

Review Article

The Abbott Vascular MitraClip: Patient Selection and How to Obtain the Best Outcomes

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Key words: **Mitral regurgitation, MitraClip, transcatheter mitral valve repair.**

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Significant mitral valve regurgitation (MR) is often encountered in clinical practice; patients present with symptoms and signs of heart failure, arrhythmias, and a progressive decline in functional capacity.^{1,2} There are several potential causes, but in general MR is characterized as primary/organic/degenerative, when it is caused by structural damage to parts of the mitral valve apparatus – leaflets, *chordae*, papillary muscles, annulus – or functional/secondary, when it is related to underlying cardiomyopathy with adverse remodeling of the mitral valve apparatus. Surgery has long been considered the gold standard treatment, with excellent results in degenerative MR (especially when repair is performed) but with equivocal results in functional MR (rarely performed as a standalone procedure). For many patients, surgery is deferred or declined because of the perceived prohibitive risk from advanced age and comorbidities.³ Multiple approaches to transcatheter mitral valve repair (TMVR) have been offered in an attempt to reduce MR grade. At present, the edge to edge approximation method with the MitraClip (Abbott Vascular) is the most widely available and clinically relevant TMVR technique.

Device characteristics and procedural steps

The MitraClip is a cobalt-chromium im-

plant covered with polyester fabric to promote tissue ingrowth. The closed clip has a length of 15 mm and a width of 5 mm. With the arms open the span of the clip arms is 17 mm (at 120°) and 20 mm (at 180°); each arm has a width of 5 mm and a length (coaptation length) of up to 9 mm (Figure 1).⁴ The implant has 2 arms that are designed to allow portions of the free edges of the anterior and posterior mitral valve leaflets to be inserted and secured with additional grippers, creating a permanent apposition that ultimately leads to the formation of a tissue bridge and a significant reduction in MR grade. The MitraClip is mounted on a delivery system that is inserted via a 24 F steerable guide catheter via the transvenous route and advanced into the left atrium via a previously performed transseptal puncture. The procedure is performed under general anesthesia and with the use of continuous transesophageal echocardiography (TEE). Once the delivery system is inserted in the left atrium, the catheter is oriented over the mitral valve with a combination of mediolateral and anteroposterior movements guided by TEE. Once in the appropriate position, i.e. the area of maximum MR flow, the clip arms are opened to verify perpendicularity to the coaptation line of the mitral valve. Next the clip is advanced slowly into the left ventricle and carefully re-

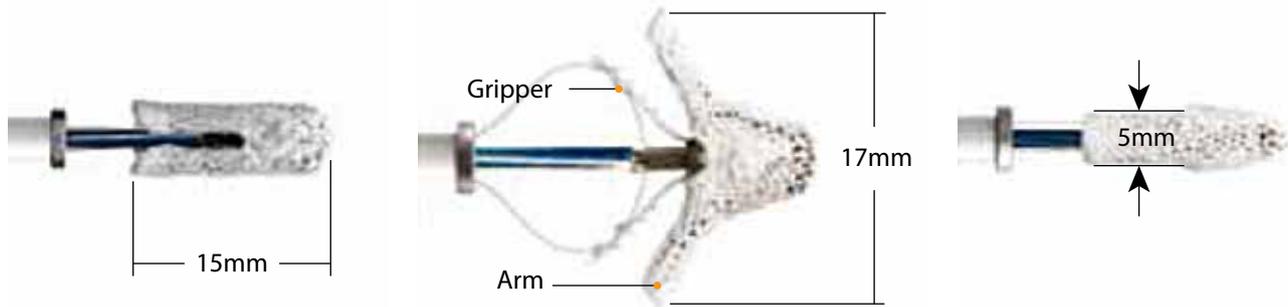


Figure 1. Technical characteristics of the MitraClip.

tracted to allow both leaflets to rest on the expanded arms. Once the leaflets are inserted, the grippers are lowered and the MitraClip arms are closed. Release of the clip is based on an adequate reduction in MR, lack of significant mitral stenosis, and verification of stability. Once the clip is released and the delivery catheter is removed from the left atrium, further assessment is performed to evaluate the need for additional clips. Finally, the steerable guide catheter is removed and hemostasis is obtained at the femoral venous puncture site.

Patient selection

Patients referred for transcatheter mitral valve repair with the MitraClip undergo a thorough clinical evaluation and detailed echocardiographic assessment. The goals are primarily to confirm the severity of mitral valve regurgitation,⁵ to identify the exact mechanism (degenerative or functional MR), and to assess whether the symptoms the patient exhibits are related to the underlying MR. In addition, the presence and significance of any coexistent coronary artery disease needs to be documented and coronary angiography is mandatory. By definition, patients referred for MitraClip therapy are at prohibitive or extremely high surgical risk⁶⁻¹² for traditional valve repair or replacement, as evaluated by existing risk scores (STS, Euroscore) while keeping in mind the limitations of these tools (for instance, not taking into account factors such as frailty, severe right ventricular dysfunction or “hostile chest”). Clinical evaluation should assess all other comorbidities (e.g. malignancy, severely debilitating conditions) and their impact on the patient’s life expectancy. Echocardiography, and specifically transesophageal imaging, are critical in

evaluating the anatomical substrate for severe mitral regurgitation, distinguishing two broad categories: degenerative MR (DMR) due to pathology of the leaflets and chordal structures, and functional MR (FMR) due to pathology of the myocardium (ischemic or non-ischemic cardiomyopathy), leading to distortion of the mitral valve apparatus and secondary MR.

In the pivotal EVEREST II trial,¹³ which compared TMVR with the MitraClip to conventional surgery, the anatomical inclusion criteria were as follows (Figure 2):

- For DMR the flail gap should be less than 10 mm and the flail width <15 mm. In addition, severe bileaflet prolapse or bileaflet flail was considered a contraindication for MitraClip therapy.
- For FMR the coaptation depth should be <11 mm and the coaptation length ≥ 2 mm.

In addition, for all patients the mitral valve orifice area had to be $>4 \text{ cm}^2$ (as measured by pressure half-time from continuous wave Doppler recording of the mitral valve inflow) and the primary regurgitant jet had to originate from the A2/P2 region, with lack of any calcification in the grasping area. Exclusion criteria also included the presence of significant clefts or leaflet perforation, the lack of both primary and secondary chordal support, restriction of the posterior leaflet, and leaflet thickness $>5 \text{ mm}$. Patients with left ventricular end-systolic diameter $>55 \text{ mm}$ or a left ventricular ejection fraction (EF) $<25\%$ were also excluded.

In “real world” clinical practice, however, patients^{10,14,15} referred for TMVR with the MitraClip are often not eligible for surgery because they have prohibitive risk. In these highly symptomatic patients with no surgical options the main criterion for

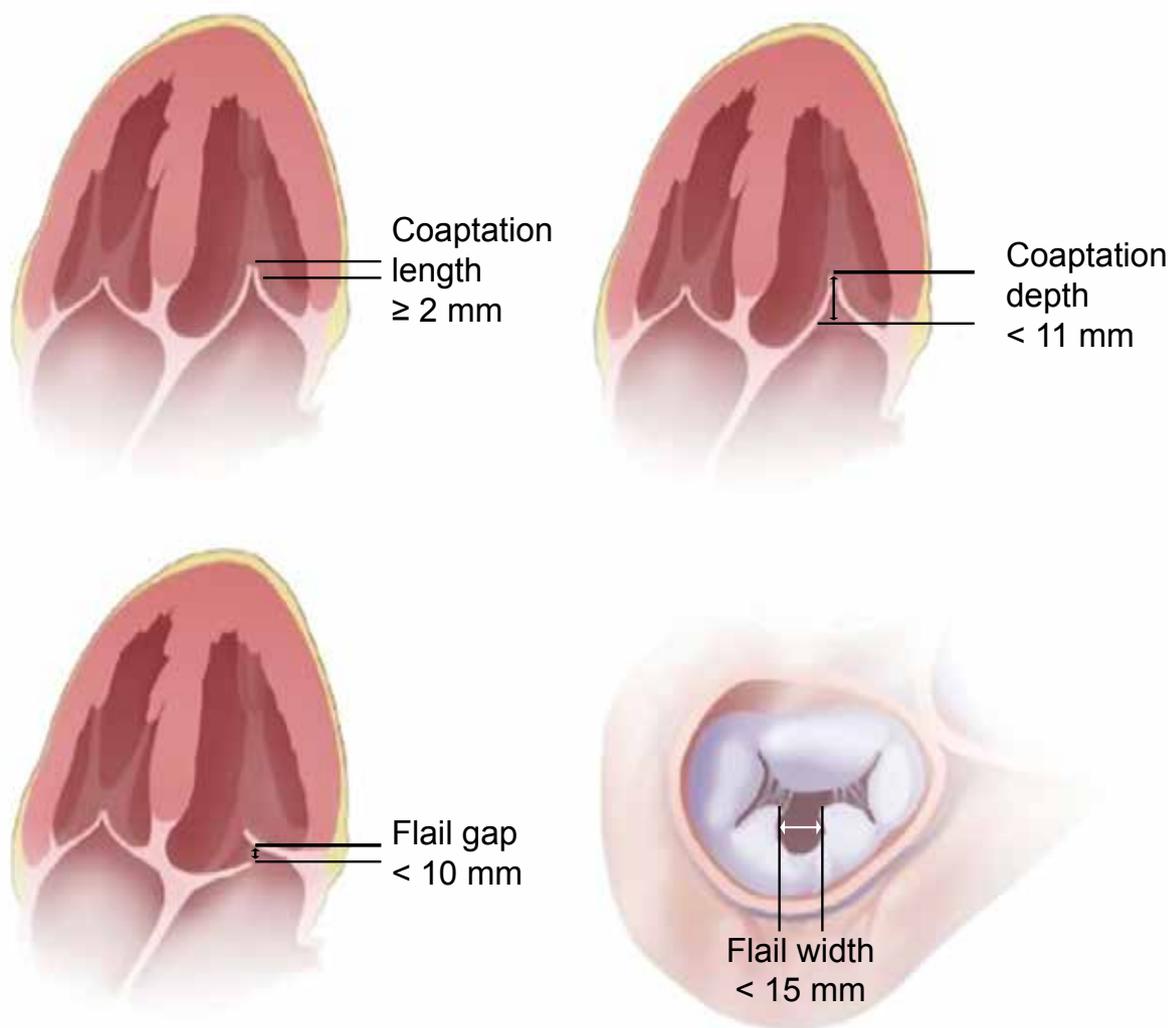


Figure 2. Anatomical criteria for MitraClip eligibility in the EVEREST II study.

MitraClip eligibility is the ability to capture both leaflets.^{6-8,10-12,15-18} Thus, non-central jets have been successfully treated by experienced operators, taking care to avoid the risk of clip entanglement in the commissural *chordae*. Mitral valve areas between 3.0-4.0 cm² can be treated successfully as long as there is adequate leaflet mobility, without significant baseline gradients. Posterior leaflet length available for grasping should be at least 10 mm, but 7-10 mm may also be attempted. Severe left ventricular systolic dysfunction has been a concern, because of the perceived risk of an acute low cardiac output state due to increased afterload in the failing left ventricle once MR was decreased, but in practice this theoretical risk has not been documented and patients with advanced heart failure have been

treated successfully, with marked clinical improvement.^{7,19} In addition, it has been shown that up to 70% of patients who had failed cardiac resynchronization therapy and significant MR showed improvement following MitraClip implantation.²⁰ Anecdotal reports also describe the use of the MitraClip as a “bridge to transplant” for patients with hypertrophic cardiomyopathy and systolic anterior motion of the mitral valve,²¹ for acute MR in the setting of myocardial infarction, or after relapse of mitral regurgitation in patients initially treated with surgical annuloplasty. Reflecting these “real world” practices, a consensus paper by the German Society of Cardiology was published recently;⁵ mitral valve morphology is classified into three categories as regards eligibility for MitraClip: optimal, conditionally suit-

able, and unsuitable (Table 1). Based on this consensus, ideal patients for MitraClip are those at high surgical risk, with severe MR, optimal anatomy, FMR with EF < 30% or DMR; on the other hand, patients with limited life expectancy, severe left ventricular dysfunction (EF < 15%), and anatomical features other than optimal should be considered for MitraClip only in exceptional cases.⁵

Current guidelines

In the United States the MitraClip has received FDA approval for the treatment of patients with severe DMR who are considered to be at prohibitive or increased surgical risk and who have a life expectancy > 1 year. This is also highlighted in the recent ACC/AHA Valvular Heart Disease guidelines,²² with level of recommendation Class IIb-B.

Table 1. Mitral valve morphology and eligibility for MitraClip. (Adapted from reference #5. Reproduced with permission.)

Ideal valve morphology	Possibly acceptable morphology	Unacceptable morphology
Central (A2-P2) pathology	Pathology in lateral (A1-P1) or medial aspect (A3-P3)	Perforation or clefts
Absence of calcifications	Mild calcifications away from MitraClip grasping area	Severe calcification in grasping area
Mitral orifice area > 4 cm ²	Mitral orifice area > 3 cm ² with good residual mobility	Hemodynamically significant mitral stenosis (area < 3 cm ² , mean gradient ≥ 5 mmHg)
Mobile posterior leaflet ≥ 10 mm	Mobile length of the posterior leaflet 7-10 mm	Mobile length of posterior leaflet < 7 mm
Coaptation depth < 11 mm	Coaptation depth ≥ 11 mm	
Normal leaflet mobility	Restricted mobility during systole (Carpentier IIIb)	Rheumatic mitral valve disease with leaflet thickening and mobility restriction in diastole and systole (Carpentier IIIa)
Flail width < 15 mm	Flail width > 15 mm, if large annulus with capacity for more than 1 MitraClip	Myxomatous degeneration (Barlows) with multiple prolapsing segments
Flail gap < 10 mm		

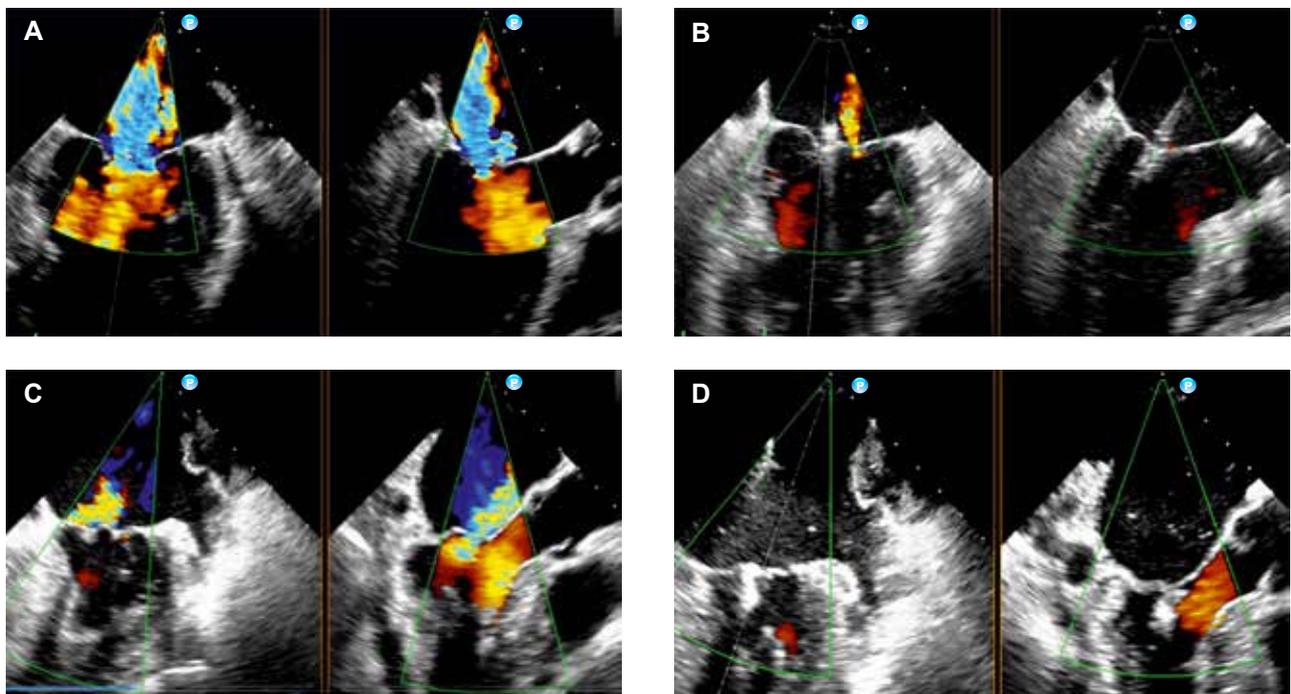


Figure 3. Examples of successful transcatheter mitral valve repair with the MitraClip system. A: Severe functional ischemic mitral regurgitation (FMR). B: Significant reduction in MR following deployment of one MitraClip. C: Severe degenerative mitral regurgitation (DMR) with P2 prolapse. D: Trivial residual MR following deployment of one MitraClip.

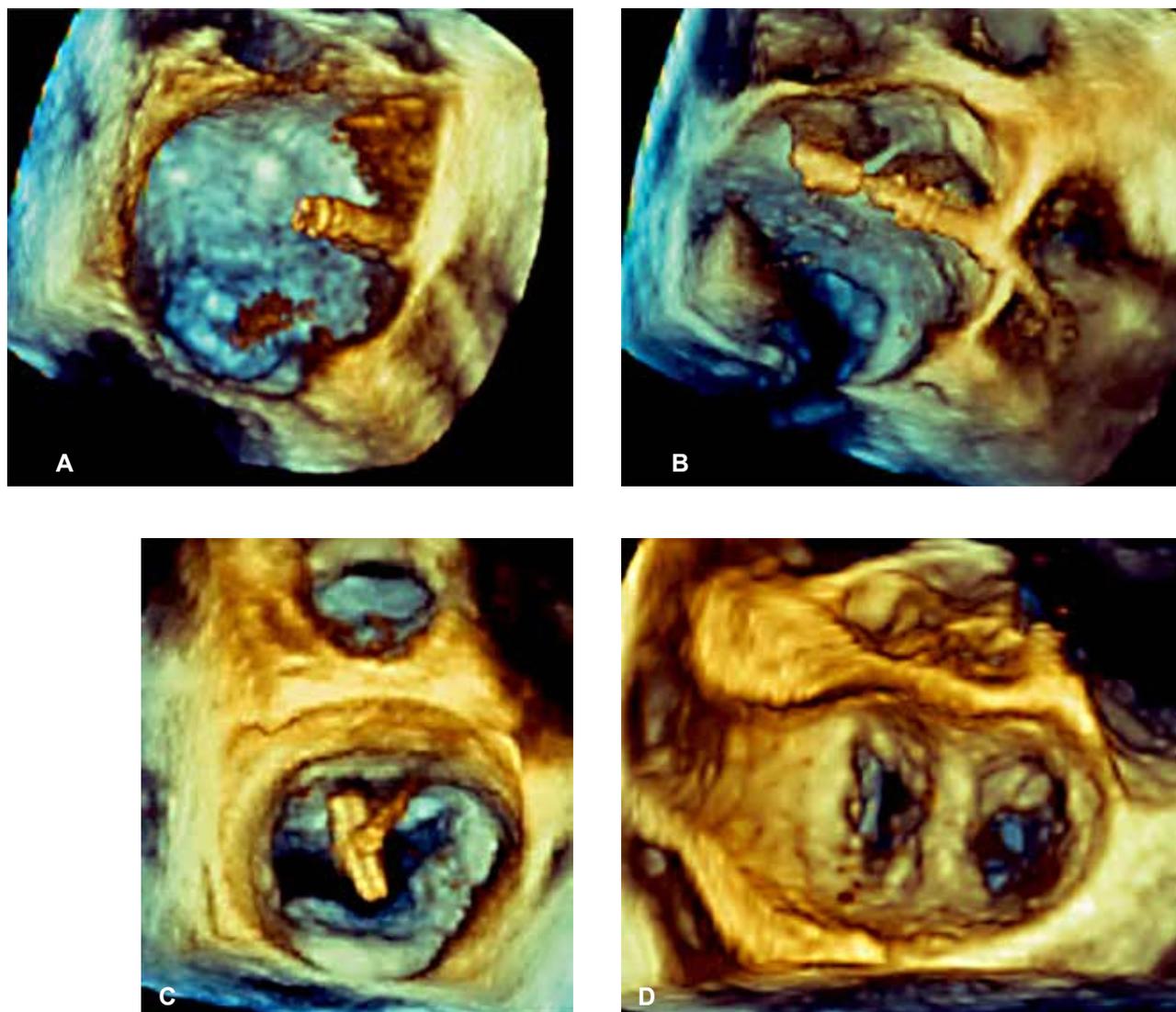


Figure 4. Three-dimensional echocardiographic imaging during MitraClip implantation. A: Steerable guide catheter positioned across the interatrial septum. B: Clip Delivery System advanced in the left atrium with arms in the closed position. C: MitraClip over the mitral valve with arms open to 180°. Evaluation for perpendicularity to coaptation line. D: Evaluation of final result with formation of a double orifice mitral valve.

In the ESC/EACTS 2012 guidelines,^{23,24} MitraClip is given a IIb-C recommendation for DMR; further, for patients with FMR MitraClip therapy may also be considered if patients are already on optimal medical therapy, which may also include cardiac resynchronization.

How to obtain the best results

Acute procedural success with MitraClip therapy is defined as implantation of the clip with an immediate reduction of MR grade to $\leq 2+$. By surgical standards this may be considered inadequate; however, in practice patients appear to improve on clinical grounds, with bet-

ter NYHA functional class and a reduction in rehospitalization rates for heart failure and with echocardiographic markers of reverse left ventricular remodeling.^{7,25} Given that this reduction can be obtained with low perioperative morbidity and mortality, and with a relatively short hospital stay, this reduction in MR grade is more than acceptable and may improve the natural history of these patients. Studies have shown that acute procedural success and discharge MR grade are strongly associated with survival;²⁶ thus, obtaining maximal MR reduction (taking care not to cause stenosis or risk entanglement with *chordae*) should be the goal of the procedure.

Transseptal puncture

The critical first step to success for the MitraClip procedure is to carefully select an appropriate area in the *fossa ovalis* along the superior and posterior aspect. This will permit easier maneuvering in the left atrium to provide adequate height over the mitral valve for the delivery system to advance without the need for more complicated steering. Thus, spending the necessary time on this step cannot be overemphasized.

Learning curve

The MitraClip procedure requires close coordination within the interventional team and the technical skills are enhanced over time. Multiple studies have shown the impact of the learning curve on device implantation times, as well as on procedural success.²⁷ Thus it would be important to establish referral centers for MitraClip procedures to allow an adequate number of procedures to be performed by each team, so that they are able to gain the necessary fluency in the technique.

Three-dimensional echocardiographic imaging

The ability to visualize in real time the mitral valve apparatus and the anatomical structures involved during transcatheter mitral valve interventions is a major breakthrough and an important contributor to success.^{28,29} Although 2D-echocardiography can be adequate in the majority of patients (Figure 3), 3D is highly encouraged. All procedural steps – transseptal puncture, steerable guide catheter insertion, clip delivery steering, evaluation of leaflet grasping, and final assessment – can be monitored, offering the interventional team the spatial orientation necessary to build confidence and familiarity with the procedure (Figure 4). An additional benefit of 3D-echocardiography is the possibility of minimizing fluoroscopic time and radiation exposure.

Anatomical criteria that may predict success were recently reported⁹ and include baseline effective regurgitant orifice area (EROA), baseline mitral valve area (MVA), and baseline mean transmitral gradient (TMPG). It has been shown that a baseline EROA $>70.8 \text{ mm}^2$ and a TMPG $>4 \text{ mm Hg}$ may be independently predictive of clip failure (inability to adequately reduce MR grade to ≤ 2), whereas an MVA

$<3.0 \text{ cm}^2$ and a TMPG $>4 \text{ mmHg}$ (markers of significant reduction in baseline mitral valve orifice area) may be independently predictive of the inability to implant/release a MitraClip. Again, these findings highlight the importance of careful patient screening for procedural success.

Single vs. multiple clips

Effective MR reduction with a single MitraClip may not be feasible. Indeed, up to 40% of cases may require two or more clips for procedural success.¹⁰ The number of clips necessary to achieve sufficient MR reduction appears to be influenced by the degree of MR, as measured by baseline regurgitant volume. In addition, anatomical factors, and in particular increased anterior leaflet thickness, appear to be associated with increased odds of implanting two devices.³⁰ A basic approach (“central clip concept”) is to implant the first clip at the center of the MR jet; if significant residual MR is observed on both sides of the clip then the clip should be repositioned more medially and a second clip may be implanted next to it. If, on the other hand, a single clip leaves significant MR only on one side, then repositioning to that side may afford enough reduction without the need for a second clip.

Heart failure reassessment and management

For patients with FMR, the underlying cardiomyopathy is the driver behind the clinical symptoms and the development of mitral valve dysfunction. Thus, TMVR in these patients should be an opportunity to confirm that optimal medical therapy (in terms of classes of medications and dosages) is already being provided. In addition, where indicated, the use of device therapy with cardiac resynchronization (\pm defibrillator) should be offered as well. Studies have also shown that patient outcomes are enhanced by earlier referral, i.e. before progression to a more severe functional class of heart failure.¹⁸

Summary

The MitraClip procedure is an important procedure for the treatment of high-risk patients with severe MR, offering an effective and clinically meaningful reduction in the degree of MR, with low perioperative morbidity and mortality. Careful screening of prospective patients and evaluation by the multidis-

ciplinary Heart Team are essential. A dedicated interventional team combining technical skills and advanced imaging is critical for success.

Disclosures

M. Chrissoheris and K. Spargias are proctors for the MitraClip procedure for Abbott Vascular.

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