Comprehensive Assessment of Mitral Valve Geometry and Cardiac Remodeling With 3-Dimensional Echocardiography After Percutaneous Mitral Valve Repair

Valentina Mantegazza, MD[a,*], Annalisa Pasquini, MD[b], Luciano Agati, MD[b], Laura Fusini, MD[a], Manuela Muratori, MD[a], Paola Gripari, MD[a], Sarah Ghulam Ali, MD[a], Carlo Vignati, MD[a], Antonio Luca Bartorelli, MD[a,c], Cristina Ferrari, MD[a], Francesco Alamanni, MD[a,d], Mauro Pepi, MD[a], and Gloria Tamborini, MD[a]

MitraClip is a validated treatment for significant mitral regurgitation (MR) in high-risk patients. Aims of the study were to evaluate immediate changes in mitral valve (MV) geometry induced by MitraClip and correlations between baseline geometry and cardiac remodeling. Eighty patients who underwent MitraClip for primary (48%) or secondary (52%) MR were enrolled. Intraoperative transesophageal echocardiographic 3D images were acquired immediately before and after the procedure for MV annulus (MVA) morphology analysis. Transthoracic 3D echocardiography was performed preoperatively and at 6 months follow-up (6MFU). Patients were classified on the basis of MR reduction (ΔMR) at 6MFU as Optimal (ΔMR $\geq$ 2) or Suboptimal (ΔMR $<$ 2). An optimal result was reached in 60 (75%) patients, whereas 20 subjects showed a ΔMR$<$ 2 at 6MFU. The Optimal showed significantly smaller baseline MVA (antero-posterior diameter 4.05 ± 0.59 vs 4.43 ± 0.68 cm; anterolateral-posteromedial diameter 4.38 ± 0.56 vs 4.70 ± 0.73 cm; MVA circumference 14.1 ± 1.7 vs 15.1 ± 2.3 cm; and 3D area 14.8 ± 3.9 vs 17.4 ± 5.3 cm^2), lower sphericity index and nonplanar angle compared with Suboptimal. A value of antero-posterior diameter $\geq$4.44 cm was identified (receiver-operating characteristic curve) as a possible cut-off for preoperative identification of Suboptimal patients. Postoperatively, MitraClip induced reduction of MVA flattening (nonplanar angle), sphericity index, and size (as expressed by antero-posterior diameter, MVA circumference and area). At 6MFU, the Optimal showed significant decrease in left ventricular volumes and pulmonary artery systolic pressure. In conclusion, MitraClip induces remarkable changes in MVA geometry and favorable left ventricular remodeling is detected in patients with optimal mid-term outcome; a preprocedural antero-posterior diameter $<$4.44 cm seems to be a potential predictor of mid-term optimal result. **(Am J Cardiol 2018;00:1−9)**

MitraClip (Abbott Vascular, Abbott Park, Illinois) implantation is a validated and safe alternative treatment of significant mitral valve (MV) regurgitation (MR) in symptomatic patients at high surgical risk.[1−3] Several studies have examined left ventricular (LV) remodeling after percutaneous MV repair,[4−6] but 3-dimensional (3D) echocardiography has never been applied for the evaluation of all cardiac chambers and MV apparatus simultaneously. Three-dimensional imaging is more reliable than 2-dimensional (2D) in computation of volumes and is a reference method for MR quantification in complex MV disease and during MV interventions.[7,8] Recently, immediate MV morphologic changes after MitraClip implantation have been evaluated.[9−13] However, no previous study has searched for correlations among preoperative MV geometry, procedural success, and cardiac remodeling at mid-term. The aim of our study was first to examine if any MV morphologic parameter could predict MR reduction at 6 months follow-up (6MFU). Second, we evaluated all cardiac chambers by transthoracic 3D echocardiography (TTE), to accurately assess mid-term reverse remodeling.

[a]Centro Cardiologico Monzino IRCCS, Milan, Italy; [b]Department of Cardiology, 'La Sapienza' University of Rome, Rome, Italy; [c]Department of Biomedical and Clinical Sciences "Luigi Sacco", University of Milan, Milan, Italy; and [d]Department of Clinical Sciences and Community Health, Cardiovascular Section, University of Milan, Milan, Italy. Manuscript received April 23, 2018; revised manuscript received and accepted June 26, 2018.

See page 8 for disclosure information.

*Corresponding author: Tel: 0039 0258002011; fax: 0039 0258002287.

E-mail address: valentina.mantegazza@cardiologicomonzino.it (V. Mantegazza).

Methods

We evaluated patients admitted to Centro Cardiologico Monzino IRCCS (Milan, Italy), affected either by secondary MR (SMR) or primary (PMR), with indication for MitraClip implantation according to guidelines,[3] MV anatomy and clinical contraindications.[1,2,14] If multiple mechanisms were responsible for MR, the cause was determined by the predominant mechanism. Patients were classified into 2 groups in accordance to outcome at 6MFU—Optimal

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(MR reduction ≥2, ΔMR ≥ 2) and Suboptimal (ΔMR < 2). The local ethics committee approved the study protocol and all participants provided written informed consent.

Patients underwent 2D and 3D TTE at baseline and at 6MFU, using Philips iE33 ultrasound Machine (Philips Medical Systems, Andover, Massachusetts), with S5-1 and X5-1 probes, respectively, for 2D and 3D acquisitions. With 2D TTE, we acquired LV end-diastolic (EDV) and end-systolic (ESV) volumes, indexed for body surface area (LVEDVi and LVESVi, respectively); LV ejection fraction (LVEF); ESV left atrial indexed volume[15]; pulmonary artery systolic pressure (PASP).[16] A score of 1 (mild), 2 (mild-to-moderate), 3 (moderate-to-severe), or 4 (severe) was assigned to MR severity integrating 6 criteria, both qualitative (Color Doppler jet characteristics, pulmonary vein flow pattern) and quantitative (vena contracta width, regurgitant volume, regurgitant fraction, and effective regurgitant orifice area).[17] Agrees with European recommendations, different cut-off values were used for grading MR in SMR and PMR patients.[18] At 6MFU, MR severity was established on the basis of 4 of 6 criteria used at baseline. As vena contracta width and regurgitant orifice area have not been validated after MitraClip implantation, these variables were not included for the assessment of MR at 6MFU.[1] Each physician was visually cross-checked by a second operator to guarantee standardization of data collection and definition of MR grading. In case of discrepancy of individual judgments on MR severity, a third expert opinion was asked to assign a definite score to residual MR. Real-time 3D TTE was performed at the end of 2D examination. Full-volume acquisitions from the 4-chamber apical view were adapted to improve the visualization of each ventricle. All data sets were digitally stored and transferred into a workstation for off-line 3D reconstruction with a dedicated software (4D LV-Analysis, TomTec Imaging Systems, Unterschleissheim, Germany). For 3D LV volumes computation, the software visualized LV cavity by the coronal, sagittal, and frontal cut-planes and, after manual selection of MV annulus (MVA) and LV apex, automatically rendered a 3D reconstruction of LV surfaces throughout the cardiac cycle providing 3D LVEDV, LVESV, and LVEF. LA systolic volume was quantified using the same software—after identification of MVA and the central part of the atrial dome, a 3D model was automatically generated and the systolic volume calculated. For the evaluation of right ventricular (RV) volumes, a dedicated system (4D RV-Function, TomTec Imaging Systems) was used. After manual selection of LV apex, tricuspid and MV annuli, the software visualized the RV cavity by the coronal, sagittal, and frontal cut-planes. Manual correction was performed to adjust the endocardial contours when needed and then 3D RV reconstruction was automatically produced and 3D RV end-diastolic (RVEDV) and end-systolic volume (RVESV), and RV ejection fraction (RVEF) computed.

Transcatheter MV repair was performed under general anesthesia, guided by fluoroscopy and real-time transesophageal echocardiography (TEE) using Philip iE33 or Epiq 7C ultrasound machine (Philips Medical Systems, Andover, Massachusetts) equipped with X7-2t TEE probe. MR severity was assessed by TEE and visually quantified on the basis of anatomical considerations, Color Doppler jet characteristics and pulmonary vein flow pattern. Three-dimensional MVA geometric evaluation was performed using 4D MV-Assessment 2.1 software (TomTec Imaging Systems). First, the mid-systolic frame was selected and 4 annular landmarks (medial, lateral, anterior, and posterior) were identified at the insertion points of MV leaflets to the annulus on 2 different longitudinal and mutually perpendicular planes. Additional landmarks were placed in the center of the aortic valve and at the apical aortic annulus as reference points for the identification of different MVA regions. Finally, the automated tracking workflow delivered geometrical MVA parameters as follows: antero-posterior (AP) diameter; anterolateral-posteromedial (ALPM) diameter; MVA circumference and 3D area; sphericity index (the ratio between AP and ALPM diameter); nonplanar angle, subtended by 2 lines connecting the middle point of the commissural diameter, respectively, with the anterior and the posterior annulus highest points. The MV was then reconstructed as a 3D rendered surface, allowing a comprehensive visualization of any structural deformation in the saddle-shaped, nonplanar configuration of MVA and any abnormality in leaflet morphology.[19]

Continuous data are presented as mean ± standard deviation and categorical variables as frequencies (percentages), as appropriate. Clinical and echocardiographic characteristics of the patients were compared based on the outcome at 6MFU (Optimal vs Suboptimal) and on the cause of MR (PMR vs SMR). Continuous variables were compared using the unpaired Student's *t* test or Mann-Whitney *U* test, and for categorical variables the chi-square test or Fisher's exact test (if the expected cell count was <5), as appropriate. A paired Student's *t* test or Wilcoxon signed-rank test was used to compare preclip and postclip TEE data as well as baseline and 6MFU TTE data. Reproducibility of 3D MV geometric parameters was assessed in a randomly chosen subgroup of 30 patients. Intraobserver variability was evaluated by the same observer repeating measurements ≥2 weeks later; interobserver variability was evaluated by a second observer, blinded to the results of previous analyses. Both intra- and interobserver variability were expressed in terms of intraclass correlation coefficients and coefficients of variation (percentage). Moreover, Bland-Altman analysis was applied to evaluate the limits of intra- and interobserver agreement. Transesophageal MV parameters with a significant p value at univariate analysis were included in a multivariate logistic regression analysis with stepwise method for the identification of independent variables predicting outcome. Furthermore, for each parameter, a receiver-operating characteristic curve was created and assessed with C-statistics. To identify the optimal threshold for outcome prediction, the Youden index was computed for the parameter with the highest area under the curve. All results were considered significant with p values <0.05. Statistical analysis was performed using SPSS 23 (SPSS Inc, Chicago, Illinois).

Results

Ninety-eight consecutive patients were considered suitable for MitraClip implantation by the Heart Team of our Institute. They were submitted to percutaneous edge-to-edge MV repair, with the exception of 1 case (precocious interruption of the procedure for cardiac tamponade). Other 3 patients were converted to conventional surgery after clip deployment for intraoperative complications (2 anterior mitral leaflet tearing and 1 chordal rupture). One patient underwent MV replacement after 48 hours because of clip detachment. Twenty-four patients (30%) were successfully treated with the deployment of 1 single clip, 49 (61%) with