Prognostic Value of Left Atrial Volume in Asymptomatic Organic Mitral Regurgitation

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Background: Basal left atrial volume (LAV) indexed to body surface area (LAVI) predicts adverse events in patients with organic mitral regurgitation, but information is lacking regarding change in left atrial volume during follow-up.

Methods: One hundred forty-four asymptomatic patients (mean age, 71 ± 12 years; 66% women; mean ejection fraction, 66 ± 4.8%) with moderate to severe mitral regurgitation were prospectively included, with a median follow-up period of 2.76 years (interquartile range, 1.86–3.48 years).

Results: Fifty-four patients (37.50%) reached the combined end point of dyspnea and/or systolic dysfunction. Both basal and change in LAV were independently associated with the combined end point on multivariate analysis: for basal LAVI ≥ 55 mL/m^2, odds ratio, 2.26 (95% confidence interval, 1.04–4.88; P = .038), and for change in LAV ≥ 14 mL, odds ratio, 7.32 (95% confidence interval, 3.25–16.48; P < .001), adjusted for effective regurgitant orifice area and deceleration time. Combined event-free survival at 1, 2, and 3 years was significantly less in patients with basal LAVI ≥ 55 mL/m^2 (75%, 58%, and 43%) than in those with basal LAVI < 55 mL/m^2 (95%, 89%, and 77%) (log-rank test = 15.38, P = .0001). The incidence of the combined end point was highest (88%) in patients with basal LAVI ≥ 55 mL/m^2 and change in LAV ≥ 14 mL.

Conclusions: Measurement of basal LAV and its increase during follow-up predict an adverse course in patients with moderate and severe asymptomatic mitral regurgitation. Hence, its assessment could be incorporated into the currently used algorithm for risk stratification and decision making in this group of patients. (J Am Soc Echocardiogr 2013;26:699-705.)

Keywords: Heart valve diseases, Asymptomatic organic mitral regurgitation, Left atrial volume

Organic mitral regurgitation (MR) is a frequent disorder encountered worldwide, and its prevalence increases with age. In fact, it is the second most frequent valve disease after aortic stenosis.[1]

Currently, the surgical approach is strongly recommended in patients with symptoms of heart failure and/or parameters of contractile dysfunction measured by echocardiography, such as left ventricular ejection fraction (LVEF) and end-systolic diameter (ESD).[2] However, the management of asymptomatic patients is less clearly defined, and although universally accepted echocardiographic predictors of surgical intervention are available, they are not completely reliable.[3-6]

Enlargement of the left atrium is a marker of the hemodynamic consequences of chronic MR.[7] Also, there is enough information to recommend using the estimation of left atrial (LA) volume (LAV), because it is the most representative measurement of LA enlargement, compared with linear measurements.[8-11] The value of LAV has already been assessed as predictor of adverse events in other disorders, such as acute myocardial infarction, hypertrophic cardiomyopathy, and dilated cardiomyopathy.[12-15] A recent study showed the independent prognostic value of LAV indexed to body surface area (LAVI) as predictor of cardiovascular events throughout the severity spectrum of this valve disease.[16]

The goal of this study was to assess LAV measured at baseline and its change during follow-up as a predictor of cardiovascular events in patients with moderate and severe MR.

METHODS

Study Population

A group of asymptomatic patients aged > 18 years with diagnoses by echocardiography of at least moderate MR (effective regurgitant orifice area [EROA ≥ 0.20 cm^2]) were included; they had to have adequate follow-up and an organic cause of regurgitation. Patients were excluded if they had any of the following: symptoms of heart failure (New York Heart Association functional class ≥ II), left ventricular systolic dysfunction (LVEF < 60% and/or ESD > 40 mm), atrial fibrillation, concomitant valve disorders (moderate or severe aortic disease, moderate or severe mitral stenosis, or significant right-sided organic valve disease), ischemic MR, prior valve or coronary surgery, cardiomyopathies and pericardial diseases, congenital heart disease, end-stage disease with survival < 1 year, or a poor echocardiographic window. All patients provided informed consent, and the study was approved by the local ethics committee.

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Abbreviations

CI = Confidence interval

DT = Deceleration time

EROA = Effective regurgitant orifice area

ESD = End-systolic diameter

LA = Left atrial

LAV = Left atrial volume

LAVI = Left atrial volume indexed to body surface area

LVEF = Left ventricular ejection fraction

MR = Mitral regurgitation

OR = Odds ratio

ROC = Receiver operating characteristic

Clinical Data

All patients underwent complete clinical evaluations at admission, and information regarding clinical and laboratory variables was collected. Patients were followed by their treating cardiologists at least every 6 months.

Echocardiography

All patients underwent comprehensive Doppler and two-dimensional echocardiography at baseline and every 6 months during follow-up. The degree of MR was quantified according to EROA.[17] EROA was calculated as the average of the quantitative measurement and the proximal isovelocity surface area method.[17,18] Quantitative measurement was performed by measuring volumetric flow through the mitral valve in diastole in comparison with a measure of forward stroke volume measured at the LV outflow tract in systole.[17]

Ventricular volumes and LVEF were measured using Simpson's biplane technique. The remaining echocardiographic variables as well as end-diastolic diameter and ESD were assessed according to American Society of Echocardiography recommendations.[11] Pulmonary artery systolic pressure was measured at rest in the apical four-chamber view with continuous-wave Doppler at the tricuspid valve by averaging three beats.[19]

Assessment of maximal LAV was performed using two-dimensional echocardiography with Simpson's biplane method.[11,20] The change in LAV was calculated as the difference between the first and last measurements (preceding the appearance of symptoms and/or LV dysfunction). The valve lesion was identified as involving one and/or both leaflets and the presence of a "new flail valve" was noted. Echocardiographic readings were averaged by two independent observers, who were blinded to the clinical information. Echocardiographic examinations were performed using General Electric Vivid Five equipment (GE Healthcare, Milwaukee, WI).

Definition of End Points

The combined end point consisted of the development of symptoms and/or LV dysfunction during follow-up. The presence of symptoms during follow-up was defined as the occurrence of New York Heart Association functional class II to IV dyspnea. The presence of LV dysfunction was defined as LVEF < 60% during follow-up. ESD > 40 mm during follow-up was also considered as systolic dysfunction. Other events were also recorded, such as valve surgery, atrial fibrillation, and death. The indication for valve surgery was defined by the referring physician according to his or her clinical assessment. Death was classified as being cardiovascular or noncardiovascular in origin according to the information provided by the attending physician, the medical report, or the autopsy, when available. Events were collected by an investigator who was blinded to the clinical and echocardiographic data.

Statistical Analysis

Continuous and categorical variables are expressed as mean ± SD and percentages, respectively. Cutoff points for each parameter were obtained from previous studies.[2] Cutoff points were assessed retrospectively according to the best performance point on the receiver operating characteristic (ROC) curve, to identify the final combined end point. A bivariate analysis was performed between each of the clinical and echocardiographic parameters and the combined end point and with the other cardiovascular events. Results are expressed as odds ratio (OR) and their respective 95% confidence intervals (CIs). We also constructed a multivariate logistic regression model with a manual strategy. Variables were entered into the model according to their statistical significance ($P < .20$) on bivariate analysis, and only those that were significantly associated ($P < .05$) with the combined end point remained in the model. Discrimination of the various models with and without LAV was assessed using ROC curve analysis. A subgroup analysis was performed assessing pulmonary hypertension, sex, and age as possible effect modifiers. Actuarial survival was assessed using Kaplan-Meier analysis for each of the LAVI strata. Statistical significance among the different strata was tested using log-rank tests. Finally, four groups were created combining the presence of a basal increased or not increased LAVI with increased or not increased LAV during follow-up. Comparisons were made using χ^2 tests, applying Bonferroni's correction. Statistical analysis was performed using Stata version 8.0 and Stata version 11.1 (StataCorp LP, College Station, TX). *P* values < .05 were considered to be statistically significant.

RESULTS

The mean age was 71 ± 12 years, 66% were women, the average EF was 66 ± 4.8%, the mean EROA was 0.47 ± 0.11 cm^2, the mean LAVI was 50 ± 19 mL/m^2, and the mean change in LAV was 14 ± 18 mL (Table 1).

The areas under the ROC curve of the different LAV values at baseline and their change during follow-up (median, 7 months since enrollment) to identify the combined end point were 0.64 (95% CI, 0.54–0.73) and 0.74 (95% CI, 0.65–0.82), respectively. According to ROC curve analysis, the optimal cutoff points were a basal LAVI ≥ 55 mL/m^2 (positive likelihood ratio, 2.16) and a change in LAV ≥ 14 mL (positive likelihood ratio, 2.87).

Patients with basal LAVI ≥ 55 mL/m^2 had significantly greater end-diastolic volume than patients with LAVI < 55 mL/m^2 (97 ± 46 vs 82 ± 26 mL, $P = .014$), greater end-diastolic diameter (5.56 ± 0.61 vs 5.06 ± 0.52 cm, $P < .001$), greater ESD (3.18 ± 0.54 vs 2.95 ± 0.51 cm, $P = .015$), greater EROA (0.52 ± 0.11 vs 0.44 ± 0.10 cm^2, $P < .001$), greater LA diameter (5.23 ± 0.66 vs 4.50 ± 0.48 cm, $P < .001$), and greater LAVI (72 ± 15 vs 40 ± 8 mL/m^2, $P < .001$) (Table 1). Sixty of 144 patients (42%) had changes in LAV ≥ 14 mL.

Events

Among the whole cohort, 54 of 144 patients (37.50%) reached the combined end point. Twelve of 144 patients (8.33%) died; seven of these deaths (58%) were cardiovascular in origin. Fifty-two of 144 patients had dyspnea (36.11%), and 10 of 144 patients (6.94%) had ventricular dysfunction. Mitral valve surgery was performed in 26 of 144 patients (18.06%). Eighteen of 144 patients (12.50%) developed atrial fibrillation.