Clinical Investigations

Increased Left Atrial Volume Index Predicts a Poor Prognosis in Patients With Heart Failure

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ABSTRACT

Background: Left atrial volume index (LAVI) is known to reflect the duration and severity of increased left atrial pressure caused by left ventricular (LV) diastolic dysfunction. However, the prognostic value of LAVI in patients with heart failure (HF) has not been fully investigated.

Methods and Results: Transthoracic echocardiography was performed in 146 consecutive patients (78 men, 68 women; mean age 72 ± 12 y) who were hospitalized for HF. There were 45 cardiac events (32%) during a median follow-up period of 448 days. There were no significant differences in LV end-diastolic dimensions or ejection fraction between patients who did or did not have cardiac events. However, LAVI was markedly higher in patients with, than those without, cardiac events (56 ± 26 vs 44 ± 22 mL/m^2; $P < .01$). Kaplan-Meier analysis showed that there was a stepwise increase in risk of cardiac events with each increment of LAVI category, and LAVI >53.3 mL/m^2 correlated with the highest risk of cardiac events (log-rank test; $P < .01$). Multivariate Cox proportional hazard analysis showed that high LAVI was an independent predictor for cardiac events (hazard ratio 1.427; 95% confidence interval 1.024−1.934; $P < .05$).

Conclusion: LAVI may be useful for stratification of risk in patients with HF. (*J Cardiac Fail 2011;17:210−216*)

Key Words: Diastolic dysfunction, left atrial volume, risk stratification, prognostic factor.

Heart failure (HF) is a major cause of death, and it has a poor prognosis despite the significant reduction in mortality achieved in clinical trials.[1−3] Therefore, the prognostic evaluation and stratification of risk in patients with HF continue to be important, involving complex assessments of multiple interacting variables. Numerous studies have shown that left ventricular (LV) systolic dysfunction and diastolic dysfunction are prognostic factors for HF.[4,5]

Because the left atrium (LA) is directly exposed to LV diastolic pressure through the mitral valve, the size of the LA reflects the duration and severity of increased LA pressure following increased LV diastolic pressure. Therefore, LA volume is reported to be a sensitive marker of LV diastolic dysfunction.[6−8] Recently, the LA volume index (LAVI) was suggested as a new marker for cardiac function. It was also reported that a high LAVI was a powerful predictor of poor prognosis after acute myocardial infarction.[9] However, the prognostic value of LAVI in patients with HF has not been fully investigated.

The aim of the present study was to examine the clinical significance of LAVI in patients with HF. We hypothesized that LAVI increases with increasing severity of HF, and that LAVI provides important prognostic information.

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Methods

Study Design

Out of 166 consecutive patients with HF, we prospectively studied 146 patients (78 men, 68 women; mean age 72 ± 12 y) who were admitted to Yamagata University Hospital, Yamagata, Japan, for treatment of worsening HF or therapeutic evaluation of HF. The diagnosis of HF was made by 2 senior cardiologists using the generally accepted Framingham criteria[10] and other relevant information, including a history of dyspnea and symptomatic exercise intolerance with signs of pulmonary congestion or peripheral edema, the presence of moist rales on auscultation, or documentation of left ventricular enlargement or dysfunction by chest X-ray or echocardiography.[11]

The functional severity of HF at admission was assessed as New York Heart Association (NYHA) functional class II in 34 patients, class III in 73 patients, and class IV in 39 patients. The etiology of HF was dilated cardiomyopathy in 40 patients (27%), ischemic heart disease in 37 (25%), valvular heart disease in 19 (13%), hypertensive heart disease in 17 (12%), and other causes in 33 (23%). Diagnoses of hypertension, diabetes, and hyperlipidemia were obtained from medical records or patient histories of current or previous medical therapy. Patients with no history of atrial fibrillation (AF), and who did not show AF on continuous electrocardiographic monitoring during hospitalization, were defined as patients with sinus rhythm, and patients with transient and chronic AF were defined as AF patients. The exclusion criteria were renal insufficiency characterized by a serum creatinine concentration >2.0 mg/dL (n = 10), severe mitral regurgitation (MR; n = 4) or previous mitral valve surgery (n = 4), mitral stenosis (n = 1), and atrioventricular block (n = 1). Informed consent was given by each of the patients before participation in the study, and the protocol was approved by the institution's Human Investigations Committee.

Blood samples were obtained at admission and discharge for measurement of plasma B-type natriuretic peptide (BNP), creatinine, uric acid, and sodium. Plasma BNP levels were measured by using a commercially available specific radioimmunoassay (Shiono RIA BNP assay kit; Shionogi Co, Tokyo, Japan).[11] Clinical data, including age, gender, and NYHA functional class at admission, were obtained from hospital medical records and patient interviews. Diuretics were administered in flexible doses on the basis of body weight and daily diuresis. The time of discharge was decided by 2 senior cardiologists.

Echocardiography

Transthoracic echocardiography was performed 3−7 days before discharge, on a Hewlett-Packard Sonos 7500 ultrasound instrument, equipped with a sector transducer (carrier frequency of 2.5 or 3.75 MHz). Therefore, all echocardiographic data were measured at the chronic compensation phase of HF.

LA volume was assessed at LV end-systole by using the biplanar area-length method from 4- and 2-chamber views.[7] Measurements of LA volume were indexed by body surface area (LA volume index; LAVI). The normal range for LAVI has been reported to be 14−26 mL/m^2.[12,13] An LAVI value ≥32 mL/m^2 is considered to indicate significant enlargement,[7] and an LAVI value ≥40 mL/m^2 is considered to indicate severe enlargement.[14]

Left atrial dimension (LAD) was measured at end-systole in the 2-dimensional parasternal long-axis view. LV internal diameter and wall thickness were measured at end-diastole and end-systole in the 2-dimensional parasternal long-axis view.[14] LV end-diastolic dimension (LVDd) was used to calculate LV mass index (LVMI), using an anatomically validated formula.[15] LV ejection fraction (LVEF) was calculated using the biplanar method of disks (modified Simpson rule).[14] The Tei index was measured as previously described.[16] All patients underwent pulsed-wave Doppler examination of mitral inflow. Peak transmitral-flow E-wave and A-wave velocities, E-wave deceleration time (DCT), and the ratio of E-wave to A-wave were measured from the apical 4-chamber view. The apical 4-chamber view was used to obtain tissue Doppler imaging (TDI) of the mitral annulus. A sample volume of the pulsed-wave Doppler was positioned at the lateral side of the mitral annulus, and the spectral signal of the mitral annular velocity was recorded. The peak early (E′) mitral annular velocity was measured and the ratio of the E-wave to E′ (E/E′) calculated. All echocardiographic measurements were calculated as mean values from 5 consecutive cardiac cycles.

Endpoints and Follow-up of Patients

Patients were prospectively followed until the occurrence of cardiac events, and no patients were lost to follow-up after discharge (median follow-up period of 502 days). The endpoints were: 1) cardiac death, defined as death due to worsening HF or sudden cardiac death; and 2) worsening HF requiring readmission to hospital.[11,17] Sudden cardiac death was defined as death without definite preceding symptoms or signs and was confirmed by the attending physician.

Statistical Analysis

Results are expressed as mean ± SD for continuous variables and as percentages of the total number of patients for categoric variables. Skewed variables are presented as median and interquartile range. The *t* test and chi-square test were used for comparison of continuous and categoric variables, respectively. When the data was not normally distributed, the Mann-Whitney test was used. A Cox proportional hazard analysis was performed to determine independent predictors of cardiac events for the entire population. Variables that were significant in the univariate analysis were entered into the multivariate model which adjusted for age, LVDd, and AF. The cardiac event−free curve was analyzed by the Kaplan-Meier method and compared by the log-rank test. The optimum LAVI for predicting cardiac events was determined as that giving the largest sum of sensitivity plus specificity on the receiver operating characteristic (ROC) curve. ROC curves were constructed to evaluate the area under the curves (AUC). Statistical significance was defined as $P < .05$. Statistical analyses were performed using a standard statistics computer program. The intraobserver and interobserver reliability of LAVI measurements were assessed by 2 echocardiologists in 20 patients, each repeated once. Based on the intraclass correlation coefficient, the mean intraobserver reliability of LAVI measurements was 98.0% and the mean interobserver reliability was 95.6%.

Results

Clinical Characteristics of the Study Subjects

The mean age of the study subjects was 72 ± 12 years, 53% of the patients were men, 36% were classified as AF patients, and 77% were in NYHA functional classes III or