Early Surgery Versus Conventional Treatment in Asymptomatic Very Severe Aortic Stenosis

Duk-Hyun Kang, MD, PhD; Sung-Ji Park, MD, PhD; Ji Hye Rim, MD; Sung-Cheol Yun, PhD; Dae-Hee Kim, MD, PhD; Jong-Min Song, MD, PhD; Suk Jung Choo, MD, PhD; Seung Woo Park, MD, PhD; Jae-Kwan Song, MD, PhD; Jae-Won Lee, MD, PhD; Pyo-Won Park, MD, PhD

Background—The optimal timing of surgical intervention remains controversial in asymptomatic patients with very severe aortic stenosis. We therefore compared the long-term results of early surgery and a conventional treatment strategy.

Methods and Results—From 1996 to 2006, we prospectively included a total of 197 consecutive asymptomatic patients (99 men; age, 63±12 years) with very severe aortic stenosis. Patients were excluded if they had angina, syncope, exertional dyspnea, ejection fraction <0.50, significant mitral valve disease, or age >85 years. Very severe aortic stenosis was defined as a critical stenosis in the aortic valve area ≤0.75 cm² accompanied by a peak aortic jet velocity ≥4.5 m/s or a mean transaortic pressure gradient ≥50 mm Hg on Doppler echocardiography. The primary end point was defined as the composite of operative mortality and cardiac death during follow-up. Early surgery was performed on 102 patients, and a conventional treatment strategy was used for 95 patients. There were no significant differences between the 2 groups in terms of age, gender, European System for Cardiac Operative Risk Evaluation score, or ejection fraction. During a median follow-up of 1501 days, the operated group had no operative mortalities, no cardiac deaths, and 3 noncardiac deaths; the conventional treatment group had 18 cardiac and 10 noncardiac deaths. The estimated actuarial 6-year cardiac and all-cause mortality rates were 0% and 2±1% in the operated group and 24±5% and 32±6% in the conventional treatment group, respectively (P<0.001), and for 57 propensity score-matched pairs, the risk of all-cause mortality was significantly lower in the operated group than in the conventional treatment group (hazard ratio, 0.135; 95% confidence interval, 0.030 to 0.597; P=0.008).

Conclusions—Compared with the conventional treatment strategy, early surgery in patients with very severe aortic stenosis is associated with an improved long-term survival by decreasing cardiac mortality. Early surgery is therefore a therapeutic option to further improve clinical outcomes in asymptomatic patients with very severe aortic stenosis and low operative risk. (Circulation. 2010;121:1502-1509.)

Key Words: echocardiography ■ stenosis ■ surgery ■ survival ■ valves

Management of asymptomatic patients with severe aortic stenosis (AS) remains controversial, and the combined risks of aortic valve (AV) surgery and late complications of AV prosthesis need to be balanced against the possibility of preventing sudden death and lowering cardiac mortality.1 Considering that sudden cardiac death occurs at a rate of ≈1%/y² and that the average postoperative mortality of isolated AV replacement is 3.0% to 4.0%,3,4 the 2007 European Society of Cardiology guidelines do not recommend AV surgery for asymptomatic patients with severe AS,5 and the 2006 American College of Cardiology/American Heart Association guidelines recommend surgery as a class IIb indication only in patients with extremely severe AS (AV area <0.6 cm²) and who are at low operative risk.1 Clinical outcomes vary widely according to the severity of stenosis in asymptomatic AS,6 and asymptomatic patients with very severe AS are often referred for AV replacement in clinical practice despite the lack of data supporting early surgery.2,6,7 Recent improvements in surgical techniques and AV prostheses also argue for early preemptive surgery in very severe AS because operative mortality has been reduced to ≈1% and morbidity of AV surgery to <5% at high-volume centers.1,2,6

Received September 16, 2009; accepted February 1, 2010.

From the Division of Cardiac Surgery, Cardiology, Biostatistics, Asan Medical Center, College of Medicine, University of Ulsan (D.-H.K., J.H.R., S.-C.Y., D.-H.K., J.-M.S., J.J.C., J.-K.S., J.-W.L.), and Samsung Medical Center, Sungkyunkwan University School of Medicine (S.-J.P., S.W.P., P.-W.P.), Seoul, Korea.

Correspondence to Duk-Hyun Kang, MD, PhD, Professor of Medicine, Division of Cardiology, Asan Medical Center, College of Medicine, University of Ulsan, 388-1, Poongnap-dong, Songpa-gu, Seoul, Korea 138-736 (e-mail dhkang@amc.seoul.kr); or Seung Woo Park, MD, PhD, Professor of Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University, 50 Irwon-dong Gangnam-gu, Seoul, Korea 135-710 (e-mail parksmc@gmail.com).

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Circulation is available at http://circ.ahajournals.org

DOI: 10.1161/CIRCULATIONAHA.109.909903

1502
No studies have compared early surgery and a conventional management strategy in patients with very severe AS, so using our prospectively collected registry data on patients with very severe AS, we sought to compare long-term cardiac mortality of early surgery with that of conventional management based on current guidelines. We also evaluated the prognostic impact of echocardiographic assessment of AS.

Methods

Study Population

A prospective registry that began in 1996 and uses a standard case report form has included all consecutive patients with AS undergoing echocardiography at our hospitals. All patients were evaluated by a cardiologist or a cardiac surgeon, and each patient’s history and clinical examination results were recorded at our institutions. Case report forms, including patient demographics, clinical presentation, and echocardiographic data, were stored in an electronic database. Clinical and echocardiographic follow-up data on study patients were collected annually and entered into the database. From 1996 to 2006, a total of 197 asymptomatic patients with very severe AS who were potential candidates for early surgery were consecutively enrolled in the present study. Following the traditional definition of severe AS, very severe AS was defined as a critical stenosis in the AV area ≤0.75 cm² fulfilling one of the following criteria: a peak aortic velocity ≥4.5 m/s or a mean transaortic pressure gradient ≥50 mm Hg on Doppler echocardiography. In line with the 1998 American College of Cardiology/American Heart Association guidelines on surgical indications for severe AS, we excluded patients with exertional dyspnea, syncope, presyncope or angina, left ventricular (LV) ejection fraction (EF) <50%, moderate or severe aortic regurgitation, or significant mitral valve disease and those who were not candidates for early surgery because of age >85 years or the presence of coexisting malignancies. Because the presence of coronary artery disease is an important prognostic factor and concomitant coronary artery bypass graft operation may increase the operative risk of AV replacement, patients with a history of coronary artery disease or regional wall motion abnormalities were also excluded, but 6 patients with incidental coronary artery disease detected on preoperative coronary angiography were included. The choice of early surgery or conventional treatment for each patient with very severe AS was at the discretion of the attending physician. The attending physicians explained the potential benefits of early surgery and the operative risks and complications associated with prostheses and considered the preferences of individual patients most important. Whereas a conventional strategy was chosen for 95 patients, early elective surgery was performed on 102 patients within 3 months of initial echocardiographic evaluation. Patients in the conventional treatment group were educated to report symptoms promptly and were observed without medical therapy because, in the absence of hypertension, there is no known indication for medical therapy in asymptomatic patients with severe AS. Informed consent was obtained from each patient, and the study protocol was approved by the ethics committees of our institutions.

Echocardiographic Evaluation

Echocardiographic evaluation was performed before surgery and annually during follow-up. Comprehensive 2-dimensional and Doppler echocardiographic examinations were performed on all patients with a Hewlett-Packard Sonos 2500 or 5500 imaging system equipped with a 2.5-MHz transducer (Hewlett-Packard, Andover, Mass). End-systolic dimension, end-diastolic dimension, and end-diastolic interventricular septal and posterior wall thicknesses of the LV were measured from parasternal M-mode acquisitions. End-systolic volume, end-diastolic volume, and LVEF were obtained with the biplane Simpson method, and LV mass was calculated with the formula validated by Devereux and associates. On 2-dimensional imaging of the AV in the parasternal short-axis view, the origin of AS was defined as bicuspid if there was clear identification of 2 leaflets during systole, rheumatic if commissural fusion and mitral valve involvement were observed, and degenerative if thickening and calcification of the leaflets were observed (Figure 1). AV calcification was graded as mild when a single spot or scattered small spots of echo brightness were observed; moderate when the calcified mass involved 1 or 2 leaflets; and severe when extensive thickening and calcified mass involved all leaflets (Figure 1). The maximal aortic jet velocity was recorded with the apical, right parasternal, or suprasternal window that yielded the highest-velocity signal. The maximal and mean pressure gradients across the AV were calculated with a modified Bernoulli equation, and the AV area was estimated from the continuity equation through the use of LV outflow tract diameter and flow velocity. After surgery, changes in LV mass and EF were monitored, and postoperative LV dysfunction was defined as an EF <0.40 on follow-up echocardiography.

Surgical Procedures

Procedures were performed with the use of standard cardiopulmonary bypass. In the early surgery group, AV replacements were successfully performed with mechanical (n=57) or bioprosthetic (n=45) valves, and concomitant coronary artery bypass graft operation at the time of AV surgery was performed on 6 patients (6%) with bypass grafts of 1.7±0.5 vessels. In the conventional treatment group, 1 Ross operation and 45 AV replacements with mechanical (n=33) or bioprosthetic (n=12) valves were performed during follow-up, and concomitant coronary artery bypass graft operation was performed on 3 patients (7%) with bypass grafts of 2.0±1.0 vessels.

Follow-Up

All study patients regularly visited their attending physicians at 3- to 6-month intervals for a clinical examination that included questions about the development of specific symptoms. Data were collected until June 2009 during annual visits to the echocardiographic laboratory and by a detailed review of all medical records or telephone interviews. Operative mortality was defined as death within 30 days of surgery. Deaths were classified as cardiac or noncardiac on the basis of medical records. For the 6 patients (3%) lost to follow-up, data on vital status, dates, and causes of death were obtained from the Korean national registry of vital statistics. The primary end point of the study was defined as the composite of operative mortality and cardiac death during follow-up, and the secondary end point was death resulting from any cause. In the conventional treatment group, progression of AS was monitored by
changes in aortic jet velocity and mean transaortic pressure gradient on annual echocardiographic follow-ups, and patients were referred for surgery if they became symptomatic during follow-up.

Statistical Analysis
Categorical variables are presented as numbers and percentages and were compared by use of the χ² test and Fisher exact test. Continuous variables are expressed as mean±SD and were compared by use of the Student unpaired t test, ANOVA, Wilcoxon signed-ranks test, or Mann-Whitney U test as appropriate. To reduce the effect of treatment selection bias and potential confounding in this observational study, we performed rigorous adjustment for the differences in the baseline characteristics by using propensity score matching.14 The propensity scores were estimated without regard to outcome variables through multiple logistic regression analysis. All specified covariates were included in the full nonparsimonious models for treatment with early surgery versus conventional strategy (Table 1). The discrimination and calibration ability of the propensity score model was assessed by means of the C statistic and the Hosmer-Lemeshow statistic. To develop the propensity score–matched pairs without replacement (a 1:1 match), the Greedy 5–digit match algorithm was used as described previously.15 After propensity score matching, the baseline covariates were compared between the 2 groups with the paired t test or the Wilcoxon signed-rank test for continuous variables and the McNemar test or marginal homogeneity test for categorical variables.

Analysis of clinical end points was performed on an intention-to-treat basis and included all patients. Event-free survival curves were constructed with Kaplan-Meier estimates and compared by use of the log-rank test. For Kaplan-Meier analysis, we analyzed all clinical events by time to first event. In the propensity score–matched cohort, the risks of clinical end points were compared by use of Cox regression models with robust SEs that accounted for the clustering of matched pairs. Unadjusted Cox proportional-hazards models were used to examine the association of baseline characteristics with cardiac mortality and cardiac events, including cardiac mortality and cardiac events, hazard ratio (HR) and 95% confidence interval (CI).

baseline clinical and echocardiographic characteristics of the matched cohort, there were no significant between-group differences for any covariates.

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
Baseline Characteristics
There were 99 men (50%) and 98 women (50%); their mean age was 63±12 years. The cause of AS was degenerative in 78 patients (39%), bicuspid in 96 patients (49%), and rheumatic in 23 patients (12%). Patients with bicuspid AV and rheumatic AS were significantly younger than those with degenerative AS (59±12 and 57±13 versus 69±9 years, respectively; P<0.001 for each). The peak velocity averaged 5.0±0.5 m/s; the mean pressure gradient was 62±13 mm Hg; and the mean AV area was 0.62±0.10 cm². A comparison of baseline clinical and echocardiographic characteristics of the elective surgery and conventional treatment groups is shown in Table 1. There were no significant differences between the 2 groups in terms of age, gender, body mass index, smoking, diabetes mellitus, hypertension, antihypertensive drug therapy, hyperlipidemia, EuroSCORE, atrial fibrillation, LVEF, LV mass index, origin of AS, degree of AV calcification, or AV area, but aortic jet velocity (P<0.001) and mean transaortic gradient (P=0.001) were significantly larger in the early surgery group. Propensity score matching for the entire population yielded 57 matched pairs of patients. In the matched cohort, there were no significant between-group differences for any covariates.

Comparison Between the Early Surgery and Conventional Treatment Groups
There were no cases of operative mortality in the early surgery group. The median follow-up was 1265 days (inter-
quartile range, 2325 to 947 days) in the early surgery group and 1769 days (interquartile range, 2423 to 1020 days) in the conventional treatment group (P = 0.295). During follow-up, there were no cardiac and 3 noncardiac deaths in the early surgery group and 18 cardiac and 10 noncardiac deaths in the conventional treatment group. The estimated actuarial 6-year survival and cardiac mortality–free survival rates were 98.1% and 100% in the early surgery group and 68.6% and 76.5% in the conventional treatment group, respectively (P < 0.001; Figure 2). The causes of noncardiac deaths were malignancy in 6 patients, stroke in 5 patients, acute cholecystitis in 1 patient, and liver cirrhosis in 1 patient. The causes of cardiac deaths were congestive heart failure in 7 patients, endocarditis in 2 patients, and sudden cardiac death in 9 patients (Figure 3). Seven cases (7%) of sudden cardiac death were asymptomatic at the last examination performed within 1 year before death, and the estimated actuarial 6-year rate of sudden death not preceded by symptoms was 10.4%. The other 2 cases of sudden cardiac death occurred after development of exertional dyspnea; 1 patient awaiting elective surgery and 1 patient who refused surgery died. All 7 patients who died of congestive heart failure were asymptomatic at the last visit and presented to the emergency room with sudden dyspnea and pulmonary edema. Their median EuroSCORE was increased significantly from 4 (interquartile range, 6 to 3) at baseline to 11 (interquartile range, 14 to 10) (P = 0.017 on Wilcoxon signed-rank test), and their median age was 77 years (interquartile range, 82 to 73 years) at admission for congestive heart failure. Urgent surgery was recommended to these patients, but they refused because of high surgical risks and old age. For the 57 propensity score–matched pairs, the risk of all-cause mortality was significantly lower in the early surgery group than in the conventional treatment group (HR, 0.135; 95% CI, 0.030 to 0.597; P = 0.008), and the estimated actuarial 6-year survival and cardiac mortality–free survival rates were also higher in the early surgery group (96±2% and 100%) than in the conventional treatment group (65±7% and 74±7%).

No patients in the early surgery group required repeat AV surgery, and 46 patients in the conventional treatment group underwent late AV surgery during follow-up. The immediate postoperative and late follow-up LV mass indexes and LVEFs of these 46 patients who underwent late AV surgery did not differ significantly from those of the early surgery group. In contrast, the incidence of immediate postoperative LV dysfunction (LVEF < 0.40) was significantly higher than that of the early surgery group (Table 2).

Clinical and Echocardiographic Predictors of Outcome in the Conventional Treatment Group

The survival rates free of cardiac mortality in the conventional treatment group were 91±3% at 2 years, 83±4% at 4 years, and 76±5% at 6 years. Using unadjusted Cox proportional-hazards analysis, we found that baseline correlates of cardiac mortality were age, male gender, EuroSCORE, degree of AV calcification, and aortic jet velocity ≥5 m/s. Aortic jet velocity ≥5 m/s was independently associated with cardiac mortality in the Cox proportional-hazard models adjusted for EuroSCORE (Table 3). Cardiac mortality was significantly different according to gender (Figure 4A) and was different between patients with aortic jet velocity <5 m/s and those with ≥5 m/s (Figure 4B).

The survival rates free of cardiac events or surgery in the conventional treatment group were 71±5% at 2 years, 47±5% at 4 years, and 28±6% at 6 years (Figure 5). On unadjusted and adjusted Cox proportional-hazards analysis (Table 4), the rate of progression in aortic jet velocity (HR, 9.75; 95% CI, 2.24 to 42.39) was associated with cardiac mortality or surgery. However, the progression rate of aortic jet velocity was not a significant correlate of sudden death.
(P=0.65) or cardiac mortality (P=0.36) but rather only AV surgery (HR, 22.94; 95% CI, 3.304 to 159.3; P=0.001). There was individual variability in the rate and pattern of hemodynamic progression, and the rate of progression did not significantly differ with respect to origin of AS or degree of calcification.

**Discussion**

This study demonstrates that in asymptomatic patients with very severe AS, early surgery improves long-term survival by decreasing sudden cardiac death and cardiac mortality compared with a conventional treatment strategy. To recommend AV surgery to asymptomatic patients with very severe AS, the following prerequisites should be met. First, the prognosis of very severe AS should be worse than that of severe AS. The severity of AS is a continuum; the more severe the AS is, the worse the clinical outcomes are.2,7,17 Compared with prospective studies that included severe AS patients only, the annual rate of sudden death (1.7%) in the conventional treatment group of this study was higher than that (1.0%) in the study of Pellikka et al,2 and the overall survival rate at 4 years was lower than that reported by Rosenhek et al 6 (78±6% versus 87±3%). A recent study also reported a worse prognosis with a higher event rate and a risk of rapid deterioration in 116 patients with very severe AS.17 Second, early surgery must prevent the small but real risk of sudden cardiac death in patients undergoing conventional treatment. A previous study reported that the risk of sudden death could not be eliminated by surgical treatment18; however, no case of sudden death occurred among 102 patients who underwent early surgery, implying that the risk of sudden death is, at the very least, greatly reduced by early surgery. The regression of LV hypertrophy and maintenance of LV systolic function on postoperative follow-up echocardiography suggest that surgery was performed before irreversible myocardial damage.

| Table 2. Comparison of Echocardiographic Results Between the Early Surgery and Late Surgery Groups |
|---------------------------------------------------------------|----------------|----------------|----------------|
| Early Surgery Group (n=102) | Late Surgery Group (n=46) |
| LV mass index, g/m² | 158±43 | 132±39 | 107±30 |
| LVEF, % | 62±7 | 58±9 | 64±6 |
| LV dysfunction, n (%) | 0 (0) | 3 (3)* | 1 (1) |

*P<0.05.

| Table 3. Correlates of Cardiac Mortality in the Conventional Treatment group |
|-----------------------------------------------|----------------|----------------|
| Unadjusted | HR | 95% CI |
| Age | <0.001 | 1.09 | 1.04–1.14 |
| Male gender | 0.002 | 7.07 | 1.99–25.07 |
| Diabetes mellitus | 0.67 | 1.37 | 0.30–6.19 |
| Hypertension | 0.74 | 0.85 | 0.31–2.34 |
| Smoking | 0.06 | 2.71 | 0.94–7.80 |
| Hyperlipidemia | 0.54 | 1.36 | 0.49–3.74 |
| EuroSCORE | <0.001 | 1.43 | 1.12–1.81 |
| Atrial fibrillation | 0.79 | 1.22 | 0.27–5.49 |
| LV mass index | 0.67 | 1.00 | 0.99–1.01 |
| LVEF | 0.97 | 1.00 | 0.94–1.07 |
| Origin of AS | | | |
| Bicuspid | 0.65 | 0.80 | 0.30–2.11 |
| Degenerative | 0.12 | 2.15 | 0.81–5.70 |
| Calcification | 0.046 | 2.37 | 1.00–5.62 |
| AV velocity ≥5 m/s | 0.032 | 2.87 | 1.07–7.71 |
| AV mean gradient ≥60 mm Hg | 0.07 | 2.36 | 0.91–6.09 |
| AV area ≤0.6 cm² | 0.43 | 0.68 | 0.26–1.79 |
| Rate of progression | | | |
| AV velocity | 0.36 | 0.03 | <0.001–58.97 |
| AV mean gradient | 0.73 | 0.98 | 0.85–1.12 |

Adjusted

| AV velocity ≥5 m/s* | 0.002 | 4.76 | 1.74–12.94 |

*Adjusted for EuroSCORE (HR, 1.589; 95% CI, 1.222 to 2.066; P=0.0006).

Figure 4. Survival free of cardiac death in the conventional treatment group according to gender (A) and baseline aortic jet velocity (B). Vmax indicates maximal aortic jet velocity.
and fibrosis occurred and could entirely prevent sudden death. Third, the risk of surgical delay and refusal of surgery after the development of symptoms should be serious in patients with very severe AS. In the Euro Heart Survey, despite the presence of severe symptomatic AS, surgery was denied in as many as 33% of elderly patients. In the present study, 9 cardiac deaths occurred in symptomatic patients who refused surgery or who were awaiting elective surgery, and the incidence of immediate postoperative LV dysfunction was significantly higher in the conventional treatment group. A recent study also reported that survival was dramatically improved by AV replacement in an observational study of 338 patients with AV areas ≤0.8 cm². Fourth, operative risk and morbidity should be very low in high-volume centers. Elective AV surgery is associated with very low operative mortality and morbidity rates in high-volume centers, and the present study confirms the very low operative risk and morbidity associated with isolated AV replacement. Although conventional treatment may decrease the number of AV replacements performed, >80% of surviving patients with very severe AS eventually required AV replacement, and they had a very poor event-free survival rate (12% at 4 years). The last issue is the definition of the echocardiographic criteria of very severe AS. The current guidelines define severe AS as an AV area <1.0 cm², but early prophylactic surgery cannot be justified in patients with AV areas of 0.8 to 1.0 cm² because individual outcomes are highly variable in such patients. Although AV area theoretically represents the ideal way to evaluate disease severity and to quantify AS, it may be susceptible to measurement errors. Because measures of jet velocity and pressure gradient are complementary to estimation of AV area for assessment of severity, all these measures should be included in the criteria for very severe AS.

In summary, the present study suggests that the clinical benefits of early surgery outweighed all risks associated with early surgery. A prospective randomized comparison trial is required to confirm the efficacy of early surgery in very severe AS.

Clinical and Echocardiographic Predictors of Outcome in the Conventional Treatment Group

This study demonstrates that baseline aortic jet velocity is independently associated with cardiac mortality and suggests that echocardiographic evaluation of AS is useful for identifying high-risk patients in whom cardiac mortality is likely to occur. A baseline aortic jet velocity ≥5 m/s can be suggested as a useful cutoff value in risk stratification of very severe AS, but the other criteria of extremely severe AS (AV area ≤0.6 cm² and mean gradient ≥60 mm Hg) were not significantly associated with cardiac mortality in this study. The recent study by Rosenhek et al also supports the concept of elective surgery in patients who present with an aortic jet velocity ≥5 m/s. The current European guidelines suggest that a calcified AV with a rapid increase in aortic jet velocity >0.3 m/s per year is a class IIa surgical indication. In the present study, the rate of progression in aortic jet velocity was significantly associated with subsequent AV surgery but not with sudden cardiac death or cardiac mortality, and echocardiographic monitoring might be insufficient to identify patients at risk of cardiac death. As in previous studies, age, gender, and EuroSCORE were significantly associated with clinical outcome in the present study. These baseline characteristics should be also considered for risk stratification and clinical decision for individual patients.
Study Limitations
Comparison of treatment strategies for very severe AS is subject to the limitations inherent to nonrandomized assignment, and the preference of each patient was considered to be of importance in the choice of treatment strategy because the optimal treatment was controversial. These limitations may have significantly affected the results owing to selection bias and unmeasured confounders. However, study patients were enrolled consecutively in a prospectively designed registry for annual clinical and echocardiographic follow-up, and all baseline characteristics except aortic jet velocity and mean transaortic gradient were not significantly different between the elective surgery and conventional treatment groups. In the propensity score–matched cohort, the early surgery group persistently showed a significantly lower rate of end points. Refusal of surgery in patients who became symptomatic might be considered a limitation. In a separate analysis in which patients of the conventional treatment group were censored at symptom onset, cardiac mortality rates were 5±2% at 2 years, 9±3% at 4 years, and 14±6% at 6 years, significantly higher than those of the early surgery group (P=0.0018).

An exercise test was not included in the study protocol because the safety of such tests has not been confirmed in patients with very severe AS. An exercise test is selectively indicated, under the supervision of an experienced physician, to elicit symptoms in patients with unclear symptomatic status,1,5 but it also has limitations in predicting symptom onset and clinical outcome.21,26 The prevalence of coronary artery disease and frequency of concomitant coronary artery bypass graft operation were relatively low, which might exert a favorable influence on postoperative outcomes. Operative mortality was very low in the present study, and our results are not applicable to low-volume centers or asymptomatic patients with high operative risk.

Conclusions
Compared with the conventional treatment strategy, early surgery is associated with improved survival by effectively decreasing cardiac mortality and sudden cardiac death in patients with very severe AS. This result suggests that early surgery can be a therapeutic option to further improve clinical outcomes in asymptomatic patients with very severe AS and low operative risk.

Disclosures
None.

References

Management of asymptomatic patients with very severe aortic stenosis remains controversial, and the combined risks of aortic valve surgery and late complications of aortic valve prosthesis need to be balanced against the possibility of preventing sudden death and lowering cardiac mortality. We prospectively evaluated 197 consecutive asymptomatic patients with very severe aortic stenosis to compare clinical outcomes of early surgery with those of the conventional treatment strategy. Very severe aortic stenosis was defined as a critical stenosis in the aortic valve area $\leq 0.75 \text{ cm}^2$ accompanied by a peak aortic jet velocity $\geq 4.5 \text{ m/s}$ or a mean transaortic pressure gradient $\geq 50 \text{ mm Hg}$ on Doppler echocardiography. Early surgery was performed on 102 patients, and a conventional treatment strategy was used for 95 patients. There were no operative deaths and no cardiac deaths in the early surgery group compared with 18 cardiac deaths in the conventional treatment group, and the risk of all-cause mortality was significantly lower in the early surgery group than in the conventional treatment group (hazard ratio, 0.135; 95% confidence interval, 0.030 to 0.597; $P=0.008$). Compared with the conventional treatment strategy, early surgery is associated with improved long-term survival by effectively decreasing cardiac mortality and sudden cardiac death. This result suggests that early surgery can be a therapeutic option to further improve clinical outcomes in asymptomatic patients with very severe aortic stenosis and low operative risk. A prospective randomized trial is required to confirm the efficacy of early surgery.
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Circulation. 2010;121:1502-1509; originally published online March 22, 2010; doi: 10.1161/CIRCULATIONAHA.109.909903

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/121/13/1502

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