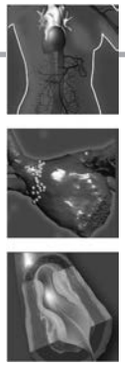

Prospects for the percutaneous repair of the mitral valve

Despite recent advances, the selection of appropriate treatment options in patients with mitral regurgitation, especially those with heart failure, represents an important clinical problem. Although mitral regurgitation is an independent predictor of worse prognosis in patients with heart failure, patients are commonly denied cardiac surgery repair procedures, owing to perceived high procedural risk and questions as to their clinical value. As a result, several less invasive techniques for percutaneous mitral valve repair have been developed and are under clinical evaluation. One of the techniques for percutaneous mitral repair is based on a surgical procedure developed by Alfieri, the so-called bow-tie mitral valve configuration. Other devices are designed to be implanted within the coronary sinus, allowing for tensioning to plicate the posterior leaflet and to reduce the septal–lateral dimension of the mitral annulus. Some of the strategies are aimed at the reduction of the annular dimensions using a ventricular or an atrioventricular approach.

KEYWORDS: heart failure ■ mitral regurgitation ■ mitral repair ■ percutaneous technique ■ ventricular dilatation

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Although much attention has recently been focused on percutaneous aortic valve therapies, there have also been continued developments in the percutaneous approach to mitral valve disease. Percutaneous treatment for mitral stenosis has become the 'gold standard' for suitable valves [1]; however, inroads have recently been made for the treatment of regurgitant valves as well. These techniques may be very attractive in comparison with currently used medical and surgical therapies [2,3], especially in the high-risk population of patients with mitral regurgitation (MR). Several novel approaches have been created and tested in animals, demonstrating the potential to percutaneously treat MR of a variety of etiologies. There is a large amount of data indicating that MR is an independent predictor of worse prognosis in patients with heart failure [3–13] and significantly affects their quality of life [14–21]. This implies that there is an important potential clinical significance to the implementation of less invasive techniques of mitral valve repair.

Although current cardiac surgery techniques remain the standard of care in patients with MR, patients with advanced heart failure are often denied surgery. In addition, current guidelines do not indicate the need for cardiac surgery in patients with ischemic MR who are not candidates for revascularization, have low ejection fraction and are symptomatic [3,15,21]. Thus, new techniques with low procedural risk may be an attractive option in these patients.

There have been several approaches for the percutaneous treatment of MR [22–26]. Some have modeled their percutaneous treatment on the surgical technique developed by Alfieri, the so-called bow-tie mitral valve configuration. Others have attempted variations on a modified annular reduction. These have included implanting a device within the coronary sinus, a structure conveniently located in proximity to the mitral annulus, allowing for tensioning to reduce the septal–lateral dimension of the mitral annulus. Alternative strategies to reduce the annular dimensions have used a ventricular or an atrioventricular approach.

Edge-to-edge technique

At present, the therapeutic approach that has been most studied has been the percutaneous approach to creating an Alfieri stitch binding the two mitral valve leaflets through the use of one or two clips or sutures in the more central aspects of the leaflets. Two different companies have developed technologies to develop this edge-to-edge concept; however, one (MOBIUS, Edwards Lifesciences Corp., CA, USA), using a stitch to bind the two leaflets, has abandoned further development at this time. The other approach, (MitraClip®, Evalve, now Abbott Vascular, CA, USA), using clips, has been studied in the Endovascular Valve Edge-to-Edge Repair Study (EVEREST) series of trials, and has received the CE mark in Europe, where the technology

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is now commercially available (Figure 1). This technology is used in sedated patients to allow for transesophageal guidance [24]. A transeptal puncture is performed to allow placement of a 24-Fr catheter-based system into the left atrium, via the femoral vein. Using a series of controls providing 3D maneuverability, the device is manipulated across the central part of the mitral valve. The arms of a clip are then used to grasp the two leaflets of the mitral valve and are then locked into place, creating the bow-tie configuration. If suitably placed, and MR is sufficiently minimized, the clip can then be released from its delivery system. If optimal placement is not achieved, the arms can be re-extended, releasing the mitral leaflets. The device can be safely pulled back into the left atrium and repositioned or removed. A second clip can be placed if insufficient reduction in MR is noted after a single clip.

This type of technology can be used in some valves with organic disease, such as mitral valve prolapse or flail leaflet, provided there are certain anatomic requirements to ensure that there is suitable anatomy for clip-capture of the two leaflets. Thus, there needs to be adequate coaptation of the leaflets, and there cannot be clefts that are too large.

This technology may also be applied to certain patients with functional MR. The term functional MR is used when leaking of the mitral valve occurs as a secondary process, which is not due to inherent abnormalities in the mitral valve apparatus. The MitraClip has been used in patients with functional MR, provided there is not so much annular dilation to inhibit leaflet coaptation. Owing to these anatomic constraints, there have been limitations in terms of left ventricular size and degree of dysfunction in which this therapy has been applied in studies of patients with functional MR thus far.

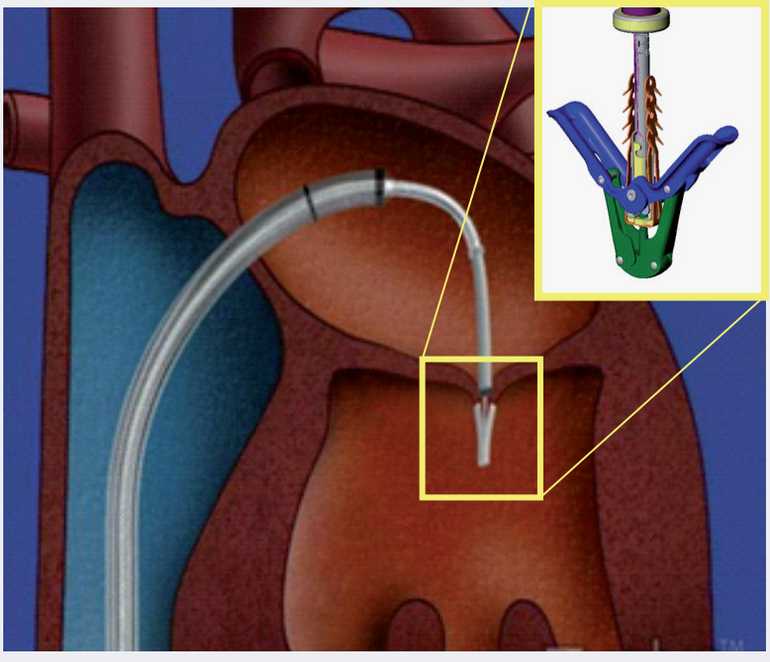

Figure 1. MitraClip® device (Abbott Vascular, CA, USA). The clip holds the edges of the mitral leaflets to mimic the Alfieri technique.

Clinical studies evaluating the MitraClip® edge-to-edge device

The EVEREST series of studies have assessed the safety and feasibility of the MitraClip system, in preparation for a pivotal trial randomizing this therapy to surgical mitral valve repair. EVEREST I was the initial feasibility, safety and efficacy study and consisted of 55 patients [2]. There was a roll-in arm for EVEREST II to provide some experience to the investigative sites prior to randomization of patients to surgery or device therapy, resulting in 52 patients receiving the MitraClip therapy in a nonrandomized manner. The results of these combined 107 patients have been presented [2]. In addition, data from a high-risk registry of 78 patients have been presented, but not yet published. These represented patients who had characteristics that made them ineligible for enrollment in the randomized trial. Data from the ongoing EVEREST II Real World Expanded Multicenter Study of the MitraClip System (REALISM) continued access registry have not yet been published.

Patients in EVEREST I and the roll-in for EVEREST II were included if they met class I indications for mitral valve surgery based upon the 1998/2006 ACC/AHA Joint Task Force Recommendations for valvular heart disease [3]. In addition, patients were required to have a regurgitation jet associated with the A2-P2 segments, have a coaptation length of at least 2 mm and a coaptation depth of no more than 11 mm. Patients were excluded for an ejection fraction of 25% or less or a left ventricular internal diameter in systole greater than 55 mm. Thus, patients with more severe forms of functional MR were not included. In this cohort of 107 patients, 21% were considered to have pure functional MR, with the rest having some form of degenerative mitral valve disease.

In this initial experience, the clip was unable to be placed in 10% of patients, with 61% receiving one clip and the rest two clips. There was no procedural mortality. A total of ten patients had a major adverse event by 30 days

(9.1%), including one death, three transseptal complications, four patients with major bleeding requiring periprocedural transfusions (and an additional patient with major bleeding after referral for surgical mitral valve repair owing to a failed MitraClip procedure) and two patients with mechanical ventilation for more than 48 h. A total of ten patients had surgery within 30 days after a failed MitraClip procedure. No patients had a clip embolization. Partial clip detachment occurred in 9% of patients, generally identified based on routine echocardiographic control.

In this initial experience, 74% of patients had acute procedural success, defined as successful clip implant with a reduction of MR of two or more. At 6 months, 76 patients had follow-up echocardiography and 66% of these had a MR of two or more. Mitral valve surgery was performed owing to recurrent MR within the first year of follow-up in 8% of patients. Overall, at nearly 2-year follow-up, 70% of patients remained free from surgery. There were no reports of surgical complications related to the previously attempted MitraClip procedure in patients undergoing surgery, with the majority of patients having successful repair of the mitral valve, and only 13% having mitral valve replacement. In total, 66% of patients were free of death, cardiac surgery or a MR greater than two at 1 year, in a population of patients who otherwise would have been offered surgery for their MR.

Percutaneous approaches to functional mitral regurgitation

While the MitraClip was used to treat patients with both organic and functional MR, the other percutaneous devices are directed at secondary, nonorganic MR. However, there are far more patients with functional MR than have an organic etiology. Since congestive heart failure is so prevalent, the incidence of functional MR may therefore be estimated as being perhaps ten-times greater than the incidence of organic mitral or aortic valve disease [4–6]. Functional MR is surprisingly common, occurring in approximately 65% of patients with dilated cardiomyopathies, with over 40% of patients having more than mild MR [7–14].

In addition, patients with MR owing to organic mitral valve disease have accepted and recommended invasive options in surgical mitral valve repair or replacement. By contrast, surgery remains controversial in patients with functional MR, owing in part to the higher risk of surgery in patients with poor left ventricular function and congestive heart failure. Current American College of Cardiology (ACC)/American Heart Association (AHA) guidelines have given surgical repair a IIb indication for functional MR [3]. The European guidelines also give a IIb indication (usefulness is less well-established) for surgical repair of an ischemic valve in patients who are not undergoing revascularization, and no recommendations are provided for patients with nonischemic functional MR [15].

Patients with functional MR are currently underserved with standard recommended therapies, as they represent a high-risk cohort of patients who are more likely to suffer from limiting symptoms. Studies looking at functional MR in association with a nonischemic-dilated cardiomyopathy, an ischemic cardiomyopathy or a combination of the two have all identified that functional MR is associated with increased mortality [7–10,14], worsening hemodynamic parameters [9,11] and higher likelihood of symptomatic congestive heart failure, as well as worse functional classification [9]. These less favorable clinical parameters have even been shown to be present when the MR is mild. In addition, it is likely that the presence of resting MR is the 'tip of the iceberg', as several studies have demonstrated that patients whose functional MR worsens with exercise are more likely to have symptoms and have a worsened prognosis, compared with those individuals whose MR does not worsen with exercise [16–20].

Therefore, functional MR may be considered to be underappreciated in patients with congestive heart failure and/or cardiomyopathy. Part of the reason for this underappreciation is likely to be caused by a lack of therapeutic options. Surgical treatment has not become the standard of care, nor is it supported by guidelines, for patients with symptomatic functional MR, with the exception that it is commonly carried out when patients are undergoing coronary artery bypass graft surgery to treat an ischemic etiology of cardiomyopathy [15,21]. Part of the reluctance to surgically treat the mitral valve of patients with functional MR is the recognition that these patients are at high surgical risk given their underlying cardiomyopathy. In addition, there are no randomized data to demonstrate whether surgical correction of functional MR has a beneficial effect on survival, both independently on procedural risk and taking into account the risk related to the surgery [27]. Therefore, it is attractive to consider a less invasive therapy to treat the functionally incompetent mitral valve.

There are a great variety of innovative therapies that have been proposed. Some of these have taken advantage of the close anatomical

relationship of the coronary sinus/great cardiac vein to the posterior mitral annulus (Figure 2). Blood that supplies the heart via the coronary arteries returns to the venous system by way of venous drainage and coalesces into the great cardiac vein, which lies in the posterior atrioventricular groove between the left atrium and left ventricle. The great cardiac vein becomes the coronary sinus, which drains into the right atrium. The great cardiac vein/coronary sinus is located slightly more on the atrial side of the atrioventricular groove, which is slightly superior to the mitral annulus. Several therapeutic approaches have proposed placing a device within the coronary sinus/great cardiac vein in order to place some force on the mitral annulus, to reduce the septal–lateral diameter of the mitral annulus and/or to 'cinch' the mitral annulus. One of these therapies, the P3 system [22], has stopped investigations, but three other companies have ongoing clinical research programs, evaluating the Monarc™ device (Edwards Lifesciences, CA, USA), the Percutaneous TransMitral Annuloplasty (PTMA) device (Viacor, Inc., MA, USA) and the Carillon® Mitral Contour System™ (Cardiac Dimensions, Inc., WA, USA).

Some of the considerations that each company has faced in evaluating this therapy include: first, how to get the device to provide tension on the system without slipping or fracturing; second, what the force and degree of tension applied to the mitral annulus is and how that relates to efficacy in reducing MR; and third, how to avoid compromising coronary arteries, which also run in the atrioventricular groove, specifically the circumflex coronary artery and its branches. Although each company has addressed these issues somewhat differently, each has also required device iterations upon initially testing the devices in humans. Much of the data available at this time reflect the early evaluations of these therapies, while investigators are exploring early safety and efficacy and identifying the need for device improvements. Therefore, the available data may be viewed as hypothesis-generating, providing information justifying further study.

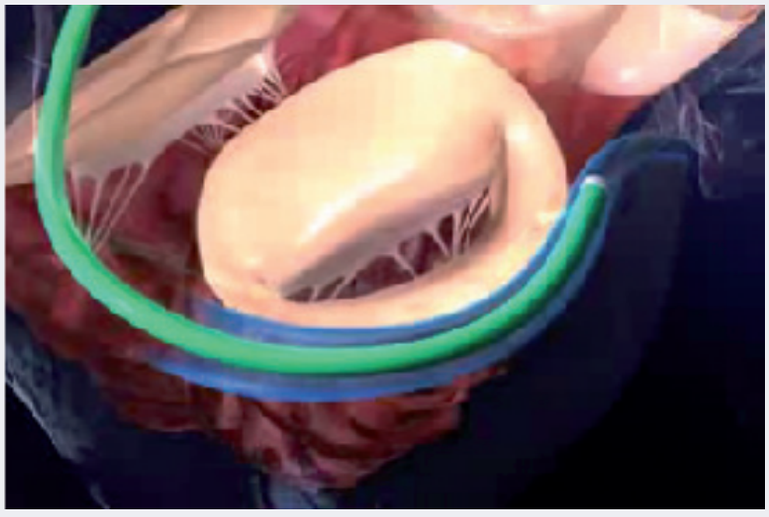

Figure 2. Relationship of the coronary sinus/great cardiac vein to the posterior annulus of the mitral valve. A catheter (which may enter from the internal jugular or subclavian veins) has been placed into the coronary sinus and advanced into the great cardiac vein nearly to the anterior interventricular vein (the termination of the great cardiac vein).

Techniques for transcoronary sinus mitral repair

The Monarc device is composed of two nitinol self-expanding stents with a connecting bridge (Figure 3). Within the bridge are dissolvable spacers. At body temperature the spacers slowly dissolve, leading to a foreshortening of the bridge and creating a reductive force on surrounding structures. The distal stent is designed to be placed within the anterior interventricular vein, which is the tributary vessel of the great cardiac vein furthermost from the coronary sinus, running near the ventricular septum. The proximal stent is placed in the coronary sinus. Thus, as the spacers in the connecting bridge dissolve, a foreshortening force is created with the intention of cinching the mitral annulus.

The PTMA device of Viacor is composed of a catheter that is placed via the right subclavian vein through the coronary sinus/great cardiac vein into the anterior interventricular vein distally, with the proximal aspect left in a pocket next to the subclavian vein, similar to a pacemaker. Into this catheter, one to three stiffening rods can be placed, which act to push the great cardiac vein in, thereby reducing the septal–lateral diameter. The choice of how many stiffening rods to be placed may be made based on efficacy, as well as the impact on coronary arteries.

The Carillon Mitral Contour System is composed of two nitinol self-expanding wire-form anchors with a nitinol curvilinear bridge. It is placed via the right internal jugular vein, with the distal anchor to be placed in the great cardiac vein; manual tension is then applied via the delivery system to plicate the periannular tissue, with delivery of a proximal anchor into the coronary sinus (Figure 4). This device has the advantage of being recapturable and removable

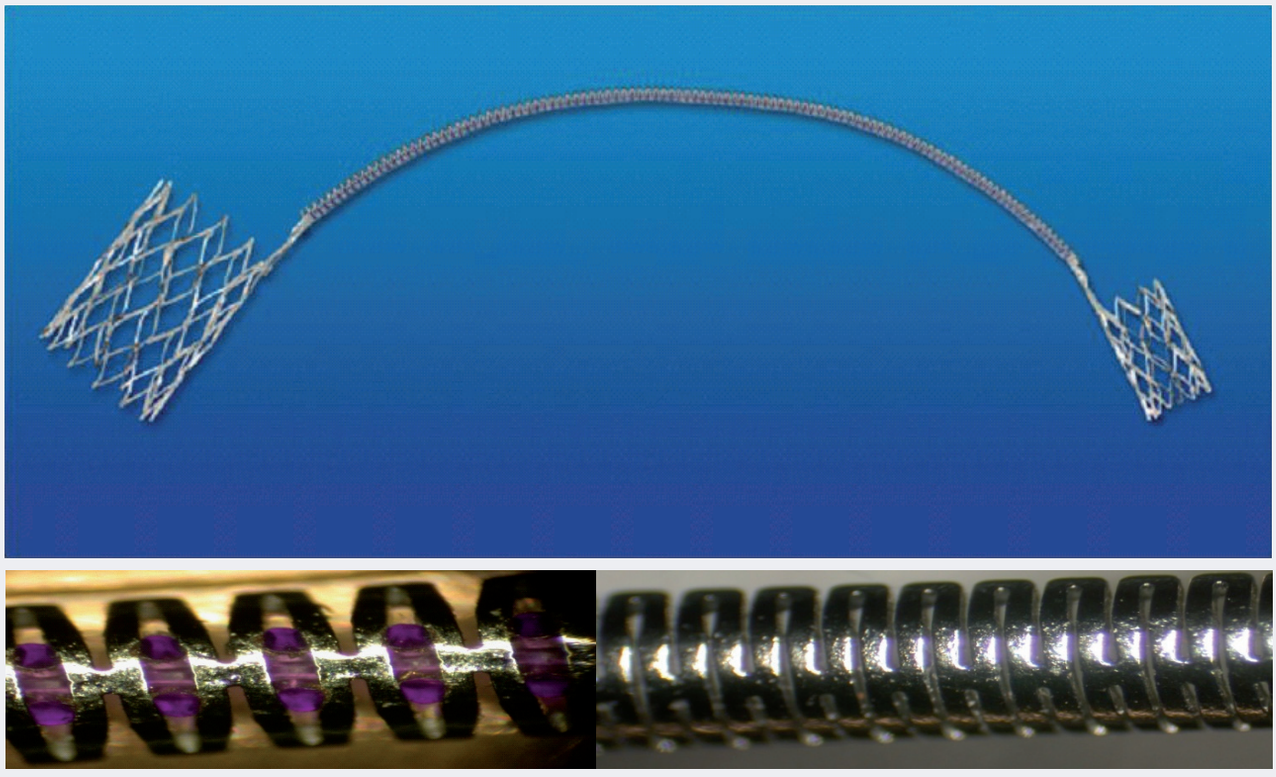

Figure 3. Monarc™ device (Edwards Lifesciences, Inc., CA, USA). This device consists of two nitinol anchors and a connecting bridge (top picture). The bottom pictures show details of the connecting bridge, with dissolvable spacers (left) and the foreshortened bridge after dissolution of the spacers (right).

until it is released from its delivery system, which may be carried out if there is inadequate efficacy in reducing MR or if coronary artery compromise is noted.

Another coronary sinus based device, mitral valve cerclage annuloplasty, has not yet been tried in humans, but results in animals have been reported [23]. This technique involves placing a wire into the coronary sinus, then puncturing from the anterior interventricular vein into a right heart chamber and snaring the wire. Traction can be applied to cinch the mitral valve.

The Monarc device was tested in the Clinical Evaluation of the Edwards Lifesciences Percutaneous Mitral Annuloplasty System for the Treatment of Mitral Regurgitation (EVOLUTION) I study, which was a safety feasibility study. This study was not designed to formally address clinical efficacy end points, although some data are available in a subset of patients. In the 72 patients enrolled, 59 received implants, with anatomic reasons limiting implants in the rest. All the patients had cardiomyopathy with 2–4+ MR, with 57% being symptomatic. The results of the first five patients were published, as this demonstrated a proof of efficacy [24]. Of the five patients, four received a device, and an acute reduction in MR was observed in three of the four patients. In these three patients, bridge separation occurred with return of MR. Thus, this therapy demonstrated effectiveness when the device was intact, and a lack of efficacy with loss of integrity. The device has since been redesigned to avoid separations. Data have recently been presented on 2-year efficacy in a subset of patients with available data. In 21 patients, the MR grade was reduced from a mean of 2.3 to 1.9 at 2 years ($p = 0.01$), and in 24 patients the New York Heart Association (NYHA) classification was reduced from 2.7 to 2.0 at 2 years ($p = 0.002$). Using quantitative assessments of MR, there appeared to be little deterioration from 1 to 2 years. A larger clinical study has been initiated in Europe, termed EVOLUTION II.

The PTMA device of Viacor has primarily been tested acutely, with only a few patients receiving a permanent implant [25]. However, several patients have received a device with immediate reduction in MR. In the few patients with permanent implantation, a reduction in

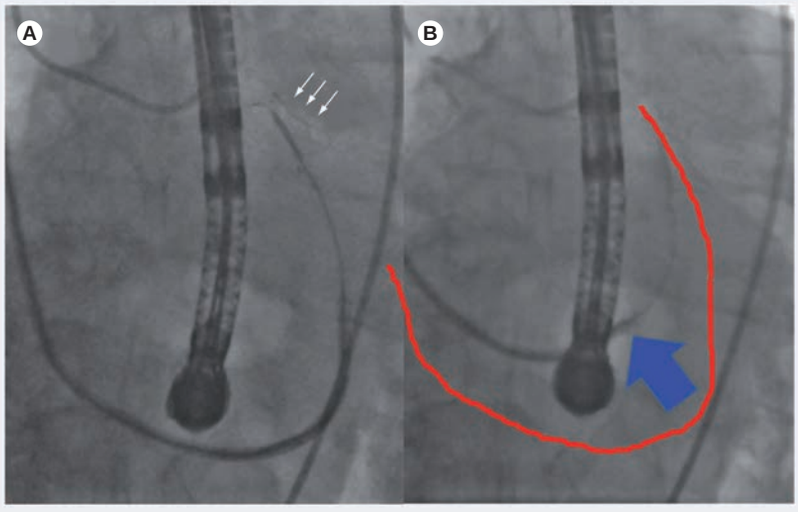

Figure 4. Carillon® Mitral Contour System™ (Cardiac Dimensions, Inc., WA, USA). (A) Carillon® device has been placed in the coronary sinus with a distal anchor (white arrows) deployed in the distal part of the great cardiac vein. **(B)** Tension is applied to the delivery system, resulting in tissue plication and reduction in functional mitral regurgitation.

mitral annular dimensions were demonstrated, and observed to persist without change over several months. A finalized version of this device is now being tested in Europe in the Percutaneous Transvenous Mitral Annuloplasty (PTOLEMY) II registry.

The Carillon Mitral Contour System has been studied in the Carillon Mitral Annuloplasty Device European Union Study (AMADEUS) [26]. This study looked at symptomatic patients with dilated (ischemic and nonischemic) cardiomyopathy, depressed left ventricular ejection fraction and 2–4+ MR as assessed by an echocardiographic core laboratory. Implantation of the Carillon device was attempted in 48 patients, with 29 receiving implants. The reasons for nonimplantation include distal anchor slipping of an early version of the device (resolved with minor redesign), inability to access the coronary sinus/great cardiac vein, insufficient reduction in MR and/or coronary artery compromise. Although coronary arteries were crossed in 84% of cases, coronary artery compromise limited implantation in only 15% of cases. There were three non-ST-elevation myocardial infarctions in this study, but impingement of the circumflex artery was not definitively demonstrated in any case. In two of these cases the patients did well, without clinical symptoms and improvement in clinical and echocardiographic parameters. In one, the event was clinically relevant, but no clear obstruction was observed. This patient developed worsening of renal failure and died 3 weeks later – the only procedural (within 30 days) death in the study. The overall 30-day major adverse event rate was 13%, which appears to be acceptable since in this high-risk cohort, there is a greater than 20% predicted 1-year mortality rate, and half of the complications were related to vascular access. Notably, a subsequent European study (Tighten the Annulus Now [TITAN]) has completed enrollment and there was only one 30-day complication in the 53 patients enrolled, providing a major adverse event rate of less than 2%. Also noted incidentally in AMADEUS were two subtle breaks in the wire-forms of the proximal anchor. These were not associated with clinical events and were identified by careful scrutiny of routine x-rays.

In AMADEUS, efficacy was assessed using a variety of modalities. MR was assessed by a core laboratory using quantitative assessments. Overall, in AMADEUS, there was a 27% quantitative reduction in MR (Figure 5). Clinical parameters improved as well. At baseline, 88% of patients were in NYHA class III or IV, whereas at 6 months, only 12% of patients receiving an implant were in NYHA class III or IV. There were marked improvements in functional capacity at 6 months, as assessed by 6-min walk tests (96 m improvement; $p < 0.001$), as well as in quality of life tests (22-point improvement in the Kansas City Quality of Life Questionnaire; $p < 0.001$).

Other techniques & devices

As previously mentioned, the PS3 system has discontinued investigations. This novel approach provided transatrial tension on the mitral annulus by linking a semirigid bar in the coronary sinus to a septal occluder device placed at the atrial septum. Animal studies and implantation in three patients demonstrated acute reduction in MR. In addition to Mobius as previously mentioned, iCoapsys (Myocor, now Edwards Lifesciences Corp., CA, USA) suffered from inadequate resources to continue further study, despite implantation in two out of three attempts resulting in successful reduction in MR. This technology was a percutaneous modification of a surgical approach to reduce left ventricular dimensions [28]. After obtaining pericardial access, pads were placed outside the left ventricle in anterior and posterior locations, with a tensioning cord connecting the two running through the left ventricle. Although procedurally complex, it had the advantage of addressing the myocardial dilation component, which is an important contributor to functional MR.

Several companies are attempting to reduce annular dimensions more directly, using a ventricular approach. The QuantumCor Endovascular Device (QuantumCor, CA, USA), which is undergoing preclinical testing, applies radiofrequency energy via an endloop catheter placed anterogradely around the mitral annulus via a transeptal puncture. The energy is designed to induce collagen shrinkage and resultant annular reduction, and has achieved approximately 20% such reduction in animal models.

The Mitralign Percutaneous Annuloplasty System (Mitralign, Inc., MA, USA) applies annular sutures into the ventricular aspect of the mitral annulus via a 14-Fr catheter from the femoral artery retrogradely across the aortic valve. A proprietary deflectable catheter is used to deliver connected pledgets around the mitral annulus, which are then tightened to cinch the posterior annulus more directly than if carried out using the coronary sinus approach. This has been performed in a small number of patients in Europe and Africa, and first-in-man studies are being planned.

The AccuCinch® device (Guided Delivery Systems, CA, USA) also approaches the ventricular aspect of the mitral annulus retrogradely across the aortic valve with a 14-Fr catheter. The proprietary catheter is used to deliver multiple anchors attached to a cable, which can then be plicated to provide a cinching force upon the posterior aspect of the mitral annulus. The device is adjustable and removable based on real-time efficacy assessment. This therapy is starting first-in-man studies.

Finally, two companies are working on percutaneous implantation of prosthetic mitral valves, Endovalve (Endovalve, Inc., NJ, USA) and CardiAQ Valve Technologies (MA, USA). Both are in preclinical stages of development. The Endovalve design is anticipated to be based on a trans-septal delivery of a foldable, nitinol device. Current studies are using a surgical access via the right atrium and are in preclinical testing [101].

Concluding remarks

Several different approaches to percutaneously treat MR are in various stages of development. Results from the EVEREST II randomized trial comparing the MitraClip to standard surgical repair will be presented in 2010. Several devices using the coronary sinus access as a means to reduce mitral annular dimensions have shown the ability to reduce functional MR, demonstrating the 'proof-of-concept' that this approach is feasible. Ongoing studies are being performed to further assess the safety and efficacy of this approach. Iterative devices and/or technique modifications are commonly required during device development as studies are transitioned from animals to humans. It is attractive to consider combining these percutaneous therapeutic approaches to mimic surgical strategies in part. For example, a direct or indirect annular reduction may be combined with an edge-to-edge leaflet repair to enhance the overall reduction in MR. However, these evaluations will necessarily follow demonstration of the value and risk–benefit of each approach individually, before combined therapies can be tested. As with every novel technique and therapy, since percutaneous treatment of MR is at an early stage of clinical experience, there have been limited long-term observations. Any new technique may have potential drawbacks. Both long-term follow-up studies and comparative randomized trials are needed to establish the potential role of these techniques in clinical practice.

Future perspective

Since MR is known to independently worsen the prognosis in patients with heart failure, there may be a need to apply techniques of mitral repair, potentially to a large segment of the heart failure population. Although improvements in cardiac surgery techniques and implementation of better postoperative patient care may allow for surgical mitral repair at an acceptable procedural risk, patients with low ejection fraction and advanced heart failure are often considered to be less than ideal candidates for surgery. Cardiac surgery procedures will probably remain

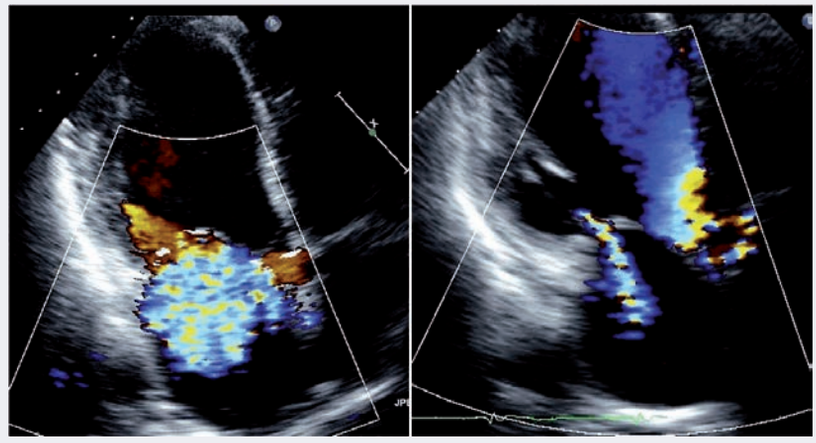

Figure 5. Color Doppler echocardiograms before (left panel) and 1 month after (right panel) implantation of a Carillon® (Cardiac Dimensions, Inc., WA, USA) device, demonstrating a marked decrease in mitral regurgitation.

an important option for patients who are otherwise candidates for surgical revascularization or have marked organic mitral valve abnormalities. Percutaneous techniques may be attractive approaches in patients with no need for surgical revascularization, perhaps most importantly in patients with low ejection fraction and advanced heart failure. Edge-to-edge technique will probably be an option in patients with MR and a certain degree of organic mitral valve disease, as it is currently considered to be important that some level of remaining coaptation is needed for successful clip implantation. Patients with pure functional regurgitation – that is, with ventricular dilatation and less leaflet coaptation – may benefit from coronary sinus techniques. Percutaneous implantable mitral valves are at very early stages of development and owing to major technical and anatomical challenges still require further development before they are ready for clinical applications.

Financial & competing interests disclosure

Steven L Goldberg is an employee of Cardiac Dimensions Inc. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties. No writing assistance was utilized in the production of this manuscript.

Executive summary

- Mitral regurgitation is known to significantly worsen the prognosis in patients with heart failure.
- Cardiac surgery remains an effective treatment of mitral regurgitation, but owing to high operational risk, it is commonly denied, especially in patients with low ejection function.
- The main goal of new percutaneous techniques for treatment of mitral regurgitation is to minimize the regurgitant volume, decrease heart failure symptoms and improve both survival and quality of life.
- The MitraClip® (Abbott Vascular, CA, USA) technique requires septal puncture and functions by placing one or two clips on the mitral valve leaflets mimicking the surgical Alfieri techniques. It has been applied in both functional cases and some cases of organic mitral regurgitation.
- Transcoronary sinus devices including the Monarc™ device (Edwards Lifesciences, CA, USA), the Percutaneous TransMitral Annuloplasty device (Viacor, Inc., MA, USA) and the Carillon® Mitral Contour System™ (Cardiac Dimensions, Inc., WA, USA) are implanted into coronary veins and exert external pressure on the mitral annulus, resulting in improvement in leaflet coaptation.
- Other percutaneous techniques to treat mitral regurgitation include direct valvuloplasty devices and modification of atrial or ventricular size, as well as mitral valve replacement techniques that are at the early stages of development.
- Establishing the clinical value of percutaneous techniques to treat mitral regurgitation will require randomized trials.

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