term follow-up.

In conclusion, percutaneous aortic valve replacement is characterized by an immediate enhancement of global and regional systolic function, even in patients with low ejection fraction. In a attempt to confirm our findings, global and regional systolic function should be explored over time and correlated to functional class and quality of life.

References
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/content/111/3/378.3.full.pdf

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In the article by Huynh et al, “Aspirin, Warfarin, or the Combination for Secondary Prevention of Coronary Events in Patients With Acute Coronary Syndromes and Prior Coronary Artery Bypass Surgery,” which published in the June 26, 2001, issue (*Circulation*. 2001;103:3069–3074), the authors now realize errors appeared in Tables 3 and 4. The percentages of events and complications were presented on the basis of the number of patients’ visits rather than on the total number of patients.

Overall, the corrected results did not change the implication of the study. There was no benefit of warfarin alone or combined with aspirin in the secondary prevention of ischemic events in this study of patients with previous coronary artery bypass surgery and an acute coronary syndrome; there was a significant excess in minor bleeding compared with the aspirin-alone group.

Corrected versions of Tables 3 and 4 appear below.

### TABLE 3. End-Point Events According to Treatment

<table>
<thead>
<tr>
<th>Events</th>
<th>Warfarin + Placebo (n=45)</th>
<th>Aspirin + Placebo (n=46)</th>
<th>Warfarin + Aspirin (n=44)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary end point, n (%)</td>
<td>18 (40.0)</td>
<td>13 (28.3)</td>
<td>11 (25.0)</td>
<td>0.27</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>1 (2.2)</td>
<td>0 (0.0)</td>
<td>2 (4.5)</td>
<td>0.34</td>
</tr>
<tr>
<td>MI, n (%)</td>
<td>4 (8.9)</td>
<td>1 (2.2)</td>
<td>2 (4.5)</td>
<td>0.34</td>
</tr>
<tr>
<td>UA, n (%)</td>
<td>16 (35.6)</td>
<td>13 (28.3)</td>
<td>10 (22.7)</td>
<td>0.41</td>
</tr>
<tr>
<td>PCI, n (%)</td>
<td>6 (13.3)</td>
<td>1 (2.2)</td>
<td>3 (6.8)</td>
<td>0.12</td>
</tr>
<tr>
<td>Repeat CABG, n (%)</td>
<td>2 (4.4)</td>
<td>2 (4.3)</td>
<td>2 (4.5)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

UA indicates unstable angina requiring rehospitalization; PCI, percutaneous coronary intervention; and MI, myocardial infarction. Primary end point is any-cause mortality, MI, or UA requiring hospitalization.

### TABLE 4. Complications and Adherence to Protocol by Patients

<table>
<thead>
<tr>
<th>Complications</th>
<th>Warfarin + Placebo (n=45)</th>
<th>Aspirin + Placebo (n=46)</th>
<th>Warfarin + Aspirin (n=44)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor bleeding, n (%)</td>
<td>10 (22.2)</td>
<td>2 (4.3)</td>
<td>9 (20.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>Major bleeding, n (%)</td>
<td>1 (2.2)</td>
<td>0 (0.0)</td>
<td>2 (4.5)</td>
<td>0.34</td>
</tr>
<tr>
<td>Blood transfusions, n (%)</td>
<td>2 (4.4)</td>
<td>0 (0.0)</td>
<td>2 (4.5)</td>
<td>0.34</td>
</tr>
<tr>
<td>Compliance, %*</td>
<td>90.1</td>
<td>86.7</td>
<td>86.1</td>
<td>0.66</td>
</tr>
<tr>
<td>Protocol completion, %*</td>
<td>77.6</td>
<td>78.5</td>
<td>69.9</td>
<td>0.22</td>
</tr>
</tbody>
</table>

*Compliance and protocol completion were calculated per visit.

DOI: 10.1161/01.CIR.00000155489.11621.70
In the article by Haïssaguerre et al, “Mapping and Ablation of Ventricular Fibrillation Associated With Long-QT and Brugada Syndromes,” which appeared in the August 26, 2003, issue (Circulation. 2003;108:925–928), the authors would like to note the following errors:

1. In the byline, Jerónimo Farré’s name incorrectly appeared as “Gerónimo Farre.”
2. José Angel Cabrera and Jerónimo Farré work at Fundación Jiménez Díaz in Madrid, Spain.
3. The work of Drs Cabrera and Farré was supported by Redes Temáticas de Cooperación, Red Cardiovascular C01/03.

In the article by McRae and Ginsberg, “Initial Treatment of Venous Thromboembolism,” which appeared in the August 31, 2004, supplement sponsored by the Society for Vascular Medicine and Biology (Circulation. 2004;110[suppl I]:I-3–I-9), an error appeared in Table 2. The footnote of the table erroneously states that “For enoxaparin, 100 anti-Xa U/kg corresponds to a dose of 100 mg/kg.” The legend should have read, “For enoxaparin, 100 anti-Xa U/kg corresponds to a dose of 1 mg/kg.”

In the article by Bauer et al, “Acute Improvement in Global and Regional Left Ventricular Systolic Function After Percutaneous Heart Valve Implantation in Patients With Symptomatic Aortic Stenosis,” which appeared in the September 14, 2004, issue (Circulation. 2004;110:1473–1476), two errors of note appeared in the table on page 1474. Under “Endocardiographic data,” the rows for “LV end-systolic volume, mm Hg” and “LV end-diastolic volume, mm Hg” should have appeared as the following:

<table>
<thead>
<tr>
<th>LV end-diastolic volume, mL</th>
<th>102±36 (baseline)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV end-systolic volume, mL</td>
<td>49±25 (baseline)</td>
</tr>
</tbody>
</table>

In the AHA Scientific Statement by Drew et al, “Practice Standards for Electrocardiographic Monitoring in Hospital Settings: An American Heart Association Scientific Statement From the Councils on Cardiovascular Nursing, Clinical Cardiology, and Cardiovascular Disease in the Young,” which appeared in the October 26, 2004, issue (Circulation. 2004;110:2721–2746), Figure 4 contained an error. The text in the figure refers to the “Angle of Lewis.” The correct name is “Angle of Louis.” The Association regrets this error.
In the article by Noujaim et al, “From Mouse to Whale: A Universal Scaling Relation for the PR Interval of the Electrocardiogram of Mammals,” which appeared in the November 2, 2004, issue (Circulation. 2004;110:2802–2808), the name of Ary L. Goldberger, MD, was misspelled as “Goldberg” in reference 12. The authors regret this error.

DOI: 10.1161/01.CIR.0000155482.89456.78

In the article by Spargias et al, “Ascorbic Acid Prevents Contrast-Mediated Nephropathy in Patients With Renal Dysfunction Undergoing Coronary Angiography or Intervention,” which appeared in the November 2, 2004, issue (Circulation. 2004;110:2837–2842), the name of author Panagiotis Iokovis was spelled incorrectly as “Panagiotis Iocovis.” The authors regret this error.

DOI: 10.1161/01.CIR.0000155487.34492.0D


DOI: 10.1161/01.CIR.0000155488.34492.E9