Aortic Valve Replacement for Aortic Stenosis in Elderly Patients (75 Years or Older)

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Background: This study evaluated the early and long-term outcomes of surgical aortic valve replacement (AVR) in elderly patients in the era of transcatheter aortic valve implantation. **Methods:** Between 2001 and 2018, 94 patients aged ≥75 years underwent isolated AVR with stented bioprosthetic valves for aortic valve stenosis (AS). The main etiologies of AS were degenerative (n=63) and bicuspid (n=21). The median follow-up duration was 40.7 months (range, 0.6–174 months). **Results:** Operative mortality occurred in 2 patients (2.1%) and paravalvular leak occurred in 1 patient. No patients required permanent pacemaker insertion after surgery. Late death occurred in 11 patients. The overall survival rates at 5 and 10 years were 87.2% and 65.1%, respectively. The rates of freedom from valve-related events at 5 and 10 years were 94.5% and 88.6%, respectively. The Society of Thoracic Surgeons (STS) score (p=0.013) and chronic kidney disease (p=0.030) were significant factors affecting long-term survival. The minimal p-value approach demonstrated that an STS score of 3.5% was the most suitable cut-off value for predicting long-term survival. **Conclusion:** Surgical AVR for elderly AS patients may be feasible in terms of early mortality and postoperative complications, particularly paravalvular leak and permanent pacemaker insertion. The STS score and chronic kidney disease were associated with long-term outcomes after AVR in the elderly.

Key words: 1. Aortic valve replacement
2. Aortic valve stenosis
3. Aged
4. Transcatheter aortic valve implantation

Introduction

Aortic valve stenosis (AS) is the most prevalent valvular heart disease in the elderly [1]. Although surgical aortic valve replacement (SAVR) has been the treatment of choice for patients with severe AS [2], recent guidelines have suggested treatment with transcatheter aortic valve implantation (TAVI) as an alternative to SAVR in high- and even intermediate-risk patients [3]. In addition, elderly patients have been targeted for TAVI regardless of their risk profile [4]. In this new era of TAVI, renewed interest has emerged in the outcomes of SAVR [5-7]. This study was conducted to evaluate the early and long-term outcomes of isolated SAVR in elderly patients and to analyze the factors influencing clinical outcomes.

Methods

1) Patient characteristics

Between January 2001 and February 2018, we recruited 94 patients with who were 75 years or older and underwent isolated SAVR at Seoul National University Hospital. Patients who underwent concomitant operations such as other types of heart valve surgery, arrhythmia surgery, ascending aorta replacement, and coronary artery bypass grafting were excluded, as were those with infective endocarditis. The study protocol was reviewed by the institutional review board, and was approved as a minimal-risk retrospective study (IRB approval no., 1805-138-948) that did not require individual consent. The baseline characteristics of the recruited patients are summarized in Table 1. Their mean age at surgery was 78.9±3.69 years, and 47 patients (50%) were female. The mean Society of Thoracic Surgeons (STS) score was 3.39%±1.85%. Sixteen patients (16.7%) had a New York Heart Association functional classification of III or IV (Table 1).

2) Operative data

All operations were performed using aortic and bicaval cannulation via a median sternotomy. Aortic valve replacement was performed using a non-everting mattress sutures buttress reinforced with polytetrafluoroethylene as a tubule (so-called 'spaghetti'). Great care was taken to avoid deep-biting sutures near the commissure between the non- and right coronary cusps to minimize the risk of conduction block. Bovine pericardial valves and porcine valves were used in 79 patients (84.0%) and 15 patients (16.0%), respectively. The sizes of the prosthetic valves were 19 mm, 21 mm, 23 mm, 25 mm, and 27 mm in 17, 25, 38, 12, and 2 patients, respectively. The mean cardiopulmonary bypass (CPB) and aortic cross-clamp (ACC) times were 152±44 minutes and 95±29 minutes, respectively.

3) Echocardiographic evaluation

Two-dimensional echocardiography and Doppler color-flow imaging were performed in all patients before surgery and during the early postoperative period. Follow-up echocardiographic evaluations were performed at the discretion of the operating surgeon.

Table 1. Preoperative characteristics and risk factors (N=94)

Characteristic	Value
Age (yr)	78.9±3.69
Male	47 (50)
Society of Thoracic Surgeons score (%)	3.39±1.85
New York Heart Association class ≥3	16 (16.7)
Degenerative : bicuspid : rheumatic	65: 21: 8
Left ventricular ejection fraction (%)	58.2±10.7
Risk factors	
Current smoker	3 (3.1)
Overweight (body mass index >25 kg/m^2)	30 (31.3)
Diabetes mellitus	21 (21.9)
Hypertension	61 (63.5)
History of stroke	10 (10.4)
Chronic obstructive pulmonary disease	9 (9.4)
Chronic kidney disease	24 (25)
Coronary artery disease	24 (25)
Atrial fibrillation	14 (14.6)
Emergency or urgency	3 (3.2)

Values are presented as mean±standard deviation or number (%).

4) Anti-thrombotic management

Warfarin anticoagulation with a target international normalized ratio (INR) of 2.0–2.5 was maintained for 3–6 months and life-long after surgery in patients with sinus rhythm and in those with atrial fibrillation, respectively. Since late 2014, however, antiplatelet therapy instead of warfarin anticoagulation has been used for patients with normal sinus rhythm.

5) Evaluation of clinical outcomes

Clinical data were assessed retrospectively, and follow-up information was acquired from patients' electronic medical records. Operative mortality was defined as any death within 30 days of surgery or during the same hospital admission. Chronic kidney disease and acute kidney injury were defined as a glomerular filtration rate <60 mL/min/1.73 m^2 and a >50% increase of the serum creatinine level from preoperative values, respectively. Postoperative atrial fibrillation was defined as any short new-onset run of atrial fibrillation. Low cardiac output syndrome was defined as a cardiac index <2.0 L/min/m^2 or a systolic arterial pressure <90 mm Hg requiring inotropic support (dopamine or dobutamine) of >5 μg/kg per minute or any need for mechanical circulatory support, such as an intra-aortic balloon pump or extracorporeal membrane oxygenation. Respiratory

Table 2. Early clinical results (N=94)	
Variable	No. (%)
Operative mortality	2 (2.1)
Postoperative complications	
Atrial fibrillation (new onset)	32 (33.3)
Acute kidney injury	6 (6.3)
Low cardiac output syndrome	4 (4.2)
Bleeding reoperation	4 (4.2)
Respiratory complications	5 (5.2)
Stroke	4 (4.2)
Any paravalvular leak	0
Complete atrioventricular block requiring permanent pacemaker	0
Infective endocarditis	0

Fig. 1. Kaplan-Meier curve for overall survival.

complications included postoperative pneumonia or >48 hours of prolonged ventilator support. Patients underwent regular postoperative follow-up at 3- to 4-month intervals at the outpatient clinic. Clinical follow-up was terminated on April 30, 2018. If patients did not visit the clinic at the scheduled time, they were contacted by telephone to confirm their condition. The median duration of follow-up was 40.7 months (range, 0.6–174 months). Valve-related events (VREs) were defined according to established guidelines [8] as structural valve deterioration (SVD), non-structural valve dysfunction (NSVD), valve thrombosis, embolism, bleeding events, prosthetic valve endocarditis, and cardiac deaths.

6) Statistical analysis

Statistical analyses were performed using IBM SPSS ver. 23.0 (IBM Corp., Armonk, NY, USA). Data are expressed as mean±standard deviation or as medians with ranges or proportions, as appropriate. Survival rates were estimated using the Kaplan–Meier method. Risk factors for time-related events were analyzed using the Cox proportional hazard model. Multi-collinearity was controlled using backward stepwise regression. All preoperative variables presented in Table 1 and the transvalvular pressure gradient on early postoperative echocardiography were included in the analyses. Variables with a p-value <0.05 in univariate analyses incorporating patient age were subsequently used in the multivariable analysis. All p-values <0.05 were considered to indicate statistical significance. The minimal p-value approach was used to estimate an optimal cut-off value
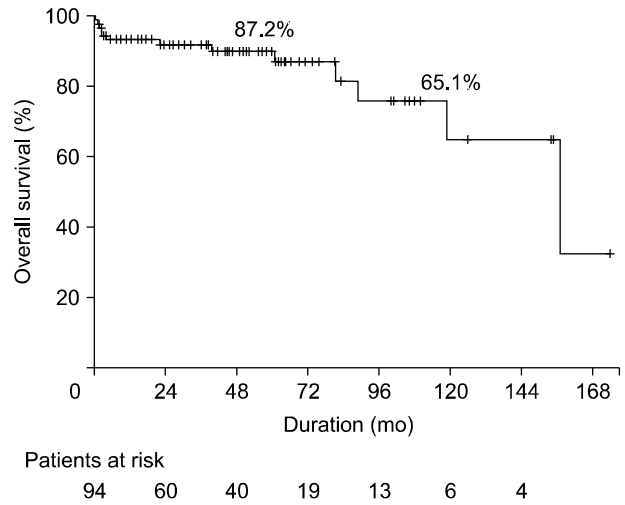
of a continuous variable predicting a time-related event [9].

Results

1) Early outcomes

The operative mortality rate was 2.1% (2 of 94 patients) and involved low cardiac output syndrome and sepsis in each. The postoperative complications included new-onset atrial fibrillation (n=32), acute kidney injury (n=6), low cardiac output syndrome (n=7), and respiratory complications (n=5) (Table 2). Paravalvular leak was found intraoperatively in 1 patient, but was corrected with a second round of CPB and ACC. None of the other patients showed any degree of paravalvular leak on either intraoperative or postoperative echocardiography. There were no instances of complete atrioventricular block requiring permanent pacemaker implantation after surgery (Table 2). The mean transvalvular pressure gradient on early postoperative echocardiography was 13.3±5.9 mm Hg.

2) Long-term outcomes

Among the 92 survivors, late death occurred in 11 patients, including 2 cardiac deaths. The overall survival rates at 5 and 10 years were 87.2% and 65.1%, respectively (Fig. 1). Other types of VREs occurred in 5 patients, although there were no instances of SVD or NSVD requiring aortic valve re-intervention. Bleeding and thromboembolic events occurred in 3
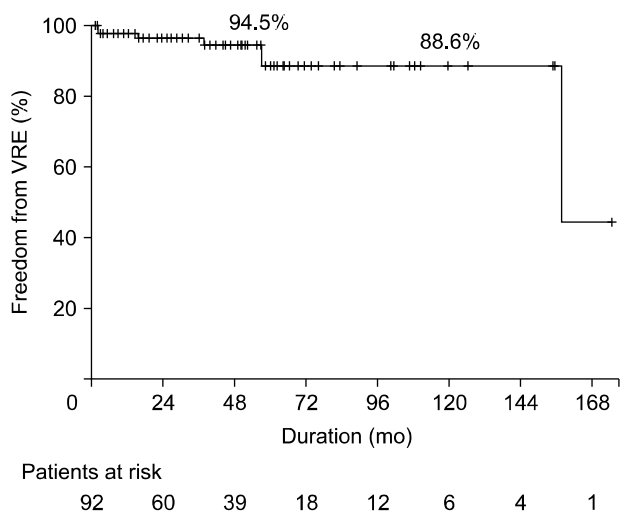
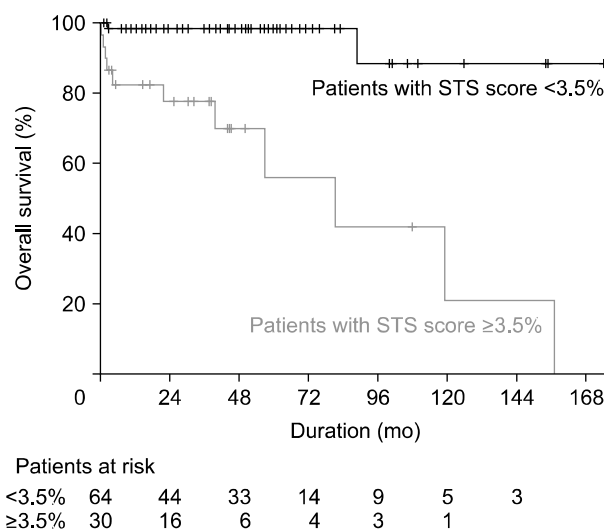Fig. 2. Kaplan-Meier curve for freedom from valve-related events (VREs).

Fig. 3. Kaplan-Meier curve for overall survival according to the cut-off value of Society of Thoracic Surgeons (STS) scores.

Table 3. Risk factor analysis for overall survival

Variable	Univariate analysis	Multivariable analysis	
	p-value	Hazard ratio (95% confidence interval)	p-value
Age	0.980	0.874 (0.721–1.061)	0.173
Chronic kidney disease	0.005	4.100 (1.149–14.629)	0.030
Society of Thoracic Surgeons score	0.006	1.455 (1.081–1.958)	0.013

and 2 cases, respectively; gastrointestinal bleeding occurred in 3 patients, of whom 2 were on warfarin due to new-onset atrial fibrillation during follow-up after surgery. Ischemic stroke occurred in 2 patients with atrial fibrillation. Both patients were also on warfarin. They had been anticoagulated properly and the INR was within the target range at the time of the events. The 5- and 10-year rates of freedom from VREs were 94.5% and 88.6%, respectively (Fig. 2). The mean transvalvular pressure gradient at the last echocardiography was 12.6±7.0 mm Hg.

3) Risk factor analysis for overall survival

The univariate analyses demonstrated that the STS score and chronic kidney disease were risk factors for overall survival. Subsequent multivariate analysis revealed that the STS score and chronic kidney disease remained independent risk factors for overall

survival (Table 3). In the minimal p-value approach, an STS score of 3.5% was the best cut-off value for predicting long-term survival after SAVR (hazard ratio, 14.735; 95% confidence interval, 3.228–67.248) (Fig. 3).

Discussion

The present study demonstrated 3 main findings. First, the early results of SAVR in the elderly were favorable in terms of mortality rate, the incidence of paravalvular leak, and the need for permanent pacemaker implantation. Second, 5- and 10-year survival rates after SAVR were 87.2% and 65.1%, respectively, and chronic kidney disease was significantly associated with long-term survival. Thirdly, an STS score of 3.5% was determined to be the best cut-off value with which to predict long-term survival after SAVR in the elderly.

Favorable early and mid-term data, along with improvements in TAVI results following device modifications and the accumulation of experience, made it possible to expand the indications of this technique to intermediate-risk patients [3,4]. Two landmark randomized trials have recently reported outcomes of TAVI in comparison with SAVR in symptomatic AS patients with intermediate surgical risk [10,11]. While these studies demonstrated no significant difference in the composite outcome of death from any

cause or disabling stroke, the primary outcomes of these studies still showed differences in the complication profiles between TAVI and SAVR, including the rates of major vascular complications (6.0% versus 1.1%), moderate or severe paravalvular leak (5.3% versus 0.6%), and permanent pacemaker implantation (25.9% versus 6.6%). In addition, the transcatheter procedure has often been used in AS patients of advanced age, rather than surgical treatment [12]. These findings have caused a resurgence in interest in terms of the outcomes of SAVR in the elderly [5-7,13-15]. Previous studies showed that early mortality after SAVR in octogenarians ranged from 0% to 13%, and that the overall survival at 5 years was over 70%. In the present study, only patients with isolated SAVR were included, whereas patients who underwent concomitant cardiovascular surgery and those with infective endocarditis were excluded, in order to present benchmark data of SAVR for patients who also could be considered candidates for TAVI. The operative mortality rate was 2.1%. This is in agreement with previous studies that demonstrated acceptable early mortality rates, even in patients of advanced age. In addition, only 1 patient experienced paravalvular leak, and none of our patients required permanent pacemaker implantation after surgery. These outcomes may represent meaningful advantages of SAVR over TAVI. The long-term results were also favorable, with 10-year survival and VRE-free rates of 65.1% and 88.6%, respectively. The durability of the stented bioprosthesis was excellent, and no SVD or NSVD required re-intervention up to 12 years after surgery. Previous studies have suggested that several factors are associated with long-term survival after surgery, including preoperative myocardial infarction, urgent or emergent procedures, and combined coronary artery disease [5,14]. In the present study, however, these factors were not associated with long-term survival because patients who needed combined myocardial revascularization were beyond the scope of the study. The STS score, initially developed to predict perioperative outcomes, has been confirmed to be associated with long-term outcomes after TAVI and cardiac surgery [16]. Similar to the current cut-off STS score of 4%, which was used to classify the intermediate-risk group, the minimal p-value approach showed that an STS score of 3.5% represented the best cut-off value for pre-

dicting the long-term survival rate.

The present study demonstrated that patient age might not be the primary exclusion criterion for SAVR. In addition, recent advances in surgical techniques could further improve the results of SAVR in the elderly [17]. Therefore, the choice between TAVI and SAVR should be individualized and not be based on patient age alone, but also on specific patient characteristics, including co-morbidities such as chronic kidney disease.

The present study has several limitations. First, this was a retrospective observational study conducted at a single institution. Second, the number of patients recruited was relatively small, making it difficult to draw definitive conclusions. Finally, the results of the multivariable analysis might be over-fitted due to the small number of events.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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