Two-Dimensional Atrial Systolic Strain Imaging Predicts Atrial Fibrillation at 4-Year Follow-Up in Asymptomatic Rheumatic Mitral Stenosis

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Background: The aim of this study was to assess systolic left atrial (LA) reservoir function in patients with mitral stenosis (MS) using two-dimensional (2D) strain (ε) and strain rate imaging and its prognostic value in predicting atrial fibrillation (AF) at 4-year follow-up.

Methods: One hundred one asymptomatic patients with pure rheumatic MS and 70 healthy controls were evaluated using standard Doppler echocardiography (mitral valve area, mean gradient, systolic pulmonary pressure, LA width, LA volumes, and LA ejection fraction) and 2D speckle-tracking.

Results: LA width, volumes, and systolic pulmonary pressure were significantly increased ($P < .0001$), and LA 2D ε and strain rate were significantly impaired in patients with MS ($P < .0001$). At 4-year follow-up, 20 patients (20%) showed AF on standard electrocardiography or 24-hour Holter electrocardiography. Patients with MS who had AF were older than those who did not, without significant differences in LA dimensions, volumes, ejection fraction, and compliance index. Instead, atrial myocardial systolic 2D ε was significantly impaired in patients with events. On multivariate analysis (age, LA volume, planimetric mitral area, average annular Ea, and LA strain) the best predictor of AF was average LA peak systolic ε (coefficient, 0.43; SE, 0.098; $P < .01$), with an area under the receiver operating characteristic curve of 0.761 (SE, 0.085; 95% confidence interval, 0.587–0.888, $P = .002$) for a cutoff value of 17.4%.

Conclusions: The results of 2D ε imaging are abnormal in patients with asymptomatic MS and predict AF at 4-year follow-up. (J Am Soc Echocardiogr 2013;26:270-7.)

Keywords: Atrial fibrillation, Atrial reservoir function, Echocardiography, Speckle-tracking, Mitral valve stenosis, Atrium

Mitral stenosis (MS) is a progressive disease in which, after a stable course without symptoms, often the initial manifestation is the onset of atrial fibrillation (AF). Patients with MS are prone to develop AF; about 30% to 40% of patients with symptomatic MS develop AF.[1] On the other hand, the onset of rapid AF in asymptomatic patients with severe MS can sometimes cause acute pulmonary edema, and this can be rapidly fatal; moreover, AF induces thromboembolic events, especially stroke, which make the prognosis worse.[1] Although encouraging data have been obtained from previous studies demonstrating that Doppler strain rate (SR) imaging is able to assess early atrial reservoir dysfunction in patients with asymptomatic MS and to identify those patients at high risk for adverse events, the analysis has major drawbacks: angle dependence, reproducibility, and time-consuming acquisition and postprocessing.[2] Recently, a new method, two-dimensional (2D) strain (ε) and SR imaging (speckle-tracking) has been developed to study ventricular function and has been used to evaluate atrial function.[3-13] It is independent of both cardiac translation and angle dependency; it is based on an automated tracking system, with very good reproducibility, unlike Doppler-based ε imaging. Two-dimensional ε and SR imaging provides automatic calculation of mean values from the pattern of speckles in predefined myocardial segments, reflecting segmental function better than the analysis of only one point in space, used in previous Doppler ε analysis. The important advantage is that 2D ε uses 2D loops (grayscale images) from the routine echocardiographic examination, and it is becoming a widespread technique, with many clinical implications.

Thus far, there have been no studies based on speckle-tracking to assess atrial function in patients with MS. Thus, our aims were to assess the effect of pure rheumatic MS on left systolic atrial reservoir function, using speckle-tracking in asymptomatic patients with normal results on stress electrocardiography (ECG), and to evaluate the prognostic value of speckle-tracking in predicting the onset of AF at 4-year follow-up.

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Abbreviations

AF = Atrial fibrillation

ECG = Electrocardiography

EF = Ejection fraction

ε = Strain

LA = Left atrial

LV = Left ventricular

MS = Mitral stenosis

SR = Strain rate

2D = Two-dimensional

METHODS

Patient Population

Among the 423 patients with MS followed at our institution, we enrolled 101 patients according to the following inclusion criteria: mild to moderate MS of rheumatic origin, sinus rhythm, recent (<2 months) negative results on exercise treadmill ECG at peak heart rate, and no need for medical therapy. According to American guidelines, MS was considered mild when the mean gradient was <5 mm Hg and valve area was >1.5 cm^2 and moderate when mean gradient was between 5 and 10 mm Hg and valve area was between 1 and 1.5 cm^2.[1]

Exclusion criteria were New York Heart Association class ≥II, diabetes mellitus, blood arterial hypertension, dyslipidemia, coronary artery disease, arrhythmias (according to history, ECG at inclusion, 24-hour Holter recording, and exercise treadmill ECG), associated valvular lesions such as more than mild aortic or mitral insufficiency, aortic stenosis, or more than mild tricuspid regurgitation, pulmonary arterial hypertension (≥45 mm Hg), left ventricular (LV) and right ventricular systolic dysfunction (LV ejection fraction [EF] <55%, right ventricular systolic annular velocity <11.5 cm/sec), LV hypertrophy (both septal and posterior wall thicknesses >11 mm), lung disease, and inadequate echocardiograms. One hundred one patients met these criteria and were included in the study.

As a reference group, we studied 70 healthy adult subjects, comparable for age and sex, without detectable cardiovascular disease and/or risk factors (family history of cardiac diseases, arterial hypertension, diabetes mellitus, hypercholesterolemia, cigarette smoking, and previous cerebrovascular disease) and without cardiovascular structural or functional abnormalities (normal results on clinical examination, ECG, and echocardiography) who were not receiving any medication.

Echocardiography

Standard Transthoracic Echocardiography. Complete mono and 2D color Doppler echocardiography was performed in each subject using the GE Vingmed System VII (GE Vingmed Ultrasound AS, Horten, Norway) with a 3.5-MHz variable-frequency harmonic phased-array transducer.

Left atrial (LA) width was measured during systole, in the long-axis view (anterior-posterior diameter) and in the four-chamber view (longitudinal and transverse diameters). The maximum and minimum LA volumes were calculated from apical four-chamber and apical two-chamber zoomed views of the left atrium, using the biplane method of disks.[14]

The difference between maximum and minimum LA volume divided by minimum LA volume was used as index of atrial compliance.[2,15]

LV global systolic function was evaluated by EF, using the biplane Simpson's method. Right ventricular systolic function was evaluated using 2D fractional area change.[16]

MS area was evaluated using 2D planimetry and the pressure half-time method, and the velocity-time integral of the mitral valve for mean transmitral gradient, according to guidelines.[1,17] Pulmonary arterial pressure was estimated from tricuspid regurgitation, always adding 5 mm Hg. Three beats in each view were analyzed and averaged. Using Doppler tissue imaging, we measured early diastolic myocardial relaxation velocities (Ea) at the four areas of the mitral annulus and then calculated average annular Ea.

2D Strain

Two-dimensional ε uses grayscale (B-mode) sector images and is based on frame-by-frame tracking of small rectangular image blocks with stable speckle patterns.[4,18] A minimum frame rate of 50 Hz was required for reliable operation of this program, and frame rates of 50 to 90 Hz were used for routine grayscale imaging. The apical four-chamber view was obtained using the same ultrasound system and probe used for standard echocardiography. By tracing the endocardial contour on an end-systolic cavitary frame after defining the thickness of the region to be considered, the software will automatically track the atrial wall on subsequent frames. Adequate tracking can be real-time verified and corrected by adjusting the region of interest or the contour (increased or decreased the width for thicker or thinner walls, respectively).

Using this technique, analysis was performed from the four-chamber and two-chamber apical views for the segments of LA septum, LA lateral wall, LA inferior wall, LA anterior wall, and near LA roof, as considered for Doppler ε imaging in previous studies, and then were averaged.[2,15]

Accordingly, for each segment, during LV systole, LA wall longitudinal lengthening was represented with a peak positive ε value; it is observed because of filling of the atrial cavity by blood coming from the pulmonary veins while the mitral valve is closed. Myocardial longitudinal shortening was represented with a peak negative ε value; it occurs during LV diastole, when the atrium empties into the LV cavity.

The tracking process and conversion to Lagrangian ε was performed offline using dedicated software (EchoPAC; GE Vingmed Ultrasound AS).

Although this software was validated for the measurement of LV ε, it has been previously used for measuring LA ε with high feasibility and good agreement in many studies.[3-13]

Follow-Up

Serial prospective follow-up (4 years) was obtained in all patients by means of a physician-directed telephone interview using a standardized questionnaire. The physicians were blinded to patient echocardiographic results. Hospitalization for cardiac cause was confirmed by review of hospital medical record. All patients were interviewed at least every 3 months during the follow-up period. After inclusion, all patients were seen every 6 months at an outpatient clinic and at any time they reported symptoms. At each examination, standard 12-lead ECG was used, and an inquiry was made about symptoms. A 24-hour Holter recording was made every month and at any time the patient had any symptoms suggesting AF.

The end point of the study was the occurrence of AF on standard 12-lead ECG or on 24-hour Holter recording.

Statistical Analysis

All analyses were performed using SPSS version 11.0 (SPSS, Inc., Chicago, IL). To compare patients with MS versus referents, or patients with MS with events versus those without events, unpaired Student's *t* tests were used for continuous variables, while for categorical variables, Fisher's exact tests were used. Quantitative values are presented as mean ± SD.