

Interventional Mitral Annular Reduction Techniques

International experience with the Carillon, Mitralign, and CardioBand mitral annuloplasty devices.

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Mitral regurgitation (MR) is the second most frequent heart valve disease, and its prevalence increases with age and cardiac comorbidities.^{1,2} Compared to the aortic valve, the anatomy and function of the mitral valve (MV) and its apparatus is more complex, and there are complicated interactions between the annulus, the leaflets, the subvalvular apparatus, and the left ventricle. There are two entities that should be defined and separated for both diagnosis and treatment: primary MR, with an abnormality of the MV itself, and secondary MR, in which the MV leaflets are more or less normal, and impairment and dysfunction of the valvular apparatus is caused by pathological left ventricular (LV) remodeling in the presence of either ischemic heart disease or other forms of cardiomyopathy (Figure 1).^{3,4} Patients with secondary MR are often at advanced age with relevant comorbidities, thus increasing the risk for interventional or surgical MV therapy.⁵⁻⁸ Current guidelines recommend cardiac surgery in symptomatic patients with severe MR or in asymptomatic patients with deteriorated LV function or concomitant factors, such as atrial fibrillation or pulmonary hypertension. Surgery may also be considered in symptomatic patients with secondary MR after optimal medical management if bypass surgery is indicated.^{3,4} MV surgery in patients with secondary MR without coronary bypass indication remains controversial and is indicated only in exceptional cases. Surgical reconstruction of the MV has been considered superior over valve replacement, and annuloplasty has been the method of choice in most of these patients, although recent research suggests differently,^{9,10} with a relapse of relevant MR in up to 54% of patients 2 years after surgical MV repair.¹¹

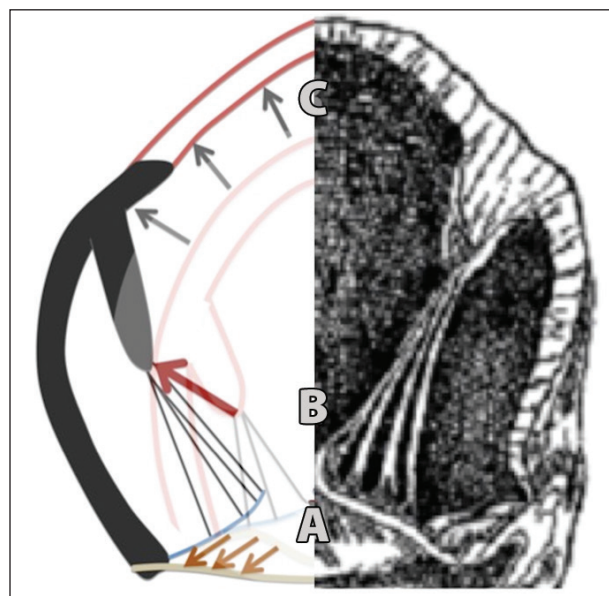


Figure 1. Two-chamber view of the left ventricle and the mitral apparatus. Dilation and distortion of the mitral annulus (A). Asymmetric or symmetric displacement of the papillary muscles (B). Global dilation and LV dysfunction may lead to dysfunction of the mitral apparatus, resulting in secondary MR (C).

Numerous interventional approaches mimicking the surgical approach have been investigated, and currently, only three devices for MV annuloplasty have received CE Mark approval for the treatment of secondary MR.

Unlike the extensive toolbox available to the mitral surgeon, transcatheter approaches for mitral annuloplasty are still limited by technical feasibility, the demand for low

invasiveness of the procedure, and other aspects, such as cost-effectiveness. This article focuses on the three currently available CE Mark–approved MV annuloplasty devices.

INDIRECT ANNULOPLASTY

The coronary sinus (CS) is in close proximity to the posterior-lateral annulus. In animal models, indirect MV annuloplasty has been demonstrated by inserting a dedicated device into the coronary sinus, thus creating continuous pressure and tension forces on the MV annulus, which leads to a decrease in annular circumference and an improvement in mitral leaflet coaptation. The Carillon Mitral Contour System (Cardiac Dimensions, Inc.), which received CE Mark approval in Europe in 2011 with more than 520 patients treated at present, is the only commercially available system still using this approach.

The Carillon Mitral Contour System is implanted using a 10-F sheath that is introduced in the internal jugular vein. The Carillon device has a proximal and distal nitinol anchor connected by a nitinol wire. After determining the dimensions of the CS with a dedicated sizing catheter and evaluating adequate device size, the Carillon device is introduced into the CS using a special guiding catheter that is part of the device kit. The distal anchor is implanted in the CS as near as possible to the anterior commissure, whereas the proximal anchor should reside near the CS ostium (Figure 2). Direct tension is placed on the delivery system, thus reducing the anterior-medial diameter of the MV annulus. Intraprocedural transesophageal or transthoracic echocardiography may be used for the assessment of acute MR reduction, and the device can be recaptured and replaced, if necessary.

Despite its easy use and very low procedural risk, several limitations of the Carillon device have been reported. Cardiac CT has demonstrated that the separation between the CS and mitral apparatus potentially increases significantly in dilated hearts compared with patients with normal hearts, suggesting that indirect MV annuloplasty might be less effective in such patients.¹² Furthermore, approximately 20% of patients present with a coronary anatomy that prohibits Carillon implantation. The left circumflex artery might cross inferiorly to the CS, and the cinching forces of the device potentially cause myocardial ischemia by compromising the circumflex artery or its major branches. This problem was observed in the AMADEUS and TITAN trials in which 15% to 17% of patients did not receive a Carillon device due to compromise of the left circumflex coronary artery.^{13,14} Another reported limitation of the second-generation devices was a relevant proportion of nitinol wire ribbon fractures, which were not associated with adverse clinical

events or outcomes. The current third-generation device wire has been tested in a model that reproduced the fractures seen in earlier versions of the device and demonstrated no recurring fractures.

Patients who received the device showed significant reductions in quantitative measures of secondary MR and favorable changes in LV remodeling after 12 months of follow-up, as well as improvement in functional New York Heart Association (NYHA) class, 6-minute walking distances, and quality of life.

Interestingly, although an acute reduction of MR grade was not as good as compared to other devices for the interventional treatment of secondary MR, MR reduction was ongoing throughout the follow-up period. The authors of the AMADEUS and TITAN trials discussed ongoing pressure on the MV annulus, with late-occurring annular and LV remodeling responsible for this “long-term” effect.

DIRECT ANNULOPLASTY

Direct mitral valve annuloplasty is considered the most promising approach for transcatheter MV treatment in patients with secondary MR. It closely reproduces the conventional surgical approach, and current publications indicate exceptional interventional results and functional outcomes.^{15,16}

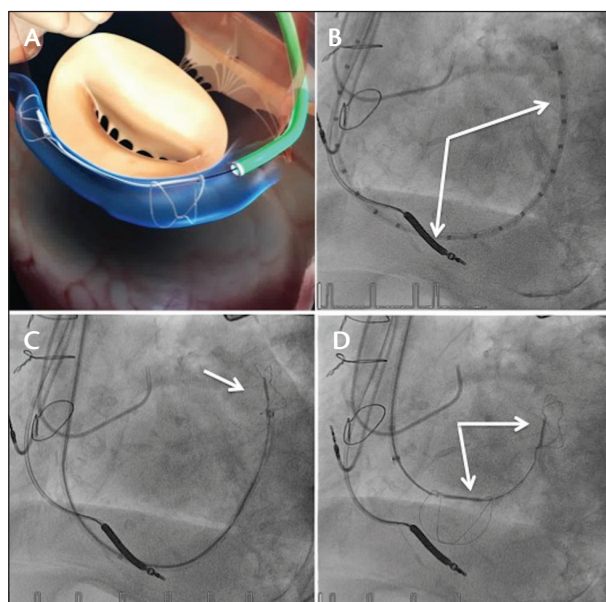


Figure 2. Carillon implantation. Illustration of the Carillon device in the CS and its relation to the mitral annulus (A). The sizing catheter (white arrow) is placed in the CS for determination of device size (B). Deployment of the distal anchor (white arrow) of the device (C). The mitral annulus is cinched after deployment of the proximal anchor (white arrow) (D).

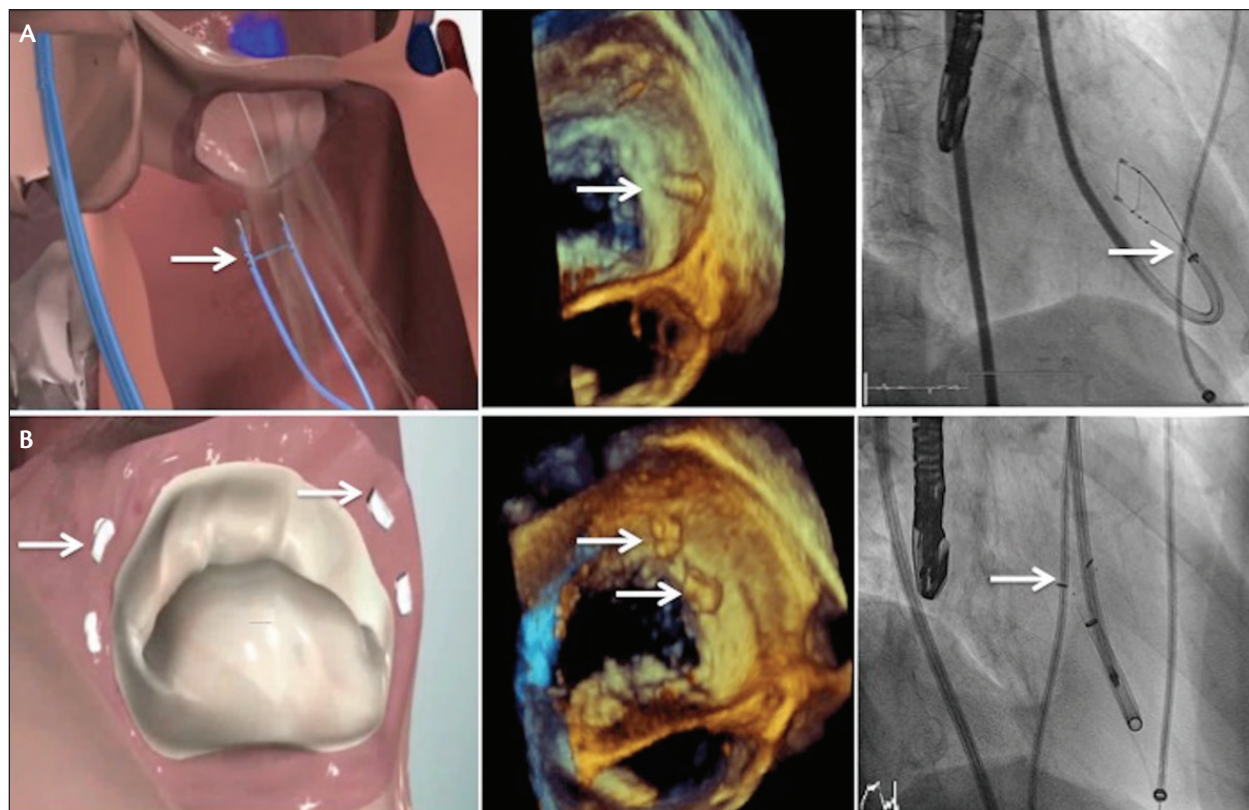


Figure 3. Steps of the Mitralign procedure. The pledgets are deployed through the “Bident” catheter (white arrows) using radiofrequency energy (A). The pledgets (white arrows) are implanted in the mitral annulus and cinched to achieve a reduction in mitral annular anterior posterior diameter (B).

The Mitralign System

The Mitralign system (Mitralign, Inc.) is a device for direct partial MV annuloplasty achieved by cinching the annulus and at least two predefined anatomical landmarks on the posterior MV annulus. The system is inserted retrograde via an arterial transventricular approach. After placing the guide catheter at the ventricular side of the mitral annulus, the MV annulus is penetrated using a radiofrequency wire. Two pairs of felt pledgets are implanted in the posterior mitral annulus (eg, next to A1–P1 and A3–P3) using a Bident catheter (Mitralign, Inc.) (Figure 3A). The pledgets are then cinched and locked by a stainless steel lock at the ventricular side of the implants to reduce the posterior circumference of the mitral annulus (Figure 3B).

Preliminary clinical experience with the second-generation Mitralign device has been reported in 15 high-risk patients with secondary MR. No periprocedural deaths were observed in this group. At 1 month, 80% of the patients had MR $\leq 2+$. Significant quality of life improvements were observed at 6 months. Reduction of the mitral annulus diameters up to 8 mm was observed in this first series of treated patients.¹⁷ Percutaneous annuloplasty with the Mitralign percutaneous annuloplasty system is

feasible and safe in high-risk patients with functional MR. The treatment initiates LV reverse remodeling and provides clinical improvement over the course of 6 months. CE Mark approval was granted in 2015.

The Valtech Cardioband

The Valtech Cardioband system (Valtech Cardio, Ltd.) is an adjustable, sutureless device delivered via a trans-septal atrial access after femoral venous puncture. The implant is a Dacron (Invista Corporation) tube that is anchored to the annulus with multiple screw anchors from commissure to commissure (Figure 4). The screw anchors are deployed from the anterolateral commissure to the posteromedial commissure in a counter-clockwise fashion at the atrial side of the mitral annulus. Controlled tension on the band reduces the annular circumference, thus reducing the degree of MR. Three-dimensional echocardiography and fluoroscopic guidance are necessary during the interventional process, which makes this procedure well controlled and safe. Once fully anchored, the implant is tensioned to create a posterior annuloplasty with reductions in mitral septal-lateral dimension of at least 30%.

The procedure is technically demanding, but to date, the interventional approach yields results closest to that of surgical ring annuloplasty, with excellent reported acute procedural success and complication rates of 0% for device-related major adverse events. MR reduction to $\leq 2+$ was reported to be 91% after 6 months, with 70% of patients having mild or no MR at 1-month follow-up. Also, functional outcome improved to NYHA class I or II by 6 months after Cardioband implantation in 81% of patients.¹⁸ The first-in-human implantation was performed in 2013 in Milan, Italy, and recently published results from a European multicenter CE Mark trial demonstrated good interventional results, favorable procedural safety, and significantly improved functional capacities.¹⁹ The Cardioband received CE Mark approval in September 2015.

CONCLUSION

Although technically challenging, transcatheter MV repair with MV annuloplasty seems the most promising approach for the treatment of secondary MR. Careful patient selection with an individualized treatment strategy will be mandatory for optimal interventional results. Patients with pronounced annular dilatation and little leaflet tethering seem to be ideal candidates for annuloplasty. In primary MR patients, annuloplasty should be considered as a complementary approach in combination with leaflet repair. ■

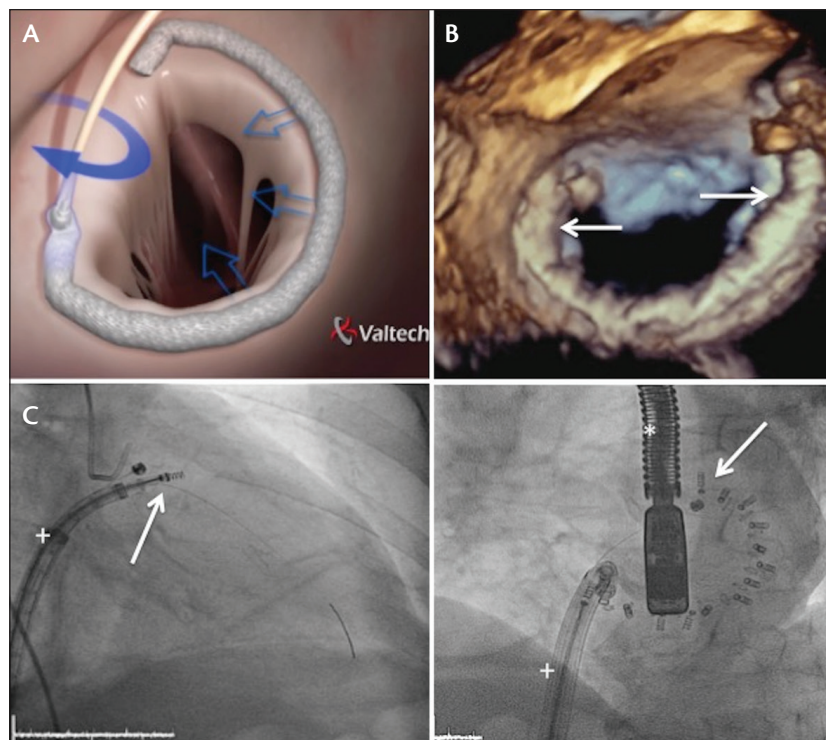


Figure 4. The Cardioband procedure. With its screw-like anchors, the Cardioband is implanted from the anterolateral commissure to the posteromedial commissure (A). Three-dimensional echocardiographic images of the implantation process and the device (white arrow) in place (B). Fluoroscopic images of the procedure and the implanted device (white arrows; *transesophageal echocardiographic probe; +guide catheter) (C, left and right panels).

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