Transcatheter mitral valve regurgitation treatment: State of the art and a glimpse to the future

Luca Testa, MD, PhD,^a Azeem Latib, MD,^b Rocco A. Montone, MD,^a and Francesco Bedogni, MD^a

ABSTRACT

Since the first transcatheter heart valve implantation in the pulmonary position in 2000 and in the aortic position in 2002, a large number of transcatheter heart valves have reached the clinical arena and thousands of high-risk patients have been treated successfully, in particular those with severe aortic stenosis. In contrast, the experience of transcatheter mitral valve repair or implantation started relatively more recently, and only a few devices are available at the moment. The aim of this review is to describe the different percutaneous systems for the treatment of mitral regurgitation. (J Thorac Cardiovasc Surg 2016;152:319-27)

MitraClip.

Central Message

The transcatheter mitral valve therapy field is quickly evolving, and the clinical need for safe and effective devices is still largely unmet.

Perspective

All current devices should be restricted to inoperable patients or to compassionate cases; however, once clinical proof of safety and efficacy has been demonstrated, extension to a broader patient spectrum seems likely. A tailored approach to the specific clinical and anatomical situation will conceivably be the future, and it will benefit from the availability of different tools.

See Article page 330.

See Editorial Commentaries page 328 and 336.

The incidence of mitral regurgitation (MR) in the general population of Western countries and in individuals older than 75 years of age is almost 1.7% and 10%, respectively,¹ and surgery is currently the gold standard for the treatment of severe MR, regardless of the adoption of minimally invasive techniques. The presence of severe comorbidities, however, precludes surgical treatment in up to 50% of patients

with severe MR.² Indeed, transcatheter mitral valve repair (MVR) may be an alternative therapeutic option,³ as proven by the encouraging results of the edge-to-edge technique with the MitraClip system (Abbott Vascular Inc, Menlo Park, Calif).

Of note, several MVR technologies are being developed (Tables 1 and 2), although successful MVR with

From the ^aDepartment of Cardiology, IRCCS Pol. S. Donato, S. Donato Milanese; and ^bS. Raffaele Scientific Institute, Emo Columbus, Milan, Italy.

Received for publication March 14, 2016; revisions received April 1, 2016; accepted for publication April 19, 2016; available ahead of print May 26, 2016.

Address for reprints: Luca Testa, MD, PhD, IRCCS Pol. S. Donato, S. Donato Milanese, Milan, Italy (E-mail: lucetes@gmail.com).

0022-5223/\$36.00

Copyright © 2016 by The American Association for Thoracic Surgery

<http://dx.doi.org/10.1016/j.jtcvs.2016.04.055>

Scanning this QR code will take you supplemental videos for the article.

Abbreviations and Acronyms

AML	=	anterior mitral leaflet
CE	=	Conformité Européenne
Fr	=	French
LV	=	left ventricle/ventricular
LVOT	=	left ventricular outflow tract
MR	=	mitral regurgitation
MV	=	mitral valve
MVI	=	mitral valve implantation
MVR	=	mitral valve repair/reconstruction/ replacement
PML	=	posterior mitral leaflet

transcatheter aortic valve implantation prostheses have been performed in patients with degenerated surgical bioprostheses or with recurrent MR after annuloplasty.⁴

MITRAL VALVE REPAIR

Current transcatheter mitral valve repair technologies are discussed in this section (Figure 1).

Leaflet Plication

As first described by Alfieri et al,⁵ the leaflet plication technique consists of creating a “double orifice” by bringing the anterior mitral (AML) and posterior mitral leaflet (PML) together, thus improving the coaptation and reducing the regurgitant orifice. As a result, leaflet coaptation is re-established and MR minimized.

The MitraClip system consists of a polyester-covered cobalt-chromium clip. (See Videos 1 and 2 for a case of degenerative MR; see Videos 3 and 4 for a case of ischemic MR. Both cases have been successfully treated with Mitraclip system.) It is introduced by a 24-French (Fr) delivery catheter via the femoral vein into the right atrium and, after transseptal puncture, advanced into the left atrium. Under 2-dimensional and 3-dimensional echocardiographic and fluoroscopic guidance, the clip is positioned above the mitral valve (MV), opened, and advanced into the left ventricle. Subsequently, it is retracted so that the free edges of AML and PML are loaded onto the clip at the origin of the regurgitant jet; closure of the clip results in a “double-orifice” MV.

The MitraClip system initially was evaluated in the EVEREST-I (Endovascular Valve Edge-to-Edge Repair Study)⁶ and EVEREST-II trials.⁷ The EVEREST-II trial⁷ allocated 279 patients in a 2:1 ratio to MitraClip or surgery. The combined safety endpoint (incidence of severe adverse events to 30 days) was reached in 15% of interventional and 48% of surgical patients ($P < .001$), even though transfusion of ≥ 2 units represented the majority of adverse events. After transfusion was excluded, no significant

difference in safety was seen ($P = .23$). Of note, 20% of MitraClip patients underwent secondary MV surgery. In 46% of interventional patients, MR was Grade 2+ or greater at 12 months. The efficacy of the MitraClip device currently is being evaluated in randomized controlled trials against best medical therapy in the COAPT (Clinical Outcomes Assessment of the MitraClip Percutaneous Therapy)⁸ and RESHAPE-HF (MitraClip Device in Heart Failure Patients with Clinically Significant Functional Mitral Regurgitation)⁹ trials.

A second device for leaflet plication is undergoing preclinical testing: The Mitraflex system (TransCardiac Therapeutics, Atlanta, Ga) combines the possibility of deploying a clip for leaflet plication and implanting an artificial chord during the same procedure via the transapical route.

Leaflet Coaptation Enhancement

The MitraSpacer device (Cardiosolutions, Stoughton, Mass), which currently is undergoing a phase 1 trial, is a balloon-shaped spacer that is delivered percutaneously via the transseptal route and made of a polyurethane-silicone polymer. It is advanced into the mitral orifice and anchored to the left ventricular (LV) apex. The device provides a surface that the leaflets can coapt against, thus reducing MR.

Another device, the Mitralix, is a spiral-shape device that is inserted into the LV to pull the chordae together. This device is at a very early stage of its development.

Leaflet Ablation

Through radiofrequency energy, fibrosis and reduced motion of the leaflets are caused. To date the feasibility of this principle was proven in animal models with the ThermoCool irrigation ablation electrode (Biosense Webster, Inc, Diamond Bar, Calif).

THE ANNULOPLASTY APPROACH**Indirect Annuloplasty**

The CARILLON Mitral Contour System (Cardiac Dimensions, Inc, Kirkland, Wash) consists of a central nitinol element that connects a distal anchor and proximal anchor. After transjugular access, the anchoring portions are placed in the vena cordis magna and proximal cardiac sinus. By foreshortening the central element, the device remodels the posterior periannular tissue.

In the prospective, multicenter AMADEUS trial (Carillon Mitral Annuloplasty Device European Union Study),¹⁰ implantation of the device was successful in 30 of 48 patients (63%). The device has Conformité Européenne (CE) mark and currently is being implanted commercially as well as being evaluated in a few prospective studies.

The MONARC System (Edwards Lifesciences, Irvine, Calif) has self-expanding distal and proximal anchoring segments connected by a central spring. After implantation, the central portion foreshortens and reduces septolateral

TABLE 1. Transcatheter mitral valve repair technology under development

Device name	Therapy type	Description	International status
MitraClip (Abbot Vascular)	Edge-to-edge repair	<ul style="list-style-type: none"> • Percutaneous mitral repair based on Alfieri edge-to-edge surgical approach, designed for both degenerative and FMR. • Features a tiny V-shaped clip. • Indication requested for FDA approval is significant symptomatic DMR in presence of prohibitive risk for mitral valve surgery 	CE Mark approval gained FDA approved
NeoChord (NeoChord DS1000)	Chordal repair	<ul style="list-style-type: none"> • Instrumentation used to enable beating heart, transapical approach, mitral valve repair by artificial chordae implantation 	CE Mark approval gained
V-Chordal-Off Pump (Valtech)	Chordal repair	<ul style="list-style-type: none"> • Designed for leaflet prolapse • Sutureless implantation of neochordae on the leaflets under direct surgical exposure • Off-pump, the chordal length can be adjusted under live echo guidance, on beating heart 	First-in-human study complete
CARILLON (Cardiac Dimensions)	Indirect annuloplasty	<ul style="list-style-type: none"> • Implantable mitral annular constraint device percutaneously placed into the coronary sinus and great cardiac vein • Constructed of nitinol wire with distal and proximal anchors connected by an intervening cable • Designed specifically for heart failure patients with significant MR due to mitral annular enlargement 	CE Mark approval gained IDE submitted for pivotal study
MVRx ARTO System	Indirect annuloplasty	<ul style="list-style-type: none"> • Transvenous delivery of 2 anchors: 1 to the atrial septum and the other to the coronary sinus; • Acutely removable and acts by reducing the anteroposterior diameter of the mitral annulus • Designed specifically for heart failure patients with significant MR due to mitral annular enlargement 	
GDS Accucinch (GDS)	Direct annuloplasty	<ul style="list-style-type: none"> • Catheter-based delivery of a subvalvular left ventricular reshaping (ventriculoplasty) system designed to reshape and resize the left ventricular base • Re-establish native mitral valve geometry while preserving native leaflet function and restore leaflet coaptation 	International feasibility trial underway
Mitralign Bident (Mitralign)	Direct annuloplasty	<ul style="list-style-type: none"> • Transcatheter annuloplasty for mitral repair • Involves delivery of polyester pledgets via LV through posterior mitral annulus • Pledgets are plicated and locked directly on the annulus 	CE Mark trial completed US feasibility trial planned

(Continued)

TABLE 1. Continued

Device name	Therapy type	Description	International status
Cardioband TF (Valtech)	Direct annuloplasty	<ul style="list-style-type: none"> An adjustable, sutureless posterior annuloplasty band implanted through transfemoral transeptal route Designed to reduce the septolateral annular diameter 	CE Mark trial underway
Millipede Ring (Millipede)	Direct annuloplasty	Nitinol ring designed for tricuspid or mitral valve repair	Preclinicals underway
Cardica Mitral Repair (Cardica)	Edge-to-edge repair	Catheter-based treatment for MR featuring a clip that holds together the leaflets of the mitral valve	Intellectual property developed
MISTRAL (Mitralix)	Chordal repair	<ul style="list-style-type: none"> Transseptally delivered (12-Fr catheter) implant (3D nitinol spiral-shaped atraumatic wire) for mitral valve repair via chord grasping This is Mitralix's first product 	Preclinicals underway
V-Chordal-Transfemoral (Valtech)	Chordal repair	Transfemoral chord repair performed via transfemoral approach that is off-pump on a beating heart	Preclinicals underway
Kardium MR (Kardium)	Direct annuloplasty	Kardium is developing a percutaneous device for treating mitral valve regurgitation	Intellectual property developed
PS3 (MVRx)	Annuloplasty	Direct leveraged transatrial shortening of the septolateral dimension of the mitral valve by providing two anchor points that are tensioned together	First-in-human study underway
MitraFlex (TransCath)	Edge-to-edge	Instruments for minimally invasive transapical mitral valve repairs	Preclinicals underway
ValCare MV Repair (ValCare)	Direct annuloplasty	A rigid, D-shaped annuloplasty ring that is delivered in a transcatheter approach to reduce MR and stabilize the mitral annulus for functional and degenerative MR	Preclinicals underway
Mitra-Spacer-Transapical (Cardiosolutions)	Enhanced coaptation	<ul style="list-style-type: none"> Catheter-based mitral valve spacer to reduce MR improving leaflet coaptation Implanted through transapical approach 	First-in-human study underway
Mitralix	Enhanced coaptation	Spiral-shaped device inserted into the LV to pull the chordae together	Animal lab underway

*FM*R, Functional mitral regurgitation; *FDA*, Food and Drug Administration; *DMR*, degenerative mitral regurgitation; *CE*, Conformité Européenne; *MR*, mitral regurgitation; *IDE*, Investigational Device Exemption; *MVRx*, mitral valve therapy; *GDS*, guided delivery system; *LV*, left ventricle; *US*, United States; *TF*, transfemoral; *Fr*, French.

circumference of the annulus. In the multicenter EVOLUTION-I (Clinical Evaluation of the Edwards Lifesciences Percutaneous Mitral Annuloplasty System for The Treatment of Mitral Regurgitation) trial,¹¹ procedural success was 82%. In 30%, compression of coronary arteries was noted. In light of these results, the device is no longer available.

Currently, devices that add a second traction force on the left atrium or right atrium, such as the device by St. Jude Medical (Minneapolis, Minn) that implants helical screws into the myocardium at the posteromedial mitral annulus, proved feasible in the animal model.¹²

A clear limitation of the indirect annuloplasty approach relies on the progressive distance between the coronary sinus and the mitral plane after the enlargement of the atrium, the variable spatial relationship between the coronary sinus and mitral annulus, and the risk of circumflex artery compression. Thus, the annuloplasty approach will probably be ideal for smaller atriums only.¹³

The MVRx ARTO System (Septal Sinus Shortening) basically delivers 2 anchors transvenously: one to the atrial septum and the other to the coronary sinus. It can be removed quickly and acts by reducing the anteroposterior diameter of the mitral annulus.¹⁴

TABLE 2. Transcatheter mitral valve implantation technology under development

Device name	Description	Status
FORTIS (Edwards Lifesciences)	<ul style="list-style-type: none"> Mitral valve replacement technology designed to minimize paravalvular leak Initial version being studied in first-in-human has a transapical delivery system 	First-in-human study underway
Tiara (Neovasc)	<ul style="list-style-type: none"> Self-expanding bovine pericardial, D-shaped trileaflet mitral valve implanted using a transapical delivery system It is anchored to the mitral annulus A transfemoral delivery system is also in development 	First-in-human study underway
TMVI-TA (CardiAQ)	Self-positioning, self-anchoring, and self-conforming system for transcatheter mitral valve implantation through transapical approach	First-in-human study completed
TMVI-TF (CardiAQ)	<ul style="list-style-type: none"> Self-positioning, self-anchoring, and self-conforming system for transcatheter mitral valve implantation Second-generation device has been developed; this profile covers transfemoral version 	First-in-human study completed
Caisson TMVR (Caisson)	Mitral valve replacement system with a transfemoral delivery system	Preclinical studies underway
MitraCath (Emory University)	Technology that enables the placement of a stent-mounted bioprosthetic heart valve in the mitral position	In development
HighLife Mitral Valve Replacement (HighLife)	Percutaneous mitral valve replacement technology with a transatrial delivery system	Preclinical studies underway
Medtronic TMVR (Medtronic)	<ul style="list-style-type: none"> Self-expanding nitinol scaffold and a bovine pericardium valve with three cusps Designed for fixation with the native mitral annulus 	Preclinical studies underway
MitrAssist Valve (MitrAssist)	<ul style="list-style-type: none"> A mitral valve that fits into the existing mitral valve Delivered through a small-diameter catheter For all forms of mitral regurgitation 	Preclinical studies underway
Navigate TMVR	<ul style="list-style-type: none"> Self-expandable mitral valve replacement device featuring a nitinol stent and dehydrated tissue for treatment of functional mitral regurgitation Transatrial, transapical, and transseptal versions are also in development 	Clinical implants have occurred
Tendyne/Lutter TMVR (Tendyne)	<ul style="list-style-type: none"> Self-expanding, transapical approach to mitral valve replacement System involves neochords with left ventricular apical tethering for fixation 	First-in-human study underway
Cardiovalve (Valtech)	Mitral valve replacement system that can be delivered using a transfemoral delivery system in a 2-step replacement procedure	Preclinical studies underway

TMVI-TA, Transcatheter mitral valve implantation-transapical; TMVI-TF, transcatheter mitral valve implantation-transfemoral; TMVR, transcatheter mitral valve replacement.

Direct Annuloplasty

The Valtech Cardioband (Valtech Cardio, Or Yehuda, Israel) is delivered via a transvenous, transseptal route and uses nitinol screws inserted into the atrial aspect of the mitral annulus in a commissure-to-commissure fashion. In a second step, the implant is cinched to reduce annular dimensions and MR. Experimental and early clinical data are available.^{15,16}

The Mitralign Percutaneous Annuloplasty System (Mitralign Inc, Tewksbury, Mass) delivers a pair of pledgets on the mitral annulus via the transventricular route. The pledgets are plicated and locked on the ventricular side.¹⁷

The QuantumCor device (QuantumCor, Lake Forest, Calif) has been tested in animal models and works with heat energy applied to the mitral annulus, causing constriction.¹⁸

THE CHORDAL APPROACH

A novel device for transapical implantation of neochordae has been evaluated clinically and recently received the CE mark (NeoChord DS1000; NeoChord Inc, Minneapolis, Minn). The delivery catheter is inserted via standard transapical access into the left ventricle. Under

2-dimensional and 3-dimensional echocardiographic guidance, the free edge of the prolapsing segment of PML or AML is grasped. Color-sensitive fiberoptics confirm grasping of sufficient leaflet tissue. Neochordae subsequently are externalized through the LV apex and fixed at the correct length under echo guidance. Clinical feasibility and safety have recently been demonstrated in the Transapical Artificial Chordae Tendineae (TACT) trial and further evaluation is being pursued in a postmarket registry at present.¹⁹

The LV Remodeling Approach

In patients with ischemic or cardiomyopathy-induced functional MR, a reduction of LV dimensions can lead to a reduction of MR. The idea is to decrease the septolateral annular distance and bring the LV papillary muscles to the leaflets by reducing the anteroposterior dimension of the LV.

Currently, there is one device that follows the concept of reducing the anteroposterior dimension of the LV by reducing the septolateral annular distance: the Mardil-BACE (Mardil, Inc, Morrisville, NC), which has been tested

FIGURE 1. Transcatheter mitral valve repair technologies. *First column from top to bottom:* MitraClip (Abbot Vascular), NeoChord (NeoChord), V-Chordal-Off Pump (Valtech), CARILLON (Cardiac Dimensions). *Second column from top to bottom:* GDS Accucinch (GDS), Mitralign Bident (Mitralign), Cardioband TF (Valtech), Millipede Ring (Millipede). *Third column from top to bottom:* Cardica Mitral Repair (Cardica), MISTRAL (Mitalrix), V-Chordal-Transfemoral, Kardium MR (Kardium). *Fourth column from top to bottom:* PS3 (MVRx), MitraFlex (TransCardiac), ValCare MV Repair (ValCare), Mitra-Spacer-Transapical.

in 15 patients. The device is implanted through a minithoracotomy with placement of a silicone band around the atrioventricular groove. It is then inflated and adjusted at the height of the mitral annulus to achieve the optimal result.

MITRAL VALVE IMPLANTATION

Nitinol-based devices that are currently under development are the Endovalve (Micro Interventional Devices, Inc, Newtown, Pa) device, the former Lutter-Lozonschi, now Tendyne valve (Tendyne Holdings, Roseville, Mich), the CardiaQ (CardiaQ valve Technologies Inc, Irvine, Calif) device, the Edwards FORTIS (Edwards Lifesciences), the MitrAssist (MitrAssist Ltd., Misgav, Israel) device, and the Neovasc Tiara (Neovasc Inc, Richmond, Canada) (Figure 2).

The Endovalve is implanted via a right minithoracotomy and delivery of the catheter-based valve through the left atrium. A true percutaneous version is under development.

The Lutter-Lozonschi, now Tendyne valve is delivered via a transapical approach. It consists of an atrial fixation system, a tubular piece with a mounted tricuspid pericardial valve, and a ventricular apical fixation system.²⁰

The Edwards FORTIS consists of a central valve body, paddles, and an atrial flange and is only available in 29 mm. The valve is nitinol-based, self-expanding, and has 3 bovine pericardial leaflets. The paddles are supposed to capture the native leaflets and secure them between the Fortis valve body and the paddles. It is delivered transapically with a 42-Fr system. First implants showed very promising results.²¹

The MitrAssist valve works with fixation of the transapically delivered valve at the papillary muscles. First-in-human procedures have not yet been performed. The Neovasc Tiara consists of a nitinol-based, self-expanding frame, bovine pericardium leaflets, and ventricular anchors to fix the valve onto the fibrous

VIDEO 1. Three-dimensional echocardiogram showing a degenerated mitral valve with a chordal rupture on the scallop 2 of the posterior leaflet. Video available at [http://www.jtcvsonline.org/article/S0022-5223\(16\)30263-X/addons](http://www.jtcvsonline.org/article/S0022-5223(16)30263-X/addons).

trigone and the posterior annulus. The valve is anatomically D-shaped. It is introduced by a 32-Fr sheathless system with a self-dilating tip via a transapical approach. First-in-human implants were successful without complications. A feasibility study with 30 patients is ongoing.²²

The CardiaQ system is made for both transfemoral and transapical access. It is placed intra- and suprannular to preserve the LV contractility and maximize the left ventricular outflow tract (LVOT) area. The anchoring frame is designed for annular attachment without the use of radial force and preservation of chordate and leaflets. It consists of a bi-level, self-expanding nitinol frame.²³ A CE mark trial with 100 patients is ongoing.

VIDEO 3. Transesophageal echocardiography showing a case of ischemic mitral valve regurgitation with 2 separated jets. Video available at [http://www.jtcvsonline.org/article/S0022-5223\(16\)30263-X/addons](http://www.jtcvsonline.org/article/S0022-5223(16)30263-X/addons).

DISCUSSION

Surgical MV repair is the reference treatment for patients with clinically significant MR. Low perioperative complication rates and excellent long-term outcomes can be achieved in centers with adequate expertise, especially in degenerative MR. Thus, although not fully clarified yet, surgery could be justified even in asymptomatic patients if repair is feasible. Of note, despite these premises, surgical MVR is denied to a large proportion of patients with significant grades of MR, especially those with functional mitral regurgitation, while at the same time, transcatheter therapies are making large steps forward. Of note, contrary to the aortic valve, the anatomy of the MV leads to a challenging and complex target regarding paravalvular leakage and LVOT obstruction. The eccentric geometry of

VIDEO 2. Three-dimensional echocardiogram showing the result after implantation of 2 MitraClips. Video available at [http://www.jtcvsonline.org/article/S0022-5223\(16\)30263-X/addons](http://www.jtcvsonline.org/article/S0022-5223(16)30263-X/addons).

VIDEO 4. Transesophageal echocardiography showing the result after implantation of a single MitraClip. Video available at [http://www.jtcvsonline.org/article/S0022-5223\(16\)30263-X/addons](http://www.jtcvsonline.org/article/S0022-5223(16)30263-X/addons).

FIGURE 2. Transcatheter mitral valve implantation technologies. *First column from top to bottom:* FORTIS (Edwards Lifesciences), Tiara (Neovasc), TMVI-TA (CardiaQ). *Second column from top to bottom:* TMVI-TF (CardiaQ), Caisson TMVR (Caisson), MitraCath (Emory University). *Third column from top to bottom:* HighLife Mitral Valve Replacement (HighLife), Medtronic TMVR (Medtronic), MitraAssist Valve (MitraAssist). *Fourth column from top to bottom:* Navigate TMVR (NCSI), Tendyne/Lutter TMVR (Tendyne), Cardiovalve (Valtech).

the mitral orifice does not allow simple solutions for device delivery and anchoring.

To date, only the percutaneous edge-to-edge approach is applied on a large scale and the MitraClip has recently been incorporated into international guidelines; however, the field of transcatheter mitral valve implantation is evolving rapidly, and major anatomical challenges remain.

MVR Versus Mitral Valve Implantation (MVI)

Both MVR and MVI have several pros and cons. In patients with chronic MR, the dilation of the annulus requires large devices to achieve optimal fixation of the prosthesis and, thus, large delivery systems, at least greater than 30 Fr. Retrograde/transseptal approaches for MVI delivery may be challenging, given the angulation, the dimensions, and stiffness of the devices. A direct transatrial approach is a possible alternative, but it has been essentially abandoned because of suboptimal coaxial alignment. The transapical approach assures optimal coaxial alignment; however, the LV wall in patients with heart failure may be particularly fragile and arrhythmogenic. Dedicated closure devices could facilitate MVI. Finally, patients with severely

depressed LV systolic function may not tolerate prolonged deployment time or rapid pacing.

Reliable fixation of the prosthesis is challenging, given the lack of heavy annular calcification in most patients. Moreover, fixation methods that rely on radial force are likely to fail as radial force poses the risk of compression of adjacent structures such as the LVOT, the conduction system, the coronary sinus, the left circumflex artery, and aortic root. Additional fixation elements are thus required.

MVR eliminates MR in a minority of the cases, and the degree of clinically meaningful MR reduction is still debatable, whereas the potential of MVI for complete and predictable abolition of MR is appealing. In patients with FMR, however, a mild degree of residual MR after repair may mitigate the acute increase in overload and serve to decompress the LV, making the procedure safer for those with severe LV dysfunction.

Because of the great anatomical variability of MR, physicians will likely need to develop expertise with more than 1 device and with advanced imaging; however, MVR will be tolerable and associated with fast recovery. MVR and MVI will probably be complementary and the future will conceivably be a tailored approach to both the valve and patient.

In conclusion, the field of transcatheter MV therapy is quickly evolving; nevertheless, all current devices should be restricted to inoperable patients or to compassionate cases. Once clinical proof of safety and efficacy has been demonstrated, however, extension to a broader patient spectrum seems likely. Likewise in the field of transcatheter aortic valve replacement, an interdisciplinary heart team is mandatory.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

References

1. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. *Lancet*. 2006;368:1005-11.
2. Mirabel M, Iung B, Baron G, Messika-Zeitoun D, Detaint D, Vanoverschelde JL, et al. What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery? *Eur Heart J*. 2007; 28:1358-65.
3. Lim DS, Reynolds MR, Feldman T, Kar S, Herrmann HC, Wang A, 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(R) system. *J Am Coll Cardiol*. 2014;64:182-92.
4. Descoutures F, Himbert D, Maisano F, Casselman F, de Weger A, Bodea O, et al. Transcatheter valve-in-ring implantation after failure of surgical mitral repair. *Eur J Cardiothorac Surg*. 2013;44:e8-15.
5. Alfieri O, Maisano F, De Bonis M, Stefano PL, Torracca L, Oppizzi M, et al. The double-orifice technique in mitral valve repair: a simple solution for complex problems. *J Thorac Cardiovasc Surg*. 2001;122:674-81.
6. Feldman T, Wasserman HS, Herrmann HC, Gray W, Block PC, Whitlow P, et al. Percutaneous mitral valve repair using the edge-to-edge technique: six-month results of the EVEREST Phase I Clinical Trial. *J Am Coll Cardiol*. 2005;46:2134-40.
7. Feldman T, Kar S, Rinaldi M, Fail P, Hermiller J, Smalling R, et al; EVEREST Investigators. 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;54:686-94.
8. Clinical outcomes assessment of the mitraclip percutaneous therapy (COAPT) clinical trial. Clinical trial: NCT01626079. Available at: <http://clinicaltrials.gov/show/NCT01626079>. Accessed April 2015.
9. A randomized study of the MitraClip device in heart failure patients with clinically significant functional mitral regurgitation (RESHAPE-HF). Clinical trial: NCT01772108. Available at: <http://clinicaltrials.gov/show/NCT01772108>. Accessed April 2015.
10. Schofer J, Siminiak T, Haude M, Herrman JP, Vainer J, Wu JC, et al. Percutaneous mitral annuloplasty for functional mitral regurgitation: results of the CARILLON Mitral Annuloplasty Device European Union Study. *Circulation*. 2009;120:326-33.
11. Harnek J, Webb JG, Kuck KH, Tschöpe C, Vahanian A, Buller CE, et al. Transcatheter implantation of the MONARC coronary sinus device for mitral regurgitation: 1-year results from the EVOLUTION phase I study (Clinical Evaluation of the Edwards Lifesciences Percutaneous Mitral Annuloplasty System for the Treatment of Mitral Regurgitation). *JACC Cardiovasc Interv*. 2011;4:115-22.
12. Sorajja P, Nishimura RA, Thompson J, Zehr K. A novel method of percutaneous mitral valve repair for ischemic mitral regurgitation. *JACC Cardiovasc Interv*. 2008;1:663-72.
13. Tops LF, Van de Veire NR, Schuijff JD, de Roos A, van der Wall EE, Schalij MJ, et al. Noninvasive evaluation of coronary sinus anatomy and its relation to the mitral valve annulus: implications for percutaneous mitral annuloplasty. *Circulation*. 2007;115:1426-32.
14. Erglis A, Thomas M, Morice MC, Narbute I, Zabunova M, Hovasse T, et al. The Arto transcatheter mitral valve repair system. *EuroIntervention*. 2015;11(suppl W):W47-8.
15. Maisano F, Vanermen H, Seeburger J, Mack M, Falk V, Denti P, et al. Direct access transcatheter mitral annuloplasty with a sutureless and adjustable device: preclinical experience. *Eur J Cardiothorac Surg*. 2012;42: 524-9.
16. Maisano F, Taramasso M, Nickenig G, Hammerstingl C, Vahanian A, Messika-Zeitoun D, et al. Cardioband, a transcatheter surgical-like direct mitral valve annuloplasty system: early results of the feasibility trial. *Eur Heart J*. 2016;37: 817-25.
17. Mandinov L, Buellesfeld L, Kuck K-H, Grube E. Early insight into Mitralign direct annuloplasty for treatment of functional mitral regurgitation. *Intervent Cardiol Rev*. 2011;6:170-2.
18. Goel R, Witzel T, Dickens D, Takeda PA, Heuser RR. The QuantumCor device for treating mitral regurgitation: an animal study. *Catheter Cardiovasc Interv*. 2009;74:43-8.
19. Seeburger J, Rinaldi M, Nielsen SL, Salizzoni S, Lange R, Schoenburger M, et al. Off-pump transapical implantation of artificial neo-chordae to correct mitral regurgitation: the TACT Trial (Transapical Artificial Chordae Tendinae) proof of concept. *J Am Coll Cardiol*. 2014;63:914-9.
20. Lutter G, Lozonschi L, Ebner A, Gallo S, Marin y Kall C, Missov E, et al. First-in-human off-pump transcatheter mitral valve replacement. *JACC Cardiovasc Interv*. 2014;7:1077-8.
21. Bapat V, Buellesfeld L, Peterson MD, Hancock J, Reineke D, Buller C, et al. Transcatheter mitral valve implantation (TMVI) using the Edwards FORTIS device. *EuroIntervention*. 2014;10(suppl U):U120-8.
22. Cheung A, Stub D, Moss R, Boone RH, Leipsic J, Verheye S, et al. Transcatheter mitral valve implantation with Tiara bioprosthesis. *EuroIntervention*. 2014; 10(suppl U):U115-9.
23. Swaans MJ, van der Heyden JAS. Mitral valve devices. In: Rajamannan NM, ed. *Cardiac Valvular Medicine*. London: Springer-Verlag; 2013:187-209.

Key Words: mitral regurgitation, transcatheter treatment, mitral valve implantation, mitral valve repair