Assessment of Biventricular Function by Three-Dimensional Speckle-Tracking Echocardiography in Secondary Mitral Regurgitation after Repair with the MitraClip System

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Background: The goal of this study was to determine changes in left ventricular (LV) and right ventricular (RV) function with three-dimensional (3D) speckle-tracking echocardiography (STE) after percutaneous mitral valve repair with the MitraClip system in high-risk surgical patients with moderate to severe or severe secondary mitral regurgitation (MR).

Methods: Thirty-two patients with MR undergoing MitraClip were prospectively included. Patients underwent two-dimensional (2D) and 3D transthoracic echocardiography before clip implantation and after 6-month follow-up. LV and RV longitudinal strain was obtained by 2D STE and 3D STE. LV circumferential, radial, and area strain was calculated by 3D STE. Data analysis was performed offline.

Results: At 6-month follow-up, significant improvements were seen in LV 2D global longitudinal strain ($P < .005$), 3D global longitudinal strain ($P = .0002$), and 3D area strain ($P = .0001$). Overall, significant improvements were also seen in 3D RV ejection fraction ($P < .05$) and 3D RV free-wall longitudinal strain ($P < .05$). A poor increase in LV strain after clip implantation (P = NS) occurred in patients with pronounced preexisting RV dysfunction. The areas under the receiver operating characteristic curves for LV and RV 3D speckle-tracking echocardiographic parameters showed high discriminative values (range, 0.87–0.91) in predicting unfavorable outcomes with persistent symptoms (New York Heart Association class > II) after the procedure.

Conclusions: Three-dimensional STE showed overall LV and RV strain improvement after clip implantation as well as lower postprocedural LV strain values in patients with worse preexisting RV function. These findings could help in guiding MR treatment strategies, suggesting different therapies in the presence of marked RV impairment or anticipating the procedure in case of evolving RV dysfunction. (J Am Soc Echocardiogr 2015;■:■-■.)

Keywords: Mitral regurgitation, MitraClip system, Echocardiography, Speckle-tracking imaging, Left ventricular function, Right ventricular function

The MitraClip device (Abbott Laboratories, Abbott Park, IL) is a novel percutaneous system to treat mitral regurgitation (MR) in patients with left ventricular (LV) dysfunction and high risk for surgical mitral valve (MV) repair.[1-6] The clip implantation over the leaflets creates a double-orifice valve and thus mimics Alfieri's surgical procedure. The Endovascular Valve Edge-to-Edge Repair Study was the first randomized controlled study to show higher safety, lower clinical efficacy, and the same improvement in clinical outcome in comparison with surgical MV repair.[2]

The hemodynamic benefit of the percutaneous procedure is usually higher in a particular subset of patients with low cardiac index values and high left-sided filling pressures.[3] However, because the acute correction of MR could lead to further impairment in cardiac output and LV function,[7] it would be useful to show noninvasively that LV performance is preserved and not decreased as a result of the acute reduction in MR. It also is known that patients with impaired right ventricular (RV) function after MV replacement have higher 5-year mortality than patients without preoperative right heart failure. The benefits of MV repair on reverse RV remodeling have been shown in patients with degenerative[8] or functional[9,10] MR using two-dimensional (2D) and three-dimensional (3D) echocardiography.

Two-dimensional speckle-tracking echocardiography (STE) represents a new means of evaluating myocardial wall movements and deformation, and the use of indexes derived from STE has been proposed as an adjunctive tool in the overall assessment of LV and RV function and is more sensitive compared with ejection fraction in detecting early changes in ventricular performance.[11,12] The capability of 2D STE is limited by the changes in heart morphology

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Abbreviations

EROA = Effective regurgitant orifice area

FWLS = Free wall longitudinal strain

GAS = Global area strain

GCS = Global circumferential strain

GLS = Global longitudinal strain

GRS = Global radial strain

LV = Left ventricular

LVEF = Left ventricular ejection fraction

MR = Mitral regurgitation

MV = Mitral valve

NYHA = New York Heart Association

PISA = Proximal isovelocity surface area

RegVol = Regurgitant volume

RF = Regurgitant fraction

ROC = Receiver operating characteristic

RV = Right ventricular

RVEF = Right ventricular ejection fraction

STE = Speckle-tracking echocardiography

3D = Three-dimensional

2D = Two-dimensional

during the cardiac cycle and the difficulty in tracking speckles in different frames because of out-of-plane motion. The newly developed 3D STE provides quick and comprehensive quantitative assessment of ventricular myocardial dynamics and has been applied in various pathologic conditions[13-16] but never in MR after clip implantation. Accordingly, the goal of this analysis was to determine the changes in LV and RV function with 3D STE after percutaneous MV repair with the MitraClip system in high-risk surgical patients with functional MR.

METHODS

Population

Thirty-two patients with moderate to severe or severe MR undergoing MitraClip were prospectively included. All patients had secondary (functional) MR from ischemic cardiomyopathy ($n = 20$) or nonischemic cardiomyopathy ($n = 12$). All of them presented with symptomatic MR despite optimal medical and device therapy and were evaluated by a multidisciplinary team composed of an echocardiologist, an interventional cardiologist, an anesthesiologist, and a cardiac surgeon. Coronary angiography was performed in all patients before clip implantation to rule out significant coronary artery disease. Patients were treated with percutaneous angioplasty before MitraClip procedure, if applicable. The group of control subjects comprised 32 healthy age- and sex-matched adults with no histories of systemic or cardiopulmonary disease, no known coronary risk factors, and normal electrocardiographic and echocardiographic results.

Transthoracic and transesophageal echocardiography was performed in all patients to assess quantitative MR analysis and morphologic suitability for clip implantation. Patients were selected for the procedure if they had moderate to severe or severe MR, met class I or II recommendations for surgery in chronic secondary MR, according to current guidelines,[17,18] and were considered high risk for surgery. A logistic European System for Cardiac Operative Risk Evaluation score > 20 defined high risk.[17] Patients were excluded if implantation was technically impossible because of valve morphology (endocarditis, mitral stenosis) or unlikely beyond the classic Endovascular Valve Edge-to-Edge Repair Study criteria,[1,2] if they had undergone coronary percutaneous procedures or bypass surgery within the preceding 30 days, or if they had severe clinical comorbidities with very poor prognosis. Patients were informed about the risks of the procedure and possible alternative treatment, and they gave written consent. Two-dimensional and 3D transthoracic echocardiography was performed before clip implantation and after 6 months of follow-up. The study was approved by the institutional research committee.

Two-Dimensional and 3D Echocardiography

Patients were examined in the left lateral decubitus position using a Vivid E9 commercial ultrasound scanner(GE Vingmed Ultrasound AS, Horten, Norway) with phased-array transducers. Grayscale recordings were optimized at a mean frame rate of ≥50 frames/sec. Measurements of cardiac chambers were made by transthoracic echocardiography according to established criteria.[19] LV mass was calculated using the Deveraux equation.[19] LV peak systolic meridional wall stress was obtained from M-mode and pressure data[20,21] with the following formula: LV peak systolic meridional wall stress = 0.86 × (0.334 × P × LV end-diastolic diameter)/[posterior wall thickness × (1 + posterior wall thickness/LV end-diastolic diameter)] − 27 × 10^3 dynes/cm^2), where P is systolic cuff blood pressure. MV orifice area was assessed using planimetry. RV systolic pressure was obtained using standard Doppler practices.[22] Mitral annular velocities(S_a, E_a, and A_a) were measured in transthoracic four-chamber views.

MR severity was graded at baseline according to the criteria of the American Society of Echocardiography[22] and the European Association of Cardiovascular Imaging.[23] Semiquantitative indices of MR severity included color jet size, pulmonary venous flow velocity, and vena contracta width. Quantitative parameters were effective regurgitant orifice area (EROA), regurgitant volume (RegVol), and regurgitant fraction (RF). For inclusion in the study, MR severity was required to be moderate to severe or severe (3+ or 4+) using multiple criteria and an integrative approach. The vena contracta is the smallest, highest velocity region of the MR jet and was measured in a plane perpendicular to mitral leaflet closure, whenever possible. EROA was determined with the proximal isovelocity surface area (PISA) method by lowering the Nyquist aliasing velocity to identify the hemispheric shell, measuring the radius from orifice to first aliasing, and applying the standard formula on the basis of the ratio between flow rate (aliasing velocity × radius) and peak orifice velocity (regurgitant jet velocity by continuous-wave Doppler). PISA is more accurate for central jets than for eccentric jets. Moreover, PISA underestimates EROA in secondary MR because of noncircular orifice geometry.[18] LV volumes were measured using the biplane method of disks. Forward stroke volume was calculated using LV outflow tract diameter and the velocity-time integral by pulsed-wave Doppler (LV outflow tract $diameter^2$ × 0.785 × velocity-time integral). RegVol was obtained by subtracting forward stroke volume from total stroke volume, where total stroke volume = LV end-diastolic volume − LV end-systolic volume. RF was calculated as RegVol/total stroke volume. According to current guidelines,[17,18,23] in primary MR, the thresholds of severity for EROA, RegVol, and RF are 40 mm^2 (moderate to severe, 30–39 mm^2), 60 mL (moderate to severe, 45–59 mL), and 50% (moderate to severe, 40%–49%), respectively. In secondary MR, although this is a controversial step,[24,25] lower cutoff values are recommended, 20 mm^2 for EROA and 30 mL for RegVol. RF remains unchanged at 50%. Although an integrative approach using multiple echocardiographic and clinical variables should be used to assess the severity of secondary MR,[25] we used a matrix of criteria and classified MR as