

Percutaneous Mitral Valve Repair Devices Beyond MitraClip

A review of devices in development for the percutaneous treatment of mitral regurgitation.

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Mitral regurgitation (MR) is present in 1.7% of the population, 7% of people older than 64 years, and 56% of individuals with congestive heart failure. MR is a major cause of heart failure and disability.¹ Severe MR compromises left ventricular function, induces pulmonary hypertension, alters the architecture of the heart, which predisposes the patient to develop atrial fibrillation.² This article reviews some of the newer methods of percutaneous treatment for MR that are being developed. Although the MitraClip device (Abbott Vascular) has been available in Europe since 2008 and has been used in more than 16,000 cases, this review highlights other devices that are being tested to treat MR, as more than one approach may be useful to percutaneously treat MR in high-risk surgical patients.

ANATOMY AND PHYSIOLOGY

Classification of MR is dependent on whether there is a structural abnormality of the valve leaflets or chordae (called *degenerative* or *primary MR*) or if the regurgitation is due to left ventricular dilation producing valve dysfunction (called *functional* or *secondary MR*). The most common cause of structural MR is valve prolapse due to myxomatous degeneration and chordal stretching. Functional MR is pro-

duced by separation of the valve leaflets due to dilatation of the mitral annulus secondary to left ventricular dysfunction.³ The annulus of the mitral valve is made up of fibro-collagenous tissue, creating an asymmetric opening.⁴ The annulus is attached to the mitral-aortic fibrous continuity anteriorly and is therefore part of the aortic valve interleaflet triangle between the noncoronary and left coronary cusps. The supporting trigons contain conduction tissue and may be injured during valvular repair or replacement. Significant MR causes volume overload that remodels the left ventricle, producing a more spherical-shaped ventricle. This change in LV geometry is associated with retraction of the papillary muscles and chordae, which widens the separation of the mitral leaflets, further exacerbating the volume of regurgitation. The posterior annulus of the mitral valve is composed of muscular tissue and is therefore capable of dilating, which produces functional MR.⁵

ANNULOPLASTY VIA THE CORONARY SINUS

Just as MitraClip is a percutaneous simulation of a surgical technique to reduce MR, there have been several attempts to percutaneously simulate surgical mitral annuloplasty. The coronary sinus and the great cardiac vein parallel the posterior leaflet of the mitral valve and posterior annulus. The

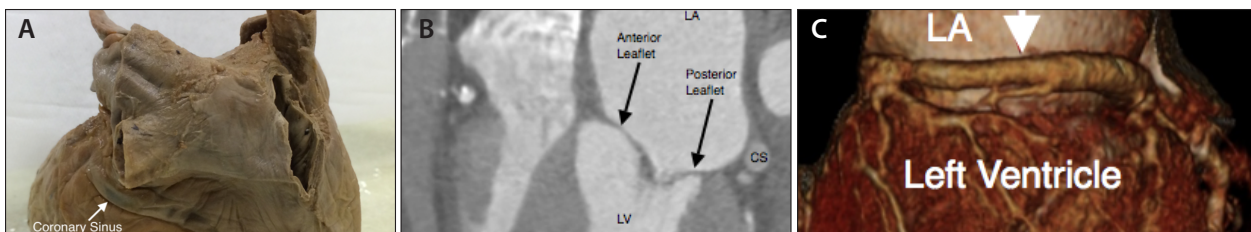


Figure 1. Anatomy of the posterior heart showing the coronary sinus circling around the left atrium and just superior to the mitral annulus and left ventricular inflow (A). CT image of the mitral valve showing the coronary sinus (CS) just lateral and superior to the mitral annulus (B). CT reconstruction of the coronary sinus (arrow) encircling the left atrium (C).

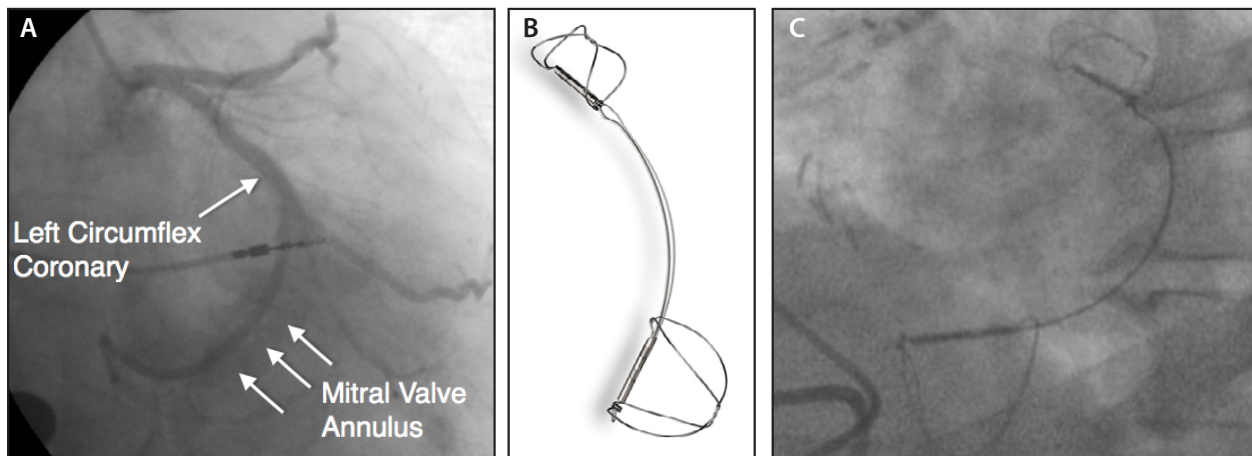


Figure 2. The position of the circumflex coronary artery and calcified annulus of the mitral valve (A). The Carillon annuloplasty device (B). The Carillon device implanted in the coronary sinus around the annulus of the valve (C).

coronary sinus runs approximately 0.5 to 1 cm on the superior atrial side of the mitral valve annulus. A device placed within the coronary sinus could potentially plicate the annulus tissue and “cinch” the mitral valve leaflets by pulling together the tissue just above the mitral annulus to approximate the mitral leaflets (Figure 1). The circumflex coronary artery also parallels the annulus of the mitral valve.⁶ In up to 27% of patients, the circumflex or obtuse marginal artery courses under the vein and could be compromised during plication of the tissue with coronary sinus annuloplasty.⁷ Venous access through the right internal jugular vein and use of the coronary sinus entrance into the right atrium does, however, afford a lower risk of vascular complications compared with transseptal or left ventricular approaches.

The Carillon mitral contour system (Cardiac Dimensions Inc.) is made of a central nitinol ribbon and a distal anchor, which is positioned in the great cardiac vein near the junction with the anterior-interventricular vein, and a proximal anchor, which is positioned at the ostium of the coronary sinus. The anchor height sizes are determined by measuring the coronary sinus venous diameter and adjusting for compliance of the venous tissue. Access is achieved with a 9-F sheath via the right internal jugular vein under ultrasound and fluoroscopic guidance. The coronary sinus is cannulated, and an angiogram is obtained in the left anteroposterior-caudal view to highlight the venous anatomy. Once the distal anchor is stabilized, the device is pulled by the external catheter at the entrance to the jugular vein, which puts tension on the tissues surrounding the coronary sinus. After the device is pulled 3 to 5 cm, the proximal anchor is deployed near the ostium of the coronary sinus. After each anchor is set, a left coronary angiogram is obtained to ensure that the obtuse marginal artery is not compromised. As the device pulls on the tissue around the mitral annulus,

the plication of tissue approximates the anterior and posterior mitral leaflets (Figure 2).⁸ The coronary veins are fragile, and care must be taken to prevent trauma during the procedure. The TITAN and AMADEUS studies demonstrated a reduction in the mitral annulus area and improvement in symptoms and 6-minute walk, which appeared to improve over time during the 12-month follow-up. The studies also met their primary safety endpoint, with a low rate of major adverse events. There was also improvement in both systolic and diastolic ventricular dimensions.⁹

The Monarc percutaneous mitral annuloplasty system (Edwards Lifesciences) had a similar concept of producing mitral annulus plication by implanting a device in the coronary sinus. It also had three sections, including self-expanding stent anchors and a connecting ribbon. Plication occurred over 3 months as spacers along the connecting ribbon dissolved. The preset shape of the nitinol ribbon contracted, causing the stent anchors to get closer. The initial results from the EVOLUTION I trial were promising, but the device had a high rate of bridge fractures. The EVOLUTION II study had low enrollment rates, and device production was suspended after several unexpected deaths occurred.¹⁰

DIRECT PERCUTANEOUS MITRAL VALVE ANNULOPLASTY

A different product that addresses MR by approximating the valve annulus is the Cardioband device (Valtech Cardio, Ltd.). Through a femoral venous transseptal access, the device delivers direct sutureless anchors around the mitral annulus to connect an annuloplasty device. The implant is adjusted under three-dimensional echocardiographic guidance (Figure 3A). The device attempts to percutaneously reproduce the effects of a surgical annu-

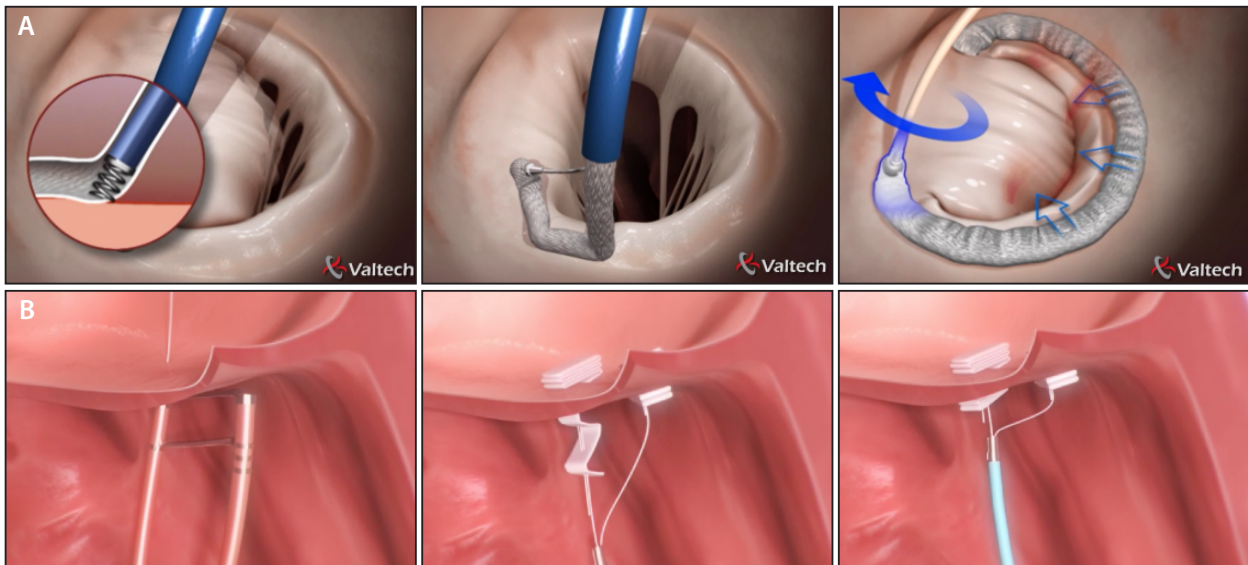


Figure 3. With the Cardioband device, anchors placed along the mitral annulus are adjusted to cinch the mitral valve leaflets together (A). With the Mitralign device, pledgets are delivered across and then plicated together to shorten the annular diameter and coapt the leaflets (B).

loplasty ring. A European multicenter study is currently underway, with more than 40 patients enrolled, to assess the safety and efficacy of the system in patients at high surgical risk.

The Mitralign device (Mitralign, Inc.) also attempts to approximate the effects of surgical annuloplasty. Access is achieved through the femoral artery, and the left ventricle is entered via a retrograde approach across the aortic valve. The catheter is retroflexed toward the mitral annulus. Using a system of wires, two pledgets are delivered through the annulus of the mitral valve. The pledgets are then pulled together, approximating that segment of the annulus (Figure 3B). The procedure may then be repeated on the other side of the annulus to further coapt the leaflets of the valve. The first clinical trial has completed enrollment of 61 patients in Europe.

The Accucinch system (Guided Delivery Systems, Inc.) also uses a retrograde arterial approach to implant a series of adjustable anchors tethered by a cable around the anterior mitral leaflet. The cable is then tightened to cinch the annulus, and the cable is locked. The device is currently being evaluated in Europe.¹¹

RESHAPING THE MITRAL ANNULUS AND VENTRICULAR REMODELING

The QuantumCor system (QuantumCor, Inc.) is a novel device that utilizes thermal injury to cause collagen shrinkage and contraction. Venous access is established, and a transeptal puncture is performed. By use of a loop containing seven electrodes with 14 thermocouples at 2-mm spacing, the area around the annulus is subjected to subablative temperatures with radiofrequency energy (Figure 4A). The

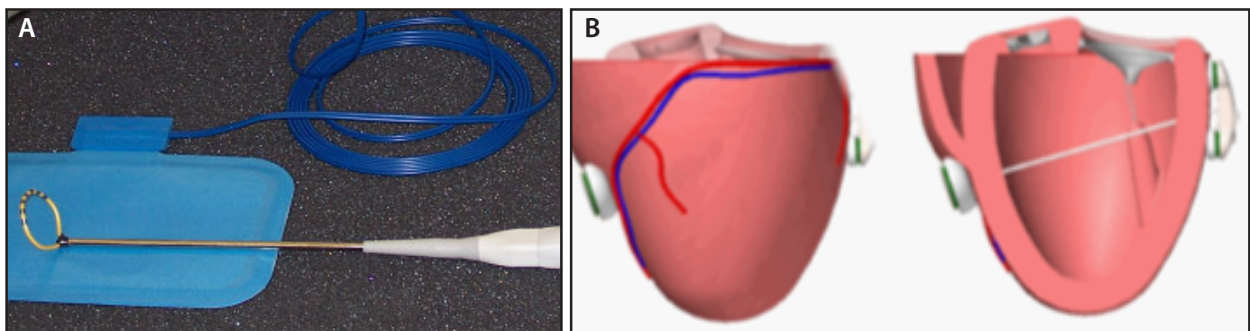


Figure 4. With the QuantumCor system, the loop containing the thermocouples subjects the mitral annulus to thermal injury and shrinkage, creating a smaller diameter (A). The iCoapsys device places a transventricular chord to reshape and shorten the left ventricular dimension (B).

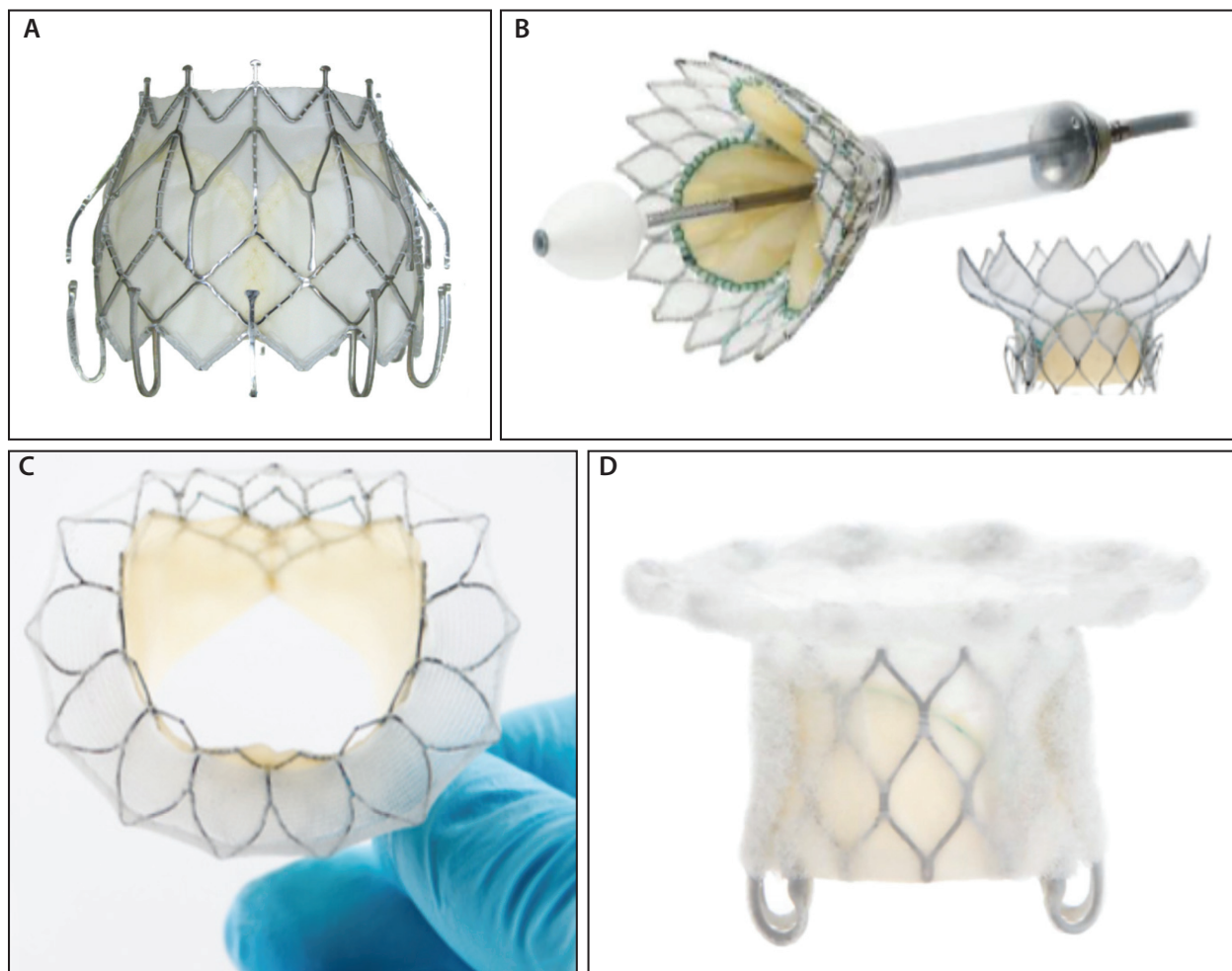


Figure 5. Percutaneous mitral valve implants. The CardiAQ valve (A). The Tendyne valve (B). The Tiara valve (C). The Fortis valve (D).

resulting injury is designed to cause the annular collagen to shrink without deforming or injuring the mitral valve leaflets. The procedure can be repeated and does not preclude other mitral interventions at a later date. The device has only been tested in animal models.¹²

Although the previously mentioned devices seek to reduce MR by percutaneous methods, the iCoapsys device (Myocor, Inc.) addresses the issue of left ventricular remodeling by more invasive but off-pump surgical techniques (Figure 4B). The device aims to reshape the left ventricle by use of a surgically placed transventricular chord. The system is positioned through a thoracotomy and adjusted under echocardiographic guidance to reduce the annular diameter and improve leaflet coaptation. The reshaping is accomplished by approximating the anteroposterior left ventricular dimensions and compressing the mitral annulus.¹³ The RESTOR-MV study demonstrated improved intraoperative MR comparable to surgical annuloplasty rings and

an improved annular dimension with use of the iCoapsys device.¹⁴

PERCUTANEOUS MITRAL VALVE IMPLANTS

With significant advances achieved in aortic and pulmonary valve implants, the techniques required to develop an adequate mitral transcatheter solution have rapidly progressed. The technology is not yet mature and is likely 5 to 10 years away from general clinical practice. However, in patients with a previously implanted tissue prosthetic mitral valve or a mitral annuloplasty ring, a currently available transcatheter aortic valve can be placed in the mitral position because the prosthetic annulus provides support to anchor the new valve implant. The currently approved Sapien XT valve (Edwards Lifesciences) has been used to treat surgically implanted prosthetic valves in the United States and has a current indication in Europe for valve-in-valve therapy.¹⁵ Without a previous tissue valve or annu-

loplasty ring, the native mitral valve does not have a rigid separate annulus or conduit into which a valve may be secured. The annulus is also asymmetric, so anchoring and precise positioning, while not interfering with the aortic valve and chordae, becomes challenging.¹⁶

Several designs of percutaneous mitral valves are being tested. The first device is the CardiAQ valve (CardiAQ Valve Technologies, Inc.) (Figure 5A). The CardiAQ valve leaflets are made of porcine pericardium and are sutured onto a nitinol self-expanding stent. The valve is then delivered via a transseptal approach. An initial in-human implantation of the device yielded significant improvement in MR and no valvular structural issues, but the patient died at day 3 due to multiorgan failure. The device has received approval in the United States to begin early feasibility testing of the second-generation prosthesis.¹⁷

A second device is the Lutter valve (Tendyne Holdings, Inc.) (Figure 5B). The Lutter valve is a fully retrievable porcine pericardial valve that is mounted on a nitinol frame. The prosthesis is available in one inner valve size and is delivered apically into position, with the option of repositioning as needed. Several implantations were performed in Europe as part of a compassionate use protocol, and the device is now being evaluated in an early feasibility study.¹⁸

The Tiara valve (Neovasc, Inc.) is composed of bovine pericardial tissue leaflets with a ventricular fabric-covered skirt to prevent paravalvular leak and is mounted on a self-expandable stent (Figure 5C). The valve has tabs for anchoring and is delivered transapically using a 32-F sheathless system. The support stent is D-shaped on the atrial side to avoid left ventricular outflow tract obstruction. Until the device is finally released, it is retrievable and adjustable. Early acute studies in animals yielded a successful implantation rate of 81% and no significant paravalvular leaks. With the success of the acute trials, long-term animal studies are in progress. The device has received a US Food and Drug Administration conditional investigational device exemption and will begin United States and international human feasibility trials this year.¹⁹

Finally, there is the Fortis mitral transcatheter heart valve (Edwards Lifesciences), which uses bovine pericardial tissue leaflets on a cloth-covered, self-expanding stent frame. A wide ventricular frame side and cloth are designed to reduce paravalvular leak (Figure 5D). The prosthesis is delivered transapically, and paddles at the base of the valve are used to secure the device to the native mitral valve and stabilize the implant. The first in-human trial began in Europe and Canada in 2014.²⁰ The trial was recently voluntarily suspended, as Edwards Lifesciences declared it has “observed evidence of valve thrombosis” and issues with leaflet mobility.

CONCLUSION

The development of percutaneous devices to treat MR is a continuation of interventional cardiology advancement to reproduce transcatheterously what cardiac surgeons have accomplished with more-invasive techniques. If this can be shown to reduce MR and improve clinical symptoms and hospitalizations for congestive heart failure with a lower risk than open surgery, then this work will represent another major step forward toward enhanced patient care. ■

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