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REVIEW

Peri-interventional echo assessment for the MitraClip procedure

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Worldwide, there have been more than 6500 MitraClip procedures performed to treat either functional or degenerative mitral regurgitation (MR). The MitraClip procedure is the only available percutaneous device available to reduce MR by creating a double mitral valve (MV) orifice and decreasing MV annular diameter. As the mitral leaflets cannot be assessed by fluoroscopy, procedural success is dependent upon echocardiographic guidance. In this review, we describe the assessment necessary to determine eligibility for the MitraClip procedure. This includes accurate assessment of MR and detailed analysis of MV morphology by 2D and 3D echocardiography. In addition, each of the intraprocedural steps involved in the deployment of this device and the guidance of these steps by 2D and 3D echo are described in detail, along with the use of echo to detect procedural complications. Thus the focus of this review is on the peri-interventional echocardiographic assessment before, during, and after the MitraClip procedure.

Keywords Mitral regurgitation • MitraClip • 2D Echocardiography • 3D echocardiography • Transoesophageal echocardiography

Introduction

In the emerging field of percutaneous approaches to treat mitral regurgitation (MR), the MitraClip® (Abbott Laboratories, Abbott Park, IL, USA) is the only technique currently available to alter the mitral valve (MV) morphology, annulus diameter, and reduce MR.[1,2] This transcatheter method using a transseptal approach to treat MR is based on the creation of a mitral double orifice, a technique first introduced by Alfieri in 1991.[3–6] He surgically sutured the free edges of the mid-portions of the anterior (A2) and posterior (P2) MV scallops. Maisano *et al.*[7,8] demonstrated that with the Alfieri technique 90 ± 5% of patients with both functional and degenerative MR are free from the combined endpoint of recurrent MR ≥2+ and re-operation after 5 years.

The MitraClip is a catheter-based technology that is similar to the Alfieri technique in that it connects the middle scallops of the anterior (A2) and the posterior (P2) leaflet of a regurgitant MV. To date, more than 6500 MitraClip implantations (Elizabeth McDermott, Abbott Laboratories, personal communication) have been performed worldwide. Initially, all procedures were performed in the setting of clinical trials in the USA which evaluated the feasibility and safety of the device.[1,2] Subsequently, a randomized trial was done to compare MitraClip implantation vs. the standard more invasive surgery for mitral repair.[9–11]

The data of the EVEREST (Endovascular Valve Edge-to-Edge Repair Study) trials[1,9] and results of registries in Europe[12] demonstrate that the MitraClip procedure is feasible, safe, and well tolerated. Even in high-risk patients in poor clinical condition, there is a low peri-interventional risk for the patient. Post-MitraClip success rates defined as a reduction of MR to 2+ or less have ranged from 72.4% in the EVEREST II trial in the MitraClip group vs. 87.8% in the surgical group[9] to 82% in a group of high surgical risk patients[12] and procedural success has been shown to increase with operator experience.[13]

The MitraClip system received CE mark in March 2008. Since then, it has been available for clinical use in Europe; in the USA, it currently can only be implanted in the setting of a defined clinical trial.

Echocardiography is the essential imaging modality for MitraClip treatment. Echocardiography in peri-interventional assessment is used for: (i) patient selection, (ii) guidance of the procedure, (iii) the identification as well as the assessment of the severity of any complications during the procedure, (iv) the evaluation of the final result after clip implantation, and (v) the assessment at follow-up of MR severity, left ventricular (LV) chamber size and function as well as pulmonary artery pressures. The focus of this review is on the peri-interventional echocardiographic assessment before, during, and after the MitraClip procedure.

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Patient selection

In order to select a patient for the MitraClip procedure, the first step is to assess the severity of MR. It is then necessary to determine the abnormal anatomic features of the MV or the abnormalities of LV function (functional MR) which are responsible for the MR.

Grading of MR severity (*Table 1*)

As shown in *Table 1*, criteria for grading MR severity have been developed by both European and American echocardiographic societies.[14,15]

The EVEREST studies classified MR by transthoracic echocardiography (TTE) into four grades.[16] To qualify for the procedure, MR needs to be moderate to severe (3+) or severe (4/− 4+). Three criteria were needed and, at least of the criteria, one had to be quantitative.[1,2,17]

Even under optimal circumstances, the grading of MR and differentiating moderate from severe MR can be difficult with poor inter-observer agreement whether using qualitative or quantitative criteria.[18]

The key points which we believe are helpful to differentiate moderate from severe MR are:

- Chronic severe MR is generally associated with left atrial (LA) and LV enlargement. (Significant chronic MR infers a state of chronic left-sided volume overload so the left-sided cardiac chambers should dilate to accommodate this added load.)[19,20]
- Severe MR as timed by CW Doppler is generally holosystolic.[21] The presence of only late systolic MR during the last third or last half of systole makes chronic severe MR unlikely as that the actual regurgitation volumes are much lower (50–80%) than the maximal colour jet area demonstrates.
- In chronic severe MR the 'E'-wave in the transmitral inflow pulsed wave Doppler profile is taller than the 'A'-wave due to the initial high transmitral gradient and inflow in early diastole. An 'E'-wave taller than 1.2–1.5 m/s usually indicates severe MR.[14,15,22] Thus, an 'A'- wave taller than the 'E'-wave is uncommon in patients with severe MR, but it could be seen in the setting of acute severe MR, where the LV is very non-compliant.

Determination of the Morphology (*Table 2*)

In addition to grading MR severity, the MV morphology and the cause of MR should be assessed in detail by transoesophageal echocardiography (TEE), as suitable MV morphology is essential to a successful MitraClip procedure. Transthoracic echocardiography is used to assess MR severity, but TEE is also useful to confirm the initial TTE findings. In cases with very eccentric MR jets, in patients with poor transthoracic echocardiographic windows the severity of MR can be underestimated by TTE.

Table 1 Echocardiographic parameters for the grading of MR severity

Parameter	Mild	Moderate	Severe
Qualitative			
Mitral valve morphology	Normal /abnormal	Normal /abnormal	Significant prolapse of a leaflet or leaflets, flail leaflet or ruptured papillary muscle, severe leaflet(s) restriction
MR colour jet	Small central jet <4 cm^2 or $<20\%$ of LA volume	Signs of MR $>$mild but no criteria for severe MR	Large central jet $>40\%$ of LA volume/ eccentric jet swirling in LA (any size)
Flow convergence	No or minimal flow convergence	Signs of MR $>$mild but no criteria for severe MR	Large flow convergence
CW-Doppler signal of MR jet	Soft density/parabolic	Dense/parabolic	Dense/triangular
Semi-quantitative			
Vena contracta width (cm)	<0.3 cm	Signs of MR $>$mild but no criteria for severe MR	≥ 0.7 cm ($>$ 0.8 cm biplane)
Pulmonary vein flow	Systolic dominant flow	Intermediate signs	Systolic flow reversal
Mitral inflow	A-wave dominant	Intermediate signs	E-wave dominant (>1.5 m/s)
LA/LV size	Normal LV size	Intermediate signs	Enlarged LA and LV
Quantitative			
Regurgitant volume (R Vol) (mL/beat)[a]	<30	Mild–moderate: 30–44, moderate–severe: 45–59	≥ 60
Regurgitant fraction (RF) (%)	<30	Mild–moderate:30–39, moderate–severe: 40–49	>50
Effective regurgitant orifice area (EROA) (cm^2)[a]	<0.2	Mild–moderate: 0.2–0.29, moderate–severe: 0.3–0.39	≥ 0.4

[a]In functional MR, lower thresholds of severity have been proposed (0.2 cm^2 for EROA and 30 mL for regurgitant volume.[15,52,53]
MR, mitral regurgitation; LA, left atrium; LV, left ventricle.

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Table 2 Morphological characterization for MitraClip eligibility

Ideal valve morphology for a MitraClip procedure (*Figure 2*)	Unsuitable valve morphology for a MitraClip procedure (*Figure 3*)
MR originating from the mid portion of the valve (degenerative or functional aetiology)	Perforated mitral leaflets or clefts, lack of primary and secondary chordal support
Lack of calcification in the grasping area	Severe calcification in the grasping area
MVA >4 cm^2	Haemodynamically relevant mitral stenosis
Length of posterior leaflet ≥ 10 mm	Length of posterior leaflet <7 mm
Non-rheumatic or endocarditic valve disease	Rheumatic valve disease—with restriction in systole und diastole or endocarditic valve disease
Flail-width <15 mm, flail-gap <10 mm	
Sufficient leaflet tissue for mechanical coaptation: coaptation depth <11 mm, coaptation length >2 mm	Gap between the leaflets >2 mm

Adapted from the EVEREST criteria and the Abbott training centre experience.
MR, mitral regurgitation; MVA, mitral valve area.

Transoesophageal echocardiography is also superior for assessing pulmonary vein flow in multiple pulmonary veins.

The MV apparatus is a very complex structure and its proper function depends on the mechanical integrity of all components involved. Mitral regurgitation can be caused by anatomical or functional abnormalities affecting any component of the MV apparatus; e.g. the MV annulus, the anterior, and posterior leaflets, the chordae tendinae, the papillary muscles as well as the left atrium and the left ventricle.

The anterior and posterior mitral leaflets can be characterized according to Carpentier as it is described hereafter[23] (*Figure 1*). The anterior mitral leaflet has a hemi-ellipsoid shape, and is often abbreviated as 'A' and is described as being segmented into three scallops by small indentations. The lateral third is named A1, the middle third A2, and medial third A3. The posterior leaflet (P) which forms two-thirds of the annular circumference has a wider circumference but a shorter leaflet length than the anterior leaflet. The posterior leaflet is often abbreviated as 'P' and again is classified as having three scallops: a lateral P1, a middle P2 (which is usually larger than the other two), and a medial P3 scallop. In addition to scallops, there are two commissures, and variable slits.[24] Thus there is considerable anatomic variability of the MV. While Carpentier's classification is extremely useful, it is a simplified description of a complex valve. It has been noted that the structure of the posterior leaflet can vary, having two to six scallops, and frequently isolated scallops of the anterior leaflet cannot be clearly identified.[24] Nonetheless, this nomenclature has been widely adopted and is particularly useful for accurately describing and localizing anatomic lesions thereby facilitating the communication between interventionalists, echocardiographers, and surgeons.

In the EVEREST studies,[1,9] morphological inclusion criteria were identified that would lead to optimal procedural results. These criteria included central origination of MR (A2/P2 segments), due to the fact that the central part of the leaflets usually have less chordae tendinae and the MitraClip is applied symmetrically on the leaflets in this area. There should be no severe calcification in the grasping area and the anatomically shorter posterior leaflet should be long enough to allow secure capturing by the Clip. In degenerative disease, an excessive flail width and an excessive flail gap should be excluded. Further, some residual coaptation length should exist in functional MR. The MV area (MVA) before a procedure should not be less than 4 cm^2 in order to avoid creating a stenotic MV post procedure.

Beyond the above-mentioned criteria for an ideal valve morphology for the MitraClip, it has been reported that in isolated patients with anatomy outside these criteria, successful treatment with the MitraClip may be achieved. These include pathology in the P1 or P3 segment, a MVA <4 cm^2 and >3 cm^2 with good leaflet mobility (e.g. patients after a surgical ring implantation), a mobile posterior leaflet length between 7 and 10 mm, leaflet restriction in systole, and a flail width >15 in patients with large rings allowing for multiple Clips to be implanted.[12,25,26]

Ideal and unsuitable morphological criteria for the MitraClip procedure are summarized in *Table 2* (*Figures 2* and *3*).

MitraClip candidates often have comorbidities that make them a less suitable candidate for surgery including impaired LV function with a left ventricular ejection fraction (LVEF) $<30-40\%$. This patient group has a significantly higher peri-operative mortality. Severely reduced LV function or extreme LV dilatation (defined in the EVEREST studies as an LV end-systolic diameter >55 mm and an LVEF $<25\%$) was considered an exclusion criteria for the MitraClip procedure in the EVEREST trials. However, Franzen *et al.*[12] demonstrated that MitraClip implantation can be safely performed with promising results in patients with very reduced LVEF (34% of the patients had an LVEF $<20\%$). In patients with severely impaired LVEF, additional studies are needed to identify what level of reduction in MR leads to optimal benefit. Moreover, Siegel *et al.*[27] and Biner *et al.*[28] have shown that the MitraClip procedure improves haemodynamics and results in an increase in stroke volume and cardiac output as well as a decrease in left-sided filling pressures in the acute setting post MitraClip deployment.

The COAPT Trial (Clinical outcomes Assessment of the MitraClip Percutaneous Therapy for High Risk Surgical Patients) which is expected to start soon will randomize high surgical risk patients with functional MR to MitraClip treatment vs. medical therapy. This trial should better define the true risks and benefits of treating these high surgical risk patients with the MitraClip.

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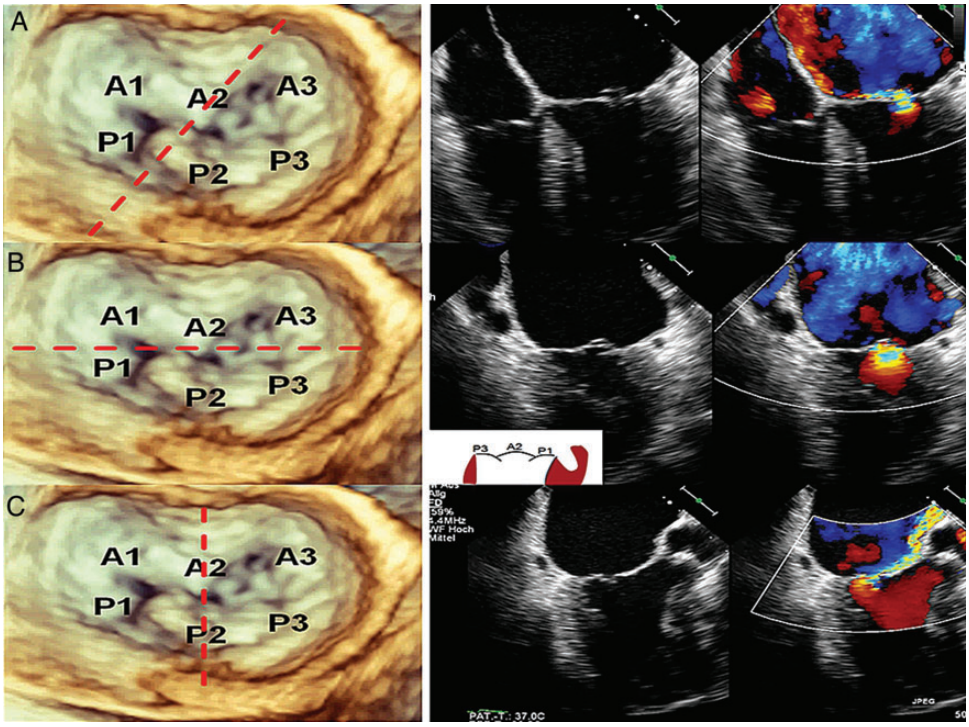

Figure 1 TEE key views for the assessment of mitral valve morphology. The key views for assessing the mitral valve are demonstrated in these images of a patient with a small P2 prolapse. A 3D TEE en-face view of the MV including segment nomenclature is shown on the left side (*A*, *B*, *C*). The red incised lines illustrate the plane of the corresponding 2D planes on the right side. A mid-oesophageal four-chamber view at 0° in (A), an intercommissural view at 60° [slightly rotated posteriorly in order to better visualize the PISA (proximal isovelocity surface area) of the MR Jet] in (B), and a LVOT view at 150° in (C). The prolapse can be identified in each plane.

Imaging assessment of mitral valve characteristics

Two-dimensional (2D) TEE MV anatomic assessment is performed using a systematic approach based on the description by Foster *et al.*[29] in 1998. Some key views (*Figure 1*) may help characterize the valve pathology. In zero-degree views (depending on the height of the probe in the oesophagus), A1 and P1 segments can be seen in the superior position, A2 and P2 segments in a more central position, and A3 and P3 segments in an inferior position of the probe. In intercommissural views (~60°), the P1, A2, and P3 segments are visible when the plane cuts both commissures properly, whereas an anterior (clockwise) rotation of the probe reveals the A1, A2, and A3 segments of the anterior leaflet, and a posterior (counter clockwise) rotation shows the P1, P2, and P3 segments of the posterior leaflet. A long-axis or LVOT view (additional 90° to the intercommissural view) shows the A2 and the P2 segment. In transgastric short-axis views, both leaflets and all segments can be evaluated.

In addition to 2D TEE, three-dimensional (3D) TEE adds remarkable benefits in the assessment of MV anatomy. Using x-plane in an intercommissural view allowing additional orthogonal views, the valve segments can be scanned from medial to lateral, including the postero-medial and the antero-lateral commissures. Using 3D TEE even more information is obtained by rendering additional views, e.g. en-face views of the MV from both LV and LA perspectives. Three-dimensional TEE provides a detailed assessment of the MV anatomy and function and all components of the mitral apparatus and neighbouring structures (such as the LA appendage, the aortic and tricuspid valve).[15]

Prolapses are best visualized from the LA side, whereas the anterior leaflet is appreciated particularly well from the LV side. In general, the detection of anterior prolapse is more difficult than posterior prolapse in all echocardiographic modalities.[30] It has been demonstrated that 3D TEE is more accurate in identifying valve segments compared with 2D TTE, 3D TTE, and 2D TEE[30] and that the determinant MV pathology was detected more accurately with 3D TEE when compared with 2D TEE.[31,32] Furthermore, 3D TEE is superior in the detection of clefts, gaps, and perforations which are frequently missed by 2D TEE evaluation.[31,33]

In addition, 3D TEE findings correlated well (in 88% of the cases) with surgery in degenerative MV disease.[34] We have also found that 3D TEE is very useful to localize and evaluate the severity of posterior leaflet restriction when viewing the MV apparatus from the LV.

The mitral annulus is also best appreciated in an en-face 3D TEE view from the LA side where the entire annular circumference is presented in one single view. Mitral annular dynamic changes can be appreciated in detail.[35] and post-processing analysis (using

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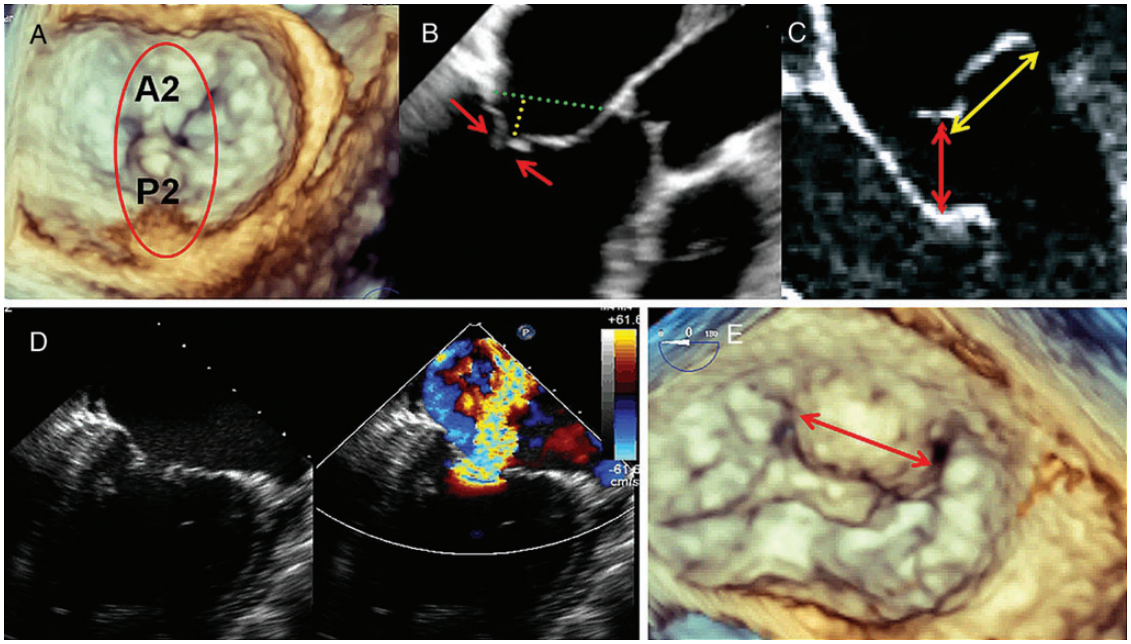

Figure 2 Ideal morphologies for a MitraClip implantation. The pathology should be located in the middle segments (*A* and *D*) with no calcification in the grasping area as shown in an intercommissural view in (*D*). (*B*) Illustrates some remaining degree of coaptation (red arrows, ideally at least 2 mm), the yellow line represents the coaptation depth (ideally < 11 mm). The yellow arrow in (*C*) follows a posterior leaflet with enough tissue for grasping (ideally ≥10 mm) and the red arrow illustrates the measurement of a flail gap (ideally <10 mm). In (*E*), the flail width is marked with a red arrow (ideally <15 mm) (P2 prolapse in a non-surgical view).

commercial software) allows for precise quantification of the size and the shape of the mitral annulus and the degree of non-planarity, thus assisting in the understanding of MV mechanics and in the evaluation of the feasibility of MV repair.

Guiding of the MitraClip procedure

MitraClip implantation is a technically demanding procedure that requires careful active imaging. As the MV leaflets are not visible by fluoroscopy, TEE is critical for optimal patient selection, for the guidance of the MitraClip procedure, for the assessment of the final result, and for the detection of complications.

Two-dimensional TEE can be used as the sole method for guidance during the MitraClip. However, 3D TEE provides valuable additional information and is therefore recommended for the guidance of MitraClip procedures.[36] Three-dimensional TEE provides en-face views of the MV, thus facilitating the assessment of MV morphology and pathology which is important for patient selection. Delivery catheters, wires, devices, and target structures can be visualized in one single view and in relation to each other, thus optimizing transseptal puncture, steering of the delivery catheter in a 3D space (LA) towards the MV and proper MitraClip positioning perpendicular to the line of coaptation in the middle segments of the MV.

As both imaging modalities are associated with advantages and limitations, the combined application of 2D and 3D TEE is of complementary value and implies benefits for the patient. Biner *et al.*[37] demonstrated that the usage of 2D and 3D TEE in combination is associated with a remarkable 28% reduction in procedure times. Fluoroscopy provides additional helpful information on the positioning and distance for delivery catheter advancement and MitraClip opening, orientation, and the final release of the device on the leaflets, most notably when a second MitraClip is implanted.

Table 3 Main procedural steps for MitraClip implantation

1. Transseptal puncture
2. Introduction of the Steerable Guide Catheter (SGC) into the left atrium
3. Advancement of the Clip Delivery System (CDS) into the left atrium
4. Steering and positioning of the MitraClip above the mitral valve
5. Advancing the MitraClip into the left ventricle
6. Grasping of the leaflets and assessment of proper leaflet insertion
7. Clip detachment

The MitraClip procedure is divided into seven main steps (*Table 3*) and in the following the specific imaging approach for each step is described in detail (adapted from Slipczuk *et al.*[17]).

Transseptal puncture

Transseptal puncture represents one of the most important aspects of the MitraClip procedure. The optimal puncture site is

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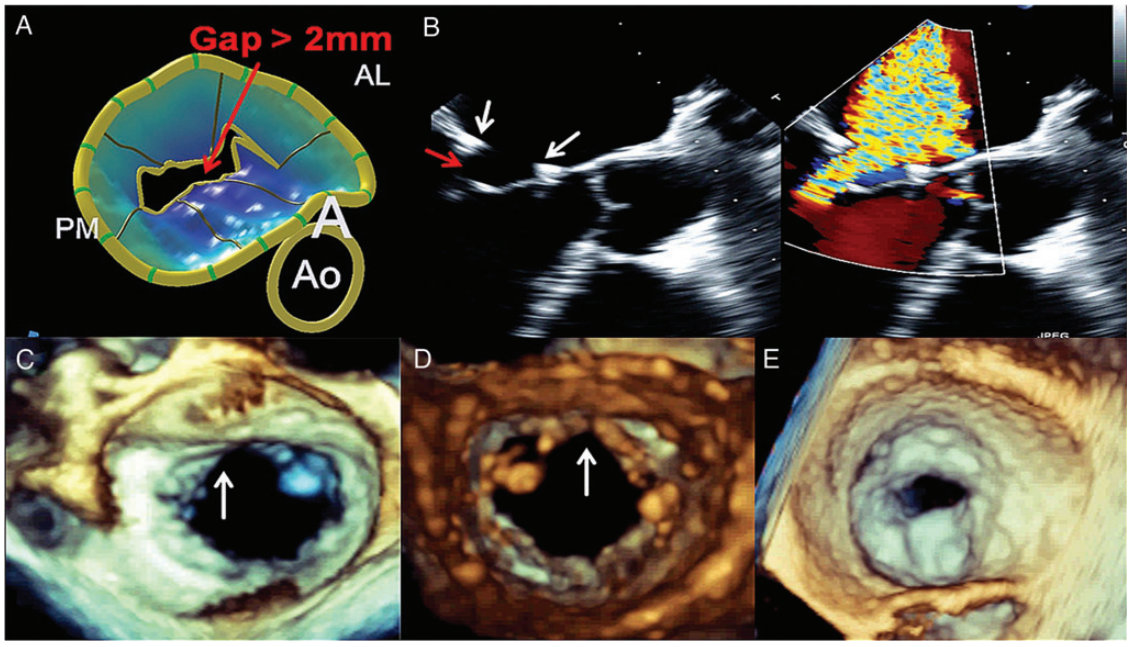

Figure 3 Unsuitable morphologies for a MitraClip implantation. In (*A*), a gap between the anterior and posterior leaflet is documented in a 3D reconstruction of the mitral valve (MVQ, Q-lab software, Philips). In (*B*), the white arrows point towards a surgically implanted mitral ring, the red arrow marks a gap as a result of a missing posterior leaflet (no tissue to grasp), the anterior leaflet is retracted in addition. An anterior cleft is illustrated in an en-face view from the LA (*C*) and an en-face view from the LV (*D*). In (*E*), an example of a severe mitral stenosis is shown in a 3D LA aspect. Ao, aorta; AL, antero-lateral; PM, postero-medial; LA, left atrium.

located superiorly and posteriorly in the interatrial septum (IAS) and three TEE planes are used to determine the correct site: a short-axis view at the base for anterior–posterior orientation (~30°), a bi-caval view for superior (cranial)-caudal (inferior) orientation (~90–120°), and a four-chamber view (~0°) to direct the height above the MV. By presenting a short-axis view at the base and a long-axis view (bi-caval) simultaneously, 3D x-plane facilitates the determination of the correct puncture site (*Figure 4A*). The position of the commonly used Brokenbrough needle can be seen by a tent-like indentation of the IAS ('tenting'). Thereby, the tip of the 'tent' points towards the LA. With a satisfactory posterior and superior location, the height above the valve is assessed in a zero degree four-chamber view (*Figure 4B*). The site of optimal transseptal puncture is different for degenerative and functional MR. In degenerative disease (e.g. prolapse), the puncture site needs to be 4–5 cm above the mitral annulus to guarantee enough space for adequate catheter and MitraClip manoeuvring. In contrast, in cases of functional MR, the line of coaptation is most often below the plane of the mitral annulus due to extensive tethering. Therefore, the puncture site in these patients needs to be more inferior and closer to the annular plane (~3.5 cm above the annular plane). A persistent foramen ovale used for transseptal access should be avoided, as this passage through the IAS is too far anterior and therefore unsuitable. The access via an atrial septal defect (ASD)—even in a superior–posterior position—is also not recommended, as most commonly the delivery sheath cannot be stabilized in the defect which is most often larger than the sheath size and carries the risk of IAS rupture.

An incorrectly chosen puncture site increases the complexity, technical difficulty, and generally the duration of the procedure. A suboptimal puncture site often necessitates additional manipulation and steering manoeuvres with the large MitraClip delivery system (CDS) and thus, should be avoided whenever possible (*Figure 5*).

Introduction of the Steerable Guide Catheter (SGC) into the left atrium

In the next step, the Steerable Guide Catheter (SGC) with the dilator is gently advanced into the LA over an Amplatz extra stiff wire (placed in the left upper pulmonary vein) under fluoroscopic and TEE guidance. The dilator can be easily identified by a cone-shaped tip and a typical echogenic appearance of ridges on the catheter system. A radiopaque echo bright double ring characterizes the tip of the guide catheter. The advancement of the SGC should be carefully visualized under continuous 2D-, 3D TEE, and fluoroscopic monitoring to avoid injuries of the free LA wall (*Figure 6*). Once the SGC is safely placed in the LA, the dilator is retrieved first, followed by the Amplatz extra stiff wire.

Advancement of the Clip Delivery System (CDS) into the left atrium

The CDS is advanced in the following step via the SGC under fluoroscopic guidance. Transoesophageal echocardiography monitoring

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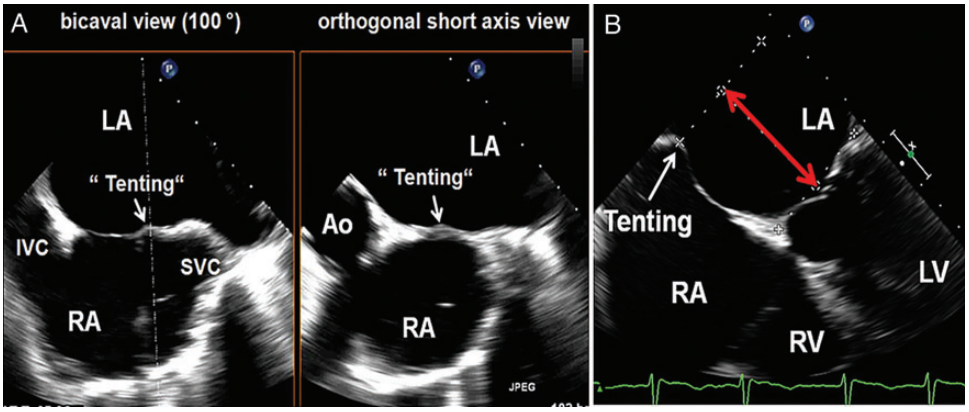

Figure 4 Transseptal puncture. (*A*) The determination of the puncture site is shown in a simultaneous x-plane view. Left side: bi-caval view, right side: short axis view at the base. The 'tenting' is marked with white arrows. In (*B*), a four-chamber view at 0° demonstrates the evaluation of the height above the valve (red arrow). LA, left atrium; RA, right atrium; IVC, inferior vena cava; SVC, superior vena cava; Ao, aorta; RV, right ventricle; LV, left ventricle.

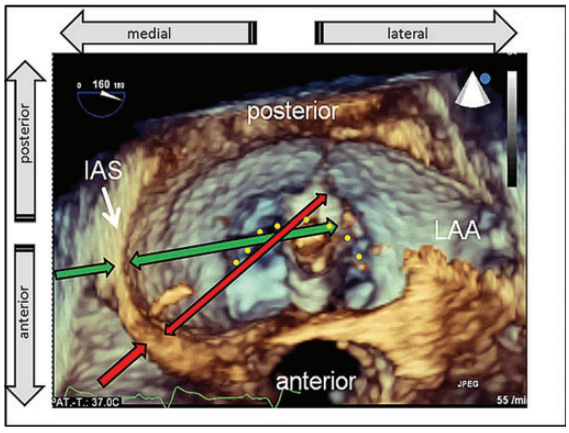

Figure 5 Consequences of a suboptimal puncture site. The red arrow marks a puncture site too far anterior. In this case, the CDS with the MitraClip is further away from the line of coaptation and any movement forward or backward of the delivery system would not only move the Clip medially or laterally but also in anterior and posterior direction. As a consequence, additional manoeuvres have to be performed to correct the position, thus increasing the complexity of the procedure. The green arrow marks a correct puncture site more posteriorly. In this case, the CDS and consecutively the Clip are closer to the line of coaptation and better aligned (more parallel to the line of coaptation). Any pushing forward or retraction of the delivery system moves the clip only medially or laterally (as desired) and less correcting manoeuvres are required. The yellow dots mark the line of coaptation. IAS, interatrial septum.

[2D- (view: short axis at the base) and 3D TEE] is additionally necessary to ensure that the tip of the SGC remains across the IAS and that the clip delivery system with the Clip at the tip does not cause injury to the free LA wall. Three-dimensional TEE and x-plane views are particularly helpful to visualize the distance of the CDS from the LA wall (*Figure 7*).

Steering and positioning of the MitraClip above the mitral valve

To position the CDS above the MV medial deflection, a posterior torque of the SGC and frequently a retraction of the whole system are required. These steps can be monitored best by 2D TEE in a short-axis view at the base or alternatively by 3D TEE. Medial–lateral Clip adjustments are monitored in a mid-oesophageal intercommissural view and anterior–posterior adjustments in an orthogonal mid-oesophageal long-axis (LVOT) view. Correct orientation of the Clip in the LA perpendicular to the line of coaptation in the mid-portion of the valve is particularly challenging with 2D imaging alone. To achieve proper Clip alignment, both arms of the opened Clip can be visualized in full length in the long-axis view (*Figure 8A*), whereas no Clip arms should be seen in the intercommissural view (*Figure 8B*). The MitraClip should split the regurgitation jet in both orthogonal views and the tip of the Clip should be directed towards the largest PISA (proximal isovelocity surface area). When only 2D TEE imaging guidance is available, the orientation of the Clip arms is confirmed in a short-axis transgastric view (*Figure 9*). Overzealous transgastric imaging has the potential to induce gastric lesions, therefore transgastric imaging should be acquired with only gentle movements of the probe. Currently, the transgastric view is generally avoidable if 3D TEE is available. A single 3D enface-view allows to determine when the Clip is adequately positioned above the middle segments of the MV and whether orientation is perpendicular to the line of MV coaptation (*Figure 8C–E*).

Advancing the MitraClip into the left ventricle

Advancing the open MitraClip into the LV can be observed best in x-plane imaging in which the intercommissural view and the LVOT

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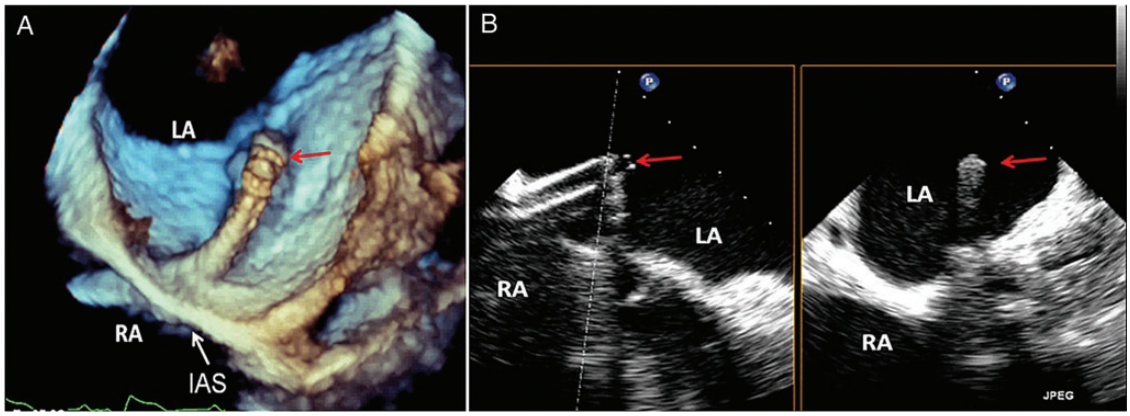

Figure 6 Introduction of the Steerable Guide Catheter (SGC) into the LA. The introduction of the SGC into the left atrium is shown in a 3D TEE image (*A*) and a 2D x-plane image (*B*). The red arrows mark the tip of the Guide. LA, left atrium; RA, right atrium; IAS, interatrial septum.

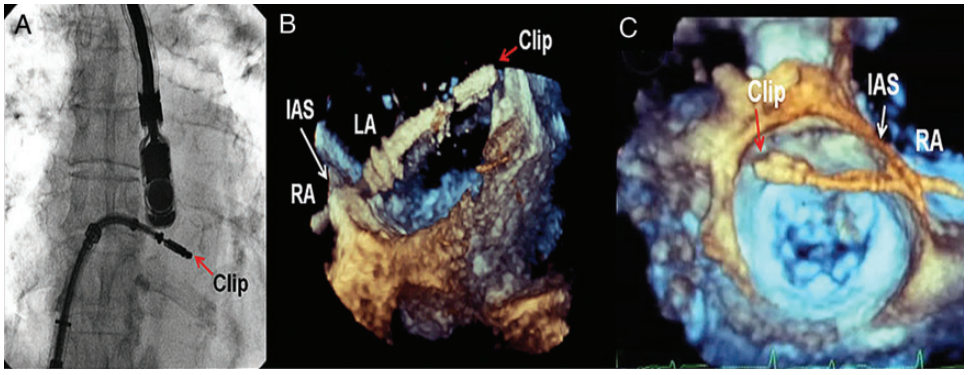

Figure 7 Advancement of the Clip Delivery System (CDS) into the LA. The entering of the CDS into the LA is shown by fluoroscopy (*A*), by a 3D TEE view (B), and by a 3D TEE wide-angle acquisition showing the relation of the MitraClip to the mitral valve (*C*). Red arrows point at the tip of the Clip. LA, left atrium; RA, right atrium; IAS, interatrial septum.

view can be judged simultaneously. In the LVOT view, both Clip arms should be clearly seen in full length, whereas in the intercommissural view no parts of the Clip arms should appear. Under fluoroscopic (*Figure 10A*) and TEE (*Figure 10B* and *C*) guidance (maintaining the Clip open), the passage across the MV is observed. The orientation of the Clip and the CDS has to be reassessed in the LV, as the Clip may rotate during translation from the LA to the LV. For this purpose, 2D TEE (intercommissural and LVOT) and 3D TEE views are used. The 2D transgastric short-axis view allows visualization of the Clip alignment relative to the line of coaptation. Alternatively, 3D en-face views from either the LA or the LV side present direct views of the MitraClip in relation to the MV and the line of coaptation. It is easiest to maintain a stable en-face LA view, and, in case the Clip orientation cannot be judged adequately, lowering the overall gain (*Figure 10D*) to get a clear impression of the Clip in the LV may help. A correct orientation of the MitraClip splitting the MR jet in intercommissural and LVOT views, a perpendicular alignment to the line of coaptation, and verifying that both mitral leaflets are freely moving above the Clip arms are crucial for a successful grasp of the MV leaflets.

Grasping of the leaflets and assessment of proper leaflet insertion

Once the MitraClip is in a satisfactory position, grasping of the leaflets as they are captured in between the Clip arms and the grippers (*Figure 11A*) is usually monitored using a 2D LVOT view (*Figure 11B* and *C*). Three-dimensional imaging has no clear benefit in this part of the procedure (*Figure 11D*). It is helpful to acquire a longer loop during the grasping of the leaflets, with the benefit of hindsight after the grasp is performed. It is recommended to initially close the MitraClip only up to 60–90° and aim for a full closure of the Clip only after determination of proper leaflet insertion and demonstration of MR reduction. For assessment of proper leaflet insertion into the MitraClip multiple planes are useful. The insertion of the posterior leaflet is

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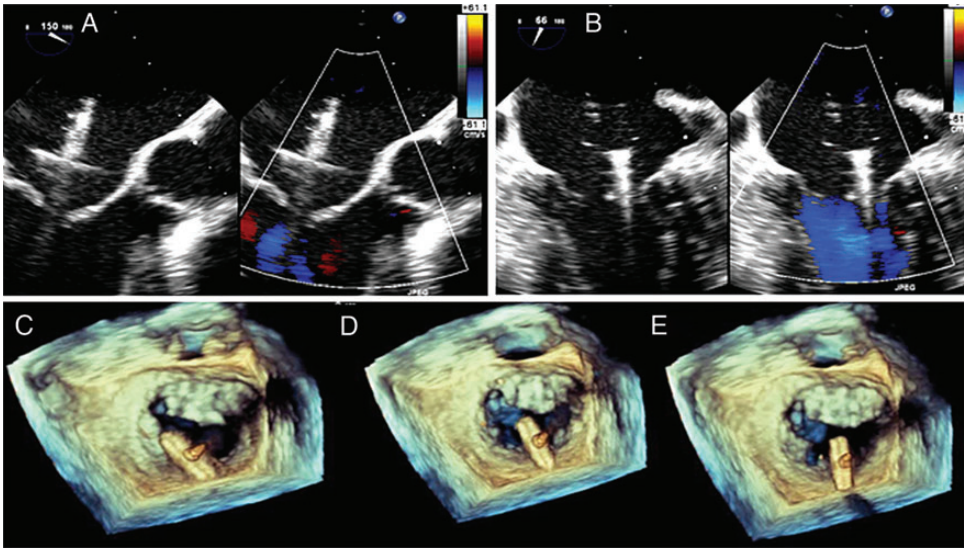

Figure 8 Steering and positioning of the MitraClip above the mitral valve. The MitraClip is opened in the left atrium above the mitral valve. In the LVOT view (*A*), both clip arms can be seen in full length, and in the intercommissural view (*B*) no parts of the Clip arms are visualized. In (*C*)–(*E*), a stepwise clockwise rotation is shown to orientate the Clip perpendicular to the line of coaptation.

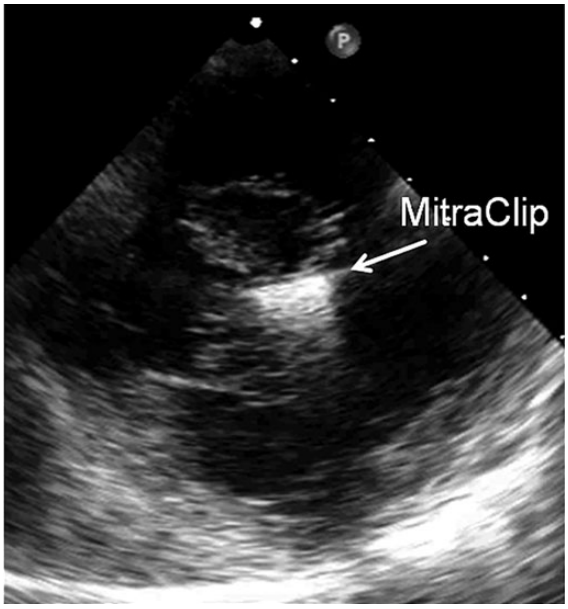

Figure 9 The transgastric short-axis view showing the orientation of the MitraClip. The orientation of the MitraClip which is not yet perfectly aligned perpendicular to the line of coaptation in this case can be appreciated in a transgastric short-axis view.

commonly best seen in the LVOT view, and the insertion of the anterior leaflet in the four-chamber view. The intercommissural view can add information such as entrapped chordae tendinae which may be visible at the free edges. Once the leaflets appear securely inserted and well positioned in between the Clip arms and the grippers and some reduction in MR is documented, the MitraClip can be fully closed.

Assessment of result and MitraClip release

Before and after the implantation of each Clip, it is necessary to evaluate the grade of regurgitation and stenosis of the MV, and in addition, the morphological result after Clip placement.

The initial evaluation of the MitraClip result is usually done at the time of the procedure under general anaesthesia. The type and the depth of anaesthesia, and the administration of medications such as inotropes, vasopressors, or vasodilators, influences pre- and afterload, the filling patterns of the LA and the LV, and MR severity. Therefore, every attempt should be made to ensure that all peri-procedural measurements and evaluations of MR are performed under similar haemodynamic conditions. In addition, there is also a need to keep ultrasound machine settings identical in pre- and post-procedural MR assessment, including colour scale and gain settings. The intra- and post-procedural evaluation of the grade of residual MR requires adjustment after a MitraClip implantation. Due to the newly created double MV orifice (or triple orifice in some cases in which two Clips are implanted), quantitative Doppler evaluation is problematic. There are no consensus guidelines or validated studies on how to best assess MR in the presence of a double orifice. As with the evaluation of native valves,[14,15] a multi-modal analysis approach is most suitable to sufficiently characterize MR after MitraClip implantation.

Echocardiography (TEE assessment is usually used as the TEE probe is still in place) plays the leading role in the evaluation of the result by using different parameters for grading residual MR. Residual MR can easily be detected by colour Doppler (*Figure 12A* and *B*). However for quantification, it has to be taken

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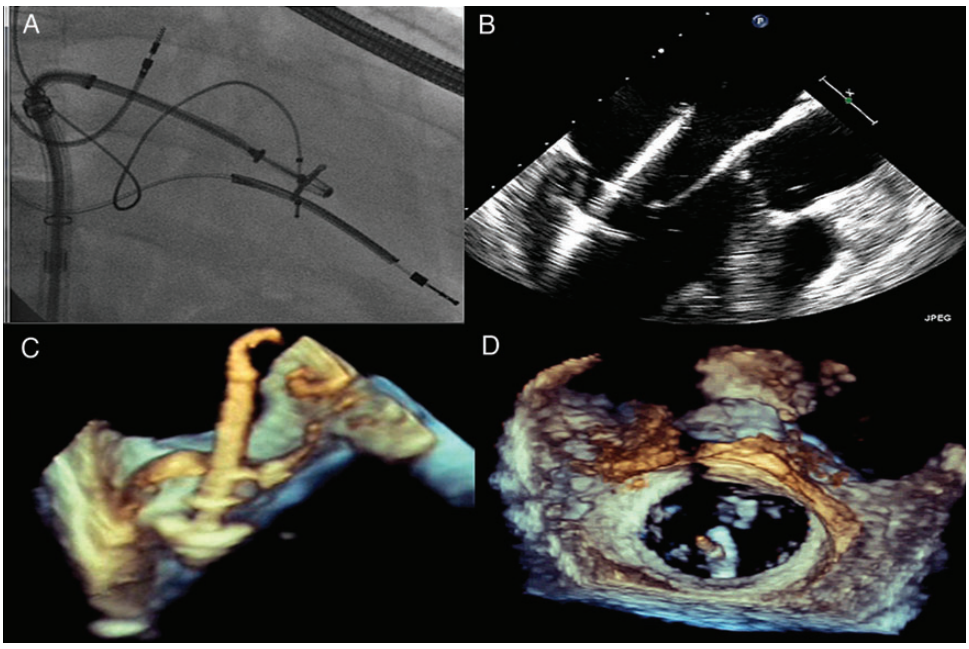

Figure 10 Advancement of the MitraClip into the Left ventricle (LV). The open clip is advanced into the left ventricle as seen by fluoroscopy in (*A*). The leaflets are moving freely above the Clip arms as shown in 2D TEE (*B*) and 3D TEE (*C*) views. The orientation of the Clip in the LV is re-assessed by lowering the overall gain as demonstrated in (*D*).

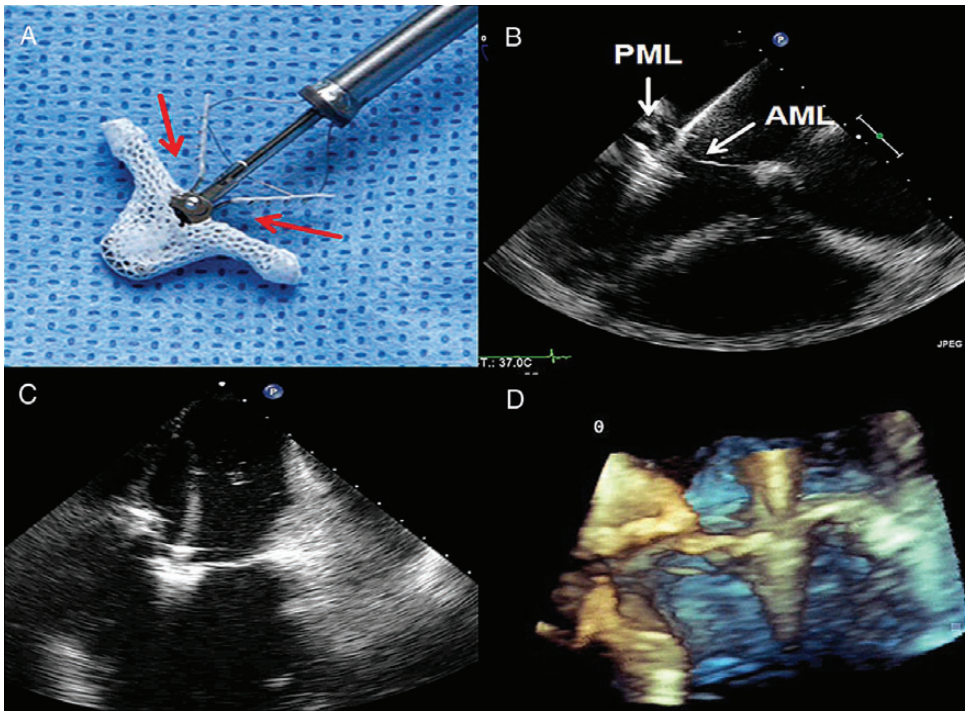

Figure 11 Grasping of the leaflets. A picture of the MitraClip demonstrates that the leaflets are grasped in between the Clip arms and the grippers (red arrows) (*A*). In (*B*), both leaflets can be clearly identified above the Clip. Proper leaflet insertion is shown in (*C*) and (*D*) by 2D TEE and 3D TEE views. Both leaflets should clearly go over the tip of the Clip arms. PML, posterior mitral leaflet; AML, anterior mitral leaflet.

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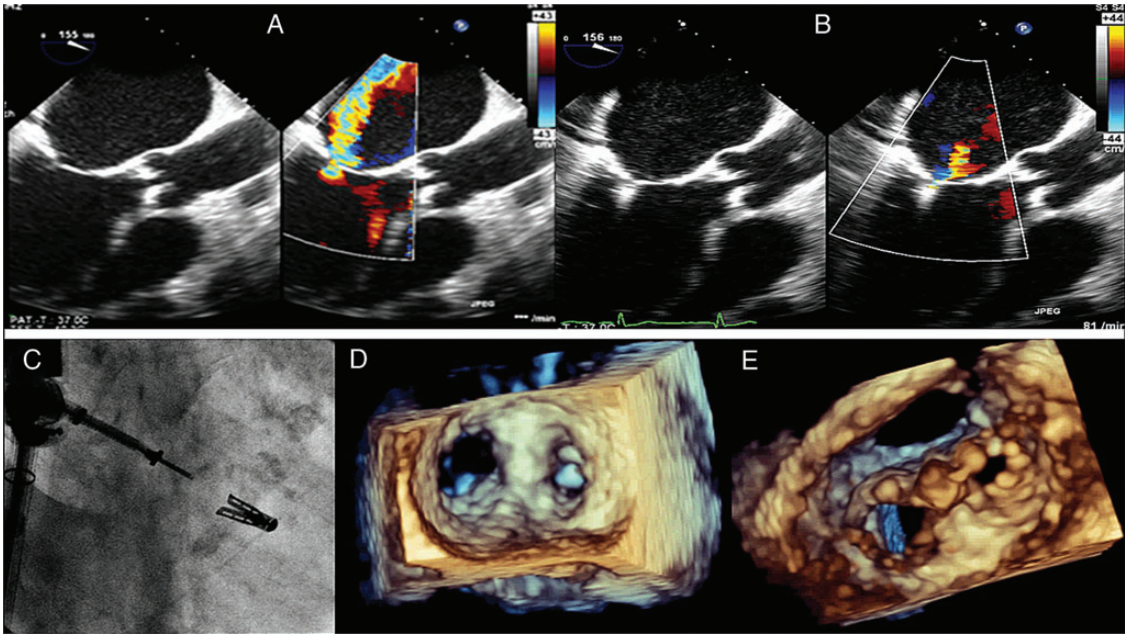

Figure 12 Assessment of result. MR reduction is assessed by comparing pre-procedural (*A*) and post-procedural images (*B*) in different views—in this example LVOT views are compared. In (*C*), Clip deployment is seen by fluoroscopy. The newly created double orifice is assessed by 3D TEE imaging using enface-views from the LA side (*D*) and the LV side (*E*).

into consideration that the area of colour jets is larger with multiple jets, which commonly occur after a MitraClip is implanted (due to the addition of multiple jet areas), than if there is a single jet. This may potentially lead to overestimating residual MR in patients with multiple jets.[38,39] In addition, artefacts caused by the MitraClip may also alter the findings. Nonetheless, small persistent colour jets, even if multiple, are certainly congruent with mild MR.

Relevant MR reduction leads to an elimination of pulmonary vein flow reversal and reduced or even normalized LA pressures. Furthermore, the pulmonary vein systolic flow reversal (if present) should disappear and the 'S' wave should become more pronounced or even dominant.

The PISA method is not validated for multiple MR jets which appear frequently after MitraClip implantation, nor for the newly created geometry of the MV with two (or even more) orifices, therefore cannot be used to quantify the MR post-procedure.

In the absence of aortic regurgitation and ventricular septal defects, the regurgitation volume can be calculated by subtracting the forward flow (velocity-time integral derived in the LVOT × LVOT area) from the total stroke volume (end-diastolic volume – end-systolic volume) thus enabling a quantification of the MR.[40] In this context, the 3D-acquisition of the LV volumes is preferable for the calculation when available.[36]

The summation of two-dimensionally measured venae contracta is not reliable in the presence of multiple jets. However, the direct measurement of the vena contracta area in 3D echocardiography shows potential for the quantification of MR with irregularly shaped vena contracta areas, although currently no reference data are available.[41,42]

In addition to echocardiography, some other parameters may be helpful for the evaluation of the severity of residual MR:

- LA pressure measurements (V-wave). A decrease or even a normalization of LA pressures may be seen in case of effective MR treatment.
- Stroke–volume measurements via right heart catheterization (thermodilution) or Picco-catheters (an increase in stroke –volumes can be expected after successful MR reduction[27]).
- LV angiography to assess the amount of regurgitation by judging the density and the expansion of the MR jet in the LA.

From a morphological point of view, it has to be confirmed that both leaflets are adequately grasped and inserted in the MitraClip. Placement of a MitraClip creates a tissue bridge between the two leaflets, which separates a medial and a lateral orifice. Final orifice size and geometry can be evaluated best in 3D enface aspects of the MV from the LA and the LV (*Figure 12D* and *E*). Two specular isosceles triangles indicate uniform and symmetrical placement of the MitraClip on both leaflets (*Figure 13*). Excessive distortion of the valve should be avoided.

After placement of each MitraClip, the MV gradient should be evaluated to exclude significant stenosis. The transvalvular diastolic gradient is usually assessed by CW-Doppler—a mean gradient of up to 5 mmHg is considered acceptable. In addition, planimetry of the two orifices should be performed, ideally with 3D TEE, alternatively with 2D TEE in the transgastric short-axis view. In the EVEREST I and II studies, a planimetric MVA <1.5 cm^2 was considered criteria for clinically significant mitral stenosis.[1,9] Once in place, it has been demonstrated that the MitraClip device did not result in clinically significant MV stenosis during 2 years of

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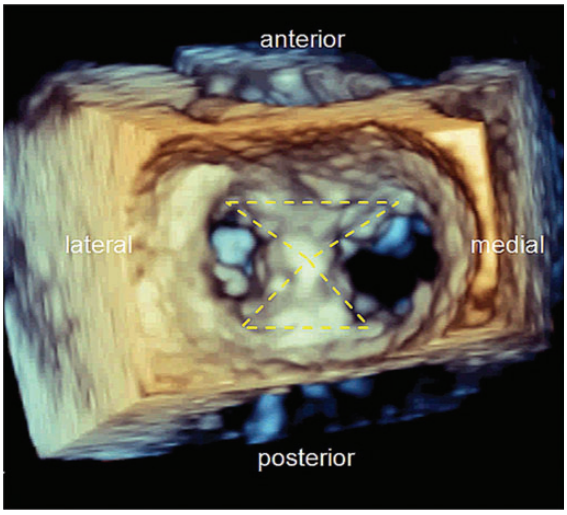

Figure 13 Tissue bridge created by the MitraClip. Specular isosceles triangles indicate uniform and symmetrical tension of the Clip on both leaflets.

follow-up. These results were not influenced by whether there were one or two MitraClips deployed, or the aetiology of MR.[43,44] However, there are limited data in patients undergoing a MitraClip that have chronic renal failure, or are on dialysis, or have a history of chest radiation that might put them at an increased risk of valve calcification and restriction.

In case of unsatisfactory MR reduction, repositioning of the Clip has to be discussed and/or the implantation of a second clip may be considered. When the Clip position and the decrease in MR are considered satisfactory, the Clip is released (*Figure 12C*). After deployment, the residual grade of MR should be reassessed as minor changes may occur when the tension transferred via the CDS is released.

Additional MitraClip implantation

With implantation of a second MitraClip, the orientation of the second Clip should be optimized by 2D, or when available, 3D echocardiography in the LA. During advancement of the MitraClip from the LA into the LV, the Clip should be closed to avoid any interference or entanglement with the chordae tendinae then re-opened in the LV. In general, fluoroscopy is more helpful than TEE for the positioning of a second MitraClip which should be aligned as parallel as possible to the first Clip. Folding of leaflet tissue between two MitraClips should be avoided as this may cause uncorrectable residual MR.

Assessment of complications

It has been demonstrated that MitraClip implantation is a remarkably safe procedure; however, complications may occur at any time of the intervention and the team performing the procedure must be aware of them and should be prepared for adequate detection and treatment. The most frequent complications are summarized in *Table 4*.

Post-procedural follow-up

For post-procedural follow-up, TTE is usually sufficient. Foster *et al.*[45] suggested several parameters for quantitative MV assessment adapted from current guidelines[14] including colour flow Doppler of the MR, MV inflow gradient, assessment of pulmonary vein flow, residual ASD evaluation, systolic pulmonary artery pressure, LV size and volume measurements in systole and diastole, and LVEF. In case there is an abnormality that needs clarification, an additional TEE should be performed.

Future perspectives

The role of 3D echocardiography in the assessment of MR severity may increase in the future, a major advantage being the ability of this modality to assess vena contracta area which is most commonly non-circular especially in patients suffering from functional MR. Usually, the vena contracta area is quantified in a post-processing step using planimetry of 3D colour regurgitation jets in orthogonal views. This method is illustrated in *Figure 14*. The 3D derived vena contracta area correlated better with effective regurgitant orifice area derived from Doppler measurements than 2D vena contracta diameter measurements.[36,46]

In addition, comparing MR jet areas, the 3D evaluation of jet volumes correlated closer with angiography as the reference standard—particularly in patients with eccentric jets—compared with the 2D assessment of jet area.[46] Direct delineation of the anatomic regurgitant orifice area in 3D enface views of the MV and calculation of the PISA in 3D flow through a MV are also emerging methods for assessing valve regurgitation and function quantitatively and may also be advantageous in the future.[47–49]

Real-time three-dimensional volume colour flow Doppler (RT-VCFD) TTE imaging with an automated quantification algorithm represents also a promising method for MR quantification. Real-time three-dimensional volume colour flow Doppler was feasible, accurate, and reproducible for mitral inflow and aortic stroke volume measurements. Aortic stroke volume by RT-VCFD correlated well with cardiac magnetic resonance values, whereas 2DTTE measurements were significantly worse compared with RT-VCFD.[50] To date, no guidelines on 3D quantification have been published by the cardiac societies and no validated reference standards are available. To which extent 3D-based echocardiographic analysis alone or in combination with other methods may lead to a better quantification of MR and post- procedural residual MR after MitraClip procedures requires further evaluation in prospective studies.

During interventional procedures including the guidance of a MitraClip implantation, there is an increasing reliance on 3D TEE.[36,51] A newly developed EchoNavigator system (Philips Healthcare) may facilitate procedural guidance by matching echocardiographic and fluoroscopic images. Although only limited clinical data are available at this time, the new features of the EchoNavigator system may support the understanding of the spatial relation between the Echo and X-ray image, thus making

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Table 4 Complications that can result from the MitraClip procedure

Complication	Aetiology	Treatment/prevention
Pericardial effusion/ tamponade	Transseptal puncture, guidewire, or catheter perforation of the LA and LV	Pericardial drainage
Air embolism	Presence of large sheaths which allows air into the venous circulation	Aspiration and flushing of catheter as well as keeping catheter hub lower than the level of heart during catheter insertion or removal
Thrombus formation	Presence of foreign objects which predispose to thrombus formation	Maintain ACT of between 250 and 300 s
Partial Clip detachment	Inappropriate positioning or device malfunction	Appropriate echo guidance, careful assessment of leaflet insertion
Clip detachment from both leaflets	Inappropriate positioning or device malfunction [to our knowledge, as of this writing, there is one report of a MitraClip detachment from both leaflets in more than 6.500 cases performed (Elizabeth McDermott, Abbott Laboratories, personal communication)]	Device retrieval if possible (either percutaneously or surgically)
Atrial and ventricular arrhythmias	Guidewire or catheter mechanical stimulation	Routine ECG monitoring during the procedure
Entrapment of chordae tendinae by the MitraClip	Inappropriate positioning	Use TEE to carefully monitor catheter and MitraClip position in the LV
Persistent ASD	Iatrogenic due to large size of MitraClip system	Most small and require no treatment (in 9 out of 10 patients a clinically insignificant ASD remains open after one month[54]), however if there is SPO2 desaturation due to left to right shunting the defect should be closed at time of the procedure

ASD, atrial septal defect; ACT, activated clotting time; LA, left atrium; LV, left ventricle; TEE, transoesophageal echocardiography.

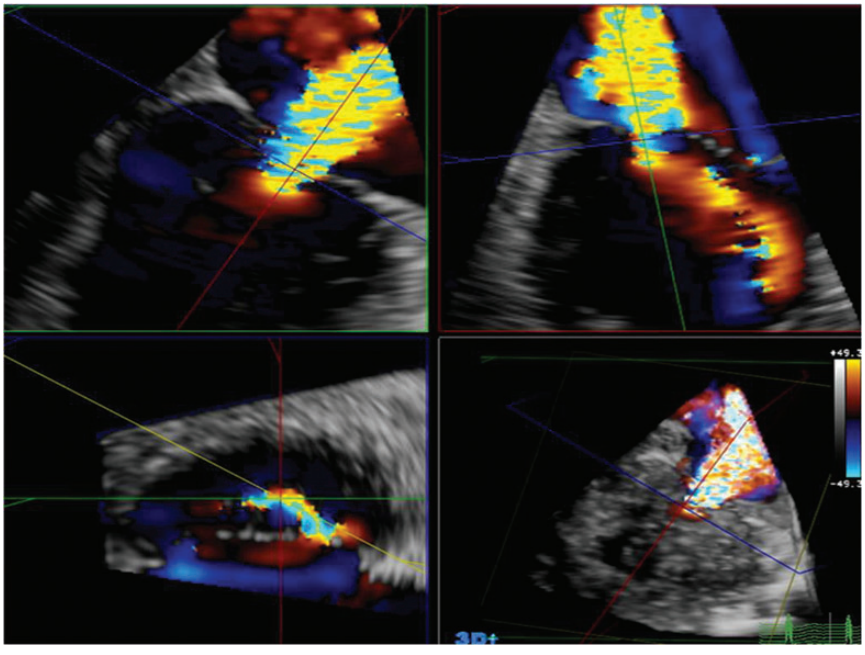

Figure 14 3D evaluation of the Vena Contracta Area (VCA). The analysis of a 3D colour data set (bottom right) reveals a small jet in a long axis view (top right) and a broader jet in an orthogonal intercommissural view (top left). The Vena Contracta Area (VCA) (bottom left) is asymmetric along the commissural line in an en-face view to the mitral valve.

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the interpretation and understanding of anatomical structures rendered by TEE easier.

Conclusions

The MitraClip device implantation is an emerging new technology for the treatment of patients with either functional or degenerative moderate-to-severe or severe MR. As the mitral leaflets cannot be assessed by fluoroscopy, procedural success relies heavily on adequate echocardiographic assessment. Patients with moderate-to-severe or severe MR and suitable anatomical characteristics must be properly defined to ensure optimal clinical outcomes. In addition, TEE plays the major role in guidance of the procedure and in follow-up. With improvement of imaging quality and a better understanding of 3D imaging, improved procedural efficacy as well as a reduction in procedure time may be expected. For pre- and post-procedural MR quantification, the most suitable parameters and measurements must be defined and standardized. New 3D quantification methods (e.g. vena contracta area, anatomic regurgitant orifice area) to assess MR are in development. New technologies that synchronize echocardiographic and fluoroscopic imaging could potentially simplify and optimize procedural guidance, improve the degree of MR reduction, and enhance safety as well as shorten the duration of both fluoroscopy and the procedure time.

Conflict of interest: R.J.S. and N.C.W. report no conflict of interest.

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