Mitral Valve Annuloplasty

Percutaneously placed coronary sinus devices may offer a viable alternative for selected FMR patients.

BY JAN HARNEK, MD

Mitral regurgitation (MR) is common in the elderly population and is seen in approximately 6% of individuals aged 65 to 74 years, increasing to 9% to 10% of individuals older than 75 years.[1] This is almost double the incidence of aortic stenosis. The prognosis of MR is directly related to the degree of MR. Echocardiography, using either quantitative or qualitative measures, is a well-established method to determine the severity of MR.[2,3]

Structural MR may occur as a consequence of an abnormality of the mitral valve apparatus, as seen in various degenerative diseases (eg, rheumatic or myxomatous). However, in the industrialized world, severe MR is most often functional (FMR), in which the mitral valve apparatus is normal but leaflet coaptation is suboptimal. In most cases, this is the consequence of ventricular dilation resulting from ischemic coronary disease.[4] Progressive dilation of the ventricle leads to dilation of the mitral annulus, along with dislocation of the papillary muscles leading to traction on the mitral leaflets. Left ventricular dilation and MR tend to be progressive and are associated with worsening heart failure.

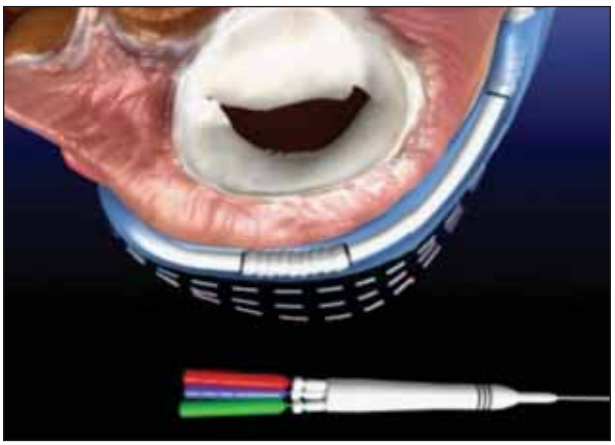
Treatment modalities for MR are limited. Pharmacological therapy and cardiac resynchronization therapy with implantation of biventricular pacemakers can reduce symptoms in selected patients.[1,5,6] However, medical therapy is unable to treat the underlying pathophysiology or halt disease progression. Mitral valve surgery is often successful, with a 90% 5-year freedom from MR grade > 2.[7] Surgical repair is generally preferred to valve replacement because it is usually effective, with a relatively lower early and late mortality.[8-12] Nevertheless, approximately one-half of patients with serious symptomatic MR do not undergo surgery due to comorbidities, advanced age, and/or poor left ventricular function.[13] For these reasons, there appears to be an unmet clinical need for new less-invasive methods for treating symptomatic FMR in patients with ischemic or dilated cardiomyopathy. Several new such catheter-based methods for treating MR are currently in various stages of development or evaluation.

DISCUSSION

"Edge-to-edge" mitral repair with the MitraClip device (Abbott Vascular, Santa Clara, CA) is an important new transcatheter technique for treating patients with MR. The method is modeled on the surgical technique developed by Alfieri and colleagues. Through a transseptal approach, a clip is implanted to approximate the posterior to the anterior leaflet of the mitral valve, creating a mitral valve with a double orifice and improved leaflet coaptation and thus reducing MR. This method has the potential to treat both FMR and structural MR that may occur with leaflet prolapse and other degenerative conditions.

However, there is considerable evidence in the surgical literature to suggest that the best long-term results with the surgical Alfieri double-orifice procedure are achieved with simultaneous implantation of an annuloplasty ring.[14] Additionally, a severely dilated annulus may be a contraindication to an edge-to-edge procedure. In the EVEREST II study, a dilated annulus (mitral valve annular area of $< 4\ cm^2$) was considered to be an exclusion for the study.[15] Thus, a large number of patients who might be excluded from repair with the MitraClip might conceivably be approached initially with a reduction annuloplasty.

Multiple approaches to percutaneous reduction annuloplasty have been pursued. Currently, the coronary sinus (CS) approaches are furthest along in evaluation. These systems were intended to replicate surgical annuloplasty by taking advantage of the proximity of the CS and the GCV to the posterior mitral annulus. Best known are the percutaneous transvenous mitral annuloplasty (PTMA) system (Figure 1), the Carillon device (Cardiac Dimensions, Inc., Kirkland, WA) (Figure 2), and the Monarc device (Edwards Lifesciences, Irvine, CA) (Figure 3). All three systems have been evaluated



(Courtesy of Viacor, Inc.)

Figure 1. The PTMA device (Viacor, Inc., Wilmington, MA) is a plastic tube that is stiffened with one to three nitinol rods that reshape the great cardiac vein (GCV). During implantation, echocardiographic imaging is used for on-line assessment of MR and efficacy.

(Courtesy of Cardiac Dimensions, Inc.)

Figure 2. The Carillon device incorporates two self-expanding nitinol anchors and a connecting nonshortening bridge segment. After expansion of the distal anchor, traction on the device shortens and cinches the GCV, thus reducing the septolateral annular diameter. The effect on MR is observed on simultaneous echocardiography. When an optimal effect is achieved, the second proximal anchor is expanded, and the device is released.

in phase I controlled multicenter studies in Europe and Canada in patients with symptomatic moderate-to-severe FMR (MR grade ≥ 2 or an effective regurgitant orifice area ≥ 0.2). It is possible that one or more of these CS devices will be available for sale in Europe soon.

The PTMA system uses a 7-F subclavian venous approach. Up to three rods of different stiffness are introduced in a multilumen catheter placed from the CS to the distal GCV. The intention is to displace the midportion (P2) of the posterior leaflet anteriorly, creating a more oval annulus with a reduced septolateral diameter and hopefully reducing FMR. The rods are attached to a small subcutaneous pocket similar to a pacemaker implant, potentially allowing the rods to be exchanged or removed at a later date. Simultaneous transesophageal echocardiography and angiography offer information on efficacy and potential compression of the left circumflex artery. Preliminary incomplete results from the PTOLEMY II study with 22 implanted patients followed to 1 year reportedly showed echocardiographic improvement in 73%, with reduction in MR of at least one grade.[16]

The Carillon device is a transjugular 9-F system and is inserted from the ostium of the CS approximately two-thirds into the GCV. Transesophageal echocardiography and coronary angiography provides information on the efficacy and potential compression of the circumflex artery. As long as the device has not been completely released, it can be removed or adjusted. The nitinol device consists of two anchors and a bridge section. After expansion of the distal anchor, traction on the device shortens and cinches the GCV, thus reducing the septolateral annular diameter. This will reduce the septolateral diameter of the annulus and thus reduce MR. At 1 year, results from the TITAN study, which included 53 patients in which 36 received an implant, have shown a 40% reduction in MR, reduction in left ventricular systolic and diastolic dimensions, an improved 6-minute walk test, and improved quality of life. In contrast, a control group of 17 nonimplanted patients showed an unchanged or worse condition.[17]

The Monarc 9-F system uses a transjugular approach and is placed from the CS ostium and reaches all the way into the anterior interventricular vein. The nitinol device consists of two anchors and a spring-like bridge section. The self-expanding anchors become securely incorporated into the wall of the CS soon after implantation. The device shortens over a 1-month period as biodegradable material incorporated into the spring-like bridge section is degraded. Because the device encircles much of the left ventricular base, from the anterior interventricular vein anterior to the left ventricle to the CS ostium posterior to the right atrium, it has been suggested that the device may allow the potential for ventricular remodeling. Computed tomographic angiography is advisable during screening to exclude patients who may be at risk of circumflex artery compression.

The long-term results from the EVOLUTION I study show that 83% of the patients are in New York Heart Association class I or II after 3 years.[18] The EVOLUTION II study was recently presented at the 2010 Transcatheter Cardiovascular Therapeutics scientific symposium. Six-month follow-up in 30 patients showed a 34% reduction in MR, reduction in left ventricular systolic and diastolic dimensions, an improved 6-minute walk test, and improved quality of life.

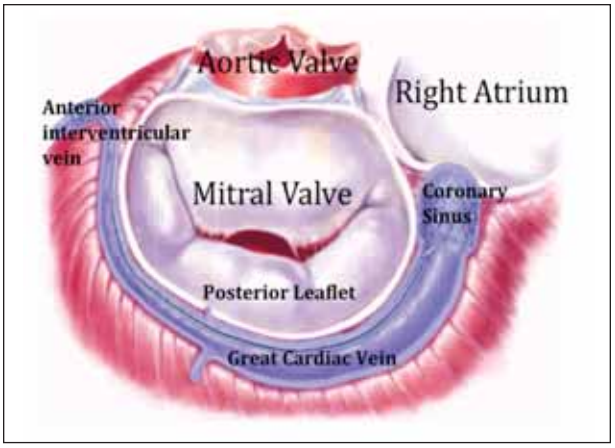


Figure 3. The Monarc is a spring-like nitinol device that has two stent-like anchors. The anchors soon become securely incorporated into the coronary venous system, after which the bridge section starts shortening, with maximal shortening achieved approximately 1 month after implantation. This shortening cinches and reduces the length of the GCV, thus reducing the septolateral diameter of the mitral annulus and thereby reducing MR.

In contrast, results from a nonimplanted control group were either unchanged or worse.

In general, the procedure for all three devices is relatively straightforward and can be performed in approximately 1 hour. Feasibility studies document that mitral valve annuloplasty using CS approaches is feasible and relatively low risk. However, long-term outcome and safety remain unproven. In all trials to date, the efficacy endpoint has been a reduction in MR by at least one grade, which is inferior to complete successful surgical repair. Whether a 1+ MR reduction is adequate to halt or slow the progressive cycle of MR and heart failure is unknown. However, because most patients with MR do not currently undergo surgical repair, a less-effective but less-invasive therapy may hold some attraction.

The risk of left circumflex artery compression is a concern in > 50% of patients in a normal population as the GCV is crossing over the artery.[19] However, because FMR is predominantly coursed by ischemia, many candidates for a CS device will have undergone protective coronary artery bypass grafting or have a chronic total occlusion of the left circumflex/M1, thereby reducing the number of patients who are at risk, as has been seen in the safety studies.[16-18] All three devices have solutions to avoid artery compression, either by the possibility of removing the device or by performing computed tomographic angiography during screening and using shorter devices.

It has been argued that because the CS/GCV is not always in the annular plane, efficacy may be lost; however, independently of one another, both in the Monarc and the Carillon trials, such a negative effect could not be demonstrated.[18,20] It has also been shown that implanted CS devices do not preclude later cardiac resynchronization therapy or mitral valve surgery.[17,18,20]

CONCLUSION

CS devices are fast and easy to implant, have acceptable safety rates (but have lower efficacy than surgery), and they may offer an alternative for selected FMR patients who are not offered surgery. ■

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