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Original article

Different indicators for postprocedural mitral stenosis caused by single- or multiple-clip implantation after percutaneous mitral valve repair

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ABSTRACT

Background: Postprocedural mitral stenosis (MS) is a main limitation for MitraClip™ (Abbot Vascular, Inc., Santa Clara, CA, USA) procedure. The purpose of this study was to detect the preprocedural predictors of high transmitral pressure gradient (TMPG) after MitraClip™ implantation, which indicated postprocedural mitral stenosis (MS).
Methods: We studied 79 patients who were implanted with MitraClip™ in our institute. Before the procedure, mitral valve orifice area (MVOA), and anterior–posterior (AP) and medial-lateral (ML) mitral annular diameters were measured at diastole using three-dimensional (3D) transesophageal echocardiography (TEE) data set. After the procedure, the mean TMPG was assessed using continuous-wave (CW) Doppler by periprocedural TEE.
Results: Preprocedural MVOA, and AP and ML diameter of left ventricular (LV) inflow orifices were larger in patients with mean TMPG ≤4 mmHg than in patients with TMPG >4 mmHg after 1-and 2-clip implantation. The large MVOA and ML diameter of LV inflow orifice strongly correlated with the low TMPG after 1- and 2-clip implantation. As a result of the receiver operating characteristic curve analysis, the preprocedural MVOA predicted the low postprocedural TMPG more accurately than the ML diameter of LV inflow orifice after 1-clip implantation either in the degenerative or functional mitral regurgitation (MR) patients. After 2-clip implantation, however, the preprocedural ML diameter of LV inflow orifice predicted it more accurately than the MVOA in the degenerative and functional MR patients.
Conclusions: 3D TEE derived MVOA predicts the postprocedural MS after 1-clip implantation, however, preprocedural ML diameter of LV inflow orifice is more useful to predict after 2-clip implantation.

Introduction

Percutaneous mitral valve repair with the MitraClip™ system (Abbot Vascular, Inc., Santa Clara, CA, USA) is a therapeutic alternative to mitral valve surgery for patients with prohibitive surgical risk [1–3]. However, the decrease in mitral valve orifice area (MVOA) or the increase in the transmitral pressure gradient (TMPG) is one of the main limitations for the MitraClip procedure.

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The mean TMPG using continuous-wave (CW) Doppler is often used as a parameter to assess the postprocedural mitral stenosis (MS) after MitraClip implantation because it is easy to apply in the catheterization laboratory [4–6]. Of preprocedural mitral parameters, small preprocedural MVOA and mitral annular size are considered to be associated with the high postprocedural mean TMPG in the previous papers [7–18]. For instance, preprocedural MVOA $<4.0\ cm^2$ was used as an exclusion criterion in the Endovascular Valve Edge-to-Edge Repair Study (EVEREST) and EVEREST II to prevent postprocedural MS [7,8]. Other studies performed with an exclusion criterion of preprocedural MVOA $<2.0\ cm^2$ or $<2.5\ cm^2$ were reported [9,10]. In addition, an increase in mean TMPG due to mitral annular deformation after surgical mitral annuloplasty [11–14] or the MitraClip procedure [15–18] were reported. However, there were no cut-off values of the preprocedural morphological parameters of the postprocedural MS based on strong evidence. Lubos et al. reported that preprocedural low MVOA calculated by the pressure half-time (PHT) method predicted procedure abortion, and they advocated that additional clip implantation should be avoided in patients with mean TMPG $\geq$4 mmHg or MVOA by PHT method $\leq 3.0\ cm^2$ [19]. As far as we know, it is the sole study on the preprocedural predictor for the MS after the MitraClip implantation. In order to find out the predictor for postprocedural high mean TMPG, we analyzed the relation of preprocedural MVOA and the mitral-annular size to the mean TMPG after 1- or 2-clip implantation.

Methods

Study population

We retrospectively reviewed the three-dimensional (3D) transesophageal echocardiography (TEE) list and found 115 patients who underwent MitraClip™ implantation from January 2011 to September 2014 in our heart institute. Of these patients, 30 without complete 3D data set of MV and 6 with preprocedural moderate or severe aortic regurgitation were excluded. The remaining 79 patients were studied. Data were retrieved from our computerized database. Clinical information was retrospectively obtained in all patients. This study was approved by the institutional review board.

Echocardiography

Of all subjects, comprehensive two-dimensional (2D) and Doppler transthoracic echocardiography (TTE) studies were obtained using a Philips iE33 ultrasound system (Philips Medical Systems, Andover, MA, USA) equipped with S5-1 phased array transducer (Philips Medical Systems) within 3 months before the procedure in our heart institute. TEE was performed using the iE33 ultrasound system equipped with an X7-2t TEE ultrasound probe providing a range frequency of 2.0–7.0 MHz and both 2D and 3D matrix arrays (Philips Medical Systems).

Functional MR was defined as impaired coaptation of the mitral leaflets due to the LV and annular dilatation and/or restricted leaflet motion. Degenerative MR was defined as disruption in any part of the mitral apparatus, such as mitral valve prolapse and/or rupture of the chordae tendineae [20]. According to the guideline of quantitative assessment of MR severity in EVEREST [21], MR severity was graded from 1+ to 4+ based on the combination of the jet area, the size of flow convergence zone and that of vena contracta. LV volume was measured at LV end-systole and LV end-diastole using the biplane method of discs (modified Simpson's rule) in the apical 2- and 4-chamber views in TTE examination [22]. After the first and the second clip were placed, the beam of the CW Doppler was located in the center of the largest orifice and the postprocedural mean TMPG was assessed [23]. 3D data set of MV was recorded by live 3D mode or by full volume mode (1–6 beats, average 2.5 beats, and 7–60 Hz, average 20.8 Hz). All volumetric images were analyzed off-line using commercial software (QLAB 9.0, Philips Ultrasound, Andover, MA, USA). Before MitraClip procedure, MVOA was measured in diastole at the time of the peak valve opening by planimetry method using the 3D quantification software (3DQ, Philips Ultrasound) after adjusting cut planes as described in previous papers (Fig. 1A) [18,23,24]. Anterior–posterior (AP) and medial-lateral (ML) inner diameters of mitral annulus were measured at the same frame using 3DQ software as described in previous papers (Fig. 1B and C) [16].

Statistical analysis

Data are presented as mean ± standard deviation for continuous variables, or as numbers with a percentage for categorical variables. Differences between groups were analyzed by *t*-test or Mann–Whitney *U*-test for continuous variables, and by chi-square test or Fisher's exact probability test for categorical variables, when appropriate. Correlations between preprocedural MVOA, AP, and ML diameter of LV inflow orifice, stroke volume calculated by Simpson's method (SV by Simpson), and the postprocedural mean TMPG after 1- or 2-clip implantation were analyzed by linear regression with Pearson's correlation coefficient or Spearman's rank correlation coefficient, when appropriate. To identify the preprocedural predicting factors of the postprocedural mean TMPG $\leq$4 mmHg after 1- or 2-clip implantation, we selected 3 candidates from the mitral morphological measurements discussed in prior studies as related to TMPG after MitraClip™ implantation; which were preprocedural MVOA [10,23,25], AP diameter of LV inflow orifice [15–18], and ML diameter of LV inflow orifice [15–18]. Receiver operating characteristic (ROC) curves and the estimation of area under the curve (AUC) of preprocedural MVOA and ML diameter of LV inflow orifice were obtained for postprocedural TMPG $\leq$4 mmHg after 1- or 2-clip implantation in the degenerative and functional MR patients. A comparison of AUCs of MVOA and ML diameter of LV inflow orifice was made with the DeLong method. Sensitivity, specificity, positive predictive value, and negative predictive value of the cut-off values of preprocedural MVOA and ML diameter of LV inflow orifice were calculated after 1- or 2-clip implantation. We analyzed intra-observer and inter-observer reproducibility for mean TMPG, MVOA, and AP and ML diameter of LV inflow orifices in 10 randomly selected patients and expressed them using Bland–Altman analysis. Two-tailed probability values less than 0.05 were considered statistically significant. Statistical analyses were performed using the SPSS 21.0 software (SPSS Inc., Chicago, IL, USA).

Results

Preprocedural measurements related to the postprocedural mean TMPG

Baseline characteristics of all patients are given in Table 1. MR grade was improved after MitraClip™ implantation (Table 1). Of all patients, 76 had mean TMPG data after 1-clip implantation (DMR 39, FMR 37). Baseline characteristics of the groups with low TMPG ($\leq$4 mmHg, $n = 63$) and high TMPG (>4 mmHg, $n = 13$) after1-clip implantation are given in the left columns in Table 2. Compared with the high TMPG group, the low TMPG group had larger body surface area, left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), SV by Simpson, MVOA, and AP and ML diameter of LV inflow orifice.

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