

# Current Options for Mitral Annuloplasty and Leaflet Repair

The benefits and limitations of today's FDA- and CE Mark–approved mitral repair technologies.

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**M**itral regurgitation (MR) is the second most common valve disease, which contributes substantially to morbidity and mortality.<sup>1</sup> The prevalence of moderate or severe MR is approximately 10% in patients older than 75 years. MR is differentiated according to its etiology as either primary or secondary, with different prognoses and treatment options.<sup>2,3</sup> Primary MR is the result of structural pathologic changes of the valve leaflets or subvalvular apparatus, whereas secondary MR is due to geometric and functional changes of the left ventricle and/or atrium itself. In secondary or functional MR, the structure of the valve itself is normal, but left ventricular or atrial dysfunction and dilatation lead to distortion of the mitral apparatus and thus lead to malcoaptation of the mitral valve leaflets.<sup>1</sup>

Treatment options for severe MR have been medical therapy or open heart surgery for many decades. In recent years, catheter-based mitral repair options have been developed. In addition to edge-to-edge leaflet repair, several annuloplasty techniques have been reported to be safe and feasible for the treatment of secondary MR and have gained CE Mark approval. In this article, we provide a description of the key procedural steps of CE Mark– and/or FDA–approved catheter-based options for the treatment of MR.

## PERCUTANEOUS MITRAL ANNULOPLASTY Indirect Annuloplasty

For secondary MR, the surgical gold standard approach is mitral annuloplasty. Several percutaneous annuloplasty devices that mimic this approach and are delivered via the coronary sinus have been developed. The Carillon mitral contour system (Cardiac Dimensions, Inc.) is the only commercially available system using this approach. It received CE Mark approval in Europe in

2011, with more than 500 patients treated at the time of this publication.

The Carillon system is implanted using a 10-F sheath that is introduced via the internal jugular vein. The system also has proximal and distal nitinol anchors that are connected by a nitinol wire. After determining the coronary sinus dimensions with a dedicated sizing catheter and selecting the appropriate device size, the Carillon device is introduced into the coronary sinus. The distal anchor is implanted in the coronary sinus as close as possible to the anterior commissure, whereas the proximal anchor should be placed near the coronary sinus ostium (Figure 1). Direct tension is applied to the delivery system, thereby reducing the anterior-medial diameter of the mitral valve annulus. The device can be recaptured and replaced before final release, if necessary.

Although it is easy to use and has a very low procedural risk profile, several limitations have been reported with the Carillon device. Cardiac CT studies have shown that the distance between the coronary sinus and mitral annulus increases in dilated hearts, thus suggesting that indirect mitral valve annuloplasty might be less effective in

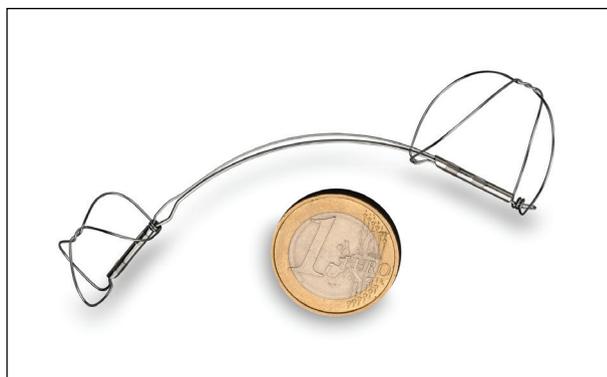


Figure 1. The Carillon device.

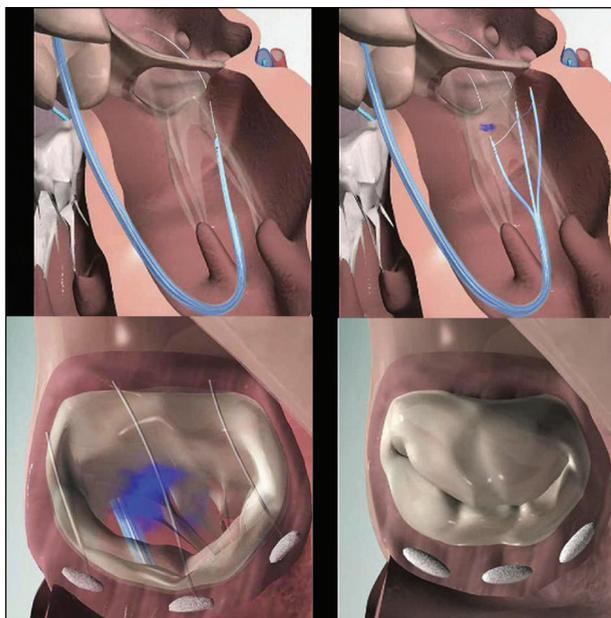


Figure 2. The Mitralign system.

patients with this anatomical presentation.<sup>4</sup> Additionally, in approximately 20% of patients, the left circumflex artery crosses inferiorly to the coronary sinus, which prohibits implantation of the Carillon device because the cinching forces of the device might compromise the circumflex artery or its major branches, inducing myocardial ischemia.<sup>5</sup>

In patients who have undergone device implantation, significant reductions have been seen in quantitative measures of secondary MR and favorable changes in left ventricular remodeling after 12 months, as well as improvement in functional capacity and quality of life. Although the acute reduction of MR severity was not as effective as compared to other interventional treatment devices, MR was persistently reduced over time during follow-up.<sup>5</sup>

The Carillon device might be a good option in patients with small annular dimensions, in which other interventional devices might induce mitral stenosis; in very dilated annuli, which prohibit, for example, the use of a MitraClip device (Abbott Vascular); or may be part of a combined approach with a MitraClip device. A randomized trial that aims to compare the effect of the Carillon device on symptoms and reduction of MR with other interventional approaches, especially the MitraClip device, for the treatment of functional MR is currently recruiting patients. Furthermore, an investigational device exemption trial designed to evaluate the effects of the treatment on MR and related symptoms will enroll 400 patients at up to 50 centers in North America, Europe, and Australia. This trial has primary safety and



Figure 3. The Cardioband device.

efficacy endpoints at 12 months and will follow patients to document long-term safety.

## DIRECT ANNULOPLASTY

### Mitralign System

Direct annuloplasty overcomes some of the limitations of the coronary sinus approach. The Mitralign system (Mitralign, Inc.) necessitates retrograde left ventricular access. The Mitralign system received CE Mark approval for the treatment of functional MR in 2016. Under transesophageal echocardiographic (TEE) guidance, the Mitralign percutaneous annuloplasty system uses a transaortic approach. With two pairs of wires, the mitral annulus is punctured using radiofrequency energy, and two pairs of pledgets are anchored in the annulus. The pledgets are connected by a Gore-Tex string (Gore & Associates) that is used to apply tension to the mitral annulus and shorten its circumference (Figure 2).

The technique has been utilized in several patients, and the results of the CE Mark approval trial have recently been published indicating favorable outcomes with regard to safety, MR severity reduction, and symptom relief.<sup>6</sup> Despite good initial results, the technique might be limited due to only partial annuloplasty, and MR may recur over time. On the other hand, the Mitralign annuloplasty device does not prohibit further treatment options (eg, other percutaneous interventions, surgical repair, or valve replacement) if the initial treatment is ineffective.<sup>5</sup> However, the company has shifted its focus toward developing a percutaneous system for treating tricuspid regurgitation, and the mitral device has not been extensively utilized since the CE Mark study ended.

### Cardioband Transcatheter Mitral Repair System

The Cardioband mitral valve repair system (Edwards Lifesciences) allows mitral valve repair that mimics surgical annuloplasty. It uses a transseptal approach that is comparable to the MitraClip procedure (Figure 3).

The Cardioband system gained CE Mark approval for the treatment of functional MR in 2015.

The Cardioband mitral repair implant includes a polyester sleeve with radiopaque markers placed every 8 mm. The sleeve covers the delivery system, which deploys the anchors. A contraction wire is mounted on the Cardioband sleeve and is connected to the adjusting spool. Activating the spool contracts the Cardioband device, thus reducing the mitral annular diameter. The implant size is adjusted under TEE guidance and can be readjusted. The implant is available in various sizes.<sup>7,8</sup>

The procedure is performed under general anesthesia with three-dimensional (3D) TEE guidance. After an echo-guided transeptal puncture, systemic heparin is administered to achieve an activated clotting time between 250 and 300 seconds throughout the procedure. The system is advanced over a super stiff guidewire into the left atrium. The delivery system is steered until the tip of the implantation catheter is securely placed at the anterior commissure. Correct positioning of the first anchoring location is crucial, and multiplanar TEE and 3D TEE views are necessary to verify correct placement. The first anchor is placed at the anterior commissure (near the P1 region), close to the leaflet hinge point.

After confirmation of the location with 3D TEE, coronary angiography may be performed to assess proximity to the left circumflex coronary artery. All anchors are released after verification of safe anchoring with a “push-and-pull” test under echocardiographic and fluoroscopic control. The Cardioband implant is deployed until the radiopaque markers of the implant catheter reach the next marker on the implant. The tip of the catheter is then further navigated to the next anchoring point along the posterior annulus. These actions are repeated until the implant catheter tip reaches the last anchoring site on the posterior commissure at the P3 region.

As the last anchor is deployed and the implant has been disconnected from the delivery system, the size adjustment tool is inserted over the implant guidewire until its distal end reaches the adjustment spool of the implant. After connection, the implant is contracted by clockwise rotation of the adjustment knob. Adequate reduction of MR severity is assessed by TEE under beating heart conditions.

The procedure has been shown to be a safe and effective method to reduce MR. In the first published study on 6-month functional and procedural outcomes, the septolateral diameters were sustainably reduced by > 30% and a MR grade reduction to  $\leq 2+$  were observed in 86% of patients. Clinical symptoms, exercise capacity, quality of life, and functional status were significantly improved.<sup>9,10</sup>

## PERCUTANEOUS MITRAL LEAFLET REPAIR

### MitraClip System

The MitraClip system is the most widely used percutaneous treatment approach for MR, with more than 50,000 patients treated to date. The MitraClip device received CE Mark approval in 2008. It is the only percutaneous mitral therapy tested in a prospective, randomized fashion comparing the device to conventional surgical valve repair or replacement.<sup>11</sup>

In the United States research trial experience, the criteria for valve suitability as well as for left ventricular size and function are strict, and multiple aspects of using the device have been published. The European experience includes patients with expanded suitability criteria without a loss of acute device efficacy.<sup>12,13</sup>

The MitraClip system itself consists of a steerable guide catheter and a clip delivery system, which includes the clip device. The clip is covered with Dacron and has two arms that are opened and closed by control mechanisms on the clip delivery system. There are “grippers” on the inner side of the clip that hold the mitral leaflets to the clip arms. Leaflet tissue is secured between the arms and each side of the gripper, and the clip is then closed and locked to effect and maintain coaptation of the two leaflets (Figure 4).

The procedure is performed under general anesthesia using fluoroscopy and TEE guidance. The right atrium is accessed via the left or right femoral vein. After transeptal puncture, unfractionated heparin is given to achieve an activated clotting time of  $\geq 250$  seconds throughout the procedure.

The ideal distance from the puncture point in the fossa ovalis to the plane of the annulus is 3.5 to 4.5 cm. In patients with severe tenting due to ischemic MR with displacement of the closure line toward the left ventricular apex or in a case where the targeted pathology is in the lateral aspect of the mitral valve, the septal puncture should be in the lower range of the mentioned optimal distance. The opposite should be considered for a medial pathology or in cases of bileaflet prolapse. As a safety



Figure 4. The MitraClip NT system.

measure, the puncture point should never be in the septum secundum.

Using 3D echocardiographic and fluoroscopic guidance, the clip is moved until the device is centered over the visible mitral regurgitant orifice. For the grasping process, the clip is closed approximately to 120° and pulled back until the mitral leaflets are captured in the arms of the clip; after proper leaflet insertion is ensured, the grippers are lowered and the clip is closed. At this point, the degree of MR reduction is assessed via echocardiography. Multiple echocardiographic views, including color and pulsed-wave Doppler, need to be used to evaluate the reduction in MR. If the MR reduction is not satisfactory or a relevant gradient > 4.5 mm Hg is found, the decision to reposition the clip or to implant a second clip can be made.

If functional results are appropriate and relevant mitral stenosis is excluded by means of echocardiography, the clip will be released from the delivery system and the delivery system and guide catheter are withdrawn. Once the system is retracted, the guide catheter is withdrawn and removed from the insertion site using figure-of-eight subcutaneous sutures, which are removed after several hours.

Novel modifications of the device, which is now called MitraClip NT, comprise easier maneuverability of the system and facilitated grasping by increased lowering of the grippers to 120° (previously 85°). Furthermore, the retraction of the clip delivery system into the guide catheter has been improved.

A coaptation length of at least 2 mm is considered ideal for efficient grasping of the mitral leaflets. In the EVEREST trials, a flail mitral leaflet, flail gap ≤ 10 mm, or flail width < 15 mm were feasibility criteria as well. The baseline mitral valve area should be > 4 cm<sup>2</sup> to avoid the creation of significant mitral stenosis after clip placement. In the European experience, the valve suitability criteria have

been expanded beyond the EVEREST criteria, but no long-term data on functional and procedural outcomes nor durability of the procedure in those patients are available.<sup>11,14,15</sup>

Potential limitations of this technique include the large device size (24-F guide catheter), technically demanding procedures, and uncertainty about the long-term durability of the results. Surgical leaflet repair has almost always been performed in combination with annuloplasty, and the lack of annuloplasty might be a limitation of this approach. The feasibility and efficacy of this technique are limited to specifically suitable anatomy and are not applicable in subsets of patients with extreme pathology of leaflets or the mitral apparatus.

### Artificial Chords

A recent change of strategy in cardiac surgery of preserving the leaflet tissue instead of resecting it encouraged the development of different approaches to implanting artificial chords into the beating heart. The NeoChord DS 1000 system (NeoChord, Inc.) allows the implantation of artificial chordae tendinae to repair mitral valve prolapse via a transapical, off-pump procedure under two-dimensional/3D TEE control.

The designated prolapsing segment is grasped using the instrument's jaws; the NeoChord is implanted and then retracted outside the heart. Under echocardiographic guidance, the NeoChord is properly tensioned to achieve correct functioning of the mitral valve leaflet. The procedure is finalized with fixation of the NeoChord on the apex of the heart (Figure 5).

Possible difficulties include mechanical stress on the myocardial and leaflet anchoring. Applying the same criticism as concerning leaflet repair when the annulus is not addressed, the future of these devices might be closely related to the success of catheter-based ring techniques. After treating 50 patients, the NeoChord DS1000 device gained CE Mark approval for primary MR in 2013.<sup>16</sup>

### CONCLUSION

In current practice, symptomatic patients with an elevated surgical risk and severe primary MR, or moderate to severe secondary MR, are typical candidates for percutaneous treatment with the MitraClip device. Careful evaluation of the echocardiographic morphology of the mitral leaflets is critical for patient selection and optimal results. Different catheter-based approaches for the treatment of functional or degenerative MR have gained CE Mark approval in recent years.

The most clinical experience exists for the MitraClip system, with more than 50,000 patients treated worldwide.

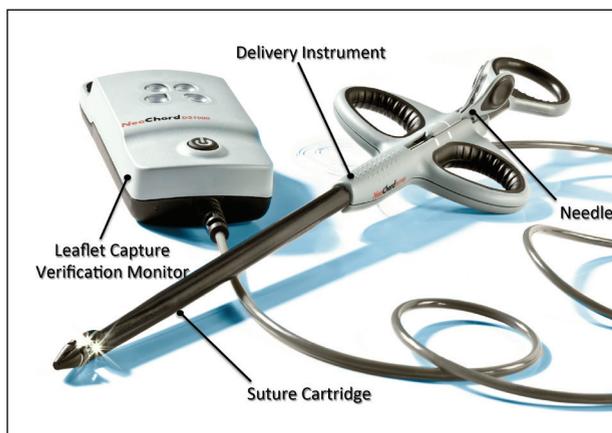


Figure 5. The NeoChord DS 1000 system.

Other devices, such as the Cardioband system, more closely mimic a surgical annuloplasty approach.

Although there are devices that reduce MR and heart failure symptoms in the setting of functional MR, none have been compared against surgical procedures in a randomized trial (except for MitraClip) nor have they been compared to standard conservative care. The impact of interventional mitral valve repair on survival is therefore an ongoing debate. ■

1. Vahanian A, Alferi O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012). *Eur Heart J*. 2012;33:2451-2496.
2. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease. *J Am Coll Cardiol*. 2014;63:e57-185.
3. Iung B, Baron G, Butchart EG, et al. A prospective survey of patients with valvular heart disease in Europe: the Euro Heart Survey on valvular heart disease. *Eur Heart J*. 2003;24:1231-1243.
4. Goodney PP, Stukel TA, Lucas FL, et al. Hospital volume, length of stay, and readmission rates in high-risk surgery. *Ann Surg*. 2003;238:161-167.
5. Schofer J, Siminiak T, Haude M, et al. Percutaneous mitral annuloplasty for functional mitral regurgitation: results of the Carillon mitral annuloplasty device European Union study. *Circulation*. 2009;120:326-333.
6. Nickenig G, Schueler R, Dager A, et al. Treatment of chronic functional mitral valve regurgitation with a percutaneous annuloplasty system. *J Am Coll Cardiol*. 2016;67:2927-2936.
7. Taramasso M, Guidotti A, Cesarovic N, et al. Transcatheter direct mitral annuloplasty with Cardioband: feasibility and efficacy trial in an acute preclinical model. *EuroIntervention*. 2016;12:e1428-e1434.
8. Maisano F, Taramasso M, Nickenig G, et al. Cardioband, a transcatheter surgical-like direct mitral valve annuloplasty system: early results of the feasibility trial. *Eur Heart J*. 2015;817-825.
9. Nickenig G, Hammerstingl C, Schueler R, et al. Transcatheter mitral annuloplasty in chronic functional mitral regurgitation: 6-month results with the Cardioband percutaneous mitral repair system. *JACC Cardiovasc Interv*. 2016;9:2039-2047.
10. Maisano F, Vanermen H, Seeburger J, et al. Direct access transcatheter mitral annuloplasty with a sutureless and adjustable device: preclinical experience. *Eur J Cardiothorac Surg*. 2012;42:524-529.
11. Feldman T, Foster E, Glover DD, et al. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med*. 2011;364:1395-1406.
12. Maisano F, Franzen O, Baldus S, et al. Percutaneous mitral valve interventions in the real world: early and 1-year results from the ACCESS-EU, a prospective, multicenter, nonrandomized post-approval study of the MitraClip therapy in Europe. *J Am Coll Cardiol*. 2013;62:1052-1061.
13. Reichenspurner H, Schillinger W, Baldus S, et al. Clinical outcomes through 12 months in patients with degenerative mitral regurgitation treated with the MitraClip device in the ACCESS-Europe phase I trial. *Eur J Cardiothorac Surg*. 2013;44:e280-288.
14. Feldman T, Kar S, Rinaldi M, et al. Percutaneous mitral repair with the MitraClip system. Safety and midterm durability in the initial EVEREST (Endovascular Valve Edge-to-Edge Repair Study) cohort. *J Am Coll Cardiol*. 2009;54:686-694.
15. Lim DS, Reynolds MR, Feldman T, et al. Improved functional status and quality of life in prohibitive surgical risk patients with degenerative mitral regurgitation following transcatheter mitral valve repair with the MitraClip system. *J Am Coll Cardiol*. 2013;64:182-192.
16. Feldman T, Young A. Percutaneous approaches to valve repair for mitral regurgitation. *J Am Coll Cardiol*. 2014;63:2057-2068.

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