Aortic Valvuloplasty in Pediatric Patients Substantially Postpones the Need for Aortic Valve Surgery
A Single-Center Experience of 188 Patients After up to 17.5 Years of Follow-Up

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Background—Aortic valvuloplasty (AoVP) is an established procedure regarded as a valid alternative for surgical management of congenital aortic valve stenosis. However, its long-term efficacy in preventing or postponing aortic valve surgery remains uncertain for the individual patient. Therefore, the aim of this study was to study the long-term results of AoVP in pediatric patients and its efficacy in preventing or postponing aortic valve surgery.

Methods and Results—We reviewed up to 17.5 years of follow-up data of all 188 patients who received AoVP at the Deutsches Herzzentrum München. The patients were divided into those 1 month of age (group 1 month; n=68) and those 1 month of age (group 1 month; n=120) at the time of AoVP. After the first and second AoVP, moderate and severe aortic regurgitation developed in 29% and 14%, respectively, of the patients in group 1 month and in 19% and 29%, respectively, of the patients in group 1 month. Survival after 10 years free from aortic valve surgery was 59% (95% confidence interval, 45 to 73) in group 1 month and 70% (95% confidence interval, 59 to 81) in group 1 month.

Conclusions—This study shows that the long-term results of AoVP of congenital aortic valve stenosis in pediatric patients and its efficacy in preventing or postponing aortic valve surgery are very good. About two thirds of the patients are free from aortic valve surgery 10 years after AoVP. (Circulation. 2008;117:1201-1206.)

Key Words: aortic valve stenosis □ balloon □ catheterization □ pediatrics □ valvuloplasty

Aortic valvuloplasty (AoVP) is the therapeutic procedure of choice in most centers for the treatment of congenital aortic valve stenosis in pediatric patients,1,2 even though no randomized controlled trials have been conducted to allow a valid comparison of aortic valve surgery (surgical valvotomy, Ross operation, mechanical aortic valve replacement) and AoVP. Only 2 comparative nonrandomized controlled trials have compared surgical valvotomy and AoVP.3,4 The immediate (in the catheterization laboratory) and short-term (before discharge) results of AoVP have been well studied.5–15

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Additionally, long-term studies have well described the rapid progressive or recurrent gradient across the aortic valve and progressive aortic regurgitation after AoVP.15–18 Therefore, it is assumed that many patients require subsequent AoVP and/or aortic valve surgery after successful AoVP.2,16 However, the long-term efficacy of AoVP in preventing or postponing aortic valve surgery remains uncertain for the individual patient.2 Therefore, the aim of this study was to determine the long-term results of AoVP of congenital aortic valve stenosis in pediatric patients and its efficacy in preventing or postponing aortic valve surgery. The long-term results of AoVP were determined by reviewing up to 17.5 years of follow-up data of all 188 patients who received AoVP at the Deutsches Herzzentrum München between January 1986 and July 2004.

Methods

Starting in January 1986, AoVP has been used in our institution as the only method of treatment of pediatric aortic valve stenosis. The indication for AoVP was based on a modification of the method of Hossack et al.17 In brief, the indication for AoVP was a Doppler peak instantaneous gradient of 75 mm Hg or a smaller gradient with signs of left ventricular strain on the ECG, syncope, angina pectoris, fatigue on exercise, cardiogenic shock, low cardiac output, severe left ventricular dysfunction, or duct-dependent circulation. In 1998, the Norwood operation was introduced in our institution for treatment of hypoplastic left heart syndrome. To determine which patients would be offered a Norwood operation, criteria according to Rhodes et al.18 were used.
In most cases, percutaneous access for AoVP was retrograde via the femoral artery. Until 1994, percutaneous access was retrograde via the brachial artery. Percutaneous access was antegrade via the foramen ovale and mitral valve in only a few cases. The most important reason for the different percutaneous access was the evolution of catheters and balloons throughout the study period.

The charts of all consecutive patients who received an AoVP at our institution were reviewed. Patients with previous cardiac intervention or surgery and patients with significant cardiac malformations other than associated coarctation of the aorta were excluded. Up to July 2004, 188 consecutive patients were treated by AoVP without having a previous cardiac intervention or surgery. All 188 patients were included in this study.

All patients were divided into 2 groups: a group of patients <1 month of age (group < 1 month) and a group of patients ≥1 month of age (group ≥ 1 month) at the time of their first AoVP.

Pressure Gradient
The systolic pressure peak-to-peak gradients across the aortic valve before and immediately after the first and, if applicable, second AoVP were evaluated. Box plots were used to display the data graphically. The box of the box plots marks the 25th (first quartile) to 75th (third quartile) percentiles; the bold line within the box marks the median. The whiskers above and below the box represent the largest and smallest data points that are <1.5 box lengths (interquartile range) away from the end of the box. Open circles highlight data points >1.5 box lengths away (outliers).

Aortic Regurgitation
Aortic regurgitation before and after the first and, if applicable, second AoVP was evaluated. Aortic regurgitation was assessed echocardiographically as trivial, mild (regurgitation without a reverse diastolic flow in the aortic arch), moderate (reverse diastolic flow in the aortic arch but not in the abdominal aorta), or severe (reverse diastolic flow in the abdominal aorta). If applicable, aortic regurgitation shortly before subsequent aortic valve surgery was also evaluated.

LVEDd, LVEF, and LVFS
Left ventricular dimension at end diastole (LVEDd), left ventricular ejection fraction (LVEF), and left ventricular shortening fraction (LVFS) at the last follow-up were evaluated in all surviving patients without subsequent aortic valve surgery who were not lost to follow-up. LVEDd was measured by echocardiography as previously described.20 LVEDd was expressed as normal or >2 SD above the mean of the normal population as determined by Kampmann et al.20 LVEDd was expressed in relation to body weight in newborn infants weighing 2 to 4 kg because an increase in body weight does not lead to a concomitant increase in body surface area at that stage of life.20 LVEDd was expressed in relation to body surface area21 in older children and adults. LVEF and LVFS were measured by echocardiography as previously described.22 LVEF and LVFS were expressed as normal, larger than, or smaller than the 95% prediction interval limits determined by Henry et al.22 LVEDd, LVEF, and LVFS were obtained from archived medical records.

Survival Analyses
End points were defined as second AoVP, subsequent aortic valve surgery, and death. Median and limits of the age of the 2 groups were calculated at the time of the first AoVP and at the end points. If the last follow-up was before 2003, the patient, the parents of the patient, or the local pediatrician of the patient was contacted to ascertain that no end point had been reached. All patients, the parents of the patients, or the local pediatricians of the patients were able to be contacted. Three Kaplan–Meier survival analyses were carried out for both groups as previously described.24 For the first survival analysis, adverse events were defined as second AoVP, surgery, or death. For the second survival analysis, adverse events were defined as surgery or death. For the third survival analysis, adverse events were defined as death. Statistical analysis was performed with SPSS version 12.0.1 (SPSS Inc, Chicago, Ill).

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

Results
Sixty-eight patients (14 female patients) were in group <1 month; 120 patients (34 female patients) were in group ≥1 month (Figure 1). The age of the patients at the time of their first AoVP was a mean of 8.1 ± 7.4 days (median, 5.5; limits, 0 to 28) in group <1 month and a mean of 5.8 ± 5.9 years (median, 4.5; limits, 0.1 to 22) in group ≥ 1 month. The age of the patients at subsequent aortic valve surgery, death, or last follow-up was a mean of 4.3 ± 4.8 years (median, 2.8 years; limits, 0.0 to 17.5) in group <1 month and a mean of 12.0 ± 6.8 years (median, 12.3; limits, 0.3 to 26.5) in group ≥1 month. The time between the first AoVP and subsequent aortic valve surgery, death, or last follow-up was a mean of 4.2 ± 4.8 years (median, 2.8; limits, 0.0 to 17.5) in group <1 month and a mean of 6.3 ± 4.5 years (median, 5.7; limits, 0.0 to 16.1) in group ≥1 month.

Pressure Gradient
The systolic pressure gradient across the aortic valve immediately after the first and second AoVP decreased significantly in both groups (Figure 2). For 7 patients in group <1 month (10%) and 14 patients in group ≥1 month (12%), the systolic pressure gradient across the aortic valve progressed or recurred after the first AoVP before the second AoVP or surgery.

Aortic Regurgitation
Moderate or severe aortic regurgitation developed after the first AoVP in 20 of 68 patients in group <1 month (29%). Seven of these 20 patients were subsequently treated surgi-
cally; 1 additional patient is awaiting surgery. Of the remaining 12 patients, 4 died shortly after the first AoVP, and 8 have moderate aortic regurgitation. Of these 8 patients, 5 have normal LVEDd. Two patients have increased LVEDd but normal LVEF and LVFS. One patient was lost to follow-up. Moderate or severe aortic regurgitation developed after the first AoVP in 23 of 120 patients in group \textit{<1 month} (19%). Of these 23 patients, 11 were subsequently treated surgically. The remaining 12 patients have moderate or severe aortic regurgitation. Only 4 of these patients had LVEDd >2 SD above the mean of the normal population. All 4 patients have normal LVEF and LVFS.

Moderate or severe aortic regurgitation developed after the second AoVP in 1 of 7 patients in group \textit{<1 month} (14%) and in 4 of 14 patients in group \textit{\geq 1 month} (29%). All 5 patients were subsequently treated surgically. The indication for surgery of the aortic valve was moderate or severe aortic regurgitation in 7 of 10 patients in group \textit{<1 month} (70%) and in 15 of 27 patients in group \textit{\geq 1 month} (56%).

**LVEDd, LVEF, and LVFS**

LVEDd was available in 32 patients in group \textit{<1 month} and in 64 patients in group \textit{\geq 1 month} at follow-up. LVEDd was >2 SD above the mean of the normal population in 9 patients (28%) in group \textit{<1 month} and in 17 patients (27%) in group \textit{\geq 1 month}. LVEF was available in 22 patients in group \textit{<1 month} and in 56 patients in group \textit{\geq 1 month} at follow-up. LVEF was larger than the 95% prediction interval limits in 9 patients (41%) in group \textit{<1 month} and in 20 patients (36%) in group \textit{\geq 1 month}. LVEF was smaller than the 95% prediction interval limits in 5 patients (23%) in group \textit{<1 month} and in none of the patients (0%) in group \textit{\geq 1 month}. LVFS was available in 34 patients in group \textit{<1 month} and in 64 patients in group \textit{\geq 1 month} at follow-up. LVFS was larger than the 95% prediction interval limits in 13 patients (38%) in group \textit{<1 month} and in 21 patients (33%) in group \textit{\geq 1 month}. LVFS was smaller than the 95% prediction interval limits in 2 patients (6%) in group \textit{<1 month} and in none of the patients (0%) in group \textit{\geq 1 month}.

**Survival Analyses**

Survival free from aortic valve surgery or second AoVP is depicted in Figure 3, and survival free from surgery is depicted in Figure 4. Figure 5 shows survival.

Seventeen (25%) of the patients in group \textit{<1 month} died during follow-up. Because the Norwood operation was introduced in our institution in 1998 for treatment of hypoplastic left heart syndrome, we analyzed the mortality of group \textit{<1 month}.
month before and after 1998. Before 1998, 15 patients (22%) in group <1 month died. After 1998, 2 patients (3%) in group <1 month died. Therefore, mortality in group <1 month decreased from 38% before 1998% to 7% after 1998.

Three patients (3%) in group ≥1 month died during follow-up. The first patient, a 25-year-old woman, had a sudden death at home awaiting aortic valve replacement surgery. She had AoVP at the age of 11 years and had endocarditis with subsequent grade 3 aortic regurgitation at the age of 18 years. The second patient, a 9-month-old prematurely born male infant with multiple respiratory tract infections, died of sepsis. He had AoVP at the age of 2 months. The third patient, a 4-month-old prematurely born female infant, also died of sepsis. She had AoVP at the age of 3 months and coarctation repair at the age of 4 months and died in the postoperative course of sepsis.

**Discussion**

This study shows that the long-term results of AoVP of congenital aortic valve stenosis in pediatric patients and its efficacy in preventing or postponing aortic valve surgery are very good. Survival after 10 years free from aortic valve surgery was 59% (95% CI, 45 to 73) in group <1 month and 70% (95% CI, 59 to 81%) in group ≥1 month. The tic marks represent the times at which patients were censored; the numbers of patients at risk are displayed above the graph.

Progressive or recurrent systolic pressure gradient across the aortic valve has previously been identified as an important indication for a second AoVP. The systolic pressure gradient across the aortic valve decreased significantly after the first AoVP in both groups (Figure 2). However, in our study, only ~10% of the patients in both groups had a progressive or recurrent systolic pressure gradient leading to a second AoVP.

Aortic regurgitation has previously been identified as the main indication for aortic valve surgery after AoVP. In addition, in our study, aortic regurgitation was moderate or severe in 70% of the patients in group <1 month and 56% of the patients in group ≥1 month shortly before aortic valve surgery after AoVP. However, immediately after the first AoVP, moderate or severe aortic regurgitation developed in only 29% of the patients in group <1 month and 19% of the patients in group ≥1 month. About half of these patients were subsequently treated surgically. The other half was closely followed echocardiographically to monitor the LVEDd, LVEF, and LVFS. Even after the second AoVP, moderate or severe aortic regurgitation developed in only 14% of the patients in group <1 month and 29% of the patients in group ≥1 month. All these patients were subsequently treated surgically. It is important to note that during the study period AoVP was carried out by only 3 interventionalists. Therefore, we assume that the avoidance of a learning curve and the consistency of treatment strategy and patient selection throughout the years may have contributed to our low aortic regurgitation rates.
It is known that a significant number of patients after both AoVP\textsuperscript{13–15} and aortic valve surgery\textsuperscript{25–29} inevitably require aortic valve replacement for progressive aortic regurgitation at some point. However, no studies exist that allow a valid comparison of AoVP and aortic valve surgery. Throughout the literature, the indication for intervention and reintervention varies significantly. All studies comparing AoVP and aortic valve surgery are retrospective and nonrandomized, consist of different age groups, and use different techniques during different periods of time. Nevertheless, AoVP and aortic valve surgery seem comparable in terms of immediate gradient relief, procedural mortality, and longer-term survival.\textsuperscript{3,4,9–14,16,25–32} Therefore, both AoVP and aortic valve surgery should be seen as palliative procedures. However, if a treatment strategy is adopted that uses AoVP as the initial palliation instead of initial aortic valve surgery, patients may benefit from at least 1 fewer open heart surgery in their life, thus lowering the risk of reoperation resulting from scar tissue and decreasing the risk of the neurodevelopmental consequences of cardiopulmonary bypass.\textsuperscript{31}

An important limitation of our study is that we do not have precise anatomic data on each valve treated. Therefore, we cannot correlate outcome with specific types of valve abnormalities. For example, the interventional cardiologist often is confronted with the problem of a severely abnormal stenotic aortic valve, usually bicuspid, unicuspid, or with a rudimentary third cusp. AoVP in these types of valves distributes circumferential force unevenly and may therefore disrupt the cusps unevenly. Hence, some of these valves were subjectively judged as not suitable for AoVP and were not included in this study. Therefore, we cannot determine which anatomic configurations are likely to lead to early failure. However, bicuspid valves are known to be a risk factor for both aortic regurgitation and subsequent reintervention.\textsuperscript{14} Therefore, it is possible that surgery would offer a greater benefit in selected subsets of patients. However, even though some have attempted to repair these valves surgically,\textsuperscript{34,35} it seems that these valves require valve replacement early regardless of the approach.\textsuperscript{36} Therefore, the high reintervention rate in this type of aortic valve may suggest an even stronger argument for AoVP as the initial palliation for patients with congenital aortic valve stenosis because it avoids the risk of reoperation in a patient in whom reintervention is almost certain.

Another limitation of our study is that the outcome was most likely influenced by patient selection. The reason is that some patients with abnormal valves were subjectively judged as not suitable for AoVP and therefore not included in this study. However, we are fairly sure that patient selection was relatively consistent because a single interventionalist (W.S.) carried out >90% of the cases.

**Conclusions**

This study shows that the long-term results of AoVP of congenital aortic valve stenosis in pediatric patients and its efficacy in preventing or postponing aortic valve surgery are very good. About two thirds of the patients are free from aortic valve surgery 10 years after AoVP.

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**Disclosures**

None.

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**CLINICAL PERSPECTIVE**

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