Chapter 25: Cardiac imaging for TMVr - TTE and TEE

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Patient Selection

Echocardiography plays a key role in the appropriate patient selection and procedural aspects of transcatheter mitral valve repair utilizing the MitraClip® system (Abbott, Abbott Park, IL, USA). This begins with an accurate diagnosis of the predominant mechanism and the severity of mitral regurgitation (MR). Excessive mitral valve (MV) leaflet motion such as MV prolapse or flail characterizes primary (degenerative) MR (Figure 1), whereas restricted systolic MV leaflet closure motion in the setting of LV dysfunction and/or dilatation is characteristic of secondary (functional) MR (Figure 2). The MitraClip is currently FDA approved only for treatment of at least moderate to severe primary MR; its application in secondary MR is currently being studied within the COAPT trial. Transthoracic echocardiography (TTE) can usually assess the main MR mechanism and its severity. Transesophageal echocardiography (TEE) may be required in patients with very eccentric MR jets or when the MR jet is not adequately visualized (see Table 1 for MR grading (1), Figures 1 and 2**)**. The assessment of the hemodynamic remodeling consequences of MR on the left ventricle (LV), right ventricle (RV) and left atrium (LA) as well as right ventricular systolic pressure and other significant valve disease is the domain of TTE, as well as an initial screening of the diastolic MV opening area at the leaflet tips (Figure 3).

Table 1. Echocardiographic Parameters of Severe Mitral Regurgitation

Structural parameters	Dilated LA
	Dilated LV
	Abnormal mitral leaflets or supporting apparatus (flail leaflet, ruptured papillary muscle)
Doppler parameters	Large central color flow jet (>50% of LA) or variable size eccentric wall-impinging jet
	Large flow convergence throughout systole
	Dominant E wave in mitral inflow PW Doppler (E wave >1.2)
	Dense, holosystolic jet on CW Doppler
	Early-peaking triangular jet contour on CW Doppler
	Minimal to no systolic flow / systolic flow reversal on pulmonary vein inflow
Quantitative Parameters	Vena contracta width ≥ 0.7cm
	Regurgitant volume ≥ 60ml/beat (may be lower in low flow conditions)
	Regurgitant fraction ≥ 50%
	Effective regurgitant orifice area ≥ 0.4cm^2 (may be lower in FMR with elliptical regurgitant orifice area)

Adapted from Zoghbi et al. (1)
Abbreviations: LA- Left atrium; LV- Left Ventricle; PW- Pulsed-wave; CW-Continuous-wave.

Once TTE imaging indicates likely favorable anatomy for MitraClip therapy, the next diagnostic step is two-dimensional (2D) and real-time 3-dimensional (3D) TEE. Pre-procedure TEE imaging allows a detailed assessment of the MV apparatus as well as the interatrial septum for transseptal puncture planning. Further benefit is a prior knowledge of TEE image quality before the MitraClip procedure, as adequate echocardiographic images/views are paramount for safe and successful intraprocedural guidance.

Accurate characterization of the MV anatomy can be achieved with a systematic evaluation of the MV leaflets and regurgitant jet(s) using 2D TEE at the mid-esophageal 0^o, 60^o, 90^o, and 120^o views (2). Transgastric en-face MV views can localize the MR jet, and can be used to measure the MV opening area with 3D orthogonal *x-plane* imaging **(**Figure 3). The 2D findings can be confirmed with real-time 3D TEE with en-face views of the MV from the LV and LA obtained at 60^o or 120^o. The aortic valve (anterior) and LA appendage (LAA, lateral) should be included in the 3D volume sections to allow standardized orientation and 3D visualization of the MV apparatus.

The morphological TTE and TEE inclusion eligibility criteria for MitraClip are based on the EVEREST trial, which are listed in Table 2 (3,4). Of note, experienced groups have successfully implanted MitraClips in patients with MV area less than $4cm^2$, but there is a risk for creating mitral stenosis physiology as MV opening area tends to decrease by half in area per MitraClip (5). The recommendation to target central, non-commissural (A2/P2) MR jets is motivated by reducing the risk for chordal entanglement of the MitraClip device and potential chordal damage as the central portions of the MV leaflets have minimal chordae tendinae insertion. Nevertheless, experienced centers have successfully utilized the MitraClip in lateral (A1/P1) and medial (A3/P3) aspects of the valve (6,7). Overall, the EVEREST trial proposed non-favorable / exclusion criteria have been “softened” with ongoing procedural experience, but extensive MV leaflet calcification in the grasping area, immobile or thick leaflets, and leaflet clefts remain challenging and undesirable MitraClip features.

Table 2. EVEREST Trial Echocardiographic Criteria for MitraClip

Central, non-commissural MR jet originating from A2/P2 scallops
Diastolic MV opening area ≥ $4cm^2$ (to avoid post-MitraClip mitral stenosis)
Absence of leaflet cleft
Minimal calcification in the grasping area
Sufficient posterior leaflet mobility and length ≥ 10mm.
For DMR: leaflet flail width <15mm; leaflet flail gap <10mm
For FMR: MV coaptation depth<11mm; MV leaflet tip coaptation length ≥ 2mm

Adapted from Feldman et al. (3,4)

Intraprocedural Guidance

Successful implantation of the MitraClip is very dependent upon high quality 2D and real-time 3D TEE imaging, and proactive and standardized communication between the interventional cardiologist/surgeon and the echocardiographer. Optimal intraprocedural TEE imaging should show the transcatheter equipment at any given time in relationship to pertinent cardiac structures. Depending on the cardiac anatomy and rotation of the heart within the chest wall this may require off axis views. A basic intraprocedural TEE stepwise approach is as follows:

1. **Mitral valve assessment, LA / LAA thrombus and pericardium**
   Prior to trans-septal puncture, a complete baseline TEE including confirmation of MR severity and pathology (including pulmonary vein inflow pattern) should be obtained and evaluation for presence / absence of pericardial effusion should be done. The LA and LAA should be assessed for thrombus, which is a contraindication for the MitraClip procedure due to the risk of embolization during catheter manipulation.

2. **Interatrial Septal Puncture (Figure 4)**
   The optimal location for interatrial septum puncture is slightly posterior and superior. The anterior-posterior interatrial septum insertions are seen at 35^o-55^o with the aortic valve located anteriorly; the superior-inferior orientation is seen in the bicaval view at 90^o -110^o with the superior vena cava usually on the right and inferior vena cava to the left. 3D *x-plane* imaging can be utilized to see both of these views simultaneously. The sheath and puncture needle position is identified by the needle artifact and tenting created over the interatrial septum towards the LA. The distance of the puncture site from the mitral annulus should be measured at 0^o and is optimally at least 4 cm superior to the level of mitral leaflet coaptation for primary MR, whereas ~3.5cm can be adequate for secondary MR given that the coaptation of leaflets is apically displaced below the annular plane. To increase transseptal puncture accuracy and safety - especially in a thick interatrial septum - a radiofrequency puncture set can be used. A patent foramen ovale, if present, should not be used to cross the septum because of its anterior location. Similarly, atrial septal defects should be avoided even if they are posterior and superior because of the inability to stabilize the delivery sheath within the defect. Once the interatrial septum has been punctured a guidewire is advanced into the LA.

3. **Steerable Guide Catheter Positioning in LA (Figure 5)**
   The LAA and left upper pulmonary vein are best seen at 60-90^o, which is the view used to advance the guidewire into the left upper pulmonary vein. The LAA should be avoided due to risk of perforation and tamponade. The interatrial septal puncture site may need to be pre-dilated to accommodate the steerable guide catheter, which is then carefully advanced under TEE guidance through the IAS into the LA. The tip of the guide catheter should be always kept in view as there is a risk of catheter tip orientation away for the center of the LA and of advancing the catheter too far, which can cause LA perforation and tamponade. The goal is that the guide catheter tip freely extends ~ 2-3 cm into the LA (from the interatrial septum) without any direct LA wall contact.

4. **Advancement of the MitraClip Delivery System and Positioning of the MitraClip in the LA (Figure 6)**

Under TEE guidance, the MitraClip device is then advanced into the LA via the steerable guide catheter. TEE monitoring is required to ensure the stability of the guide catheter position and to avoid injury of the LA by the exiting MitraClip. The device is then oriented towards the MV with its tip pointing towards the LV apex. The MitraClip arms are opened to 180 degrees. The starting rotation of the device arms in the LA should be perpendicular to the line of MV leaflet coaptation, with the MitraClip located ~ 1 cm above the leaflets in a central A2/P2 position. Proper MitraClip arm alignment can be confirmed in the long axis view, which should show both device arms wide open, whereas no arms are seen in the intercommisural view. 3D TEE can be very helpful in visualizing and confirming the MitraClip arm alignment both from the LA and LV. The device should then be repositioned to target the site of the main MR jet / MV leaflet pathology. Optimal positioning and MitraClip arm orientation in the LA is essential prior to advancing the device into the MV and LV, as repositioning / orienting the arms within the subvalvular apparatus can result in chordal entanglement and injury. Practice runs advancing the MitraClip and following its trajectory towards the MV can give clues about any torque buildup in the delivery system as the MitraClip may twist, and dive medial or lateral and posterior or anterior requiring repositioning of the starting position.

5. **Advancement of the MitraClip into LV (Figure 7)**
The MitraClip is then advanced into the LV under TEE and fluoroscopic guidance. Utilization of 3D *x-plane* imaging is necessary to visualize the arms of the device in the intercommisural and long axis views. As the device is advanced into the LV, the MitraClip may, as above, rotate or move. Therefore, the MitraClip orientation should be reassessed in the LV to confirm proper orientation, which can be again achieved with simultaneous orthogonal 3D *x-plane* imaging and real-time 3D en-face views from either the LA or the LV with reduced gain settings.

6. **Grasping the leaflets and proper leaflet insertion (Figure 7, 8)**
Once an intra-LV MitraClip position is achieved that targets the main MR jet and MV leaflet malcoaptation, the device is slowly retracted towards the LA. Under constant TEE imaging, the aim is to catch both leaflets edges in-between the outer- and gripper MitraClip arms. Adequate posterior leaflet insertion can be confirmed in the 2D LVOT view at ~120^o and anterior leaflet insertion in the same view or the 2D 4-chamber view at 0^o. If the leaflets are difficult to catch, rapid pacing (or adenosine) can be helpful as those interventions limit leaflet mobility. Once the leaflets are caught, the MitraClip gripper arms are "dropped" against the outer arms, and the whole device closed to 60 degree and further. Adequate leaflet insertion and a successful reduction of MR should be documented on TEE. Minimal leaflet motion / slack and overall taut leaflets when visualized with the closed MitraClip in view and the formation of a stable anterior – posterior leaflet tissue bridge and double orifice MV by 2D and 3D TEE usually indicate a good grasp. Parameters for MR quantification with a MitraClip in place are not well established. The PISA method is not validated for multiple MR jets. Subtracting the forward flow of the MV from the LV stroke volume may quantify the residual MR, but this method requires absence of aortic regurgitation, ventricular septal defect, and mitral annular calcification. 3D measurements of multiple vena contracta areas may be utilized (9). Obtaining post MitraClip PV inflow and comparing it with the baseline PV inflow pattern can be very helpful to estimate significance of MR reduction. The transmitral inflow gradients through both neo-orifices should be measured

with continuous wave Doppler. Depending on the remaining MR volume and flow a mean gradient ≤5 mmHg is usually acceptable (8). Once adequate MV leaflet grasp and MR reduction have been demonstrated with the fully closed MitraClip, the device can be deployed and permanently detached from the delivery catheter, with subsequent removal of the delivery catheter under TEE guidance. Remaining MR severity and stability should be immediately reassessed as MR may increase with the MitraClip freely deployed.

7. **Additional MitraClip Deployment (Figure 8)**
   It is not uncommon that a second (rarely a third MitraClip) is required to further reduce MR. Depending on the overall quality of the first MitraClip grasp and the overall MV leaflet anatomy / morphology a 2^{nd} MitraClip may also aid to "reduce the load" on the first MitraClip and the MV leaflet edges. The additional MitraClip is advanced into the LA via the existing steerable guide catheter, and LA orientation of the second (or third) clip can be optimized as described above. Depending on where the main remaining MR originates, the additional MitraClip is then positioned medial or lateral to the first clip. After above outlined MitraClip positioning and arm orientation steps the 2^{nd} MitraClip is then advanced into the LV in a closed position and positioned not too close to the first MitraClip (fluoroscopy can be helpful). The MitraClip arms are then reopened in the LV and the leaflet catching / grasping steps as outlined above are repeated.

Assessment of possible complications

Once the MitraClip(s) are permanently deployed and the guiding catheter is pulled out, the post-procedure atrial septal defect and the presence or absence of a pericardial effusion should be assessed (the absence / presence of a pericardial effusion should be periodically confirmed throughout the procedure). A complete post procedure TEE should be obtained prior to removing the TEE probe.

Follow-up

The degree of residual MR, MitraClip stability, MV inflow gradient, assessment of the pulmonary vein inflow pattern (if possible), residual atrial septal defect, pulmonary arterial systolic pressure, and LV / RV function / dimension should be evaluated by TTE prior to discharge, at ~ 1 month post procedure, and then yearly.

References:

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Figure 1. Primary degenerative MR. Parasternal long axis (A) and apical 4-chamber (B) views of significant posterior leaflet prolapse. (C) Color Doppler Flow in the apical 4-chamber view showing significant anteromedially directed MR jet. (D) TTE parasternal long axis view in a patient with a partially flail posterior leaflet. (E) TEE left ventricular outflow tract view on the same patient. The flail portion of the MV is seen in LA associated with severe eccentric MR (F). The pathology is confirmed on real time 3D TEE imaging. LA- Left atrium; MV- Mitral valve; MR- mitral regurgitation; P2- middle scallop of the posterior leaflet of MV.

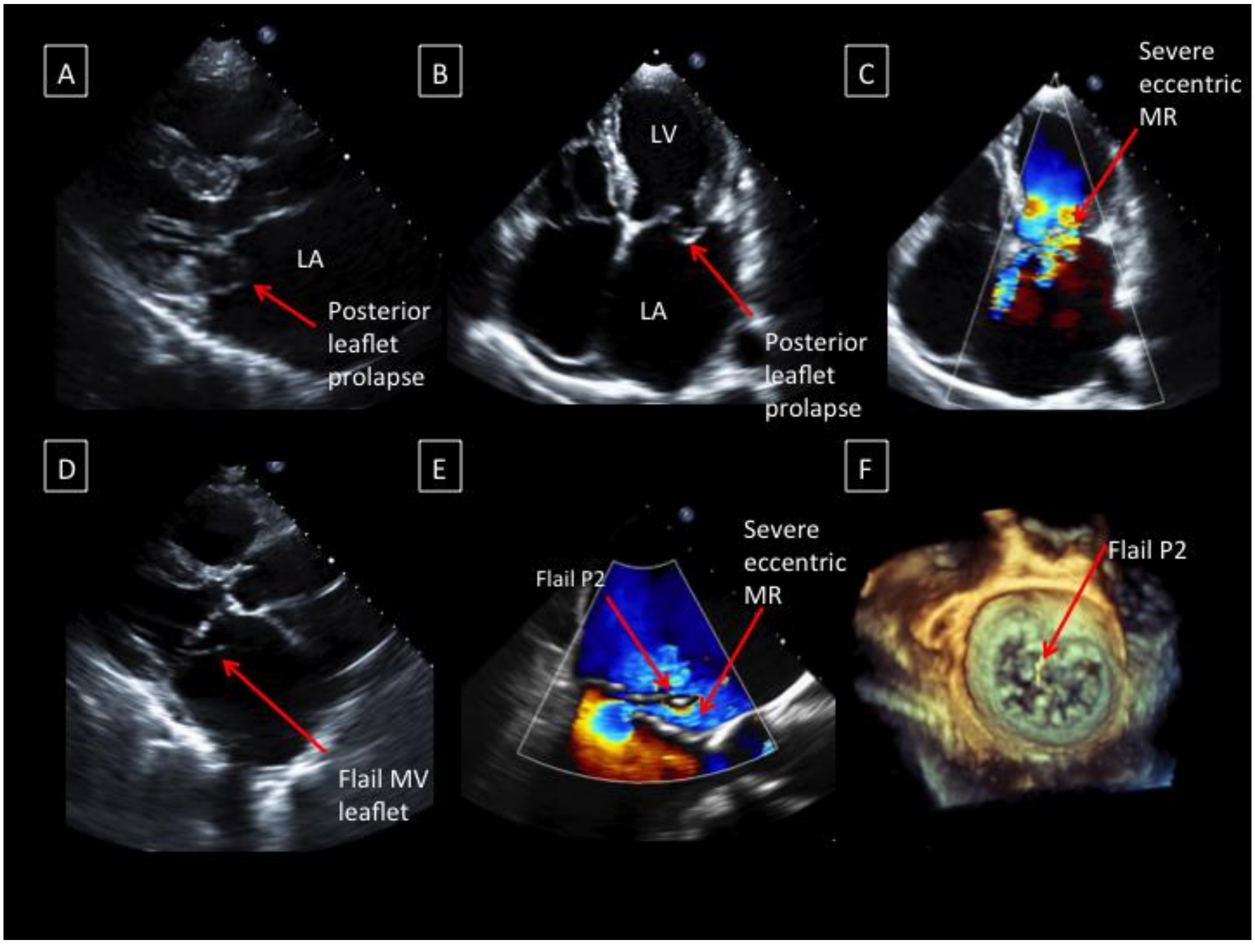

Figure 2. Secondary functional MR**.** (A) Parasternal long axis view of a dilated left ventricle; the mitral leaflets are tethered and coaptation point is apically displaced. (B) Color Doppler shows severe typically central MR.(E) Parasternal short axis view of the MV at the tips (left) with color flow (right) confirming MR jet origin,. (G) Pulmonary vein pulsed-wave Doppler profile shows systolic flow reversal (systolic flow is depicted with asterisks). MV- Mitral valve; MR- Mitral regurgitation; PV- Pulmonary vein.

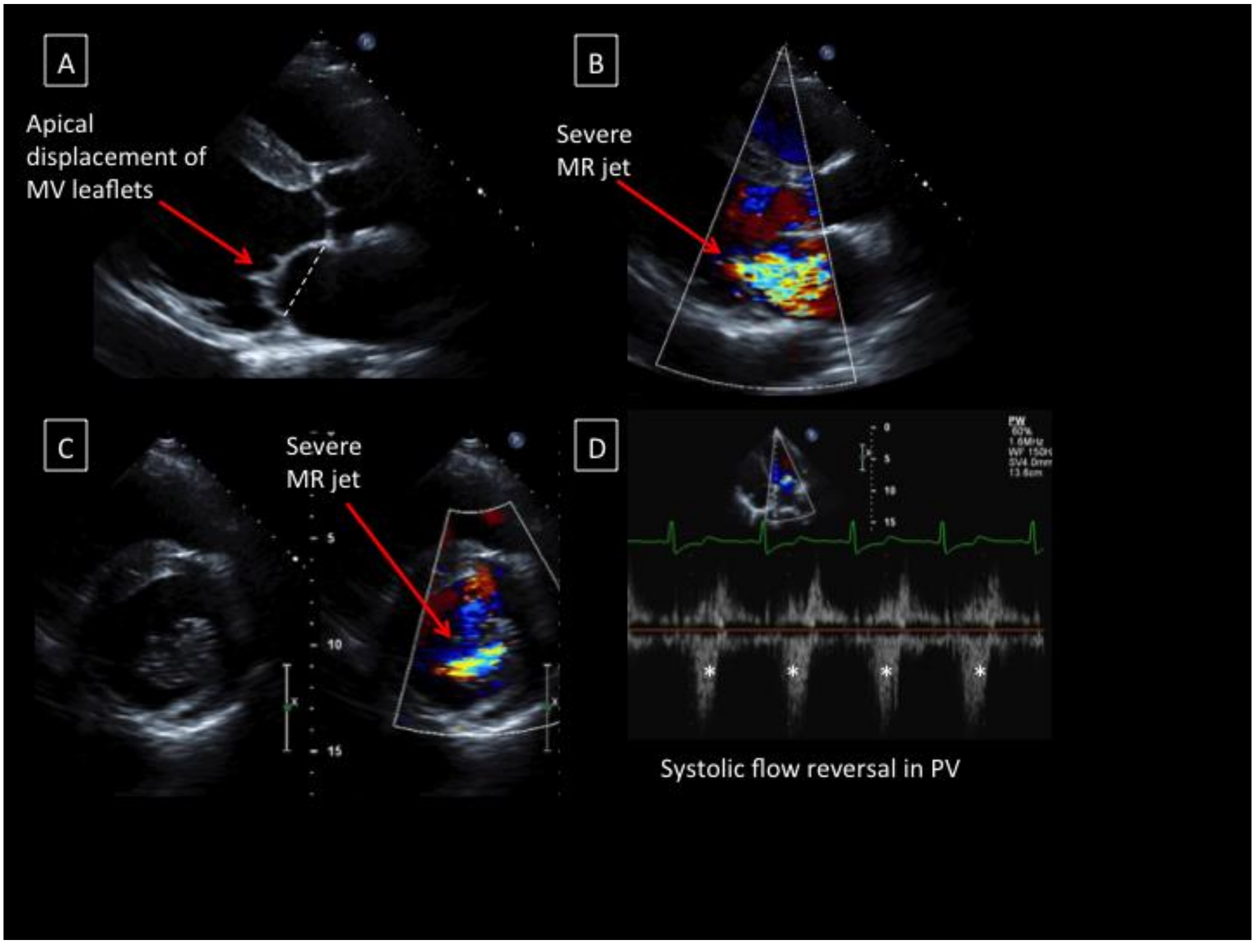

Figure 3. Mitral valve diastolic opening area at the leaflet tips / edges can be measured with TTE and TEE imaging. (A) MV opening area in an optimal TTE parasternal short axis view. (B) Transgastric MV opening area view on TEE of the same patient. On TEE, the diastolic MV opening area can be measured by planimetry using *x-plane* (B) or RT-3D TEE (C) imaging to accurately locate the tips of the MV leaflets. All the different techniques yielded a similar MV opening area in the same patient. MVA- Mitral valve area; MV- Mitral valve; LV- left ventricle; LA-Left atrium; LAA- Left atrial appendage.

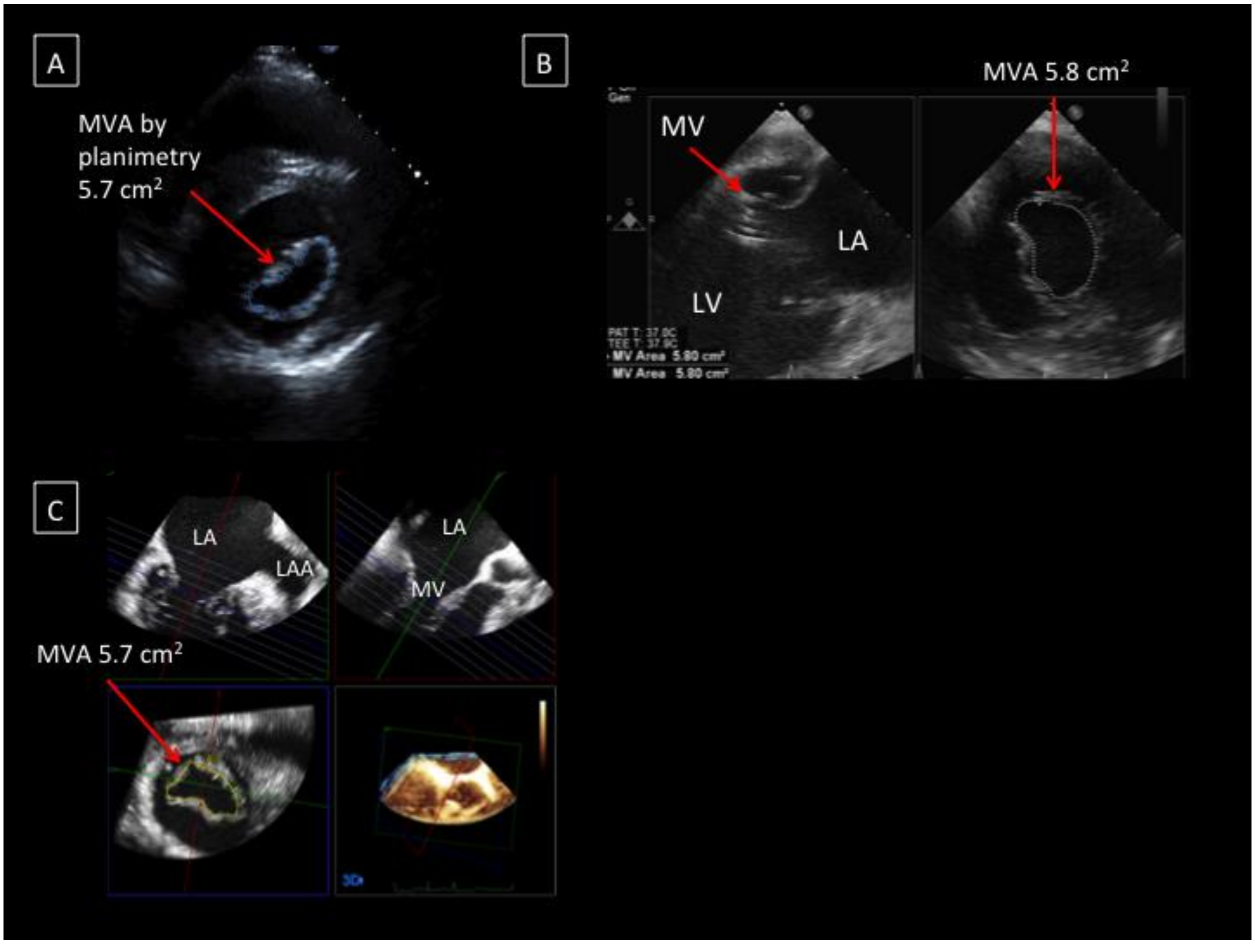

Figure 4. IAS puncture. Assessment of the IAS can be achieved in two orthogonal views. (A) Superior and inferior orientation is seen in bicaval view (90^o-120^o) and (B) the anterior and posterior orientation is seen at the 35^o-55^o view. Tenting of the IAS is visualized in both anterior-posterior and superior-inferior aspects. The distance of the puncture site from the MV should be measured in a modified 0^o view. This measurement can be done from the puncture site to the MV annulus (white dotted line) or to the level of the leaflet coaptation (blue line depicts the level of leaflet coaptation and yellow dotted line depicts the distance from puncture site). For DMR, the distance should be at least 4cm; for FMR, the distance can be ~3.5 cm since there is apical displacement of the leaflet coaptation. SVC- Superior vena cava; RA- Right atrium; IAS- Interatrial septum; LA- Left atrium; AV- Aortic valve; LV- Left ventricle; RV- Right ventricle; RA- Right atrium.

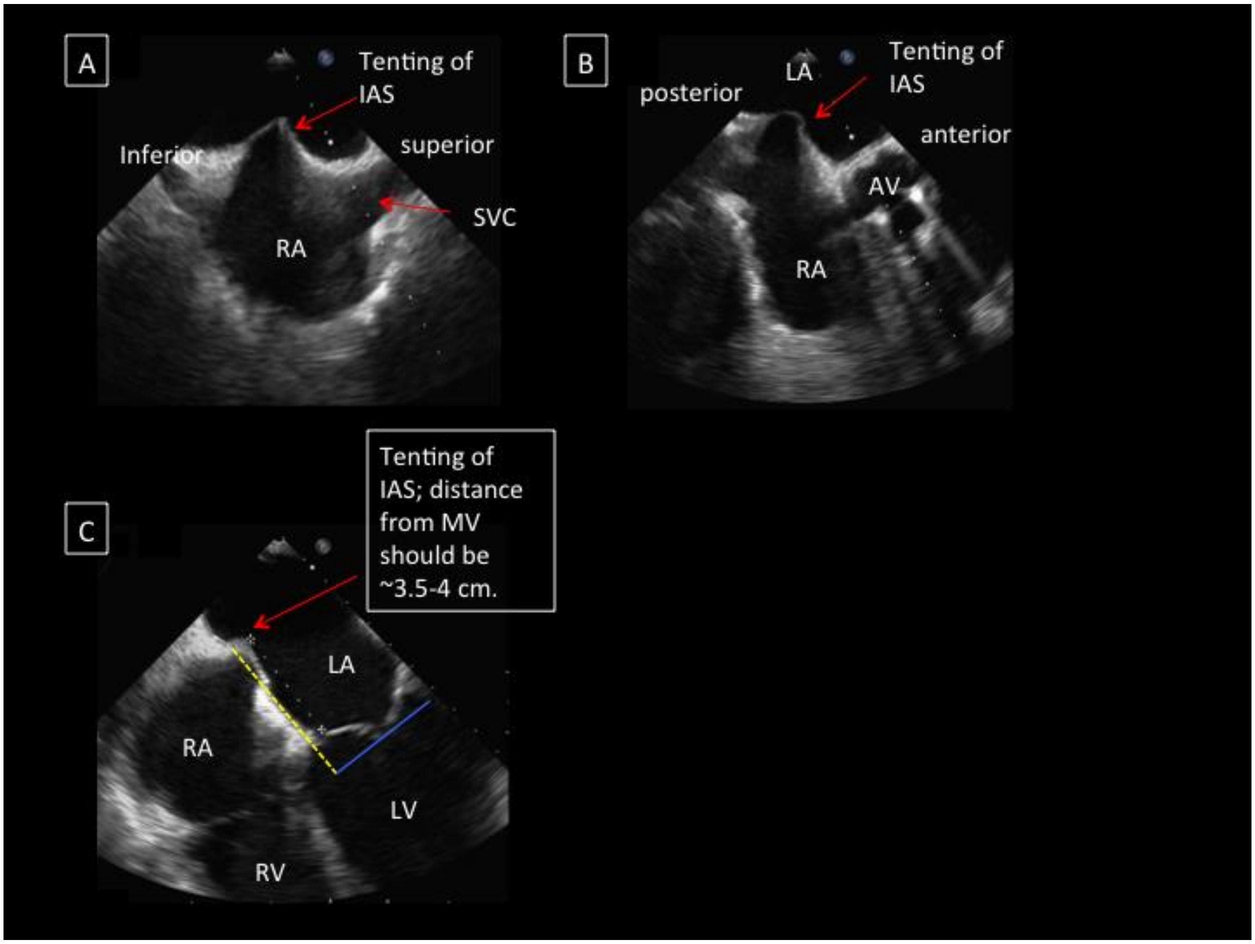

Figure 5. Advancement of the guidewire and positioning of the steerable guide catheter (SGC) in the LA. (A) The guidewire is carefully advanced into the left upper pulmonary vein. (B) The IAS puncture site may need to be dilated to accommodate passing of the SGC through the septum. (C, D) The SGC tip is readily identified by its characteristic shape and by small exiting bubbles and should be continuously imaged to prevent injury to LA wall. To avoid losing intra-LA SGC position a safe insertion depth should be at least ~2cm. LUPV- Left upper pulmonary vein; LAA- left atrial appendage; IAS- Interatrial Septum; AoV- Aortic valve; RA- Right atrium; LA- Left atrium

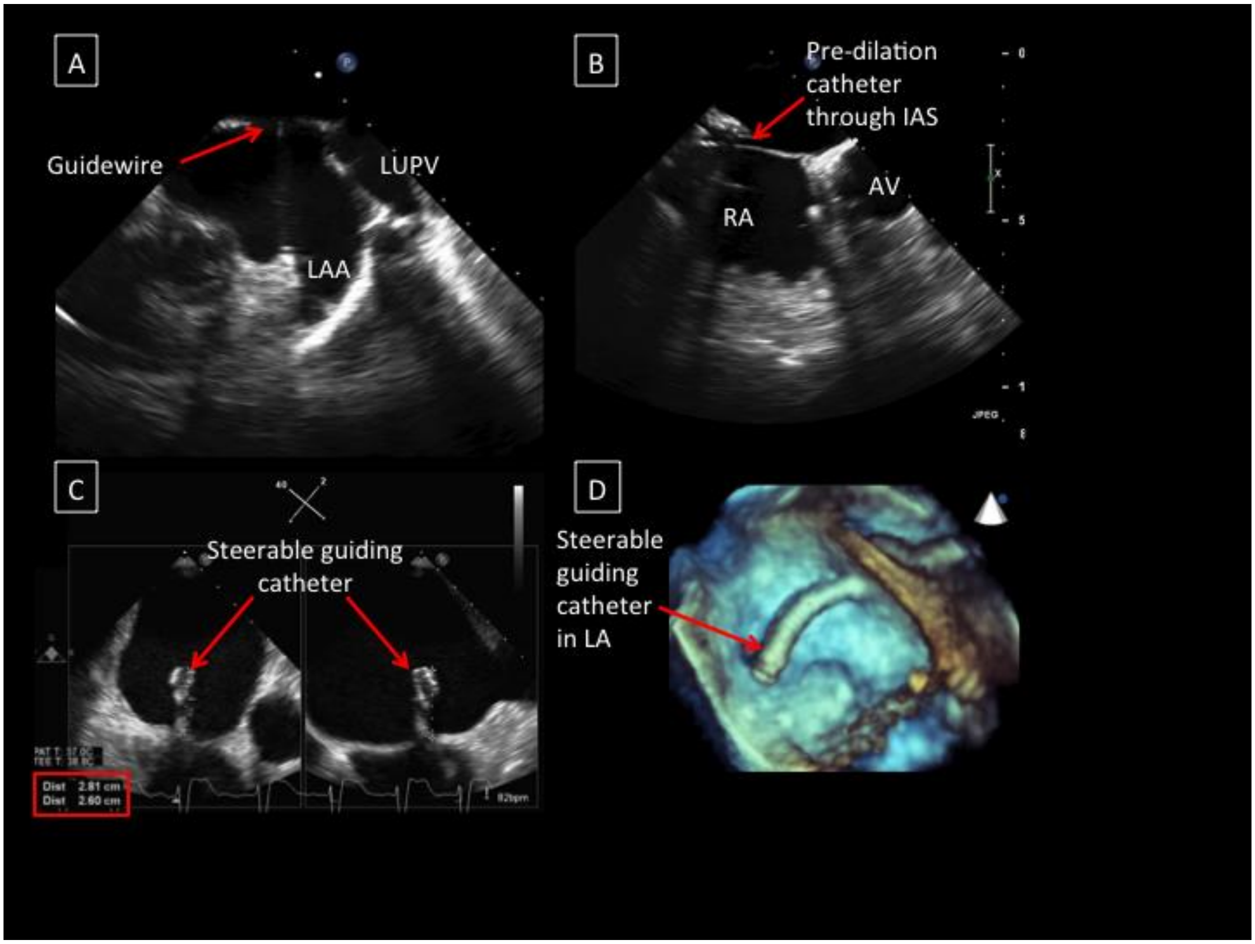

Figure 6. Advancement of delivery system and positioning of the MitraClip in the LA. (A) The MitraClip device, mounted on the delivery catheter, is advanced via the steerable guide catheter into the LA. (B) The MitraClip at the tip of the delivery catheter is readily appreciated on 2D and 3D TEE (C) The MitraClip is positioned centrally over the MV and the arms (D) fully opened. (E) The optimal orientation of the arms over the MV is perpendicular to the leaflet coaptation line, and can be guided with RT-3D TEE assistance. The appropriate position of the device is based on the leaflet malcoaptation site, main regurgitant jet location, and clipping strategy chosen to reduce MR. Clockwise or counter-clockwise rotation of the device can be visualized on RT-3D TEE. LA- Left atrium; LV- Left ventricle; MV- Mitral Valve; AV- Aortic valve.

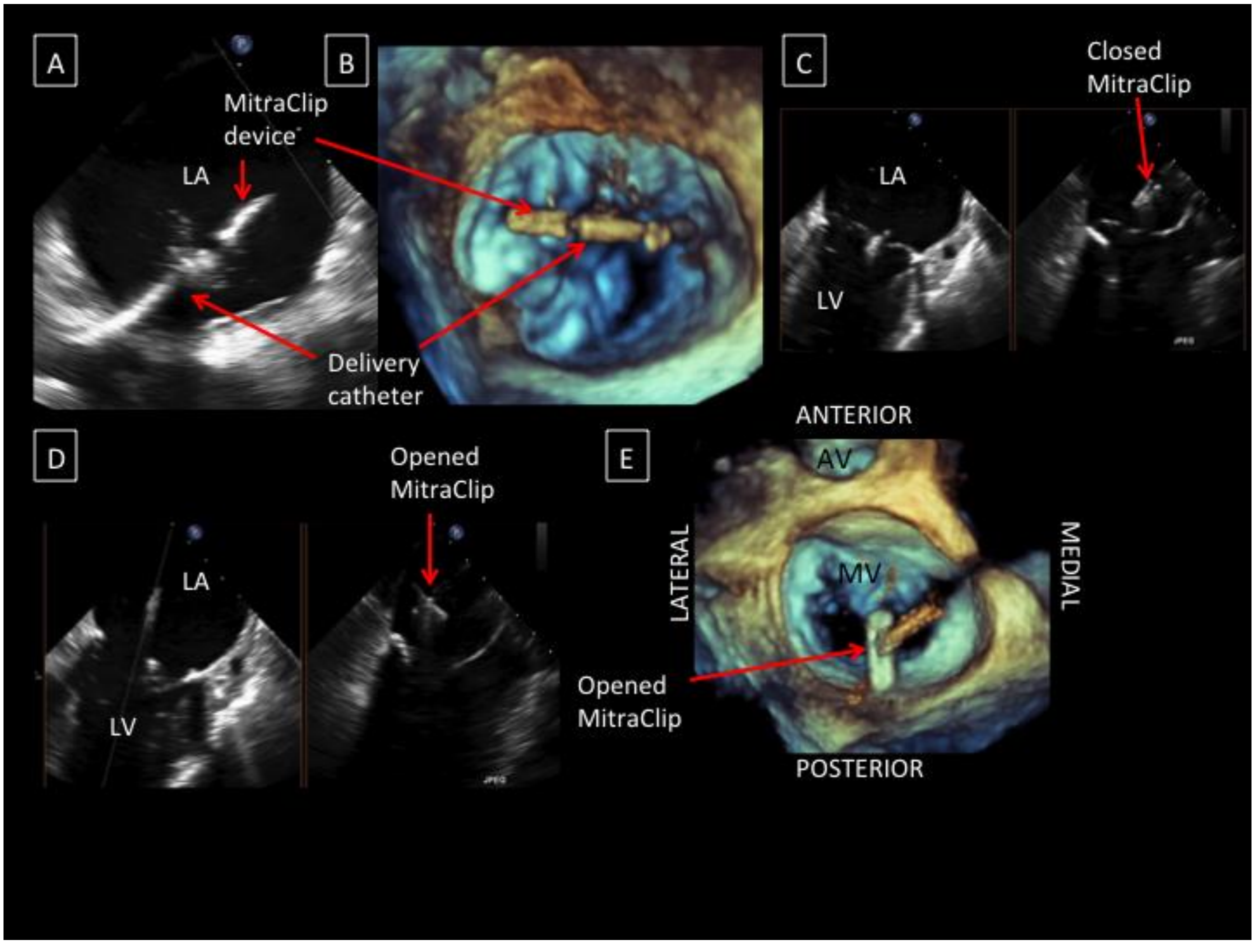

Figure 7. Advancement of the MitraClip into the LV and grasping of the leaflets. (A) The open-armed MitraClip is carefully advanced into the subvalvular apparatus. Orthogonal imaging is used to visualize the arms fully open in LVOT view. (B) The MitraClip is in the LV, below the MV leaflets. The image on the left is with normal gain settings and the device is difficult to visualize; the image on the right is with much reduced gain setting and the MitraClip is easily seen. The correct positioning and orientation of the device arms should be confirmed by RT-3D imaging. (C) Once appropriate positioning and orientation is established, the MitraClip delivery catheter is slowly pulled back towards the LA to catch the anterior and posterior leaflets. (D & E) Once a good catch and insertion of both leaflets is present the gripper arms are dropped and the device slowly closed. After a successful grasp, the leaflets have decreased mobility. The arms of the device are then further closed. LA- Left atrium; Ao- Aorta; AV- Aortic valve.

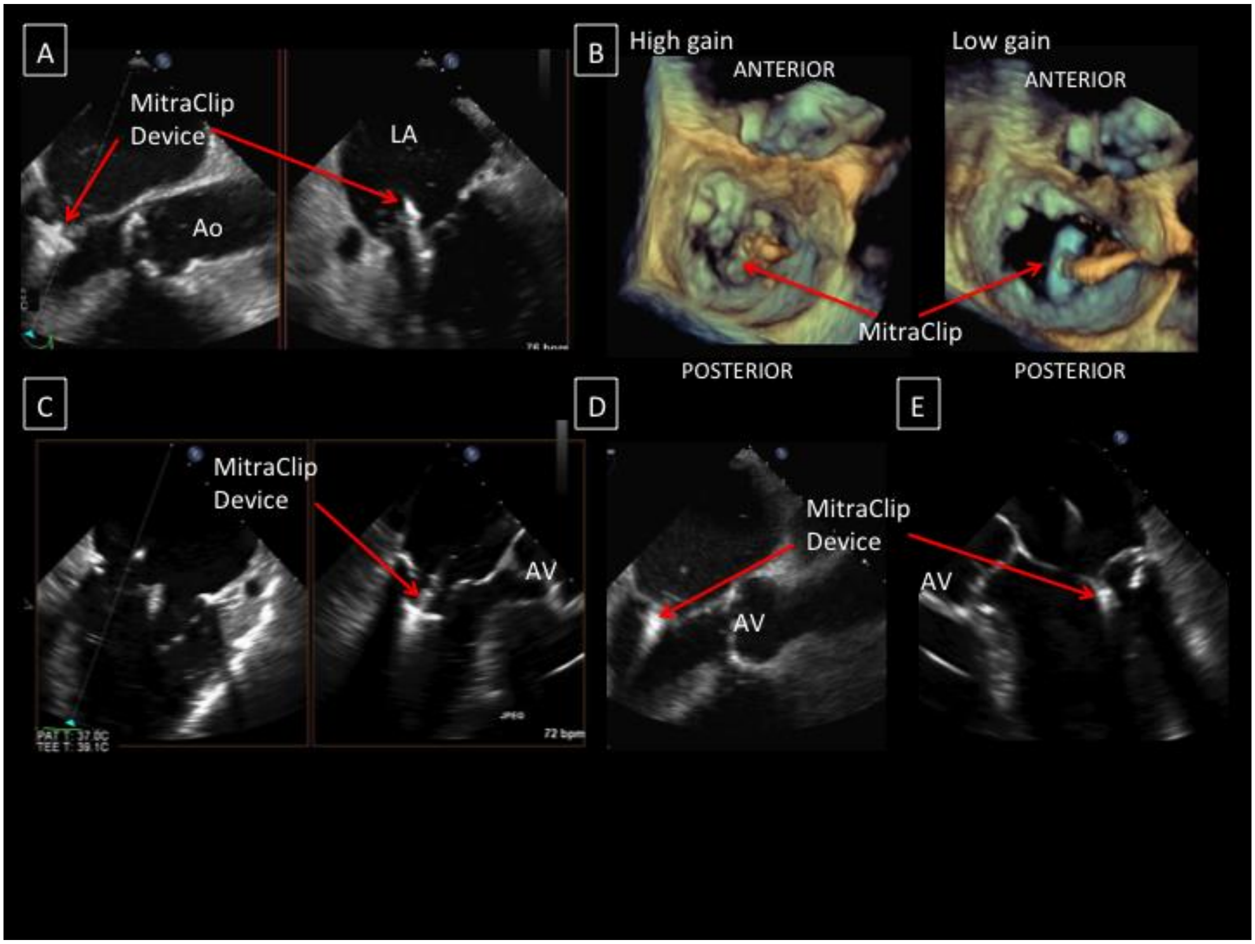

Figure 8. Evaluation of MR reduction and hemodynamics with a MitraClip in place. (A, B) Formation of a double orifice MV is seen on RT-3D imaging, with the MitraClip creating a bridge between the two leaflets. (B) In the absence of significant mitral stenosis (average MV mean gradient ≤ 5mmHg) after the original clipping strategy with inadequate MR reduction, a second (or a third) device may be deployed. (C)Residual MR is assessed by Color Doppler, with multiple smaller jets commonly seen after MitraClip implantation. (D, E) Continuous-wave Doppler is used to measure the gradients across the two neo-orifices of the MV. The recommended mean gradient is less than 5mmHg. If the results are acceptable, the MitraClip is deployed. (F) The change in pulmonary vein inflow pattern (disappearance of systolic reversal) is a finding suggesting significant MR reduction. The asterisk depicts the forward blunted systolic flow in right upper pulmonary vein. The creation of an atrial septal defect is also seen. LAA- Left atrial appendage; IAS- Interatrial septum; ASD- Atrial septal defect.