Analysis of Procedural Effects of Percutaneous Edge-to-Edge Mitral Valve Repair by 2D and 3D Echocardiography

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DOI: 10.1161/CIRCIMAGING.112.974691

Journal Subject Codes: [23] Catheter-based coronary and valvular interventions: other
[19] Valvular heart disease
Abstract

Background—Analysis of procedural effects in patients undergoing percutaneous mitral valve edge-to-edge repair (PMVR) is complex and common techniques to define mitral regurgitation severity based on 2-dimensional (2D) echocardiography are not validated for post procedural double-orifice mitral valve. This study used 3-dimensional (3D) transesophageal echocardiography (TEE) to determine functional and morphological effects of PMVR

Methods and Results—In 39 high-surgical risk patients with moderate to severe functional mitral valve regurgitation 3D TEE with and without color Doppler as well as 2D transthoracic and transesophageal echocardiography was performed before and after PMVR (MitraClip™ device). Mitral valve regurgitant volume (RV) by color Doppler 3D TEE was determined as the product of vena contracta areas defined by direct planimetry and velocity time integral using CW Doppler. RV was reduced from 84.1±38.3 ml pre intervention to 35.6±25.6 ml post intervention. Patients in whom vena contracta area could be reduced >50% had a smaller pre procedural mitral annulus area compared to patients with ≤50% reduction (11.9±3.9 vs. 16.1±8.5 cm², respectively; p=0.036) and tended to have a smaller mitral annulus circumference (13.0±2.0 vs. 14.8±4.1 cm, respectively; p=0.112). At 6 months follow-up left atrial and left ventricular end-diastolic volumes were significantly more reduced in patients in whom regurgitant vena contracta area was reduced by >50% compared to those with less reduction (-11.4±5.2 vs. -4.8±7.7%; p=0.005, and -11.0±7.2 vs. -4.5±9.3%; p=0.028). The maximum diastolic mitral valve area decreased from 6.0±2.0 to 2.9±0.9 cm² (p<0.0001).

Conclusions—3D transesophageal echocardiography demonstrates significant reduction of regurgitant volume after PMVR. The unique visualization of the mitral valve by 3D TEE allows improved understanding of the morphological and functional changes induced by PMVR.

Key Words: 3-dimensional echocardiography, image guided intervention, mitral regurgitation, transesophageal echocardiography, valvular repair
Percutaneous mitral valve repair (PMVR) using the edge-to-edge technique has been shown to be safe and effective for treatment of mitral regurgitation considering specific indications (1-3). Analysis of the morphological and functional effects of PMVR is complex. 2-dimensional (2D) echocardiography provides only limited access to morphological changes induced by mitral valve repair and commonly used techniques based on 2D echocardiography to evaluate functional changes of the mitral valve are not validated for post procedure double-orifice mitral valve (4). In contrast, 3-dimensional (3D) echocardiography provides improved visualization of the complex mitral valve morphology. It has been shown to allow accurate analysis of mitral regurgitation severity based on direct measurement of regurgitant orifice areas in 3D images with or without color Doppler (5-9).

This study evaluated (1) morphological and functional changes of the mitral valve induced by percutaneous edge-to-edge repair using 3D transesophageal echocardiography (TEE), (2) preprocedural morphological characteristics determined by 3D TEE with impact on functional effectiveness of PMVR, (3) changes of the left atrial and left ventricular (LV) volumes at 6 months follow-up related to PMVR effectiveness.

Methods

Patients. In 39 consecutive high-surgical risk patients with moderate to severe mitral valve regurgitation (age 73±9 years; 24 male) and LV ejection fraction of 46±16%, 2D transthoracic echocardiography (TTE), 2D and 3D TEE with and without color Doppler were performed within 24 hours before and after percutaneous mitral valve edge-to-edge repair using the MitraClip™ device (Abbott Vascular Structural Heart, Menlo Park, CA). Only patients with functional mitral regurgitation and at most trace aortic regurgitation were included in this study. Previously described inclusion and exclusion criteria for the procedure were acknowledged (1-3). 24 of the 39 patients had a history of atrial fibrillation. 12 patients had atrial fibrillation at the time of the procedure. In 30 patients 1 clip was applied and in 9
patients 2 clips. 3 patients died within the 6 months follow-up period, one due to pneumonia
3 months after PMVR, the second with severe COPD due to pulmonary sepsis at 4 months
follow-up and the third due to myocardial infarction two months after PMVR. Patient
characteristics are given in Table 1. Clinical follow-up and 2D TTE was performed in all
patients alive at 6 months. This study was approved by the ethical committee of the
University Aachen. All patients gave written informed consent.

**Image acquisition.** Echocardiographic studies were performed with a commercially available
echocardiographic system (iE 33, Philips Medical Systems, Andover, Massachusetts) with a
2D TTE probe (S5-1) and a TEE probe (X7-2t) allowing 2D and real-time 3D TEE. 3D TEE
studies included: zoom mode and full-volume wide-angle acquisition with and without color
Doppler flow imaging of the mitral valve. 3D analysis was performed with dedicated
software (3DQ and MVQ, QLAB-Version 7.0, Philips Medical Systems, Andover,
Massachusetts). Care was taken to perform image acquisition with similar hemodynamic
conditions before and after PMVR. This included administration of fluid challenges and
vasodilators to obtain similar blood pressures.

**Left atrial and left ventricular volumes.** Left atrial and LV systolic and diastolic volumes
were determined before and 6 months after PMVR based on transthoracic 2-chamber and 4-
chamber views. Left atrial volumes were determined by manual tracing of endocardual
contours at enddiastole of the left atrium in the 4-chamber view using the Simpson rule. LV
enddiastolic and endsystolic volumes were determined by manual tracing of endocardial
contours in the 4-chamber and 2-chamber view using Simpson biplane rule.

**Grading of mitral regurgitation severity.** Mitral regurgitant severity was graded
considering previously published EVEREST criteria (10). Furthermore, the mitral regurgitant
jet area was assessed by 2D TEE color flow Doppler in an intercommissural view using a
Nyquist limit of 50 to 60 cm/s, and a color gain that just eliminated random color speckle
from non-moving regions. Accordingly, these areas were assessed separately post
intervention for the jet located medial and lateral to the clip. The medial and the lateral areas were summed up to a total jet area.

**3D TEE to assess mitral valve morphology and function.** Mitral regurgitation vena contracta area (VCA) was assessed by analysis of 3D TEE full volume color flow Doppler data sets as previously described (7,11,12). After adjusting a cut plane orthogonal to the regurgitant jet at level of mitral valve commissural line direct planimetry of VCA could be done before the procedure. The regurgitant volume was calculated by multiplying VCA and velocity time integral obtained by continuous-wave Doppler. Similarly, areas of the medial and the lateral regurgitation jet were determined by planimetry and summed up to a total VCA post intervention (Figure 1). The medial and lateral regurgitant volumes were calculated by multiplying each VCA with the velocity time integral obtained by continuous-wave Doppler.

Maximum diastolic mitral valve area (MVA) was assessed by 3D TEE zoom mode. Direct planimetry was done after adjusting cut planes before and after PMVR for each orifice. Medial and lateral areas were summed up to a total MVA after PMVR (Figure 2). Mean diastolic mitral valve pressure gradient (Pmean) was measured by continuous-wave Doppler before and after PMVR for one orifice. The impact of MVA pre intervention on Pmean post procedure was evaluated. In patients with atrial fibrillation measurements of 5 cardiac cycles were averaged.

**Clip position.** The commissural line was defined as the line between the posteromedial and the anterolateral edge of the mitral valve in diastole. After PMVR the position of the clip or the two clips relative to the center of the commissural line was measured using 3D TEE zoom mode (Figure 3).

**Mitral annulus dimensions.** Before PMVR the mitral valve annulus area, annulus circumference, anterior to posterior diameter and posteromedial to anterolateral diameter were calculated by analysing 3D TEE full-volume wide-angle acquisition data sets with a
quantification software as previously described (13) (Figure 4). The impact of mitral annulus dimensions on the success of PMVR was evaluated. Procedural success was defined as reduction of the total regurgitation VCA >50%.

**Analysis of mitral valve regurgitant volume by 2D echo techniques.** Mitral valve regurgitant volume was determined by subtracting forward LV outflow from 2D TTE total LV stroke volume as described before (4,14).

Based on 2D TEE effective regurgitant orifice area (EROA) was calculated using the flow convergence method as previously described. The regurgitant volume was calculated by multiplying EROA and velocity time integral obtained by continuous-wave Doppler (4). After PMVR the EROA and regurgitant volume were calculated separately for the medial and the lateral jet by measuring the radius of each flow convergence zone in the intercommissural view and the peak regurgitant velocity and velocity time integral by continuous-wave Doppler. The medial and lateral regurgitant orifice areas and volumes were summed up to a total EROA and a total regurgitant volume.

**Observer agreement.** In 15 randomly selected studies, two observers independently measured the regurigitant volume by subtracting forward outflow from 2D total LV stroke volume and by 3D TEE direct planimetry of VCA before and after PMVR, and interobserver agreement was assessed by analysis of deviation of each measurements. These same studies were also reexamined by one observer at a separate time 1 month later to determine intraobserver agreement.

**Statistics.** Statistical analysis was performed using the MedCalc software (Version 9.5.1.0, Mariakerke, Belgium) and R statistical software (Version 2.14.1). Continuous data are presented as mean±SD and are compared with paired Student´s t-test or ANOVA as adequate. Categorical data were presented as frequencies and compared with the Pearson chi-square test. Pearson correlation coefficient (r) was calculated to express agreement between MVA before PMVR and mean diastolic mitral valve gradient post procedure. Bland-Altman
analysis was performed to determine differences in regurgitant volumes defined by the different analysis methods (15). Intraclass correlation coefficients (ICC) were calculated between regurgitant volumes determined by the different methods. Regression analysis was performed to identify predictors for reduction of vena contracta area >50% after PMVR. Variables included in the analysis were severity of valvular regurgitation, mitral annulus area, mitral annulus circumference, mitral annulus diameters, and use of one or two mitral valve clips. Receiver operating characteristics (ROC) analysis was performed to define the impact of mitral valve area pre intervention on mean diastolic pressure gradient post intervention. A p<0.05 was considered significant.

Results

Patient characteristics are given in Table 1. Considering the EVEREST criteria, 29 of the 39 patients had mitral regurgitation grade III and 10 patients had mitral regurgitation grade IV before the procedure. After the procedure 30 patients had grade I, 8 patients had grade II and 1 patient had grade III mitral regurgitation. In 28 of the 36 patients alive at 6 months follow-up, the NYHA functional class improved by at least one grade, while in 8 patients it did not change. The average NYHA functional class improved from 3.3±0.5 pre intervention to 2.0±0.7 at 6 months follow-up (p<0.0001). Using 3D TEE to assess mitral regurgitant severity before PMVR, VCA was found to be 0.50±0.22 cm² and regurgitant volume was 84.1±38.3 ml.

Impact of edge-to-edge repair on mitral regurgitation. The remaining medial and lateral regurgitant jet orifice areas after PMVR determined by direct planimetry of VCA using 3D TEE were 0.12±0.10 and 0.09±0.08 cm², respectively, indicating a reduction of regurgitant area by 58.9% to VCA_{total\ post} = 0.21±0.13 cm² (Figure 5). The calculated remaining regurgitant volume after PMVR by 3D TEE VCA method was 35.6±25.6 ml indicating a reduction of regurgitant volume by 59.2%. Patients with improvement in NYHA functional
class at 6 months follow-up after PMVR had a greater reduction of VCA compared to patients without improvement in NYHA functional class (-61.1±17.0 vs. -47.7±7.9%; p=0.040). There was no significant difference in the reduction of regurgitant volume between patients with and without improvement in NYHA functional class when 2D TTE based LV outflow-LV stroke volume method was used (-64.7±19.1 vs. -74.8±19.0%; p=0.193) or 2D TEE flow convergence method was applied (-75.5±16.8 vs. -70.5±16.1%; p=0.460).

Regurgitant volumes before and immediately after PMVR determined by the different 2D and 3D imaging methods are provided in Table 2. Considering regurgitant volume analysis based on calculation of 2D TTE LV stroke volume-LV outflow a reduction of 66.4% was seen post intervention and considering regurgitant volume analysis based on 2D TEE flow convergence method a reduction of regurgitant volume by 74.5% was seen. Difference in means determined by Bland-Altman analysis between regurgitant volume defined by 3D TEE and 2D TEE was 28.1 ml (95% CI -39.4 to -16.8 ml) before PMVR and 21.3 ml (95% CI -29.0 to -13.6 ml) after PMVR. ICC between 3D TEE and 2D TEE was 0.363 before PMVR and 0.177 after PMVR.

After PMVR a residual medial and lateral regurgitation jet could be defined by 2D echocardiography in all patients with a remaining bigger color Doppler jet area located medial (1.5±1.1 cm²) and a smaller jet area located lateral to the clip (1.2±1.1 cm²).

**Clip position relative to the commissural line.** Post procedural analysis of the clip position using 3D TEE demonstrated a location slightly lateral to the center of the mitral valve commissural line (0.03±0.23 cm lateral), with a range from 0.35 cm medial to 0.67 cm lateral to the central position.

**Effectiveness of PMVR related to annular size.** Before PMVR, the mitral valve annulus area determined by 3D TEE was 13.2±5.8 cm², the annulus circumference was 13.5±2.9 cm, the anterior to posterior mitral annulus diameter was 3.7±0.7 cm and the posteromedial to anterolateral diameter was 4.1±0.8 cm. Patients with a reduction of 3D TEE regurgitant VCA
>50% after the procedure (n=27) had a smaller preprocedural mitral annulus area compared to patients with a reduction ≤50% (n=12) (11.9±3.9 vs. 16.1±18.5 cm²; p=0.036). Mitral annulus circumference, mitral annulus anterior to posterior diameter and annulus posteromedial to anterolateral diameter tended to be smaller in patients with reduction of 3D TEE regurgitant VCA >50% (Table 3). Mitral annulus area was the only predictor for reduction of regurgitant VCA >50% (OR 0.964 per additional cm² VCA pre PMVR; 95%CI 0.913 – 0.991; p=0.0323).

6 months follow-up echocardiography. Regurgitant volumes determined by subtracting forward stroke volume from 2D LV stroke volume were unchanged at 6 months after PMVR (15.0±11.9 ml) compared to immediately after the procedure (15.3±10.4 ml; p=0.8949). Left atrial and ventricular volumes decreased significantly at 6 months follow-up after PMVR. The reduction in left atrial volume as well as LV enddiastolic volume at 6 months follow-up was significantly greater in patients with a reduction of regurgitant VCA >50% after PMVR as defined by 3D TEE compared to those patients with a reduction of regurgitant VCA ≤50% (Table 4). 2D TTE based analysis of regurgitant volumes (subtraction of LV outflow from 2D LV stroke volume) demonstrated only non-significant differences between patients with a reduction of regurgitant volume >50% and ≤50% in subsequent changes of left atrial, LV enddiastolic and endsystolic volumes at 6 months follow-up (-8.9±6.7% vs. -11.3±6.1%; p=0.382, -9.6±9.1% vs. -7.0±4.7%; p=0.442 and -6.3±7.5% vs. 5.0±7.8%; p=0.669). Similarly, if analysis of regurgitant volumes based on 2D TEE flow convergence method was applied, there was no significant difference between patients with reduction of regurgitant volume >50% and ≤50% with regards to subsequent remodeling of left atrial, LV enddiastolic and endsystolic volumes (-9.3±6.9 vs. -11.1±4.4%; p=0.666, -9.5±8.5 vs. -3.6±4.1%; p=0.240 and -6.3±7.7 vs. -2.4±1.2%; p=0.394).

Change of mitral inflow function. The maximum diastolic MVA area before the procedure determined by planimetry in 3D zoom mode was 6.0±2.0 cm². Diastolic MVA was reduced
after the procedure. The remaining maximal medial valve area was 1.5±0.7 cm² and the maximal lateral valve area was 1.4±0.5 cm², resulting in a total remaining valve area of 2.9±0.9 cm² (reduction by 52.5% after PMVR). Mitral valve mean diastolic pressure gradient increased from 1.6±0.9 mmHg pre to 3.3±1.8 mmHg post intervention (p<0.001). There was an inverse correlation between MVA before PMVR and postprocedural Pmean (r=-0.63). Using a ROC analysis, a MVA <4.1 cm² was an excellent predictor for a Pmean >5 mmHg after PMVR (AUC 1.0). Patients with a maximal MVA pre intervention ≥4.1 cm² (n=33) had a lower postprocedural Pmean compared to patients (n=6) with a MVA <4.1 cm² (2.6±1.1 mmHg vs. 6.7±0.8 mmHg; p<0.001).

Observer agreement. The intraobserver variability for the regurgitant volume determined by subtracting LV outflow from 2D total LV stroke volume was 12.8±12.1% (ICC=0.909) before and 39.3±86.8% after PMVR (ICC=0.941), while the interobserver variability for this method was 14.3±12.6% (ICC=0.887) before and 42.2±12.1% (ICC=0.913) after PMVR. Intraobserver variability of regurgitant volume based on 3D TEE direct planimetry of VCA was 8.4±5.6% (ICC=0.983) before and 16.2±10.0% (ICC=0.959) after PMVR, while the interobserver variability for this methods was 10.1±6.1% (ICC=0.978) before and 18.8±11.8% (ICC=0.942) after PMVR.

Discussion

The major findings of this study are (1) mitral regurgitation volume is reduced by 59% after PMVR as assessed by 3D TEE, (2) PMVR effectiveness as well as postprocedural mitral valve gradient are related to parameters of preprocedural mitral valve morphology defined by 3D echocardiography, (3) greater effectiveness of PMVR is associated with greater reduction of left atrial and LV volumes at 6 months follow-up, (4) while the relative reduction in mitral regurgitation volume is similar for the different echocardiographic modalities, the absolute mitral regurgitation volumes defined by 3D and 2D imaging techniques are significantly
different.

**Analysis of mitral regurgitation severity.** Planimetry of regurgitant jet area by 2D color Doppler is known as a semi-quantitative method for assessment of mitral regurgitation severity. In a phantom model planimetry of the regurgitant jet area has been shown to overestimate regurgitation severity in case of multiple jets (16). Numerous technical, physiologic and anatomic factors affect the size of the regurgitant area and therefore alter its accuracy as an index of regurgitation severity (17). In this study an intercommissural view was used for assessment of the regurgitant jet areas, because only in this view could both post procedural jets be visualized in one plane.

Analysis of regurgitant volume by subtracting LV systolic outflow from 2D TTE stroke volume is applicable even in case of multiple jets. However, this method is known to underestimate mitral valve regurgitation severity due to underestimation of LV volumes (4,14). Nevertheless, this has been the only quantitative method used in previous studies to assess procedural success of PMVR (1,13). Both, 3D TEE data sets with or without color Doppler have been used for direct visualization of mitral regurgitant orifice areas (6,7,9,11,12). Direct planimetry of vena contracta area by 3D color Doppler echocardiography has been shown to allow precise quantification of mitral valve regurgitation validated against magnetic resonance imaging (9). Similarly, analysis of mitral regurgitant areas and volumes based on 3D TEE without color has recently been validated against magnetic resonance imaging (18). In patients with mitral regurgitation, regurgitant orifice area was found to be the most robust parameter for quantification of lesion severity (19). A transfer of the excellent results obtained in one-orifice mitral valve morphology to the two-orifice post PMVR morphology seems adequate as this modality for quantification of regurgitant severity is based on direct visualization of mitral regurgitant orifice areas. In this study, mitral regurgitation volumes were found to be substantially greater using quantification based on direct planimetry of VCA by 3D color Doppler TEE compared to a definition of
regurgitation volumes by subtracting LV outflow from 2D TTE stroke volume. This difference was seen before as well as after the procedure. The difference should be explained by the known underestimation of volumes by the 2D method (4,19). However, reduction of mitral regurgitation fraction was of the same magnitude irrespective of applied method for quantification. 3D TEE has a unique advantage in that it allows analysis of mitral regurgitation severity for each orifice of the double-orifice mitral valve after PMVR. Assessment of EROA before and sum of the medial and the lateral EROA after edge-to-edge repair by 2D color Doppler TEE seems to overestimate the procedural reduction of mitral regurgitation compared to subtracting LV outflow from total stroke volume or direct planimetry of VCA by 3D TEE. The smaller intra- and interobserver variability of regurgitant volume measures by 3D echocardiography allows better detection of regurgitant volume changes during serial studies compared to 2D echocardiography.

**Mitral valve area.** 3D echocardiography has been shown to be a precise technique to assess maximum diastolic mitral valve area (20,21). In an in-vitro model the hemodynamic behavior of a double-orifice mitral valve did not differ from a physiologic one-orifice valve of same total area and same pressure gradient (22). In previous studies total MVA was reduced by 31 to 44 % after PMVR (2,23,24). In this study, a post procedural reduction of MVA by 52.5% has been shown by 3D TEE planimetry. The minor reduction seen in previous studies may be due to the obliquity when measuring the valve areas after PMVR in only one plane by 2D echocardiography. This can overestimate each area of post procedural mitral valve double-orifice resulting in an underestimation of the procedural reduction of MVA.

In most studies patients with a MVA <4.0 cm² at baseline were excluded from PMVR (2,23,24). Mean pressure gradient ≥5 mmHg is a criterion of moderate mitral stenosis (25). In this study all patients with a MVA <4.1 cm² by 3D TEE pre intervention had a mitral valve diastolic mean pressure gradient ≥5 mmHg after edge-to-edge repair, confirming that the previously arbitrarily applied exclusion criteria for PMVR is correct if postprocedural mitral
stenosis should be prevented.

**Impact of mitral annulus dimensions on effective reduction of mitral regurgitation.** In this study PMVR was associated with less procedural success in patients with enlarged preprocedural mitral annulus. This finding relates to previous reports on the surgical edge-to-edge repair which has been shown not to be successful in patients with significant annulus dilation and enlarged septal to lateral annulus distance (26). However, only mitral annulus area defined by 3D TEE was found to be a predictor of a reduction in mitral regurgitant VCA >50%, while diameters were not significant. This finding supports the importance of 3D imaging for preprocedural patient selection and prediction of procedural effectiveness.

**Impact of procedural effectiveness on left atrial and ventricular volumes.** PMVR has been demonstrated to be similarly effective in reducing LV volumes at follow-up compared to surgical repair (3). This study extended this observation of reduced volumes at follow-up to the left atrium. In addition, changes in left atrial and LV volumes were significantly greater in patients with a reduction of regurgitant VCA >50% than in those with a reduction ≤50% after the procedure.

**Limitations.** Patients were evaluated within 24 hours before, within 24 hours after PMVR and at 6 months follow-up. No information on long-term results was obtained. Only echocardiographic methods have been used for quantification of mitral regurgitation severity while no independent imaging method was applied. The applied 2D echocardiography based methods to evaluate mitral regurgitation are not validated for post procedural double-orifice mitral valve morphology. However, there is no validated method for quantification of mitral regurgitation after the PMVR procedure which can be applied in the majority of patients. Cardiac magnetic resonance tomography has been shown to be feasible in patients after PMVR (27), but pre-existing cardiac device therapy prevents the use of magnetic resonance imaging for precise assessment of mitral regurgitation in a high rate of patients undergoing PMVR.
Clinical implications. This study showed that mitral valve regurgitant volumes pre- and post percutaneous mitral valve repair can be evaluated with lower intra- and interobserver variability using 3D transesophageal echocardiography compared to 2D echocardiography based methods. This may allow better assessment of procedural effects during serial analysis of mitral regurgitant severity pre- to post procedure. 3D transesophageal echocardiography used for pre-procedural analysis of mitral valve morphology allows definition of patients with greater procedural effectiveness and greater risk of postprocedural mitral valve stenosis. Furthermore, the 3D TEE based analysis of procedural effectiveness allows an improved definition of patients with subsequent remodeling of left atrial and LV remodeling.

Conclusions. 3D echocardiography demonstrates significant reduction of regurgitant volume after PMVR. The unique visualization of the mitral valve by 3D TEE allows improved understanding of the morphological and functional changes induced by PMVR as well as prediction of procedural success.

Disclosures
None.

References


Table 1. Patient characteristics

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<th>Characteristic</th>
<th>Value</th>
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<tr>
<td>N=39</td>
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<tr>
<td>Age (years)</td>
<td>73±9</td>
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<tr>
<td>Male / female</td>
<td>24 (62%) / 15 (38%)</td>
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<tr>
<td>Logistic Euroscore (%)</td>
<td>18±12</td>
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<td>NYHA*</td>
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<td>III</td>
<td>27 (69%)</td>
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<tr>
<td>IV</td>
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<td>Ejection fraction (%)</td>
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<tr>
<td>2-vessel</td>
<td>4 (10%)</td>
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<tr>
<td>3-vessel</td>
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<td>Left atrial area (cm²)</td>
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<td>I / II</td>
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<td>29 (74%)</td>
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<tr>
<td>IV</td>
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<td>Color Doppler mitral regurgitation jet area (cm²)</td>
<td>7.5±3.2</td>
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<td>Effective regurgitant orifice area by flow convergence method (cm²)</td>
<td>0.33±0.15</td>
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<td>Mitral valve area (cm²)</td>
<td>6.0±2.0</td>
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*New York Heart Association (NYHA) functional classification for the extent of heart failure

#Mitral regurgitation grade according to EVERST criteria (10)
Table 2. Mitral valve regurgitant volume before and after PMVR determined by different methods

<table>
<thead>
<tr>
<th>Regurgitant volume by subtracting LV outflow from 2D TTE LV stroke volume (ml)</th>
<th>Before PMVR</th>
<th>After PMVR</th>
<th>Change (%)</th>
<th>P-value</th>
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<td>40.0±16.5</td>
<td>15.3±10.4</td>
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<tr>
<th>Regurgitant volume by 2D TEE flow convergence method (ml)</th>
<th>Before PMVR</th>
<th>After PMVR</th>
<th>Change (%)</th>
<th>P-value</th>
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<tr>
<td>56.0±27.4</td>
<td>14.3±10.9</td>
<td>-74.5%</td>
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<tr>
<th>Regurgitant volume by 3D TEE VCA method (ml)</th>
<th>Before PMVR</th>
<th>After PMVR</th>
<th>Change (%)</th>
<th>P-value</th>
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<tr>
<td>84.1±38.3</td>
<td>35.6±25.6</td>
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<td>&lt;0.0001</td>
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Table 3. Impact of mitral valve annulus dimensions on reduction of the total mitral regurgitation VCA after PMVR determined by 3D TEE color Doppler direct planimetry

<table>
<thead>
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<th>Reduction of VCA</th>
<th>Reduction of VCA</th>
<th>P-value</th>
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<td></td>
<td>&gt; 50% (n=27)</td>
<td>≤ 50% (n=12)</td>
<td></td>
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<tr>
<td>Mitral valve annulus area (cm²)</td>
<td>11.9±3.5</td>
<td>16.1±8.5</td>
<td>0.036</td>
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<tr>
<td>Mitral annulus circumference (cm)</td>
<td>13.0±2.0</td>
<td>14.8±4.1</td>
<td>0.112</td>
</tr>
<tr>
<td>Mitral annulus anterior to posterior diameter (cm)</td>
<td>3.5±0.7</td>
<td>3.9±0.8</td>
<td>0.163</td>
</tr>
<tr>
<td>Mitral annulus posteromedial to anterolateral diameter (cm)</td>
<td>4.0±0.7</td>
<td>4.4±1.1</td>
<td>0.263</td>
</tr>
</tbody>
</table>
Table 4. Left atrial volume, LVEDV and LVESV at baseline and relative volume changes at 6 months after PMVR defined by 2D TTE related to reduction of the total mitral regurgitation VCA after procedure as determined by 3D TEE.

<table>
<thead>
<tr>
<th>Reduction of VCA</th>
<th>Reduction of VCA</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50% (n=25)</td>
<td>≤ 50% (n=11)</td>
<td></td>
</tr>
<tr>
<td>LA volume at baseline (ml)</td>
<td>160.6±68.0</td>
<td>157.5±52.9</td>
</tr>
<tr>
<td>LVEDV at baseline (ml)</td>
<td>205.2±106.7</td>
<td>205.0±107.1</td>
</tr>
<tr>
<td>LVESV at baseline (ml)</td>
<td>123.6±98.6</td>
<td>120.8±95.1</td>
</tr>
<tr>
<td>Δ LA volume 6 months after PMVR (%)</td>
<td>-11.4±5.2</td>
<td>-4.8±7.7</td>
</tr>
<tr>
<td>Δ LVEDV 6 months after PMVR (%)</td>
<td>-11.0±7.2</td>
<td>-4.5±9.3</td>
</tr>
<tr>
<td>Δ LVESV 6 months after PMVR (%)</td>
<td>-6.5±8.5</td>
<td>4.9±4.3</td>
</tr>
</tbody>
</table>

LA: left atrium, LVEDV: left ventricular end-diastolic volume, LVESV: left ventricular end-systolic volume, VCA: vena contracta area.
Figure Legends

**Figure 1.** 3D TEE full-volume color Doppler view from the anterior roof of the left atrium towards the mitral valve in midsystole before PMVR (A). A cut plane orthogonal to the regurgitant jet allows direct visualization of the proximal vena contracta area (0.52 cm²) (B). After PMVR a view from the anterior roof of the left atrium towards the mitral valve in midsystole allows assessment of the device effect (C). Orthogonal cut planes of the remaining medial and lateral regurgitation jets can be adjusted allowing direct visualization of the medial (0.16 cm²) (D) and the lateral vena contracta area (0.04 cm²) (E). PMVR=percutaneous mitral valve repair; PM=posteromedial; AL=anterolateral; VCA=vena contracta area.

**Figure 2.** 3D TEE view from the roof of the left atrium in diastole before PMVR (A) with direct visualization of the maximum diastolic mitral valve area (B). It can be noted that after PMVR the two resulting orifices are not in one plane (D). Direct planimetry of diastolic mitral valve areas was done separately for the medial (C) and the lateral orifice (E). PMVR=percutaneous mitral valve repair; PM=posteromedial; AL=anterolateral; Ao=aortic valve; MVA=mitral valve area.

**Figure 3.** 3D TEE view from the anterior roof of the left atrium towards the mitral valve after PMVR (A). The double-headed arrow shows the orientation of the commissural line as defined as the line between the posteromedial and the anterolateral edge of the mitral valve in diastole. The distance (d) between the center of the mitral valve commissural line (white dot) and the position of the clip (red dot) was assessed (B). PM=posteromedial; AL=anterolateral; Ao=aortic valve.
**Figure 4.** Analysis of 3D TEE data sets enables accurate visualization of the mitral valve annulus with anterior and posterior leaflets as well as position of the papillary muscles. The mitral valve including the mitral annulus can be shown from different views, in particular from a lateral view (A) and a superior view from the roof of the left atrium towards the mitral valve (B). Mitral annulus area, mitral annulus circumference as well as the anterior to posterior and anterolateral to posteromedial diameter (white double-headed arrows) can be determined. A=anterior; P=posterior; PM=posteromedial; AL=anterolateral; Ao=aortic valve.

**Figure 5.** VCA determined by direct planimetry in 3D TEE color Doppler images before PMVR and VCA of the remaining medial and lateral regurgitation jets after PMVR for each patient.
Figure 2

A: Before PMVR

B: After PMVR

C: MVA Medial

D: Ao

E: MVA Lateral
Figure 5

*VCA before vs. after medial, after lateral and after total
†VCA after medial vs. after lateral
Analysis of Procedural Effects of Percutaneous Edge-to-Edge Mitral Valve Repair by 2D and 3D Echocardiography
Ertunc Altiok, Sandra Hamada, Kathrin Brehmer, Kathrin Kuhr, Sebastian Reith, Michael Becker, Jörg Schröder, Mohammad Almalla, Walter Lehmacher, Nikolaus Marx and Rainer Hoffmann

Circ Cardiovasc Imaging. published online September 21, 2012;
Circulation: Cardiovascular Imaging is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-9651. Online ISSN: 1942-0080

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