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Left Ventricular Geometry Predicts Optimal Response to Percutaneous Mitral Repair via MitraClip – Integrated Assessment by Two- and Three-Dimensional Echocardiography

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Abstract

Objectives: To assess impact of left ventricular (LV) chamber remodeling on MitraClip (MClp) response.

Background: MitraClip (MClp) is the sole percutaneous therapy approved for mitral regurgitation (MR) but response varies. LV dilation affects mitral coaptation; determinants of MClp response are uncertain.

Methods: LV and mitral geometry were quantified on pre- and post-procedure two-dimensional (2D) transthoracic echocardiography (TTE) and intra-procedural three-dimensional (3D) transesophageal echocardiography (TEE). Optimal MClp response was defined as mild MR at early (1-6 month) follow-up.

Results: 67 degenerative MR patients underwent MClp: Whereas MR decreased 1 grade in 94%, 39% of patients had optimal response (mild MR). Responders had smaller pre-procedural LV end-diastolic volume (94 ± 24 vs. 109 ± 25 ml/m², $p=0.02$), paralleling smaller annular diameter (3.1 ± 0.4 vs. 3.5 ± 0.5 cm, $p=0.002$), and inter-papillary distance (2.2 ± 0.7 vs. 2.5 ± 0.6 cm, $p=0.04$). 3D TEE-derived annular area correlated with 2D TTE ($r=0.59$, $p<0.001$) and was smaller among optimal responders (12.8 ± 2.1 cm² vs. 16.8 ± 4.4 cm², $p=0.001$). Both 2D and 3D mitral annular

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size yielded good diagnostic performance for optimal MClp response (AUC 0.73-0.84, $p<0.01$). In multivariate analysis, sub-optimal MClp response was associated with LV end-diastolic diameter (OR 3.10 per-cm [1.26 – 7.62], $p=0.01$) independent of LA size (1.10 per-cm² [1.02 - 1.19], $p=0.01$); substitution of mitral annular diameter for LV size yielded an independent association with MClp response (4.06 per-cm² [1.03 - 15.96], $p=0.045$).

Conclusions: Among degenerative MR patients undergoing MClp, LV and mitral annular dilation augment risk for residual or recurrent MR, supporting the concept that MClp therapeutic response is linked to sub-valvular remodeling.

Introduction

Mitral regurgitation (MR) is a leading cause of valvular heart disease,(1,2) for which percutaneous mitral repair is an emerging therapeutic strategy. MitraClip (MClp) is the sole percutaneous therapy commercially approved to treat MR in patients not suitable for surgical intervention.(3) Despite high success rates in initial research trials,(4,5) subsequent reports have yielded mixed clinical results: Longitudinal studies have reported some degree of residual or recurrent MR (mild) in as many as half of patients undergoing MClp;(6,7) residual or recurrent MR after MClp has been linked to mortality and heart failure risk. (8-11) Other studies – including two recent large scale trials in functional MR (MITRA-FR, COAPT) have yielded conflicting results regarding impact of MClp on clinical outcomes, possibly due to underlying physiologic differences in patient profiles that impact device efficacy.(12,13) Given the prevalence of MR and growing diversity of surgical and investigational percutaneous alternatives for its treatment, elucidation of structural predictors of MClp therapeutic success is of substantial importance.

Whereas MitraClip is intended to induce focal leaflet coaptation, MR is itself impacted by left ventricular (LV) remodeling. Myocardium underlying the mitral valve is an intrinsic component of the mitral apparatus that provides support for valve closure. LV dilation can contribute to MR by augmenting leaflet tethering, altering papillary mechanics, and geometrically distorting the mitral annulus. Mitral valve incompetence has been strongly linked to adverse LV remodeling in patients with functional MR.(14) Whereas MClp is commercially approved for degenerative MR, it is commonly implanted in older patients with contraindications to surgery in whom coronary artery disease (CAD) and adverse LV remodeling are common,(15-17) and MR etiology is mixed (degenerative and functional components). LV dilation can potentially impair MClp efficacy by augmenting tensile force required to achieve adequate mitral coaptation. The impact of adverse LV remodeling as a predictor of MClp response is poorly understood.

This study examined structural predictors of MR response to MClp. To do so, transthoracic echocardiograms (TTE) were analyzed pre- and early post- (within 6 months) MClp implantation - analyses included quantification of MR, LV and left atrial (LA) geometry. As a reference, three-dimensional (3D) transesophageal echo (TEE) was also used to quantify mitral annular geometry. The goal was to test the hypothesis that pre-procedural sub-valvular mitral apparatus remodeling augments risk for suboptimal MR response to MClp.

Materials and Methods

The population comprised patients with advanced (>moderate) degenerative MR who underwent MClp at Weill Cornell Medicine (NY, NY) in whom TTE was performed pre- and post- (1-6 months [target 6 months]) procedure: No otherwise eligible patients were excluded based on procedural outcomes, imaging findings, and/or clinical indices. Demographic data were collected in a uniform manner, including cardiac risk factors and medications. Number and location of MClp devices were also recorded, together with hemodynamic indices at time of MClp implantation. This protocol was approved by the Weill Cornell Institutional Review Board, which approved analysis of pre-existing data for research purposes.

Image Acquisition

To comprehensively test LV geometry as a predictor of MClp response, imaging data were derived from both TTE and TEE, each of which was acquired via a standardized protocol:

- TTEs were obtained using commercial equipment (Philips: iE33, EPIQ7 [Andover, MA]). Images were acquired in parasternal long, parasternal short, and apical 2-, 3-, and 4- chamber orientations. Color and pulsed wave Doppler was used to assess MR; continuous wave Doppler included assessment of tricuspid regurgitant velocity (to quantify pulmonary artery [PA] systolic pressure).
- TEEs were acquired intra-procedure in a mid-esophageal view using a Philips iE33 system equipped with a matrix array transducer (X7-2t). 3D images of the mitral apparatus, including the annulus, leaflets, and basal LV were acquired in 70% of patients (n=47). 3D images were optimized for coverage and gain using single beat acquisition (Zoom 3D); datasets were selected for analysis based on image quality.

Image Analysis

Mitral Regurgitation—Echoes were interpreted by dedicated ACC/AHA level III trained readers in a high-volume laboratory, for which expertise in MR quantification has previously been reported.(1,18) MR was graded per consensus guidelines based on an aggregate 4-point scale (1=mild – 4=severe),(19) for which key components included vena contracta, regurgitant fraction, regurgitant volume, and effective regurgitant orifice area (EROA). Additional data including jet area and density and mitral and pulmonary vein flow pattern were also examined.

LV Chamber Quantification—LV chamber size, function, and mass were quantified on TTE based on standardized linear dimensions measured in parasternal long axis orientation, concordant with established methods validated in prior research.(20,21) In brief, LV end-diastolic and end-systolic internal dimensions were measured in parasternal long axis at the level of mitral leaflet tips. LV mass was quantified using antero-septal and posterior wall thickness, in accordance with previously validated methods.(22) Additional analyses included quantification of LA area/volume and Doppler-based measurement of PA systolic pressure.

Tailored mitral apparatus remodeling indices were quantified in accordance with established methods:(14,23,24) Mitral annular diameter was defined as the distance between annular insertion into the lateral LV wall and inferoseptum as discerned at LV end-diastole in apical 4-chamber orientation. Inter-papillary diameter was defined as the distance between the anterolateral and posteromedial papillary muscle in mid parasternal short axis.

Three Dimensional Mitral Annular Geometry—3D TEE analysis was performed using a semi-automated program (TomTEC 4D MV [Munich, Germany]) tailored for mitral annular geometry. A mid-systolic frame was selected for initiation of mitral annular tracking; landmarks including antero-posterior (AP) diameter, anterolateral-posteromedial (AL-PM) diameter, anterior and posterior annulus, aortic valve and coaptation points were identified. The annulus was then tracked automatically throughout the cardiac cycle; contours were manually edited to ensure optimal border delineation. Figure 1 provides a representative example of both conventional two-dimensional (2D) TTE (**1A**) and 3D TEE (**1B**) analyses of mitral annular indices.

Intra-procedural 3D TEE and pre-procedural 2D TTE were analyzed blinded to one another, as well as to MClp response (i.e. change in MR).

Statistical Methods

Comparisons between groups were made using Student's t test (expressed as mean $\pm$ standard deviation) for continuous variables. Categorical variables were compared using chi-square or (when < 5 expected outcomes per cell) Fisher's exact test. Bivariate correlation coefficients were used to evaluate associations between continuous variables. Univariable and multivariate modeling was performed via binary logistic regression. Statistical calculations were performed using SPSS 22.0 (SPSS Inc. [Chicago, IL]). Two-sided $p < 0.05$ was considered indicative of statistical significance.

Results

Population Characteristics

67 patients with advanced ($>$ moderate) MR who underwent MClp between 2013-2018 were studied. Whereas all patients had degenerative mitral valve pathology (61% valve thickening, 43% annular calcification, 39% prolapse), concomitant conditions pre-disposing to adverse LV remodeling and mixed mitral valve dysfunction were common: Over half (54%) of patients had known CAD, and nearly one quarter (24%) had prior MI. 55% of patients had multiple MClp implants placed during the index procedure, constituting an average of 1.6 ± 0.6 distinct devices.

Follow-up TTE (2.8 ± 2.6 months) was performed to assess short term procedural durability: Nearly all (94%) patients had some MClp response (≥ 1 grade MR reduction) and 90% had moderate MR, whereas 39% had optimal MClp response ($\leq$ mild MR). Table 1 details clinical and imaging characteristics of the population, as well as comparisons between patients with and without optimal MClp response. As shown, groups were similar with respect to clinical indices, including history of CAD, atherosclerotic risk factors, and clinically reported heart failure severity (all $p = \text{NS}$).

Two Dimensional Mitral Annular Geometry

Table 2 compares baseline cardiac structural and functional indices, as well as MR severity in relation to subsequent MClp response. As shown, patients with optimal MClp response had smaller LA size, irrespective of whether quantified based on area or volume (both $p < 0.05$). LV indices similarly demonstrated lesser chamber enlargement among patients with optimal MClp response: Global LV size was smaller among optimal responders ($p = 0.005$), paralleling smaller mitral annular ($p = 0.002$) and inter-papillary diameter ($p = 0.04$). LV geometric differences were independent of LV contractile function, as evidenced by similar LV ejection fraction and cardiac output (both $p = \text{NS}$) between response groups.

Three Dimensional Mitral Annular Geometry

Mitral annular geometry as quantified by the reference of TEE provided further confirmation of TTE results. As shown in Table 2, 3D mitral annular area was nearly 25% smaller among patients with, compared to those without, optimal MClp response ($12.8 \pm 2.1 \text{ cm}^2$ vs. $16.8 \pm 4.4 \text{ cm}^2$, $p = 0.001$). TEE-derived 2D mitral annular area and circumference demonstrated comparable differences in relation to MClp response (both $p = 0.001$). Regarding mitral geometry, data shown in Table 2 demonstrate that prevalence of prolapse, annular calcification, and mitral valve thickening were similar between groups. Flail mitral valve pathology was present in 16% of the study population- among affected patients, neither flail gap ($p = 0.25$) nor flail width ($p = 0.35$) differed between patients with and without sub-optimal MClp response.

Figure 2 provides scatter plots relating TEE derived 2D and 3D mitral annular area to linear TTE measurements. As shown, mitral annular diameter as quantified by 2D TTE yielded good correlations with annular area as measured on 2D and 3D TEE ($r = 0.589$ - 0.590 , $p < 0.001$). LV chamber size quantified on 2D TTE also correlated with other adverse mitral apparatus remodeling indices measured on the reference of 3D TEE including mitral tenting area ($r = 0.52$, $p < 0.001$), tenting volume ($r = 0.45$, $p = 0.003$), and posterior leaflet length ($r = 0.43$, $p = 0.002$).

Structural Predictors of MitraClip Response

Figure 3 reports prevalence of optimal MR response in relation to population-based quartiles of LV and LA remodeling indices. As shown, optimal MR response was nearly 4-fold more common among patients in the highest versus those in the lowest quartile of LV chamber size (59% vs. 16%), paralleling an equivalent difference in MClp response rates between patients stratified based on left atrial volume (71% vs. 17%), or mitral annular size on 2D TTE or 3D TEE (all $p < 0.05$ for trend). ROC analysis demonstrated both 2D and 3D mitral annular size to yield good diagnostic performance (AUC 0.73-0.84, $p < 0.01$) for optimal MClp response (Figure 4), corresponding to good maximal sensitivity/specificity for 3D TEE (80% and 82% respectively, using a partition of 14.1 cm^2) and lesser sensitivity/specificity for 2D TTE (80% and 59% respectively, using a partition of 3.1 cm).

Multivariate analysis was used to further test the association of pre-procedural LV remodeling with MClp response when controlling for LA remodeling. As shown in Table 3A, sub-optimal MClp response was associated with increased LV chamber size ($p = 0.01$)

independent of LA area ($p=0.01$). As shown in Table 3B, substitution of mitral annular diameter in place of LV chamber size again demonstrated mitral apparatus remodeling to be independently associated with greater residual MR ($>$ mild) after MClp implantation.

Discussion

This study provides new insights concerning impact of LV remodeling on MClp response. Key findings are as follows: First, optimal therapeutic response to MClp (mild MR) was negatively associated with sub-valvular dilation on TTE, irrespective of whether quantified by mitral annular diameter, LV end-diastolic volume, or inter-papillary distance (all $p<0.05$). Second, intra-procedural 3D TEE confirmed TTE results, as evidenced by a similar association between smaller mitral annular area and optimal MClp response ($p=0.001$), as well as good diagnostic performance for annular size with respect to identification of optimal responders (AUC 0.73-0.84, $p<0.001$). Finally, multivariate analysis demonstrated LV and LA size to each be independently associated with optimal MClp response; a similar independent association was present when mitral annular area was substituted for LV size. Applied clinically, these data indicate that degenerative MR patients with marked LV or mitral annular dilation are less likely to derive optimal therapeutic results from focal mitral valve apposition as induced by MClp.

While our data provides new insights regarding the impact of LV sub-valvular remodeling with therapeutic success, our findings build upon prior research that has identified LV chamber size as a predictor of MClp-related outcomes. For example in a U.S. registry data of 564 patients undergoing MClp (91% of whom had degenerative MR), increased LV end-diastolic diameter was negatively associated with likelihood of reduced MR at index hospitalization.(7) LV chamber size has also been reported to impact prognosis: Among patients with functional MR, Rudolph et al. found that increased LV volume stratified risk for re-hospitalization after MClp.(17)The notion that LV and/or mitral annular dilation can impact procedural success may provide an explanation for conflicting results of two recent trials testing MClp for functional MR - whereas COAPT demonstrated marked impact of MClp on clinical outcomes, no benefit was found in MITRA-FR. Of note, LV chamber volume was over 25% greater among patients in MITRA-FR (135 ± 35 ml/m²) compared to COAPT (101 ± 34 ml/m²), paralleling increased rates of recurrent MR.(12,13) It is important to note that mechanism for MClp response likely differs in part between patients with functional MR (as were studied in COAPT and MITRA-FR) and patients with degenerative or mixed MR (as comprised our cohort), given that the latter group has primary mitral valve pathology that would be expected to impact MClp durability. On the other hand, degenerative and functional MR may share some common features that impact LV remodeling and MClp, such as MR-induced chronic LV volume loading that has the potential to alter biomechanical strain caused by implanted devices.

LA dilation has also been linked to procedural success: Among 74 patients undergoing MClp (62% functional, 38% degenerative), Toggweiler et al. found LA volume to stratify risk for post-procedure recurrence of MR but did not report on the role of LV dilation.(9) Whereas these data support a link between chamber dilation and outcomes, prior data are lacking as to whether impact of LV and LA dilation stem solely from changes in mitral

annular geometry, or reflect broader alterations in the mitral apparatus (i.e. valve, annulus, underlying myocardium). Our finding of increased inter-papillary diameter among MR patients with sub-optimal MClp results supports the notion that systemic changes in LV geometry influence procedural success. In another study, Stolfo et al. reported LV size to be a predictor of device failure, but the cohort was limited to patients with functional MR and advanced heart failure (LVEF<40%).(25) Of note, the cohort studied by Stolfo et al. did not include patients with degenerative MR – the population in whom MClp is currently commercially approved in the United States and that mechanisms for MClp response in patients with functional MR cannot necessarily be extrapolated to other causalities of MR, providing a logical rationale for our study.

It is important to recognize that our study assessed MClp response using a cutoff of mild (1+) MR, to test LV remodeling in relation to procedural success. The approach is consistent with that employed in several prior studies, and supported by data showing MClp patients with greater residual MR (2+) to have worse clinical prognosis.(8,9) Despite this, a variety of cutoffs for adequate MR reduction have been used in prior MClp studies, which may explain discordances in reported procedural success rates.(6,8,9,26-29) Of note, even tailored research data – as was acquired for the EVEREST II trial – demonstrated that whereas MClp yielded near uniform acute post-procedure reductions in MR, only 43% of patients had mild MR by 1 year post procedure(6) – a proportion similar to our study (39%). Other studies have supported the notion that MR recurrence after MClp is common: Among 85 patients who had initial optimal MClp implantation (residual MR 1+ at discharge), De Bonis et al reported that 32.5% developed recurrent MR (2+) by 1 year post procedure.(30) Taken together, these data suggest a dynamic process, whereby acute procedural success may be impacted by factors that subsequently contribute to LV and myocardial stress, impaired mitral valve coaptation, and recurrent MR.

Regarding mechanism, we speculate that MClp failure is in part due to increases in leaflet stress and/or remodeling strain in the proximal LV myocardium and that these two unintended consequences would be expected to increase in the setting of LV dilation. (16,31,32) The notion that focal restriction of the mitral apparatus can be less efficacious in the context of LV dilation has been shown in patients with functional MR, in whom LV/annular mismatch has been shown to predict MR recurrence.(33) Whereas MClp is intended to exert localized valvular effects, increased risk for residual MR in context of degenerative MR with LV dilation may stem from augmented leaflet stress tethering forces required for MClp to achieve durable valve apposition in context of annular distortion as compared to normal annular geometry. It is also possible that myocardial tissue properties may impact this process due to increased LV stiffness as induced by sub-valvular infarction or non-ischemic fibrosis. Consistent with this, prior studies by our group have shown focal non-ischemic fibrosis to increase in proportion to LV dilation, and other studies have shown extracellular volume (a marker of diffuse fibrosis) to increase with adverse LV remodeling. (34,35) Whereas our study employed echo to assess LV remodeling, our observed association between LV dilation and residual MR, as well as known associations between dilation and fibrosis support the need for further research using MRI or other methods to test the modulating impact of myocardial fibrosis as a determinant of recurrent and/or residual MR after MClp.

Several limitations should be noted: First, our study employed a standardized semi-quantitative grading criteria to assess MR severity rather than a singular criterion. However, our approach is consistent with that applied in prior multicenter studies of MClp, for which post-procedural MR severity has been similarly assessed.(5,6) More broadly, all analyses performed in this study are consistent with methods applied and validated by our group and others in prior large epidemiologic and outcomes research.(1,18,20,22,36) Second, whereas our sample size (n=67) was similar to several other studies that have tested imaging predictors of MClp response (n=50-77),(9,25,37,38) larger multicenter prospective studies are warranted to confirm our findings and test LV remodeling as a predictor of post-MClp clinical outcomes. On the other hand, prior studies examining MClp response have linked recurrent or residual MR to prognosis, and shown mortality to parallel MR severity.(8-11) Third, it should be noted that our multivariate analysis tested LV size as a predictor of suboptimal MitraClip response while controlling for LA size, given that these two indices were each strongly related to MR in univariate analysis and that the role of LV (independent of LA) remodeling as a predictor of MitraClip response in patients with degenerative MR is uncertain. On the other hand, our cohort only included 26 patients with optimal MitraClip response, prohibiting development of models inclusive of a broader array of chamber remodeling, leaflet based, and clinical predictors. Finally, whereas an array of alternative percutaneous devices are being developed for treatment of MR, our study solely tested MClp. Given our observed link between LV dilation and MR response, it is possible that devices aimed at altering annular remodeling could provide utility as an alternative intervention in patients with marked LV dilation being considered for MitraClip. To this end, external compression devices have been tested in pilot studies but have yet to be widely applied as a strategy to treat MR.

In conclusion, findings of this study demonstrate that among patients with degenerative or mixed MR undergoing MClp, pre-procedure LV and mitral annular dilation predict sub-optimal procedural success. Future larger scale studies are necessary to further validate current findings and determine whether extent of LV remodeling can be used to guide therapeutic decision making for patients being considered for percutaneous mitral valve repair.

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Figure 1. 2D and 3D Annular Geometric Indices

Representative examples of echo derived LV and mitral apparatus remodeling parameters used to assess MCIp response. **1A.** Inter-papillary distance and mitral annular diameter as respectively acquired in mid LV short axis and 4C long axis on 2D TTE. **1B.** Mitral annular area as quantified on 3D TEE (single beat) acquisition. Analytic output included 3D area as well as projected 2D area, circumference and linear indices.

Figure 2. Linear Annular Dimension in Relation to TEE Quantified Mitral Area

Scatter plots comparing 2D and 3D TEE derived mitral area in relation to 2D TTE linear dimension; note similar magnitude of correlation for 2D TTE in relation to both TEE indices ($p < 0.001$ for both).

Figure 3. MR Response Prevalence in Relation to Chamber Remodeling

Prevalence of optimal MClp response (mild MR) in relation to LV (top left), LA (top right), and mitral annular (bottom left and right) size. As shown, prevalence of MR response decreased stepwise in relation to LV, LA, and annular remodeling parameters ($p < 0.05$ for all).

Figure 4. Receiver Operating Characteristics Curves

ROC curves for 3D and 2D TEE as well as 2D TTE quantified mitral annular size in relation to optimal MR response. As shown, 3D TEE yielded highest overall diagnostic performance for stratifying MCIP response, although all approaches similarly demonstrated annular size to predict procedural success ($p < 0.01$).

Table 1.

Clinical Characteristics

	Overall (n=67)	MC _{RSP} + (n=26)	MC _{RSP} – (n=41)	P
CLINICAL				
Age (year)	81 ± 8	81 ± 7	80 ± 9	0.87
Male gender	61% (41)	62% (16)	61% (25)	0.96
Body surface area (m ²)	1.8 ± 0.3	1.8 ± 0.3	1.8 ± 0.2	0.72
Heart rate (bpm)	70 ± 12	70 ± 14	70 ± 10	0.84
Systolic blood pressure (mmHg)	116 ± 18	120 ± 18	113 ± 17	0.12
Diastolic blood pressure (mmHg)	65 ± 11	66 ± 12	65 ± 10	0.70
Atherosclerosis Risk Factors				
Hypertension	84% (56)	89% (23)	81% (33)	0.51
Hypercholesterolemia	64% (43)	62% (16)	66% (27)	0.72
Diabetes mellitus	25% (17)	35% (9)	20% (8)	0.17
Tobacco use	63% (42)	58% (15)	66% (27)	0.50
Coronary Artery Disease				
Prior Myocardial Infarction	24% (16)	15% (4)	29% (12)	0.25
Prior Revascularization	43% (29)	39% (10)	46% (19)	0.53
Prior Percutaneous Intervention	31% (21)	35% (9)	29% (12)	0.65
Prior Coronary Artery Bypass Grafting	22% (15)	19% (5)	24% (10)	0.62
Atrial fibrillation/flutter	51% (34)	46% (12)	54% (22)	0.55
Prior CVA/TIA	8% (5)	8% (2)	7% (3)	1.00
NYHA Class (1/2/3/4)	9% (6)/ 27% (18)/ 51% (34)/ 13% (9)	0% (0)/ 42% (11)/ 46% (12)/ 12% (3)	15% (6)/ 17% (7)/ 54% (22)/ 15% (6)	0.71
Cardiovascular Medications				
Beta-blocker	78% (52)	81% (21)	76% (31)	0.62
ACE-Inhibitor/Angiotensin Receptor Blocker	57% (38)	50% (13)	61% (25)	0.38
Loop diuretic	84% (56)	85% (22)	83% (34)	1.00
HMG CoA-Reductase Inhibitor	69% (46)	77% (20)	63% (26)	0.25
Aspirin	61% (41)	58% (15)	63% (26)	0.64
Number of Clips (1/2/3)	45% (30)/ 49% (33)/ 6% (4)	46% (12)/ 54% (14)/ 0% (0)	44% (18)/ 46% (19)/ 10% (4)	0.56

* MC_{RSP} defined as mild MR after MitraClip.

Table 2.**Pre-MitraClip Imaging Characteristics**

	Overall (n=67)	MC_{RSP} + (n=26)	MC_{RSP} - (n=41)	p[¶]
Left Ventricle				
LV Function				
Ejection fraction (%)	49 ± 15	50 ± 15	49 ± 15	0.83
LV dysfunction (LVEF < 55%)	51% (34)	54% (14)	49% (20)	0.69
Cardiac Output (L/min)	6.3 ± 2.2	5.8 ± 2.5	6.5 ± 2.1	0.22
LV Structure				
Inter-papillary distance (cm)	2.4 ± 0.7	2.2 ± 0.7	2.5 ± 0.6	0.04
End-diastolic diameter (cm)	6.1 ± 0.7	5.7 ± 0.6	6.3 ± 0.7	0.005
End-diastolic volume (ml/m ²)	103 ± 26	94 ± 24	109 ± 25	0.02
End-systolic diameter (cm)	4.5 ± 1.0	4.2 ± 0.9	4.7 ± 1.0	0.07
End-systolic volume (ml/m ²)	55 ± 28	48 ± 26	59 ± 29	0.14
Myocardial mass (g/m ²)	112 ± 30	108 ± 28	116 ± 31	0.30
Mean wall thickness (cm)	0.8 ± 0.1	0.9 ± 0.1	0.8 ± 0.1	0.32
Relative wall thickness	0.26 ± 0.05	0.29 ± 0.05	0.25 ± 0.05	0.008
Eccentric hypertrophy (%)	59% (38)	58% (14)	60% (24)	0.90
Mitral Valve Geometry				
TTE				
Mitral annular diameter (cm)	3.3 ± 0.5	3.1 ± 0.4	3.5 ± 0.5	0.002
TEE				
AP diameter (cm)	4.1 ± 0.6	3.8 ± 0.4	4.3 ± 0.6	0.002
AL-PM diameter (cm)	4.5 ± 0.6	4.2 ± 0.4	4.7 ± 0.6	0.001
Sphericity Index	0.91 ± 0.09	0.90 ± 0.07	0.92 ± 0.09	0.57
2D Mitral annular area (cm ²)	15.0 ± 4.1	12.5 ± 2.1	16.3 ± 4.3	0.001
3D Mitral annular area (cm ²)	15.3 ± 4.2	12.8 ± 2.1	16.8 ± 4.4	0.001
Annular circumference (cm)	14.3 ± 1.9	13.1 ± 1.1	15.0 ± 1.9	<0.001
Right Ventricle				
TAPSE (cm)	1.8 ± 0.6	1.8 ± 0.6	1.8 ± 0.7	0.88
S' (cm/s)	10.9 ± 3.1	10.6 ± 2.7	11.0 ± 3.3	0.62
RV diameter (cm)	4.6 ± 0.8	4.6 ± 1.0	4.5 ± 0.8	0.71
Left Atrium				
Diameter (cm)	5.1 ± 1.1	4.8 ± 1.0	5.3 ± 1.2	0.06
2-Chamber area (cm ²)	33 ± 12	28.9 ± 8	35.5 ± 14	0.01
4-Chamber area (cm ²)	34 ± 10	29.1 ± 8	36.6 ± 11	0.003
Volume (ml/m ²)	76 ± 38	62 ± 28	85 ± 42	0.02
Mitral Regurgitation				
Regurgitant Severity				
Regurgitant fraction (%)	55 ± 17	52 ± 12	57 ± 19	0.24
EROA (cm ²)	0.6 ± 0.2	0.5 ± 0.2	0.6 ± 0.2	0.18

	Overall (n=67)	MC_{RSP} + (n=26)	MC_{RSP} - (n=41)	p[¶]
Regurgitant volume (ml)	86 ± 37	79 ± 36	90 ± 38	0.25
<i>Mitral Valve Morphology</i>				
Prolapse	39% (26)	39% (10)	39% (16)	0.96
Mitral annular calcification	43% (29)	46% (12)	42% (17)	0.71
Mitral valve thickening	61% (41)	62% (16)	61% (25)	0.96
Flail pathology	16% (11)	15% (4)	17% (7)	1.00
Pulmonary arterial systolic pressure (mmHg)	53 ± 16	56 ± 19	51 ± 14	0.19
Pulmonary hypertension (PASP ≥ 35mmHg)	86% (57)	84% (21)	88% (36)	0.72

* MC_{RSP} defined as mild MR after MitraClip.

¶ Bold value indicates p<0.05

Table 3.

Structural Predictors of Sub-Optimal Response (>mild MR) After MitraClip *

3A.				
Univariate Regression			Multivariate Regression <i>Chi square =17.08; p<0.001</i>	
Variable	Odds Ratio (95% Confidence Interval)	P [¶]	Odds Ratio (95% Confidence Interval)	P
LV End-Diastolic Diameter	2.90 (1.33 – 6.33)	0.008	3.10 (1.26 – 7.62)	0.01
LA Area (4 Chamber)	1.10 (1.03 – 1.18)	0.008	1.10 (1.02 – 1.19)	0.01
3B.				
Univariate Regression			Multivariate Regression <i>Chi square =14.20; p=0.001</i>	
Variable	Odds Ratio (95% Confidence Interval)	P	Odds Ratio (95% Confidence Interval)	P
Mitral Annular Diameter	6.59 (1.86 – 23.30)	0.003	4.06 (1.03 – 15.96)	0.045
LA Area (4 Chamber)	1.10 (1.03 – 1.18)	0.008	1.07 (0.99 – 1.15)	0.08

* LV end-diastolic diameter, LA area, and mitral annular diameter were quantifiable in all (100%) patients.

¶ Bold value indicates p<0.05