Noninvasive estimate of left ventricular filling pressure correlated with early and midterm postoperative cardiovascular events after isolated aortic valve replacement in patients with severe aortic stenosis

Sung-A Chang, MD,[a] Pyo-Won Park, MD,[b] Kiick Sung, MD,[b] Sang-Chol Lee, MD,[a] Seung Woo Park, MD,[a] Young Tak Lee, MD,[b] and Jae K. Oh, MD[a,c]

Objectives: The aim of this study was to investigate whether preoperative estimated left ventricular filling pressure predicts the postoperative outcome in patients with severe aortic stenosis.

Methods: Two hundred ten patients who underwent isolated aortic valve replacement because of severe aortic stenosis were analyzed. Left ventricular filling pressure was noninvasively assessed based on the ratio between early diastolic mitral inflow and mitral annular velocity (E/E′), which was calculated based on results of mitral inflow and mitral annular tissue Doppler scanning. Early postoperative hospital events were reviewed. Postoperative mortality and morbidity were searched and compared according to left ventricular filling pressure.

Results: Preoperative functional class was associated with increased E/E′ values. Postoperative hospital events were higher in patients with increased preoperative E/E′ values. Midterm mortality of the overall population was very low after aortic valve replacement (2%). Cardiovascular event-free survival, including hospital visits caused by heart failure symptoms, embolic cerebral infarction, and sudden cardiac death, was significantly lower in the patients with increased left ventricular filling pressure and E/E′ values of greater than 12 ($P = .03$). Multivariable analysis showed a high hazard ratio of increased E/E′ values of greater than 12 (hazard ratio, 41; $P < .001$).

Conclusions: The incidence of postoperative mortality after isolated aortic valve replacement caused by severe aortic stenosis is relatively low in the current era. E/E′ representing diastolic filling pressure is the most important preoperative predictor of risk of early postoperative hospital course and postoperative morbidity. (J Thorac Cardiovasc Surg 2010;140:1361-6)

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Prolonged pressure overload in patients with severe aortic stenosis (AS) induces remodeling of the left ventricle and alteration of both systolic and diastolic function. As a result, left ventricular (LV) filling pressure is commonly increased in patients with severe AS.[1,2] The increased filling pressure results in pulmonary hypertension and dyspnea[2] in this patient population. However, most patients with increased LV filling pressure in the setting of severe AS have a normal left ventricular ejection fraction (LVEF). It is also likely that the increased filling pressure is partly related to superimposed diastolic dysfunction independent of severe AS. After aortic valve replacement (AVR), LV afterload rapidly decreases and LV function improves, but LV filling pressure can remain increased in some patients for years after surgical intervention and affects postoperative outcomes.[3,4]

Increased LV filling pressure is associated with diastolic dysfunction and hence is a reliable parameter to evaluate LV diastolic dysfunction.[5] Previous reports suggested that diastolic dysfunction,[6] pulmonary hypertension,[7] and more severe functional class[4] were associated with poor patient outcomes, and all of these factors can be explained by increased LV filling pressure. Therefore the single parameter of LV filling pressure might predict postoperative outcomes after AVR because of severe AS.

The velocity of mitral annular motion can be easily measured online by using echocardiography with the Doppler tissue-imaging technique. Because early diastolic velocity of the mitral annulus is a relatively load-independent index of LV relaxation and early mitral inflow velocity is associated with relaxation and LV filling pressure, the simple ratio between early diastolic mitral inflow and mitral annular velocity (E/E′) has been shown to be a reliable method for noninvasive estimation of LV filling pressure.[8,9] It is now routinely used in clinical practice, including in patients with moderate-to-severe AS.[10] The primary aim of this study

From the Cardiovascular Imaging Center, Cardiac and Vascular Center,[a] and the Department of Thoracic and Cardiovascular Surgery,[b] Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; and the Division of Cardiovascular Diseases,[c] Mayo Clinic College of Medicine, Rochester, Minn.

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Address for reprints: Jae K. Oh, MD, Division of Cardiovascular Diseases, Mayo Clinic College of Medicine, Gonda 6 South, 200 1st st SW, Rochester, MN 55905 (E-mail: oh.jae@mayo.edu); and Pyo-Won Park, MD, Department of Thoracic and Cardiovascular Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 IL Won-Dong, Kangnam-Ku, Seoul, 135-230, South Korea (E-mail: pwpark@skku.edu).

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Abbreviations and Acronyms

AS	= aortic stenosis
AVR	= aortic valve replacement
E/E′	= Ratio between early diastolic mitral inflow and mitral annular velocity
LA	= left atrial
LV	= left ventricular
LVEF	= left ventricular ejection fraction

was to investigate whether preoperative E/E′ values (noninvasively estimated LV filling pressure) predict postoperative adverse outcomes in patients with severe AS.

MATERIALS AND METHODS

Study Population

Two hundred forty-eight patients who underwent isolated AVR for degenerative severe AS from January 2003 to December 2008 in Samsung Medical Center were retrospectively reviewed. Patients who had rheumatic AS, other severe valve diseases requiring a valve operation, and a history of previous cardiac surgery or recent myocardial infarction in the last 6 months were excluded from this study. Patients who presented with acute coronary syndrome with left main disease or multivessel disease were also excluded. Of the 248 patients, 210 who had complete preoperative echocardiographic analysis, including tissue Doppler parameters, were our study subjects. Hospital records were reviewed, and clinical variables, including age, sex, cardiovascular risk factors, and/or other variables regarding AVR, were investigated.

Echocardiographic Examination

Preoperative echocardiographic parameters were acquired from our electronic medical database. Preoperative echocardiographic analysis was usually performed within 2 weeks before the operation. As a routine protocol, our laboratory measures LV systolic and diastolic dimensions, end-diastolic LV wall thickness, LVEF, and pulsed-wave Doppler velocities of mitral inflow. The LV mass index was calculated based on M-mode echocardiographic analysis, as previously described,[11] and the left atrial (LA) volume index was calculated with the prolate–ellipsoid biplane method.[12] Peak early (E) and late (A) diastolic velocities of mitral inflow were measured by using pulsed-wave Doppler scanning at the tip of the mitral valve leaflets. Peak early (E′) and late (A′) diastolic mitral annular velocities were acquired at the septum in the apical 4-chamber view. Aortic valve mean and peak transvalvular gradients were calculated from the peak aortic valve Doppler velocities interrogated from multiple transducer locations. Aortic valve area was calculated by using the continuity equation.[13]

Outcome Measures

The postoperative hospital course was reviewed regarding in-hospital cardiovascular events. In-hospital complications were divided into surgical and cardiovascular complications. The former included wound problems, including infection or bleeding and redo operations caused by technical failure. Cardiovascular complications were defined as cerebral embolism, cardiopulmonary resuscitation, and arrhythmia requiring cardioversion or pacemaker insertion before discharge. If a cardiovascular complication was associated with a surgical complication, that event was excluded from the cardiovascular events. Early postoperative mortality was defined as death within 30 days after AVR.

Postoperative outcomes and events after discharge were acquired from the review of medical records, direct telephone interviews with patients or their families, and national registry of birth and death data. Cause of death was classified as cardiac (sudden death, heart failure, or myocardial infarction) or noncardiac. Cardiovascular events were defined as heart failure requiring hospital admission or an early hospital visit, embolic cerebral infarction, or cardiac death during the follow-up period. This study protocol for retrospective review and follow-up analysis was approved by our institutional review committee (Samsung Medical Center).

Statistical Analysis

Continuous variables are expressed as means ± standard deviations. Time variables were expressed as medians ± interquartile ranges. Categorical variables are expressed as numbers and percentages. For comparison between 2 groups, the χ^2 test or Fisher's exact test was used for categorical variables, and the independent *t* test or Mann–Whitney test was applied for continuous variables, where appropriate, according to normality. The optimal cutoff value of E/E′ to predict postoperative morbidity was determined by using receiver operating characteristic curve analysis. Postoperative clinical outcomes were demonstrated by using the curve derived from the Kaplan–Meier estimation method and were compared by with the log-rank test. For multivariable analysis for cardiovascular events, the proportional hazard assumption was tested with Schoenfeld residuals and the Supremum test for proportional hazards assumption. Possible predictors were tested by using Cox proportional hazard regression with the bootstrapping method. Each proportional hazards model was subjected to 1000 bootstrap replications by using random samples generated from and consisting of the same number of patients as the original model. Bootstrap estimates of hazard ratios and 95% confidence intervals were calculated by using a bias-corrected method derived from the 1000 replications. All statistical analyses were performed with the Statistical Analysis Software package (SAS version 9.1, SAS Institute, Inc, Cary, NC).

RESULTS

Patient Characteristics

Clinical and echocardiographic characteristics of the 210 patients are summarized in Table 1. The ethnicity of all the patients was Korean. Severe dyspnea with New York Heart Association functional class 3 or 4 was present in 22% of the patients before AVR. LVEF was less than 50% in 18% of the patients. The mean E/E′ value was increased at 16.8 ± 8.6, and the LV mass index was increased at 151 g/m^2. E/E′ values were correlated with LVEF (r = –0.34, P < .001), aortic valve area (r = –0.24, P = .001), LV mass index (r = 0.23, P < .001), LA volume index (r = 0.42, P < .001), pulmonary hypertension (r = 0.48, P < .001), and the functional class of the patients (r = 0.30, P < .001). A history of coronary artery disease was presented in 17% of the patients, and coronary artery bypass grafting during AVR was performed in 11% of the patients.

Postoperative Hospital Course

None of the patients experienced early postoperative death within 30 days after AVR. Postoperative ventilator time was 11.0 ± 8.3 hours. Mean postoperative intensive cardiac unit and hospital stays after valve surgery were 1.0 ± 1.0 days and 8.0 ± 3.0 days, respectively.

Postoperative surgical complications were present in 5 (2.3%) patients, and in-hospital cardiovascular complications were present in 13 (6.2%) patients (embolic cerebral

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