Indexed left atrial size predicts all-cause and cardiovascular mortality in patients undergoing aortic valve surgery

Victor X. Mosquera, MD, PhD,[a] Alberto Bouzas-Mosquera, MD, PhD,[b] Miguel González-Barbeito, MD,[a] Victor Bautista-Hernandez, MD, PhD,[a] Javier Muñiz, MD, PhD,[c] Nemesio Alvarez-García, MD, PhD,[b] and José J. Cuenca-Castillo, MD[a]

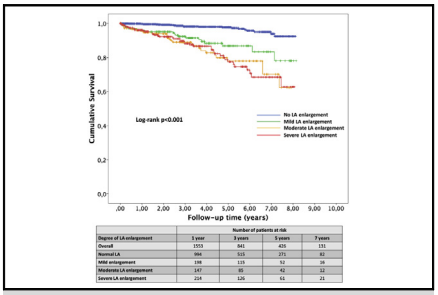
ABSTRACT

Objectives: The enlargement of the left atrium has been identified as a marker of chronically increased left ventricular filling pressure and left ventricular diastolic dysfunction. This study aims to evaluate the association of indexed left atrial diameter with stroke, cardiovascular mortality, the combined event, and all-cause mortality in patients who underwent aortic valve surgery.

Methods: Indexed left atrial diameter was measured in 2011 adult patients (mean age, 70.9 ± 10.8 years; 58.7% were men) who underwent aortic valve surgery between January 2008 and March 2016.

Results: On the basis of the criteria of the American Society of Echocardiography, indexed left atrial diameter was normal in 64% of patients, mildly enlarged in 12.4% of patients, moderately enlarged in 9.2% of patients, and severely enlarged in 14.3% of patients. Over a mean follow-up period of 3.2 ± 2.1 years, there were 334 deaths and 97 strokes. Cardiovascular mortality survival at 5 years among patients with normal, mild, moderate, and severe left atrial enlargement was 91.6%, 86.8%, 77.9%, and 77.4%, respectively ($P < .001$). After covariable adjustment, Cox regression analysis showed indexed left atrial diameter as an independent predictor of all-cause mortality (hazard ratio per 1-cm/m^2 increment, 1.545; 95% confidence interval, 1.252-1.906, $P < .001$), cardiovascular death (hazard ratio per 1-cm/m^2 increment, 1.971; 95% confidence interval, 1.541-2.520; $P < .001$), and the combined event (hazard ratio per 1-cm/m^2 increment, 1.673; 95% confidence interval, 1.321-2.119; $P < .001$).

Conclusions: Indexed left atrial diameter is a strong predictor of long-term outcomes in patients with aortic valve diseases who undergo surgery. (J Thorac Cardiovasc Surg 2017;■:1-10)



Kaplan–Meier curves for cardiovascular survival stratified according to indexed LA diameter.

Central Message

Indexed LA diameter is a strong predictor of long-term outcomes in patients undergoing AVS.

Perspective

Indexed LA measurements reflect the burden of elevated LV filling pressure and LV diastolic dysfunction in patients undergoing AVS and have demonstrated their value to predict the long-term outcomes of these patients. Further research should address whether indexed LA diameters may be useful to guide the best therapy for aortic valve diseases.

ACQ

Different left atrial (LA) measurements have been proposed as predictors of long-term outcome in the general population,[1,2] but also in specific subgroups of patients, such as those with left ventricular dysfunction,[3] myocardial infarction,[4] or hypertrophic cardiomyodiopathy.[5] However, little information is available in the literature on the relationship between indexed LA size and outcome among patients who are referred for aortic valve surgery (AVS).

The enlargement of the left atrium has been identified as a marker of chronically increased left ventricle (LV) filling pressure and LV diastolic dysfunction.[6] Increased nonindexed LA diameter has been described as a marker of diastolic dysfunction among patients with asymptomatic aortic stenosis,[7] as well as a factor of poor outcome in patients undergoing AVS.[8] However, little is known about the long-term prognostic value of indexed LA diameter in

Scanning this QR code will take you to the supplemental tables and video for this article.

From the Departments of [a]Cardiac Surgery and [b]Cardiology, Complejo Hospitalario Universitario de A Coruña; and [c]Instituto Universitario de Ciencias de la Salud, Universidad de A Coruña, A Coruña, Spain.

Received for publication July 31, 2016; revisions received Jan 5, 2017; accepted for publication Jan 25, 2017.

Address for reprints: Victor X. Mosquera, MD, PhD, Cardiac Surgery Department, Complejo Hospitalario Universitario de A Coruña, As Xubias n°84, CP 15006 A Coruña, Spain (E-mail: Victor.X.Mosquera.Rodriguez@sergas.es).

0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2017.01.054

Abbreviations and Acronyms

AVS = aortic valve surgery
BSA = body surface area
CABG = coronary artery bypass grafting
CI = confidence interval
euroSCORE = European System for Cardiac Operative Risk Evaluation
HR = hazard ratio
LA = left atrial
LV = left ventricle
VKA = vitamin K antagonist

patients with chronic LV pressure or volume overload due to an aortic valve condition.

The aim of this study is to determine the association between indexed LA diameter with all-cause mortality and cardiovascular mortality, as well as with stroke and the combined event cardiovascular death or stroke in a large cohort of patients with aortic valve diseases who underwent AVS.

MATERIALS AND METHODS

Between January 2008 and March 2016, 2460 adult patients (age >18 years) underwent AVS at Complejo Hospitalario Universitario de A Coruña. For each patient, the first comprehensive transthoracic echocardiogram was selected. We excluded 400 patients for whom the LA indexed size was not reported and 49 patients for whom no follow-up data were available. Thus, 2011 patients were finally included. The study was approved by the local research ethics committee (Comité Ético de Investigación Clínica de Galicia) (Study Identification Number 2016/259).

Clinical Data

Demographic, clinical, and echocardiographic data were entered in our surgical database. The study was completed using linked clinical and administrative databases, as well as electronic medical records through the Department of Information Technology of Complejo Hospitalario Universitario de A Coruña. Data sources were linked using unique identifiers.

A history of atrial fibrillation was defined as atrial fibrillation recorded at the time of the admission for AVS or any previously known episode of atrial fibrillation. Creatinine clearance was calculated using the Cockcroft–Gault formula. Extracardiac arteriopathy was defined as 1 or more of the following factors: claudication, carotid occlusion or more than 50% stenosis, amputation for arterial disease, and previous or planned intervention on the abdominal aorta, limb arteries, or carotid arteries. Chronic lung disease was defined as long-term use of bronchodilators or steroids for lung disease. Active endocarditis was considered when the patient was still receiving antibiotic treatment for endocarditis at the time of surgery.

Postoperative standard anticoagulation with vitamin K antagonists (VKAs) and heparin was initiated after surgery in all patients receiving a mechanical prosthesis, patients with chronic or new-onset atrial fibrillation or atrial flutter, or patients with other less common indications to the appropriate target international normalized ratio, as recommended by current practice guidelines.

Echocardiographic Data

Echocardiograms were performed in the left lateral decubitus position using standard imaging planes, according to the recommendations of the American Society of Echocardiography.[9] LA diameter was measured using M-mode or 2-dimensional echocardiography, from the posterior aortic wall to the posterior LA wall, in the parasternal long-axis view at the end-ventricular systole (ie, just before the mitral valve opening), as we have previously reported.[10]

LA size was indexed by dividing by body surface area (BSA) according to the recommendations of the American Society of Echocardiography.[9] Although there are sex differences in LA size, these are nearly completely accounted for by variation in body size.[9,11,12]

LA enlargement was defined as an indexed LA diameter of 2.3 cm/m^2 or greater; an indexed LA diameter below this value defined normal LA size. LA enlargement was further classified as mild (indexed LA diameter, 2.4-2.6 cm/m^2), moderate (2.7-2.9 cm/m^2), or severe ($\geq$3 cm/m^2) in accordance with the recommendations of the American Society of Echocardiography.[9]

Left ventricular ejection fraction (LVEF) was estimated using the Teichholz formula or Simpson's rule. Normal LV function was defined as LVEF 55% or greater.[9] Left ventricular systolic dysfunction was classified as mild (LVEF 45%-54%), moderate (30%-45%), or severe (<30%) in accordance with the recommendations of the American Society of Echocardiography.[9]

Pulmonary hypertension was classified according to the systolic pulmonary artery pressure classified as moderate (31-55 mm Hg) and severe (>55 mm Hg). Significant mitral valve disease was defined as more than mild mitral regurgitation or significant mitral valve stenosis.

Follow-up and Outcome Measures

Follow-up data were retrieved from healthcare databases, electronic medical records, and death certificates. The outcomes were stroke, cardiovascular mortality, the combined event, and all-cause mortality.

Cardiovascular death was defined as death due to acute myocardial infarction, sudden cardiac death, heart failure, stroke, cardiovascular procedure, cardiovascular hemorrhage, and other cardiovascular causes (ie, nonstroke intracranial hemorrhage, nonprocedural or nontraumatic vascular rupture, or pulmonary hemorrhage from a pulmonary embolism) as recommended by the American College of Cardiology.[13] Ischemic stroke was defined as codes 433.x1, 434.x1, and 436 of the International Classification of Diseases, Ninth Revision.

Statistical Analysis

The quantitative variables are expressed as mean and standard deviation or median and rank, when appropriate; the qualitative variables are expressed as an absolute value (n) and the percentage. For bivariate analysis, proportions were compared with contingency tables by means of the chi-square test. Student *t* test or Wilcoxon rank-sum test was used to compare means. One-way analysis of variance was used to determine potential differences in several quantitative variables among the different LA sizes.

Survival was determined with Kaplan–Meier methodology. Differences in the probability of survival between groups were analyzed with the log-rank (Mantel–Cox) test. Binary logistic regression analysis was performed to study the potential impact of indexed LA diameter on operative mortality.

Cox proportional hazards regression models were used to assess the associations between indexed LA diameter and outcomes. Adjusted hazard ratio (HR), 95% confidence intervals (CIs), and *P* values were derived. The assumption of proportionality of hazards was verified using log-minus-log survival plots. Separate analyses were performed using indexed LA diameter as a continuous variable or categorized according to the severity criteria of the American Society of Echocardiography.[9] The linearity assumption of the continuous variables in the model was evaluated by applying restricted cubic spline transformations to the continuous measures using 3 degrees of freedom.

Fine-Gray proportional hazard regression for competing events (death) was used to assess the associations between indexed LA diameter and stroke, also adjusting for covariates. Multivariate Cox proportional hazards