Prospectively Randomized Evaluation of Stentless Versus Conventional Biological Aortic Valves

Impact on Early Regression of Left Ventricular Hypertrophy

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Background—The aim of this prospectively randomized study was to evaluate left ventricular hypertrophy and its regression after stentless versus conventional biological aortic valve replacement.

Methods and Results—From March 1996 through April 1998, 180 patients were prospectively selected; 106 patients received a stentless aortic valve (SAV), and 74 received a conventional stented bioprosthesis (CSB). Of these patients, 95% and 96%, respectively, had aortic stenosis. Their mean age was 72.3 and 74.8 years, and there were no significant differences in left ventricular function, preoperative pressure gradients, and NYHA functional status. Aortic annulus diameter indexes were comparable at 13.46 (SAV) versus 13.55 (CSB) mm ($P=\text{NS}$). Larger SAVs were implanted because of the oversizing technique. In-hospital mortality ($n=3$ and 1 for SAV and CSB) was not valve related. At follow-up, all patients were in NYHA class 1 or 2. Baseline end-diastolic left ventricular posterior wall thickness was 15.6 (SAV) and 14.8 (CSB) mm ($P=\text{NS}$) and decreased to 11.8 (SAV) and 13.2 (CSB) mm ($P<0.05$) at 6 months. Left ventricular mass index was 213 and 202 g/m$^2$ at baseline ($P=\text{NS}$), whereas after 6 months, it was 141 (SAV) and 170 (CSB) g/m$^2$ ($P<0.05$).

Conclusions—Regression of left ventricular hypertrophy occurs in all patients after aortic valve replacement but is significantly enhanced after SAV implantation. This possibly is due to improved transvalvular hemodynamics. (Circulation. 1999;100[suppl II]:II-6–II-10.)

Key Words: valves ■ echocardiography ■ hypertrophy ■ stentless bioprosthesis

In patients with aortic stenosis, left ventricular hypertrophy (LVH) develops as an adaptation to the increased pressure load. Being an independent cardiac risk factor, LVH is associated with a higher incidence of cardiovascular clinical events and death.1 Regression of LVH occurs after aortic valve replacement (AVR), but little is known about the impact of the type of prosthetic aortic valve implanted. None of the currently available artificial heart valves provides all functional properties of the native valve.2,3 Nevertheless, in addition to conventional stented bioprostheses (CSBs), stentless aortic valves (SAVs) have been used increasingly with good functional and hemodynamic results during the past 10 years.4–8 In longitudinal studies, early LVH regression after stentless valve implantation has been demonstrated.9,10 However, none of these trials was randomized. The aim of this prospectively randomized study was to evaluate the course of LVH regression after stentless versus conventional AVR.

Methods

From March 1996 through April 1998, 180 patients with aortic valve disease were prospectively evaluated. The study was approved by the local ethics committee, and all patients gave informed consent after the study protocol was outlined in detail.

Patients amenable for bioprosthetic aortic valve implantation were randomized to receive an SAV, either Freestyle (Medtronic Inc) or Toronto SPV (St Jude Medical Inc), or a CSB, a Carpentier Edwards porcine valve (Baxter Healthcare Inc). Follow-up was performed at our outpatient clinic after 6 months. No patient was lost to follow-up. Because of longer distances to the hospital, 15% of the patients were followed up by their family physicians. At all visits, patients were assessed for functional state and quality of life through the specific activity questionnaire11 and had routine transthoracic echocardiography (TTE).

Patient Population

We included 180 patients in the study from March 1996 through April 1998. Of these, 74 patients received CSBs and 106 patients received SAVs (Freestyle, $n=49$; Toronto, $n=57$). The patients were randomized after preoperative echocardiographic examination. Severe calcification of the aortic sinuses diagnosed intraoperatively, very low coronary ostia in relation to the annulus, and atypical insertion of the coronary ostia made it impossible to implant stentless valves. These patients were excluded, which explains the differences in group sizes.

Patient age was 74.8±4 (CSB) and 72.3±7 (SAV) years ($P<0.05$). Roughly half of the patients (54% receiving CSBs and
50% receiving SAVs) were female. The preoperative NYHA class was 2.6±0.6 (CSB) versus 2.6±0.6 (SAV) (P=NS).

The predominant aortic valve lesion was stenosis in 96% and 95% for CSB and SAV, and left ventricular ejection fraction assessed by angiography was 57±15% and 59±16% (P=NS). Maximum preoperative transaortic pressure gradients were 81±25 and 76±25 mm Hg (P=NS). Preoperative body surface area was 1.74±0.2 (CSB) and 1.82±0.2 m² (SAV) (P<0.05).

**Surgery**

All operations were performed with the use of complete or partial median sternotomy and standard extracorporeal circulation with hypothermic cardiopulmonary arrest (Bretschneider HTK solution, Kohler Chemie).

For further comparison, aortic annulus diameter was measured intraoperatively by use of a standard set of sizers before the new valve was implanted.1,12 This was performed after excision of the diseased aortic valve and after complete decalcification. Annulus diameter was divided by body surface area to obtain the annulus index as a baseline value.

Aortic valve implantation was performed according to standard techniques as described previously.1,13 SAV implantation was performed with single 4-0 Tvedek stitches at the annulus without pledgets and a continuous 4-0 Prolene suture line at the commissures. CSBs were implanted in a supra-annular position with 2-0 Teflon armed U stitches.

**Echocardiography**

The System Five (Sonotron Vingmed) was used by 2 experienced echocardiographers at standard views. Cardiac morphology (chamber and wall sizes, wall motion, valve structure) and function (fractional shortening, ejection fraction with the Simpson method) and transvalvular hemodynamics with Doppler and color Doppler were assessed. Intraoperative TEE was applied to confirm the underlying pathology and to control postoperative valve and ventricular function.

All hemodynamic measurements were performed with patients in stable conditions. Aortic valve flow velocities were assessed by use of continuous-wave Doppler. Transvalvular pressure gradients were calculated using the Bernoulli equation with correction for left ventricular outflow tract velocities.14 End-diastolic left ventricular posterior wall thickness >12 mm was considered hypertrophied; left ventricular mass was calculated with a standard formula.14 Aortic valve incompetence was judged as transvalvular or paravalvular and graded according to the regurgitant jet area in relation to left ventricle as mild (<20%), moderate (20% to 40%), or severe (>40%).

**Statistical Analysis**

Absolute and relative frequencies were calculated. Results are given as mean±SD. After tests for normal distribution, Student’s t test for matched pairs or independent samples was applied. A value of P<0.05 was considered significant. The χ² test was used for comparison of outcome variables. Postoperative valve-related morbidity and mortality were evaluated according to standard guidelines.15

**Results**

After decalcification, the annulus diameter was 24.4±2.2 (SAV) and 23.5±2 (CSB) mm. Consequently, the aortic annulus index was 13.46±1.3 (SAV) and 13.55±1.6 (CSB) mm (P=NS). Larger SAVs than CSBs were implanted; mean valve diameters were 25±2 and 23.2±2 mm (P<0.05). For implantation of stentless valves, longer aortic cross-clamp time was required, 75±19 and 55±13 minutes (P<0.05).

**Surgical Outcome, Morbidity, and Mortality**

All patients were safely transferred to ICU. Rethoracotomy for bleeding had to be performed in a total of 5 patients, 3 after SAV and 2 after CSB implantation (P=NS). One of these patients required prolonged mechanical ventilation; all others had an uneventful recovery. Extubation was performed after a median of 9 and 10 hours, respectively. Reintubation for respiratory failure had to be performed in 3 patients, all on the first postoperative day. Severe ventricular arrhythmias requiring intravenous antiarrhythmic therapy occurred in 2 patients each. New-onset AV block was seen in 11 (SAV) and 7 (CSB) patients postoperatively (P=NS). In 7 and 4 patients, regular conduction was completely restored after a maximum of 5 days as documented by 24-hour ECG. The remaining 4 (SAV) and 3 (CSB) patients required permanent pacemaker implantation before discharge. These patients had heavily calcified aortic annuli requiring extensive decalcification. Transient confusion was observed in 3 and 2 patients; it had resolved until the third postoperative day in all of them.

There were 4 in-hospital deaths, 3 after SAV, all not valve related. Causes of death were respiratory failure requiring prolonged mechanical ventilation and subsequent pneumonia in 1, prolonged ICU stay because of low cardiac output syndrome complicated by multiple organ failure in 2, and intraoperative stroke with severe progressive neurological deficit in 1 patient. At early follow-up, 2 patients had died (1 after SAV, 1 after CSB), both because of malignancies. Thus far, no thromboembolic or hemorrhagic events or endocarditis occurred. At 6 months, 1 patient in each group presented with new-onset moderate to severe paravalvular incompetence. On reoperation, torn sutures were found in both patients at sites where the aortic annulus had significant calcification.

**Postoperative Hospital Stay and Follow-Up**

All other patients were discharged from the hospital in time according to the German standards of postoperative cardiac care. Wound healing was uneventful in all patients. After stentless valve implantation, permanent anticoagulation with warfarin was prescribed only if additional atrial fibrillation was present. Patients in the conventional group received a 3-month course of warfarin. Because there have been no problems regarding thromboembolic events, this protocol was recently changed. Currently, no patient receives systemic anticoagulation therapy. At discharge, 84% (SAV) and 79% (CSB) were in stable sinus rhythm. At follow-up, all patients had clinically improved and tolerated more physical activities at no or only little dyspnea. NYHA functional class was 1.1±0.4 (SAV) and 1.1±0.3 (CSB) (P=NS). The specific activity questionnaire had improved in all patients, to 5.5±1 (SAV) and 5±1 (CSB).

**Echocardiography**

Intraoperatively perfect SAV function with central valve closure was seen in all patients. Trivial transvalvular incompetence (closing volume) was present in 7%. The typical laminar systolic transvalvular flow profile after SAV compared CSB implantation is demonstrated in the Figure.
Postoperative TTE was performed on the fifth to seventh day. Good views were obtained in 85% (SAV) and 84% (CSB) of the patients, and moderately good views were obtained in 12% and 11%. In 3% and 5%, only part of the measurements could be performed because of imperfect visualization. TTE revealed normal aortic valve function in all patients postoperatively.

Maximum transaortic blood flow velocities were 2.33 ± 0.5 (SAV) and 2.47 ± 0.5 (CSB) m/s (P = NS) postoperatively. At follow-up, they had decreased to 2.23 ± 0.4 and 2.43 ± 0.4 m/s (P < 0.05). Postoperative maximum transvalvular pressure gradients were lower after stentless valve implantation without reaching significance at that time (18.1 ± 9 and 20.8 ± 9 mm Hg). At 6 months, maximum transvalvular pressure gradients were 16.7 ± 7.7 (SAV) and 20.1 ± 7.3 (CSB) mm Hg (P < 0.05). Calculated cardiac indexes were 2.6 ± 1 (SAV) and 2.8 ± 1 (CSB) L · min⁻¹ · m⁻² postoperatively (P = NS); after 6 months, they were 3.2 ± 1 and 3.0 ± 1 L · min⁻¹ · m⁻² (P = NS).

Measurements of end-diastolic left ventricular posterior wall diameter are given in Table 1. There was a significant difference in favor of SAVs after 6 months, reaching almost normal diameters. In Table 2, left ventricular mass indexes are shown. No relevant difference was seen postoperatively, whereas left ventricular mass index was significantly lower after SAV implantation at follow-up.

**Discussion**

Despite good clinical results, the obstructive nature of a stent has a negative impact on biological valve performance. SAVs were reintroduced in 1997 to yield a more ideal prosthesis, and encouraging results have been report-

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**TABLE 1.** Left Ventricular Posterior Wall Thickness During Diastole From Parasternal M-Mode Echocardiography

<table>
<thead>
<tr>
<th></th>
<th>CSB</th>
<th>P</th>
<th>SAV</th>
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<tbody>
<tr>
<td>Postoperative</td>
<td>14.8 ± 2.4</td>
<td>NS</td>
<td>15.6 ± 2.4</td>
</tr>
<tr>
<td>P &lt; 0.05</td>
<td></td>
<td>P &lt; 0.05</td>
<td></td>
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<tr>
<td>6-mo follow-up</td>
<td>13.2 ± 2.4</td>
<td>&lt; 0.05</td>
<td>11.8 ± 2.5</td>
</tr>
</tbody>
</table>

Results are given for SAV versus CSB postoperatively and after 6 months of follow-up.

**TABLE 2.** Left Ventricular Mass From Parasternal M-Mode Echocardiography Indexed for Body Surface Area

<table>
<thead>
<tr>
<th></th>
<th>CSB</th>
<th>SAV</th>
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<tbody>
<tr>
<td>Postoperative</td>
<td>202 ± 72</td>
<td>NS</td>
</tr>
<tr>
<td>P &lt; 0.05</td>
<td></td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>6-mo follow-up</td>
<td>170 ± 43</td>
<td>&lt; 0.05</td>
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Results are given for SAV versus CSB postoperatively and after 6 months of follow-up.
In combination with effective anticalcification treatments, SAVs may become the first choice in future.

**Aortic Stenosis and LVH**

LVH as present in aortic stenosis correlates with overall cardiovascular morbidity and mortality, especially that caused by congestive heart failure, sudden death, myocardial infarction, and stroke. Regression of LVH has been reported after conventional stented AVR. Nevertheless, incomplete regression of LVH was shown to be associated with decreased survival. Incomplete regression of LVH may be related to the obstruction caused by the stent or to the nonflexible annulus. By enhancing LVH regression, stentless valves may lead to a decreased postoperative risk and thus improved long-term outcome for patients.

Our own initial results compared with stented mechanical and biological valves were in favor of stentless bioprostheses. In the present study, SAVs and CSBs were compared for the first time in a prospectively randomized fashion.

**Evaluation of Results**

Comparison of the SAV and CSB groups was possible and justified because there were no differences in annulus index. It has been previously shown that exact sizing of the patient’s annulus after complete decalcification is crucial for further comparison of different valves. Furthermore, the importance of indexing results after valve replacement for body surface areas has been emphasized. Thus, the concept of indexing aortic annulus diameters before further comparison of different implanted valves is helpful and is gaining increasing acceptance. This prevents differences in outcome that are related to preexisting patient-related variables rather than type of prosthetic valve. In the present study, larger SAVs than CSBs were implanted. This can be explained by 2 factors. First, the oversizing technique is used for SAV selection. Second, patients in the stentless group had slightly larger body surface areas, requiring larger implants.

The hemodynamic results are intentionally given as continuous-wave Doppler recordings of transvalvular blood flow velocities. All further data were calculated from these initial baseline measurements. In this study, postoperative instead of preoperative data were compared with follow-up results. The difference between these 2 sets of data reveals the true changes that can be attributed to the implanted valve over time.

Hemodynamic results were in favor of stentless valves. This can be easily explained by the larger effective orifice areas resulting from the lack of an obstructing stent and larger valve size selection at a given annulus diameter. From an echocardiographic perspective, stentless valves resemble native aortic valve function and can be considered close to an ideal artificial heart valve. Paravalvular leakage was not a major issue in this series and should not occur in the presence of 2 suture lines.

There were no relevant differences between the 2 groups in overall clinical outcome. Intraoperative aortic cross-clamp time was longer in the stentless group, but the overall duration was acceptable because it did not result in any excess morbidity. The operative mortality was low and not valve related.

Regression of LVH was seen in all patients after AVR. In this prospectively randomized trial, it also has been proved that use of SAVs leads to significant enhancement of LVH regression. The increase in LVH regression can be explained by better hemodynamics and the flexible design compared with conventional valves. As such, the stentless valve design allows more physiological blood flow and a larger effective orifice area at any given aortic annulus diameter. LVH was assessed with routine TTE. Nevertheless, 3-dimensional echocardiography or ultrafast MRI may result in even more exact measurements in the future.

Further follow-up must be performed to prove long-term outcome and the benefit of early LVH regression after SAV implantation.

**Conclusions**

This is the first prospectively randomized trial comparing LVH regression after stentless versus conventional biological AVR. The indexed aortic annulus diameter is essential for objective comparison of different valves. At a 6-month follow-up, hemodynamic and left ventricular morphological measurements were in favor of stentless valves. Enhanced regression of LVH after stentless AVR may be of clinical benefit for patients. When combined with effective anticalcification treatments, SAVs that resemble native valve function will be the prostheses of choice in the future.

**Acknowledgment**

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**References**


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