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Aortic Valve Replacement for Aortic Stenosis and Concomitant Coronary Artery Bypass: Long-term Outcomes and Predictors of Mortality

Won-Chul Cho, M.D.*, Dong-Gon Yoo, M.D.**, Joon-Bum Kim, M.D.*, Jae-Won Lee, M.D.*, Suk-Jung Choo, M.D.*, Sung-Ho Jung, M.D.*, Cheol-Hyun Chung, M.D.*

Background: We evaluated the surgical results and predictors of long-term survival in patients who underwent coronary artery bypass grafting (CABG) at the time of an aortic valve replacement (AVR) due to aortic stenosis. ***Materials and Methods:*** Between January 1990 and December 2009, 183 consecutive patients underwent CABG and concomitant aortic valve replacement for aortic stenosis. The mean follow-up period was 59.8±3.3 months and follow-up was possible in 98.3% of cases. Predictors of mortality were determined by Cox regression analysis. ***Results:*** There were 5 (2.7%) in-hospital deaths. Follow-up of the in-hospital survivors documented late survival rates of 91.5%, 74.8%, and 59.6% at 1, 5, and 10 postoperative years, respectively. Age ($p<0.001$), a glomerular filtration rate (GFR) less than 60 mL/min ($p=0.006$), and left ventricular (LV) mass ($p<0.001$) were significant predictors of mortality in the multivariate analysis. ***Conclusion:*** The surgical results and long-term survival of aortic valve replacement with concomitant CABG in patients with aortic stenosis and coronary artery disease were acceptable. Age, a GFR less than 60 mL/min, and LV mass were significant predictors of mortality.

Key words: 1. Aortic valve stenosis
2. Coronary artery disease
3. Coronary artery bypass surgery

INTRODUCTION

Aortic stenosis and coronary atherosclerosis can independently cause myocardial ischemia and the sequelae of myocardial ischemia including angina, myocardial infarction, and death. A review of the results of combined aortic valve replacement (AVR) and coronary artery bypass grafting (CABG) in several centers shows more variable mortality than that seen after isolated aortic valve replacement [1-6]. Therefore, the present study analyzed the surgical results and predictors of long-term survival in patients who underwent combined AVR and CABG for aortic stenosis and coronary artery disease.

MATERIALS AND METHODS

1) Patients

The present study examined the records of 183 patients who underwent combined AVR and CABG for aortic stenosis and co-existing coronary artery disease at our institution be-

*Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine
**Department of Thoracic and Cardiovascular Surgery, Gangneung Asan Hospital, University of Ulsan College of Medicine
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Corresponding author: Jae-Won Lee, Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, 388-1, Pungnap 2-dong, Songpa-gu, Seoul 138-736, Korea
(Tel) 82-2-3010-3580 (Fax) 82-2-3010-6966 (E-mail) jwlee@amc.seoul.kr

tween January 1990 and December 2009. Data collection involved reviewing in-patient and out-patient medical records, and conducting telephone interviews. The study protocol was approved by the Institutional Review Board of the Asan Medical Center, Seoul, Korea. The requirement for informed patient consent was waived by the board because of the retrospective nature of the study.

2) Definitions

All patients underwent preoperative cardiac catheterization and echocardiography within 2 months prior to surgery. Coronary arteries with greater than 70% narrowing were considered significantly stenosed. Categorization of the extent of coronary artery disease (CAD) (one-, two-, or three-vessel disease) was based on the significant stenosis of major arteries (left anterior descending, left circumflex, or the right coronary artery) or branches thereof. Revascularization was considered incomplete if any major artery or one of the branches had a significant stenosis that was not revascularized with a bypass graft at the time of surgery. The severity of aortic stenosis was defined as mild, moderate, or severe by using the ACC/AHA guidelines for the management of patients with valvular heart disease [7]. Glomerular filtration rate (GFR) means the estimated GFR in this study [8].

Operative variables included completeness of myocardial revascularization, type of aortic prosthesis implanted, global ischemic time, total cardiopulmonary bypass time, and use of the internal thoracic artery. The selection of aortic valve prosthesis type was based on surgeon and patient preference. Operative mortality was defined as death prior to discharge or any death within 30 days following surgery. Major adverse cardiac events (MACE) included anticoagulation complication, thrombo-embolism including cerebrovascular attack, re-interventions for aortic valve or coronary artery, and infective endocarditis.

3) Statistical analysis

Categorical variables were presented as frequencies and percentages, and were compared using the chi-square test or Fisher's exact test. Continuous variables were expressed as mean±SD or medians with ranges, and were compared using the Student's unpaired *t* test or Mann-Whitney *U* test, as appropriate. Kaplan-Meier curves were employed to delineate overall survival, and log-rank tests were used to compare the differences in survival rates between groups. Stratified survival curves were plotted to explore unadjusted differences for variables of interest. For multivariate analyses, updated covariate Cox's proportional hazard regression models were used to examine the association of baseline characteristics with time to death. Variables with a probability value <0.05 in univariate analyses were candidates for the multivariable Cox models. Multivariate analyses involved a backward elimination technique and only variables with a p-value of <0.05 were used in the final model. Results were expressed as hazard ratios (HR) with 95% confidence intervals (CI). All reported p-values are two-sided, and p-values of less than 0.05 were considered to indicate statistical significance. SPSS version 14.0 was used for the statistical analysis.

RESULTS

1) Preoperative clinical characteristics and operative variables

The mean age at surgery was 68.0±8.8 years and 60.7% of patients were male. Clinical follow up was complete in 98.4% of patients, with a mean follow-up duration of 59.8±3.3 months. The clinical details and results of cardiac catheterization and echocadiography are shown in Table 1. Mean cross-clamp time and cardiopulmonary bypass time were 104.3±42.5 minutes and 170.1±63 minutes, respectively. A total of 103 bioprostheses (56.3%) and 80 mechanical prostheses (43.7%) were used. Overall, 65% (n=119) of patients used an internal mammary artery graft. Among all of the patients in our study cohort were 40 (21.9%) patients who were considered incompletely revascularized. For all patients, the reason for incomplete revascularization was poor distal target or quality.

2) Early outcomes

Significant postoperative morbidities occurred in 24 patients (Table 2). There were five cases of stroke and four cases of bleeding. Five (2.7%) in-hospital deaths occurred. Three patients died in the immediate postoperative period, and of these, two deaths occurred from low cardiac output and the

Table 1. Preoperative clinical characteristics

Variable	Number (%)
Mean age (years)	68.0±8.8
Male	111 (60.7)
Preoperative	
NYHA III	79 (43.2)
NYHA IV	12 (6.6)
Diabetes	52 (28.4)
Hypertension	96 (52.5)
Hypercholesterolemia	50 (27.3)
Angina	104 (56.8)
COPD	18 (9.8)
Hx of MI	18 (9.8)
Smoking	72 (39.3)
A-fib	14 (7.7)
eGFR <60	51 (27.9)
CAD	
1 Territory	69 (37.7)
2 Territories	63 (34.4)
3 Territories	51 (27.9)
Severity of aortic stenosis	
Mild	0
Moderate	19 (10.4)
Severe	164 (89.6)

Values represent mean±SD. Values in parentheses are percentages. NYHA=New York Heart Association functional class; COPD=Chronic obstructive pulmonary disease; Hx=History; MI=Myocardial infarction; A-fib=Atrial fibrillation; eGFR=Estimated glomerular filtration rate; CAD=Coronary artery disease.

Table 2. Mortality and significant postoperative morbidities

	Number (%)
Significant postoperative morbidities	
Stroke	5 (2.7)
Congestive heart failure	2 (1.1)
Pneumonia	3 (1.6)
Renal failure (requiring dialysis)	3 (1.6)
Bleeding	4 (2.2)
Others	7 (3.8)
Mortality	
Operative mortality	5 (2.7)
Late mortality	48 (26.2)

Values in parentheses are percentages.

other was secondary to a hemorrhagic diathesis and complications. The remaining two deaths were attributable to sepsis and postoperative atrioventricular block, respectively.

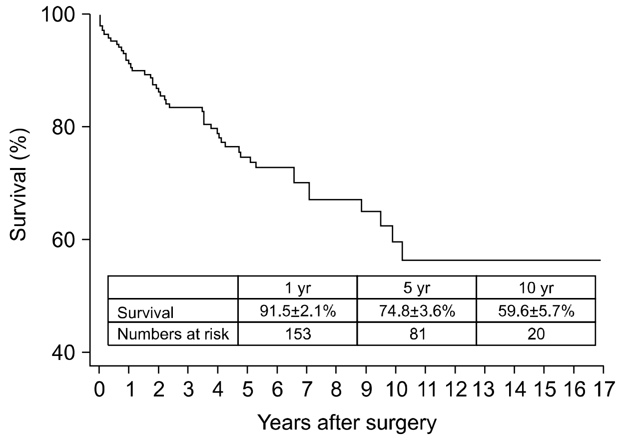

Fig. 1. Long-term survival rate.

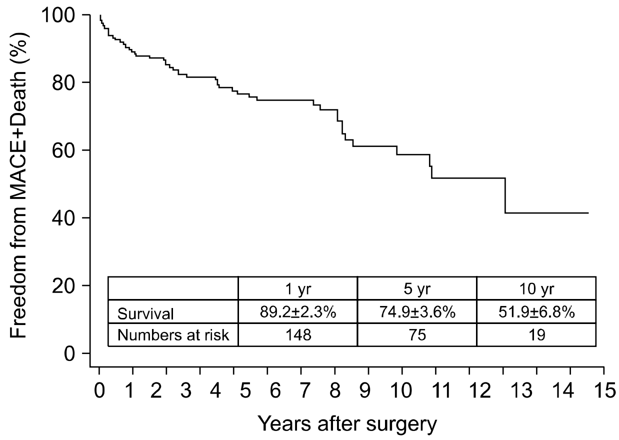

Fig. 2. Freedom from Major adverse cardiac events (MACE) and mortality.

3) Late outcomes

Late death occurred in 48 patients including 31 cardiac and 17 non-cardiac deaths. Non-cardiac deaths included cancer in 3 patients, infection in 3 patients, multiorgan failure in 3 patients, and accidents and other causes in 6 patients. Overall survival was 91.5±2.1% at 1 year, 74.8±3.6% at 5 years, and 59.6±5.7% at 10 years (Fig. 1).

Three reoperations were performed. One patient underwent a redo-CABG because of the occlusion of a saphenous vein graft to the left anterior descending artery (LAD). The other two patients underwent redo-AVR because of prosthetic aortic valve failure (Fig. 2).

Univariate analysis identified older age, a GFR less than

Table 3. Univariate and multivariate analysis for risk factors of mortality

	Univariate analysis		Multivariate analysis	
	Hazard ratio	p-value	Hazard ratio (CI)	p-value
Age	1.083	<0.001	1.081 (1.034～1.130)	0.001
eGFR <60	3.032	<0.001	2.307 (1.222～4.215)	0.007
History of AMI	2.672	0.008		
COPD	4.079	<0.001	2.176 (1.021～4.634)	0.044
Bioprosthetic valve	1.817	0.055		
Echocardiography data				
LV mass >280 g	1.729	0.08		
LVIDs	1.029	0.039	1.040 (1.009～1.073)	0.012
ESV	1.005	0.023		
EDV	1.004	0.057		
LV EF	0.977	0.016		
Incomplete revascularization	1.575	0.229		

Cox proportional hazard model (backward LR). AMI=Acute myocardial infarction; CI=Confidence Interval; eGFR=Estimated glomerular filtration rate; AMI=Acute myocardial infarction; NYHA IV=New York Heart Association functional class IV; LV=Left ventricle; LVIDs=Systolic left ventricular internal diameter; ESV=End-systolic volume; EDV=End-diastolic volume; EF=Ejection fraction.

Table 4. Univariate and multivariate analysis for risk factors of major adverse cardiac events and mortality

	Univariate analysis		Multivariate analysis	
	Hazard ratio	p-value	Hazard ratio (CI)	p-value
NYHA IV	3.28	0.004		
eGFR <60	3.155	<0.001	3.551 (1.964～6.420)	<0.001
Echocardiography data				
LV mass >280 g	2.28	0.009	1.960 (1.008～3.814)	0.047
LVIDs	1.029	0.075		
Aortic jet velocity	0.991	0.085		
Mean gradient	0.987	0.1		
ESV	1.004	0.02		
EDV	1.005	0.019	1.005 (1.000～1.010)	0.049
LV EF	0.982	0.06		
Incomplete revascularization	1.836	0.083		

Cox proportional hazard model (backward LR). CI=Confidence interval; eGFR=Estimated glomerular filtration rate; AMI=Acute myocardial infarction; NYHA IV=New York Heart Association functional class IV; LV=Left ventricle; LVIDs=Systolic left ventricular internal diameter; ESV=End-systolic volume; EDV=End-diastolic volume; EF=Ejection fraction.

60 mL/min, history of myocardial infarction (MI), presence of chronic obstructive pulmonary disease (COPD), left ventricular internal dimension of systole (LVIDs), end-systolic volume (ESV) and lower ejection fraction as factors associated with overall mortality. Multivariate analysis revealed that older age, a GFR less than 60 mL/min, and LVIDs were independent factors affecting long-term survival (Table 3).

In terms of MACE and death, univariate analysis identified a GFR less than 60 mL/min, New York Heart Association class IV, echocardiographic data including LV mass greater than 280 g, ESV, and EDV as significant factors. Multivariate analysis revealed that a GFR less than 60 mL/min, EDV, and LV mass greater than 280 g were also independent factors in MACE and death (Table 4).

DISCUSSION

The present study examined surgical and long-term clinical outcomes following combined AVR and CABG in patients with aortic stenosis and coronary artery disease. The outcomes and survival rates were acceptable. The operative mortality rate was 2.7%. This rate was similar to rates reported by others, which ranged from 3.4% to 6.5% [2,9-13], and which were no different from those for patients undergoing isolated AVR and not CABG [14-16]. In the current study, the 10-year cumulative survival rate was 59.6%, which was similar to rates reported by others (52% in [10] and 55% in [9,11]).

The present study included 18 patients (10.8%) with moderate aortic stenosis. It is broadly accepted that AVR should be performed in conjunction with CABG if aortic stenosis is severe or if the patient has symptoms. However, controversy exists regarding the treatment of asymptomatic patients with mild or moderate stenosis [17,18]. A recent study showed that AVR at the time of CABG for mild or moderate aortic stenosis appeared to convey a survival advantage on patients with moderate aortic stenosis but not on those with mild aortic stenosis [11,19,20].

1) Risk factors for long-term clinical outcomes

The present study found that older age had a negative effect on long-term survival, as reported elsewhere [3,10,12]. We found that in patients ≥70 years old, the 10-year survival rate was 24.5±10.7%, and that the rate decreased with greater age. This shorter life expectancy for patients older than 70 years should be taken into account when considering surgery in such patients.

We found that incomplete CABG revascularization did not influence late survival. An early study by Kobayashi and colleagues [21] showed that although extensive CAD negatively influenced early mortality, this did not negatively affect late survival. In addition, the number of diseased territories, the number of bypass grafts, incomplete revascularization, aortic stenosis, and aortic insufficiency did not predict late mortality in the cited study or our present work.

The present study found that survival was not affected by valve type (mechanical or bioprosthetic). These findings are consistent with previous studies showing satisfactory long-term results using either mechanical or bioprosthetic valves in AVR [22,23] and AVR-CABG [24,25] patients.

LV mass is proportional to the total force that contracting LV walls must receive at end-systole. As aortic stenosis becomes more severe, the measured values of LV mass, EDV, and LVID also become greater. These changes in the measured value mean LV hypertrophy (LVH). The results of the present study found that preoperative LVH might be a negative effect of both mortality and MACE, including mortality, because LVH caused problems with myocardial protection and remodeling due to scar change. Early surgery might therefore be a therapeutic option to further improve clinical outcomes and lessen operative risk [26,27].

The analysis of left ventricular function and its influence on long-term survival is complex in patients with both aortic valve disease and coronary disease. Segmental dysfunction secondary to myocardial infarction will not be improved by surgery and may theoretically have a more profound effect on risk than will generalized impairment of left ventricular function caused by aortic stenosis [9]. Previous studies [10,12,21] showed that a low EF increased the risk of undergoing AVR-CABG. However, EF was not found to influence long-term survival in the current study.

Several studies have documented ten-year cumulative survival rates similar (52% [10], 55% [9,11]) to the 59% from this study. Although this study contains younger patients with higher preoperative ejection fractions, several factors were also identified in this study as significant predictors of mortality.

CONCLUSION

The surgical results and long-term survival rates were acceptable for patients undergoing a combined CABG for aortic stenosis and coronary artery disease. Multivariate analysis found that older age, a GFR less than 60 mL/min, and greater LVIDs were independent variables affecting long-term survival in such patients.

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