Predictive Value of Left Atrial Deformation on Prognosis in Severe Primary Mitral Regurgitation

Li-Tan Yang, MD, Yen-Wen Liu, MD, Jhih-Yuan Shih, MD, Yi-Heng Li, MD, PhD, Liang-Miin Tsai, MD, Chwan-Yau Luo, MD, and Wei-Chuan Tsai, MD, *Tainan, Taiwan*

Background: Impaired left atrial (LA) deformation is noted in patients with severe primary mitral regurgitation (MR), but its prognostic value is unknown. The aim of this study was to investigate the prognostic significance of LA deformation parameters in patients with chronic severe primary MR.

Methods: A total of 104 patients with asymptomatic chronic severe primary MR (Carpentier type II) and preserved left ventricular systolic function were prospectively recruited. Global peak positive strain of the left atrium (LASp) and strain rate in the LA filling phase (LASRr) as well as strain rate in the LA conduit phase were identified using two-dimensional speckle-tracking echocardiography.

Results: During a mean follow-up period of 13.2 ± 9.5 months, 22 patients reached a composite end point of death and mitral valve repair or replacement prompted by heart failure development. Among the clinical and echocardiographic parameters, LV end-systolic volume index (19.5 ± 9.5 vs 15.7 ± 6.3 mL/m^2, P = .028), LASp (22.7 ± 10.4% vs 27.2 ± 9.1%, P = .049), and LASRr (1.97 ± 0.6 vs 2.33 ± 0.6 1/sec, P = .013) varied between the two groups in terms of end points but not age, LA volume index, left ventricular ejection fraction, pulmonary artery systolic pressure, and presence of atrial fibrillation. After multivariate analysis, low LASp (odds ratio, 3.606; 95% CI, 1.294–10.052; P = .014) and low LASRr (odds ratio, 2.857; 95% CI, 1.078–7.572; P = .035) remained powerful outcome indicators.

Conclusions: In patients with asymptomatic severe primary MR, reduced LASp and LASRr predicted a worse prognosis. These findings may offer additional information to guide early surgery. (J Am Soc Echocardiogr 2015;■:■-■.)

Keywords: Left atrium, Mitral regurgitation, Strain rate, Speckle-tracking echocardiography

Severe primary mitral regurgitation (MR) is a public health burden that occurs most commonly in the senescent population and is associated with a nonnegligible yearly mortality rate of up to 6% if treated medically.[1] Surgery is currently the only option to restore quality of life and improve outcomes.[1] However, optimal surgical timing in asymptomatic patients without left ventricular (LV) dysfunction remains controversial.[2,3] This conflict is reflected in the current international consensus statements, in which a class IIA recommendation is made in the North American guidelines in favor of early surgical repair,[4] versus a class IIB recommendation in Europe.[5] This difference stems in part from diverging opinions regarding the consequences of uncorrected severe MR, which is considered a benign disease to which a strategy of watchful waiting should be applied,[6] as opposed to an unfavorable process requiring early surgery.[7]

This clinical dilemma exists not only because of the unpredictable outcomes in stable individuals with severe primary MR but also because of the unknown threshold of normal cardiac adaptive response. Patients are often free of symptoms, with an adequate forward stroke volume, until the heart fails to accommodate. Consequently, early recognition of indicators of poor prognosis is paramount in risk stratification to guide treatment, including timely mitral valve (MV) surgery.

In a previous study (see Figure 1 for participants included in both studies), we demonstrated the added value of left atrial (LA) deformation analysis by two-dimensional (2D) speckle-tracking echocardiography (STE) in patients with severe primary MR with preserved LV ejection fractions (LVEFs).[8] Impaired LA deformation was linked to a deterioration in functional capacity despite a similar degree of chamber size and the absence of subclinical LV dysfunction (evaluated by global longitudinal strain [GLS]), but not conventional parameters for surgical decision making, including pulmonary artery systolic pressure (PASP) and atrial fibrillation (AF).[4] As a result, we speculated that LA deformation parameters may be used to predict outcomes in asymptomatic patients with severe primary MR, of which little is currently known.

From the Division of Cardiology, Department of Internal Medicine (L.-T.Y., Y.-W.L., Y.-H.L., L.-M.T., W.-C.T.); the Department of Public Health (L.-T.Y.), and the Department of Surgery (C.-Y.L.), National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan; the Department of Internal Medicine, Tainan Hospital, Tainan, Taiwan (L.-T.Y.); and the Department of Internal Medicine, Chi-Mei Hospital, Tainan, Taiwan (J.-Y.S.).

This study was supported by grant NSC 101-2314-B-006-074 from the National Science Council, Executive Yuan, Taipei, and grant NCKUH-10302001 from the National Cheng Kung University Hospital, Tainan, Taiwan.

Reprint requests: Wei-Chuan Tsai, MD, National Cheng Kung University Hospital, Department of Internal Medicine, 138 Sheng-Li Road, Tainan 704, Taiwan (E-mail: *wctsai@seed.net.tw*).

0894-7317/$36.00

http://dx.doi.org/10.1016/j.echo.2015.07.004

Abbreviations

AF = Atrial fibrillation

GLS = Global longitudinal strain

LA = Left atrial

LASp = Peak positive strain of the left atrium

LASRc = Strain rate in the left atrial conduit phase

LASRr = Strain rate in the left atrial filling phase

LAVd = Left atrial volume during left ventricular end-diastole

LAVi = Left atrial volume index

LAVs = Left atrial volume during left ventricular end-systole

LV = Left ventricular

LVEF = Left ventricular ejection fraction

LVESVi = Left ventricular end-systolic volume index

MR = Mitral regurgitation

MV = Mitral valve

PASP = Pulmonary artery systolic pressure

STE = Speckle-tracking echocardiography

2D = Two-dimensional

METHODS

Participants

Figure 1 is a diagram of our present and previous studies. Between December 2010 and August 2013, a total of 520 patients with chronic severe MR undergoing echocardiography in the outpatient clinic were screened. The initial exclusion criteria were (1) LVEF < 60%; (2) MR of Carpentier type I or III, caused by regional or global LV remodeling without structural abnormalities of the MV (functional or ischemic MR) and MR caused by rheumatic heart disease; (3) coexistent aortic valve disease and mitral stenosis of more than a mild degree; (4) prior open heart surgery; and (5) congenital heart disease.

The remaining 168 patients with chronic severe primary MR (caused by diseases involving the MV) and LVEFs ≥ 60% received surgical referrals guided by current recommendations[5] and were excluded if any of the following was present: (1) symptoms of heart failure or effort-related limitations in daily activities (unable to climb two flights of stairs, to run a short distance, or to walk uphill) on the basis of a medical record, (2) prior admission for heart failure, (3) planned MV surgery at the time of index echocardiography, and (4) inadequate image acquisition. Finally, only asymptomatic patients (New York Heart Association functional class I) with MR designated as Carpentier type II (MV prolapse or flail, adjudicated by two cardiologists)[9] entered our study, including (1) asymptomatic patients without surgical indications, (2) asymptomatic patients with class IIA surgical indications (LV end-systolic dimension > 40 mm, pulmonary hypertension, or AF rhythm)[5] but refused surgery.

Severe MR was diagnosed using a multiparametric approach, including evaluation of the vena contracta width, the effective regurgitant orifice area, the regurgitant volume, and the presence of systolic pulmonary venous flow reversal aligned with American Society of Echocardiography criteria.[10]

Every 1 to 3 months, patients were followed up at the clinic by their original cardiovascular specialists, and symptoms and signs of heart failure were carefully evaluated. For patients who developed symptoms, surgical referrals were made, and follow-up echocardiography was arranged, whether at the outpatient clinic or during hospitalization (different vendors might be used). The final surgical decision, however, was based on the patient's preference after communication with independent surgeons blinded to the study. For asymptomatic patients, whether follow-up echocardiography was arranged was left to the discretion of the primary care physician. The composite end points of our study after index echocardiography were designated as cardiovascular mortality or MV surgery (repair or replacement) caused by new-onset heart failure (symptom exacerbation requiring hospitalization with radiographic evidence of pulmonary congestion or heart failure progression identified in the outpatient clinic). This rationale reflects what is commonly seen in Taiwan; most asymptomatic patients declined MV surgery until symptoms were patent, regardless of the presence of a class IIA surgical indication. Hence, MV surgery triggered by symptoms was denoted as an end point.

All patients were followed until they either reached the study end point or reached the end of study follow-up. There was no loss to follow-up as of August 2014. If a patient experienced any cardiac event eventually leading to cardiovascular death or a subsequent firm surgical decision, the time to the end point was signified as the time to that cardiac event. Functional class at enrollment, medical history, any adverse cardiac events, and the composite end point (including the cause) during follow-up were obtained from medical records and adjudicated by two cardiologists. Telephone interviews were conducted to assess the condition of patients between office visits. In the study, brain natriuretic peptide level was not routinely acquired. The study adhered to the Declaration of Helsinki and received approval from the Human Research and Ethics Committee of National Cheng Kung University Hospital (A-ER-102-322).

Echocardiography

Standard echocardiography was performed with Doppler studies (Vivid 7; GE Vingmed Ultrasound AS, Horten, Norway), with a 3.5-MHz multiphase-array probe in subjects lying in the left lateral decubitus position. Chamber dimension and wall thickness were measured using the 2D-guided M-mode method, and LVEF was measured using the 2D biplane method of disks, according to American Society of Echocardiography recommendations.[10] LV mass was measured using the M-mode method and indexed to body surface area. Transmitral Doppler flow velocity was obtained from an apical four-chamber view, and peak early fllling velocity (E), peak atrial velocity (A), early fllling–to–atrial velocity ratio (E/A), and mitral deceleration time were measured.[11,12] Pulse Doppler tissue imaging was performed from the medial and lateral annulus, and peak systolic annular velocity (S) and the average value of early diastolic annulus velocity (e′) were measured. The E/e′ ratio was used as an index of LA pressure.[13] Two-dimensional images were acquired from apical four-chamber and two-chamber views for three cardiac cycles and digitally stored, at a frame rate of 50 to 90 frames/sec.[14] The images were analyzed offline using computer software (EchoPAC PC 09; GE Vingmed Ultrasound AS).

Volumetric Measurements of the Left Atrium

LA volume was measured using the biplane area-length method from 2D echocardiography.[15] LA area was measured with planimetry for four-chamber and two-chamber views by tracing the endocardial border, excluding the confluence of the pulmonary veins and the LA appendage. LA length was measured from the midline of the plane of the mitral annulus to the opposite aspect of the left atrium. LA volume was measured at end-systole and end-diastole and calculated as 0.85 × four-chamber area × two-chamber area/average of the two lengths.[13] The maximal LA volume during LV end-systole (LAVs) and the minimal LA volume during LV end-diastole (LAVd) were obtained. LA total emptying fraction (LATEF) was calculated as [(LAVs − LAVd)/LAVs] × 100%. LA size was represented by