

# iREVIEW

STATE-OF-THE-ART REVIEW

## Transcatheter Interventions for Mitral Regurgitation Multimodality Imaging for Patient Selection and Procedural Guidance



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**CME/MOC/ECME Objective for This Article:** Upon completion, the reader should be able to: 1) identify which patients with severe mitral regurgitation can be candidates for each of the currently available transcatheter devices for mitral valve repair (targeting leaflets of mitral annulus) or replacement; 2) select the most appropriate imaging techniques to plan and guide the transcatheter mitral valve/replacement procedures; and 3) discuss the important questions that need to be addressed when evaluating a patient with severe mitral regurgitation who may be referred for transcatheter mitral valve intervention.

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# Transcatheter Interventions for Mitral Regurgitation

## Multimodality Imaging for Patient Selection and Procedural Guidance

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### ABSTRACT

Transcatheter therapies to treat mitral regurgitation are rapidly developing. Currently, there are several devices commercially available to treat mitral regurgitation. The underlying cause of mitral regurgitation and specific anatomical aspects of the mitral valve and surrounding structures are considered when patients with symptomatic severe mitral regurgitation for transcatheter mitral valve therapies are selected. Multimodality imaging plays an important central role in the selection of patients, providing information about the mechanism of mitral regurgitation, the anatomy of the mitral valve and spatial relationships with the coronary sinus, the circumflex coronary artery and left ventricular outflow tract and to predict the procedural outcomes. During the transcatheter procedure, transesophageal echocardiography and fluoroscopy are key for monitoring the procedural steps to maximize the outcomes and minimize the complications. This paper provides a comprehensive review of the most important aspects to visualize in order to appropriately select patients for transcatheter mitral valve repair and replacement and to guide the procedure for the different transcatheter devices. (J Am Coll Cardiol Img 2019;12:2029-48) © 2019 by the American College of Cardiology Foundation.

**T**he growing number of patients who present with symptomatic severe mitral regurgitation (MR) and with contraindications to surgery or high operative risk pose an important therapeutic challenge. The advent of transcatheter mitral valve (MV) therapies has provided feasible and safe alternatives to medical and surgical treatments. Adequate patient selection for these therapies requires accurate assessment of MV anatomy and function and procedural access; moreover, accurate procedural guidance is needed. Combinations of noninvasive imaging techniques such as echocardiography and computed tomography permit patient selection for each specific transcatheter MV device. The procedure is usually guided by fluoroscopy and echocardiography. Technological advances allow current real-time integration of echocardiography and fluoroscopy, facilitating the communication between the interventionalist and the imaging specialist. This review paper provides a comprehensive overview of

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the imaging needs of select patients with symptomatic severe MR for transcatheter therapies and to guide the procedure.

**MITRAL VALVE ASSESSMENT: STATE-OF-THE-ART**

Proper function of the MV complex requires the structural and functional integrity of all components, including the leaflets, mitral annulus, chordae, papillary muscles, left ventricle (LV) and left atrium (LA). Functional, morphological or geometric distortion of one or more of these components may cause MV dysfunction, leading to regurgitation or stenosis.

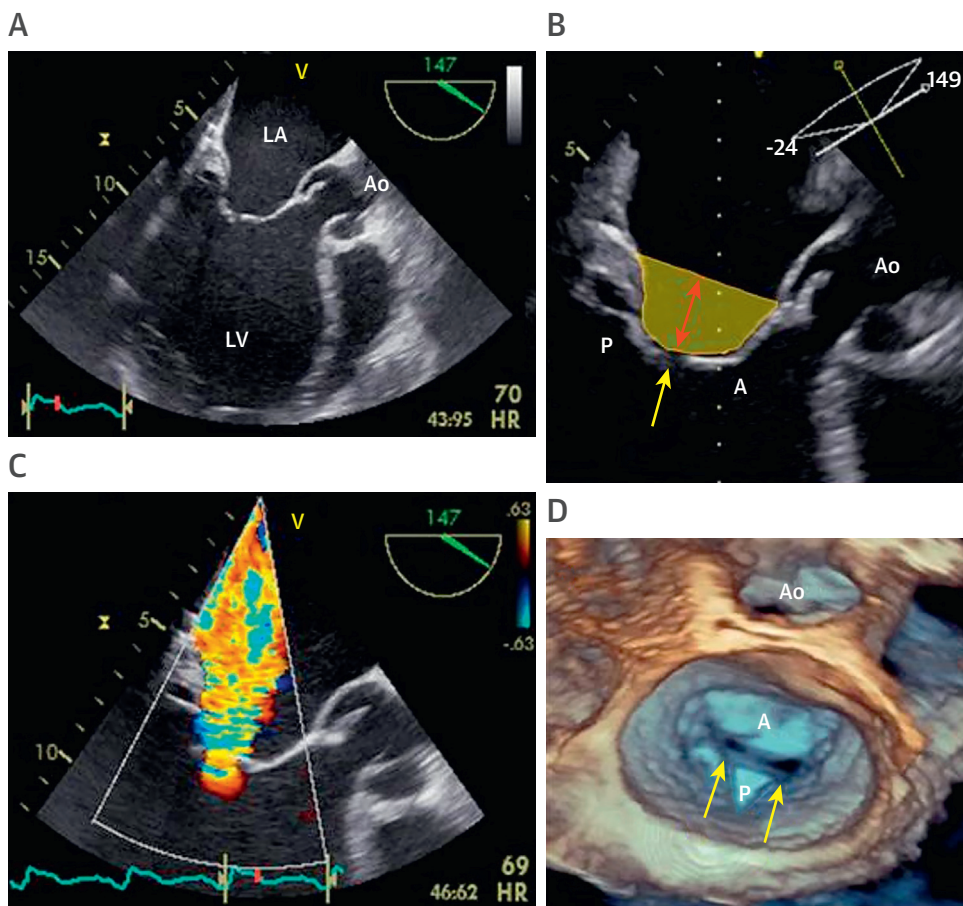
**MITRAL VALVE ANATOMY.** With a much larger area, the anterior mitral leaflet covers approximately

two-thirds of the MV orifice, whereas the posterior mitral leaflet covers one-third of the orifice. The respective lateral and medial continuity between both leaflets is provided by the anterolateral and posteromedial commissural leaflets. Small indentations from the tip to the body of the posterior leaflet represent morphological landmarks to demarcate the lateral (P1), central (P2), and medial (P3) scallops. Despite the absence of indentations, similar terminology is applied to identify the anterior leaflet scallops (A1, A2, and A3, respectively) (1). This nomenclature is useful for communication during the guidance of transcatheter procedures for MR. Competent MV closure is defined by a “tenting area”

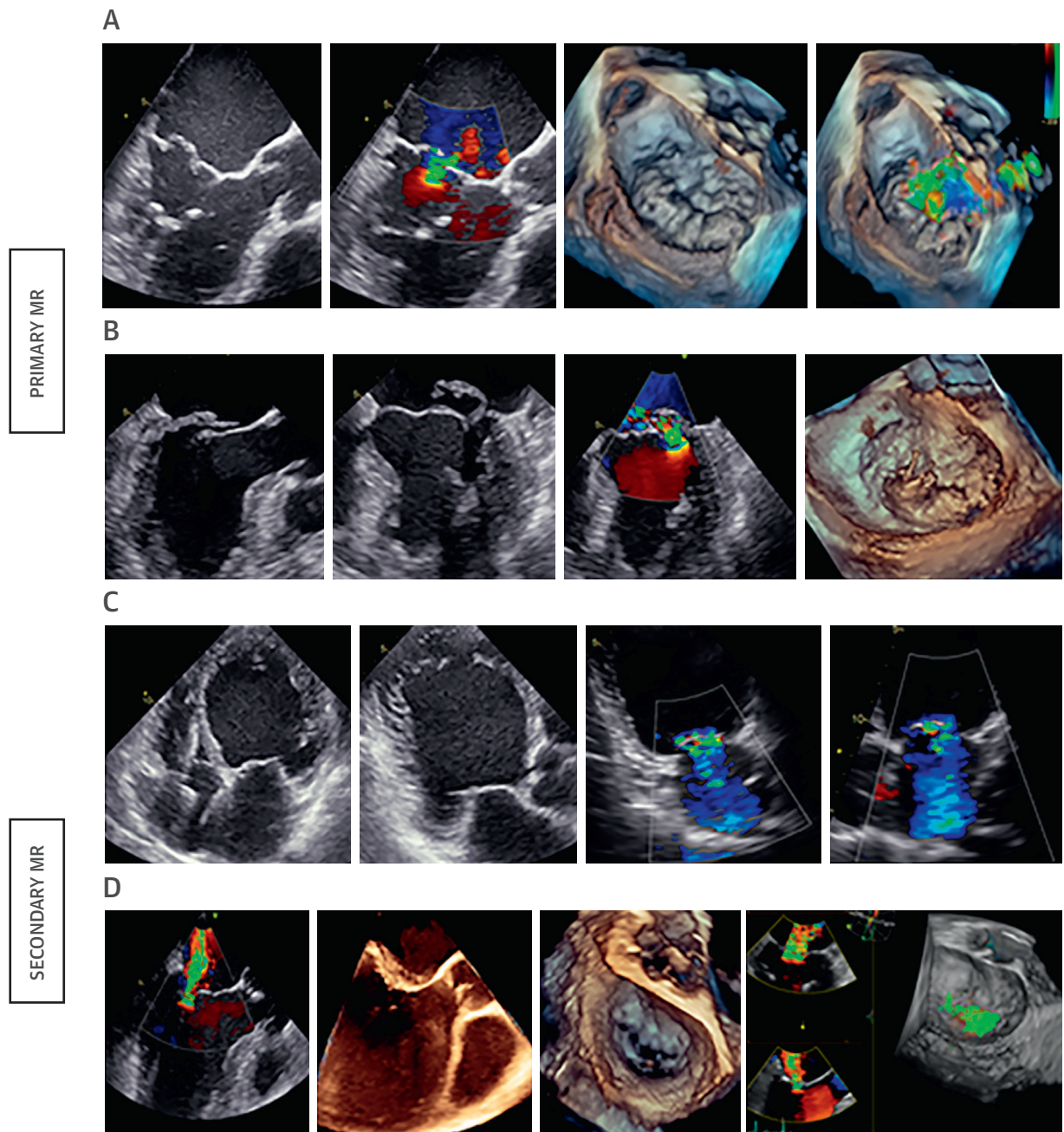
**ABBREVIATIONS AND ACRONYMS**

- CMR** = cardiac magnetic resonance
- LA** = left atrium
- LV** = left ventricular
- LVOT** = left ventricular outflow tract
- MDCT** = multidetector row computed tomography
- MR** = mitral regurgitation
- MV** = mitral valve
- TMVR** = transcatheter mitral valve replacement

**FIGURE 1** Significant Mitral Valve Leaflet Tethering Causing Severe Mitral Regurgitation



In dilated cardiomyopathy, the remodeling of the left ventricle leads to significant tethering of the mitral valve leaflets which cannot coapt and secondary mitral regurgitation (A). (B) Increased tenting area (yellow zone), absent leaflet coaptation (yellow arrow) and elevated coaptation depth (red arrow) leading to large regurgitant jet (C). The en face view of the mitral valve on 3-dimensional transesophageal echocardiography (lower right) shows the lack of coaptation at the central to central-medial level (D). A = anterior leaflet; Ao = aorta; LA = left atrium; LV = left ventricle; P = posterior leaflet.

**FIGURE 2** Assessment of Mitral Regurgitation Cause With Echocardiography

**(A)** 2-Dimensional versus 3D transesophageal echocardiography (with and without color Doppler) in a patient with severe MR due to Barlow's mitral valve disease, with bi-leaflet prolapse and billowing. **(B)** 2D versus 3D transesophageal echocardiography in a patient with severe MR due to chordal rupture (fibroelastic deficiency) of the P2 scallop. **(C)** 2D transthoracic echocardiography in a patient with severe MR secondary to left ventricular dilation with mitral annulus dilation and displacement of the papillary muscles with chordal tethering. **(D)** 2D and 3D transesophageal images of the same patient showing tethering of both mitral valve leaflets and the typical functional MR along the coaptation line (color Doppler). MR = mitral regurgitation; P2 = central scallop of the posterior mitral leaflet.

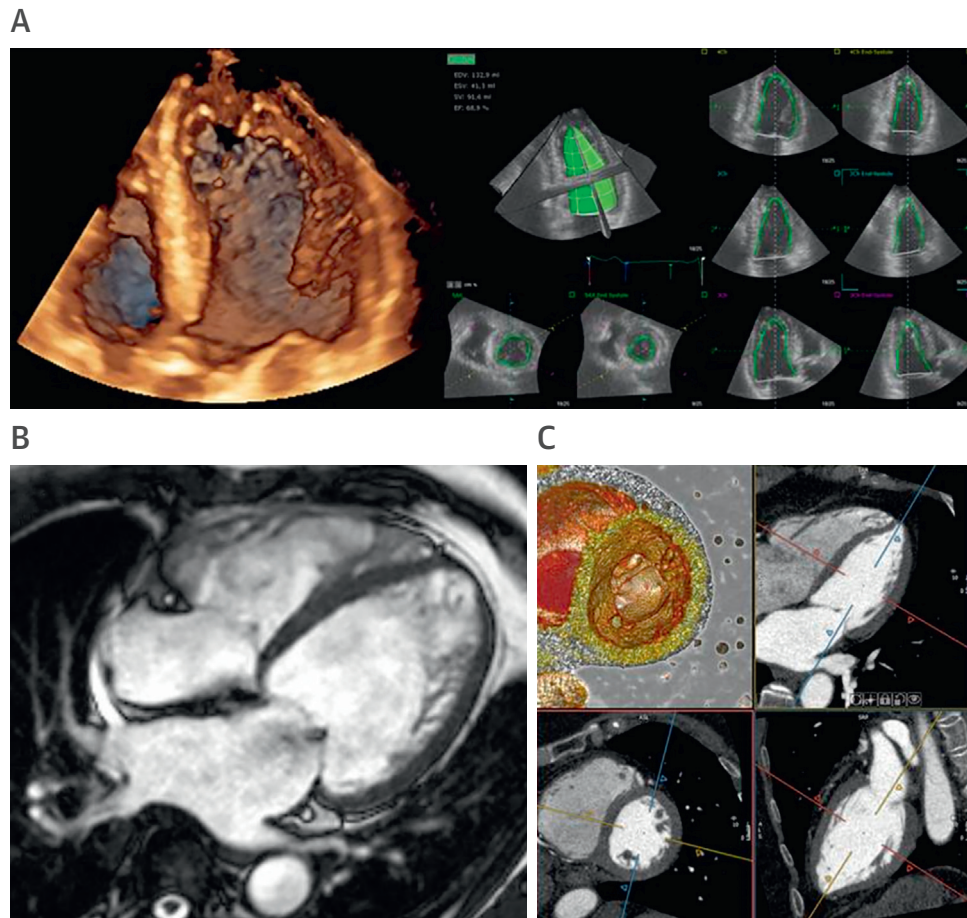
**TABLE 1** Criteria for the Definition of Severe Mitral Regurgitation

	2013 EACVI (8)		2017 ASE (9)	CMR (10,11)
<b>Qualitative</b>				
Valve morphology	Flail leaflet/ruptured papillary muscle/large coaptation defect		Severe valve lesions (primary: flail leaflet, ruptured papillary muscle, severe retraction, large perforation; secondary: severe tenting, poor leaflet coaptation)	As for EACVI and ASE
Color flow regurgitant jet	Very large central jet or eccentric jet adhering, swirling and reaching the posterior wall of the left atrium		Central jet >40% left atrium/holosystolic eccentric jet	-
CW signal of regurgitant jet	Dense/triangular		Holosystolic/dense/triangular	-
Other	Large flow convergence zone		Large throughout systole	-
<b>Semiquantitative</b>				
Vena contracta width, mm	≥7 (>8 for biplane)		≥7 (>8 for biplane)	-
Upstream vein flow	Systolic pulmonary vein flow reversal		Minimal to no systolic flow/systolic flow reversal	-
Inflow	E-wave dominant ≥1.5 m/s		E-wave dominant (>1.2 m/s)	-
Other	TVI mitral/TVI aortic >1.4		-	-
<b>Quantitative</b>				
EROA, mm <sup>2</sup>	Primary ≥40	Secondary ≥20	Primary/secondary ≥40 (may be less in secondary MR with elliptical ROA)	-
Regurgitant volume, ml/beat	≥60	≥30	≥60 (may be less in low-flow conditions)	≥55 (10)/60 (11)
Regurgitant fraction, %			≥50	≥40 (10)
Enlargement of cardiac chambers	Enlarged left ventricle/left atrium			
AHA/ACC = American Heart Association/American College of Cardiology; ASE = American Society of Echocardiography; CMR = cardiovascular magnetic resonance; CW = continuous wave; EACVI = European Association of Cardiovascular Imaging; EROA = effective regurgitant orifice area; ESC/EACTS = European Society of Cardiology/European Association for Cardiothoracic Surgery; MR = mitral regurgitation; ROA = regurgitant orifice area; TVI = time velocity integral.				

(space encompassed between the closed leaflets and the annular surface) and a “coaptation depth: (distance from the annulus to the coaptation point) (Figure 1) (1). The mitral annulus is a discontinuous D-shaped fibrous ring at the atrioventricular junction with 2 different parts: the anterior annulus is enforced by the aortomitral curtain that provides a fibrous continuity with the aortic valve, whereas the posterior annulus spans the right and left fibrous trigone and is formed by myocardium, making this region prone to annular dilation. The circumflex coronary artery and the coronary sinus are located in the vicinity of the left atrioventricular junction, in close spatial relationship with the posterior part of the mitral annulus, and are important landmarks for transcatheter annuloplasty techniques (2). Arising from the papillary muscles, the tendinous chords spread out into small chords attached to the tip (primary chords) or to the ventricular body of the leaflets (secondary chords). In addition, commissural chords stem from the papillary muscle underneath and provide suspension of the leaflets to the papillary muscles and/or directly to the ventricle (few tertiary chordae attached to the posterior leaflet) (1). Although the anterolateral papillary muscle originates from the distal apicolateral third of the LV, the posterolateral muscle is implanted at the

LV mid-inferior portion and is characterized by highly variable morphology (3). Finally, local or global LV dysfunction typically causes secondary MR by its influence on the subvalvular apparatus. Similarly, LA dilation and dysfunction may induce mitral annular dilation and dysfunction, indirectly affecting MR severity. In addition, atrial dilation redirects the posterior wall downward and posteriorly, increasing tension on the posterior leaflet through its direct continuity with the atrial wall, and impairing leaflet coaptation.

**CAUSE OF MITRAL REGURGITATION.** Two main mechanisms have been identified that underlie MR (4) (Figure 2). Primary MR is due to intrinsic involvement of MV leaflets and chordae tendinae, and secondary MR is caused by LV pathology. Another classification of MV dysfunction based on leaflet motion was proposed by Carpentier et al. (5) in 1983 and is still widely used. According to this classification, type I MR is defined as normal leaflet motion, type II MR is characterized by excessive leaflet motion, and type III MR is characterized by restrictive leaflet motion. This functional classification can be further refined by segmental MV analysis, including scallops and commissures assessment, which permits

**FIGURE 3** Assessment of Left Ventricular Dimensions and Function With 3D Imaging Modalities

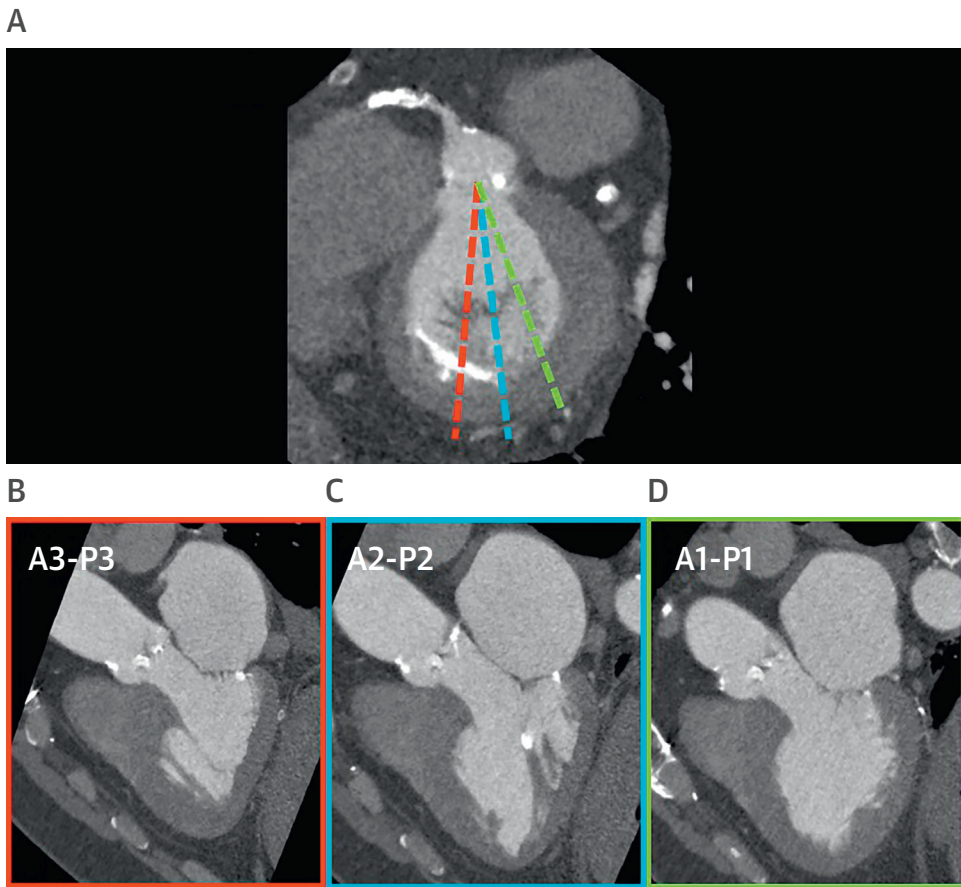
**(A)** 3D volume rendering (**left**) and the measurement of end-systolic and end-diastolic volumes from the reconstructed apical 4-, 2-, and 3-chamber views and the short-axis view. **(B, C)** Examples of LV dimensions and function assessment with cardiovascular magnetic resonance and computed tomography, respectively. LV = left ventricle.

precise localization of valve dysfunction. Particularly in primary MR caused by degenerative MV disease, this analysis allows the distinction between the 2 most common forms: Barlow disease, where the MV shows multisegment redundancy, billowing and thickened tissue, and fibroelastic deficiency, where the typical lesion is a chordal rupture with involvement of 1 single scallop (**Figure 2**) (6). Characterization of the cause of MR and MV dysfunction is performed mainly by echocardiography. Both standard 2-dimensional (2D) transthoracic and transesophageal echocardiography (TEE) permit good morphological analysis of MV and subvalvular apparatus with >85% accuracy compared to surgical inspection (7). The introduction of real-time 3D (transesophageal) echocardiography has significantly improved diagnostic accuracy, showing a >95% agreement with surgical

findings and providing a detailed description of MV dysfunction even in complex lesions, allowing a better communication with the surgeon or interventionist (7).

**ASSESSMENT OF MR SEVERITY.** Transthoracic echocardiography is recommended as the first-line imaging mode for MR assessment and provides useful information including valve anatomy, valve hemodynamics, and hemodynamic consequences. When transthoracic echocardiography has nondiagnostic value or when further diagnostic refinement is required, TEE is advocated. Additionally, recent studies have shown the additional value of cardiovascular magnetic resonance imaging (CMR) in assessing the MR severity. The criteria for defining severe MR with echocardiography and CMR are described in **Table 1** (8,9).

**FIGURE 4** Mitral Valve Analysis With Multidetector Row Computed Tomography



From the double oblique reconstruction of the short-axis view of the mitral valve (A), the planes across the medial (B, A3-P3), central (C, A2-P2), and lateral (D, A1-P1) scallops of the anterior (A) and posterior (P) mitral leaflets provide the longitudinal display of the mitral valve similar to transesophageal echocardiography. Note that the reconstructed short-axis of the mitral valve is visualized from the LV perspective. Abbreviation as in Figure 3.

Qualitatively, color Doppler imaging is used mostly to assess MR severity. The presence of a large eccentric jet adhering, swirling, and reaching the posterior LA wall supports significant MR. The presence of flow convergence at a Nyquist limit of 50 to 60 cm/s should alert to the presence of significant MR, whereas a vena contracta width of  $\geq 7$  mm defines severe MR. Quantitatively, the flow convergence method is the most recommended quantitative approach. The radius of the proximal isovelocity surface area is measured at mid-systole using the first aliasing velocity. Regurgitant volume and effective regurgitant orifice area are obtained by using the standard formula. In eccentric jets, multiple jets, or complex or elliptical regurgitant orifices, the proximal isovelocity surface area method is less accurate

or not feasible. Assessment of MR using CMR is reasonable to provide additional information about cause and severity, especially for measurements of regurgitant volume and fraction (10,11), whereas the feasibility of CMR for assessing the mechanism of MR and valve reparability has not yet been defined. In patients with isolated MR (no other concomitant valvular regurgitant lesions), CMR quantification of the regurgitant fraction or volume has been validated with in vitro and in vivo measurements and, in contrast to echocardiography, is less influenced by geometric assumptions, jet direction, or multiple regurgitant jets. Of note, although CMR is more reproducible, each modality has its potential errors and limitations and is technically demanding. In addition, specific CMR thresholds of regurgitant

volume and fraction to define severe MR have not been extensively investigated, and therefore, CMR thresholds are those established for echocardiography. Finally, the presence of severe MR has significant hemodynamic effects, primarily on the LV and LA.

**LV FUNCTION, SIZE, AND SHAPE.** In both primary and secondary MR, accurate measurement of LV ejection fractions and dimensions are important in the decision making of treatment for patients with severe MR (4). The size, shape, and function of the LV are typically assessed using 2D transthoracic echocardiography. However, 2D echocardiography may be inaccurate in some patients, and interobserver variability remains debated. These limitations for LV assessment may be overcome by 3D assessment, including 3D echocardiography, CMR, or multidetector row computed tomography (MDCT) (Figure 3). Nevertheless, it has been suggested that LV ejection fraction may not be an accurate marker of LV systolic function in severe MR because the calculated differences between LV end-diastolic and end-systolic volumes do not reflect the true “forward stroke volume.” Due to significant backward flow into the LA, LV systolic function may be overestimated when derived from LV volumes. In contrast, LV strain analysis may be a more accurate method to assess LV systolic function (12,13). It has been demonstrated, that both in primary (13) and secondary (12) MR, global LV longitudinal strain may be impaired. Kamperidis et al. (12) studied 2 groups of patients with nonischemic cardiomyopathy who were matched for LV ejection fraction. In 75 patients, severe MR was present, whereas the other 75 patients had no or less than trivial MR. Global LV longitudinal strain was significantly reduced in the patients with severe MR compared to patients without MR ( $-8.08 \pm 3.33\%$  vs.  $-9.78 \pm 3.78\%$ ;  $p = 0.004$ ), despite similar LV ejection fractions in both groups. Therefore, accurate assessment of LV systolic function in patients with severe MR may require more dedicated parameters than LV ejection fraction alone.

In addition to LV systolic function, it is important to assess LV size and shape for the invasive treatment of MR. In secondary MR, geometric alterations of the LV result in tethering of the MV with subsequent malcoaptation of the leaflets. For conventional surgical MV repair, specific parameters of LV remodeling have been identified that predict procedural outcome (8). However, for transcatheter MV procedures, these LV parameters are less clear, partly because of the different mechanisms of action of the various procedures. A 3D imaging modality such as echocardiography or MDCT provides the most detailed

**TABLE 2** Multidetector Row Computed Tomography Analysis of the Mitral Valve for Transcatheter Mitral Valve Therapies

• Mitral valve annulus dimensions <ul style="list-style-type: none"> <li>○ Perimeter</li> <li>○ Intertrigonal distance</li> <li>○ Intercommissural distance</li> <li>○ Septal-to-lateral distance</li> </ul>
• Mitral annulus calcification
• Length of mitral valve leaflets
• Distance between papillary muscles
• LVOT area <ul style="list-style-type: none"> <li>○ Predicted neo-LVOT</li> </ul>
• Coronary sinus course relative to mitral annulus
• Circumflex coronary artery course relative to mitral annulus <ul style="list-style-type: none"> <li>○ Distance between the circumflex coronary artery and lateral trigon</li> </ul>

neo-LV = a native anterior mitral leaflet that protrudes into the LVOT forming a new anatomical compartment known as the neo-LVOT.

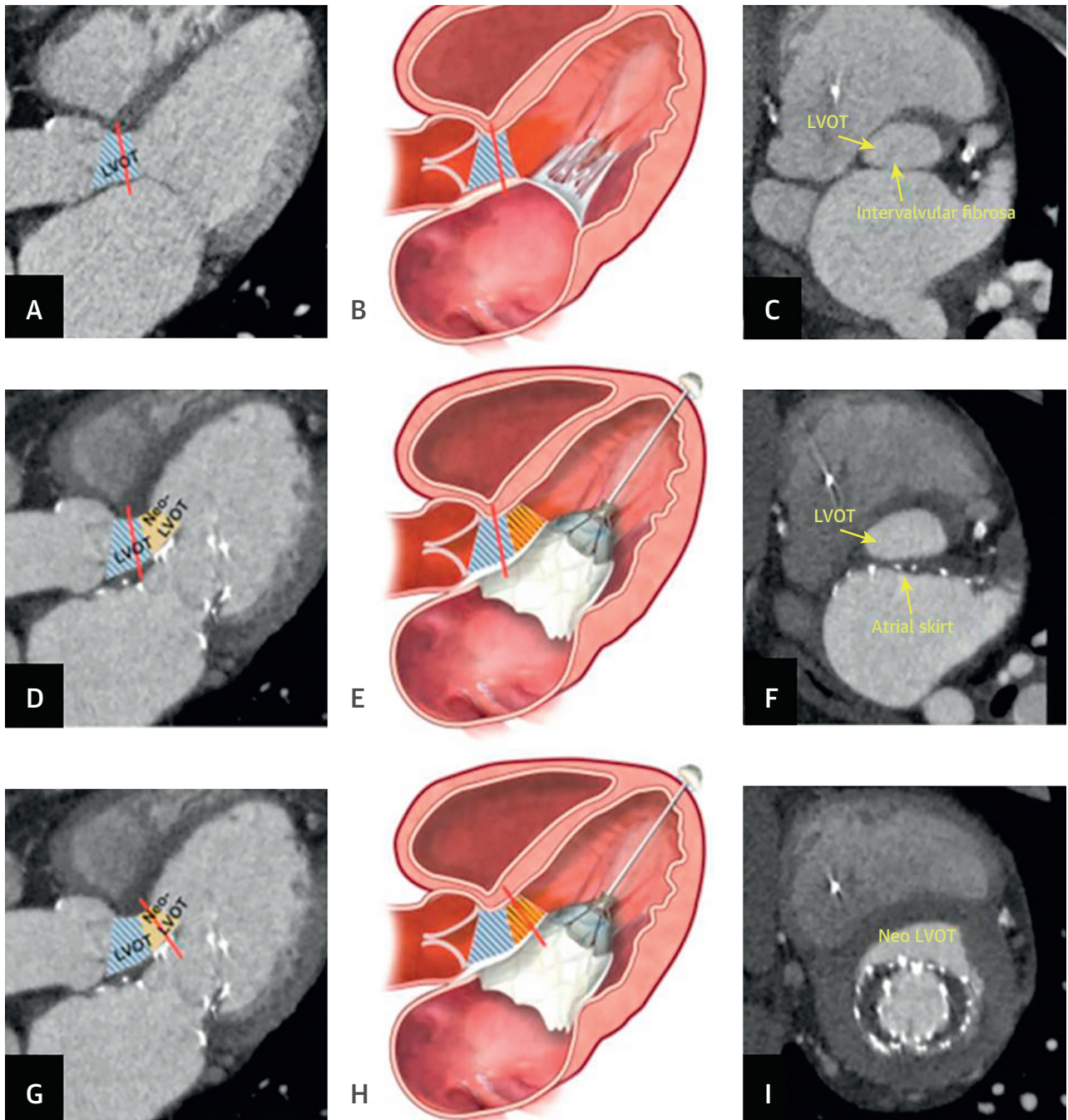
information for LV size and shape. Use of MDCT can accurately assess the exact geometric changes of the LV in relation to the MV, and its subvalvular apparatus can be assessed accurately (3).

## ROLE OF MULTIDETECTOR ROW COMPUTED TOMOGRAPHY IN TRANSCATHETER MV THERAPIES

**MITRAL VALVE ANATOMY AND FUNCTION.** In transcatheter mitral interventions, MDCT is becoming an important imaging modality for characterizing the anatomy of the MV and its spatial relationships. Electrocardiographically gated MDCT permits retrospective acquisition of data throughout the entire cardiac cycle, which can be subsequently reconstructed at each 5% or 10% of the RR interval and in multiple reformation planes resembling echocardiography or CMR. The short axis of the MV can be reconstructed with the double-oblique transversal plane, and the orthogonal plane can be oriented across the lateral (A1 to P1), central (A2 to P2) and medial (A3 to P3) segments of the MV (Figure 4). By performing this reconstruction in the end-systolic phase, the mechanism underlying MV dysfunction (MR or mitral stenosis) can be defined. In Carpentier type I MR (5), the MV leaflet is normal, but the MV annulus is dilated. In Carpentier type II MR, the prolapsing MV leaflet segments can be defined, whereas in Carpentier type III MR, the extent of MV leaflet tethering can be assessed. In patients with at least moderate secondary MR due to LV systolic dysfunction (in ischemic and nonischemic cardiomyopathy), the central and posterior MV segments showed significantly larger tethering angles than those in patients without MR (3).



**FIGURE 5** Predicting Left Ventricular Outflow Tract Obstruction After Transcatheter Mitral Valve Implantation



From the reconstructed LVOT (A, D, G) and short-axis (C, F, I) views, the LVOT area can be measured before and after the transcatheter mitral valve implantation, using the Tendyne TMVR system (Abbott Vascular). (B, E, H) Schematic renderings. The new device prolongs the outflow tract into the left ventricle, referred to as the neo-LVOT (yellow-shaded area). LVOT = left ventricular outflow tract. Adapted with permission from Blanke et al. (17).

In addition, the grade of mitral stenosis or MR can be estimated by measuring the anatomic MV area and the anatomic regurgitant orifice area, respectively. When Doppler echocardiography is not

conclusive, MDCT may help to finally determine the severity of MV dysfunction. By aligning the reformation planes to bisect the tips of the MV leaflets in diastole, the MV area can be planimetered in mitral

stenosis patients (14). In patients with MR, the alignment of the multiplanar reformation planes across the MV leaflets in systole, the anatomical regurgitant orifice area can be measured. The regurgitant volume can be subsequently estimated by integrating Doppler echocardiographic data. In 73 patients (62% with secondary MR and 38% with primary MR), the integration (fusion) of the velocity of the regurgitant flow on echocardiography with the anatomical regurgitant orifice on MDCT led to a reclassification of the MR severity in a significant proportion of patients. MR was downgraded from severe to nonsevere in 10% of patients and was upgraded from nonsevere to severe in 14% of patients (15). However, this method is not currently recommended by current American and European guidelines (8,9).

For transcatheter MV repair or replacement techniques, the MDCT parameters of the MV that need to be assessed with MDCT is still under investigation and most are empirical (Table 2). The dimensions of the MV annulus are important to select the size of transcatheter MV annuloplasty devices and transcatheter MV prostheses. In addition, the severity of MV annulus calcification is important to assess the feasibility of various transcatheter therapies. For example, the length of the MV leaflets is important for the feasibility of MitraClip implantation (Abbott Vascular, Menlo Park, California). The distance between the heads of the papillary muscles indicates the displacement of these structures in patients with secondary MR, which may be relevant for future transcatheter MV therapies. Specific devices for transcatheter MV therapies demand accurate imaging of anatomical relationships with surrounding structures that may be damaged during the procedures. Transcatheter MV replacement may obstruct the LV outflow tract, whereas transcatheter MV annuloplasty may impinge the circumflex coronary artery. MDCT is the optimal imaging technique to obtain this information.

**NEO-LV OUTFLOW TRACT.** The obstruction of the LV outflow tract during transcatheter MV replacement procedures is caused by the native anterior mitral leaflet that protrudes into the LV outflow tract, forming a new anatomical compartment known as the neo-LV outflow tract (LVOT). In a multicenter registry including 116 patients at very high surgical risk, with severe mitral annulus calcification undergoing transcatheter MV replacement, LVOT obstruction with hemodynamic compromise occurred in 11.2% and was associated with high in-hospital mortality (16). Importantly, the axis or center line of this neo-LVOT is different from the axis of the native LVOT,

which is essential to define the orientation of the imaging planes to quantify the cross-sectional neo-LVOT area and predict the risk of LVOT obstruction after transcatheter MV replacement. MDCT in combination with advanced post-processing allows for assessment of the mitral annular geometry and its spatial relationship to the LVOT and the LV (Figure 5) (17). A recent multicenter registry including 194 patients undergoing MDCT prior to transcatheter MV replacement (including valve-in-valve, valve-in-ring, and valve-in-mitral annulus calcification) showed that an estimated neo-LVOT area  $\leq 1.7$  cm<sup>2</sup> predicted LVOT obstruction during the procedure with a sensitivity and specificity of 96% and 92%, respectively (18).

**CORONARY SINUS AND CIRCUMFLEX CORONARY ARTERY.** A coronary sinus coursing extremely high relative to the mitral annulus will reduce the efficacy of devices for indirect mitral annuloplasty because the cinching effect will affect only the LA. In addition, the presence of a circumflex coronary artery coursing underneath the coronary sinus where the distal anchoring of the device for indirect mitral annuloplasty should be placed needs careful monitoring of the patency of the coronary artery during the procedure due to the increased risk of arterial impingement. The course of the circumflex coronary artery is also important for the implantation of direct mitral annuloplasty devices that use anchoring systems or pledgets that are implanted directly into the myocardium of the atrioventricular groove. MDCT is the imaging modality that provides the best spatial resolution to assess these anatomical relationships of the mitral annulus. In most patients, the coronary sinus courses along the left atrial wall rather than along the mitral annulus (2). Importantly, in patients with heart failure, the distance between the coronary sinus and the mitral annulus may increase, potentially resulting in less favorable outcome after indirect transcatheter MV annuloplasty.

#### SELECTION AND GUIDANCE FOR CURRENTLY AVAILABLE DEVICES

Transcatheter MV replacement (TMVR) therapies can be divided according to the target structure or mechanism by which MR will be reduced:

- MV leaflets. MitraClip (Abbott Vascular), Pascal TMVR (Edwards Lifesciences, Irvine, California), NeoChord DS 1000 (NeoChord, Inc, St Louis Park, Minnesota), Harpoon mitral valve repair system (Edwards Lifesciences).
- MV annulus. Cardioband (Edwards Lifesciences), Mitralign (Mitralign, Tewksbury, Massachusetts),

Carillon (Cardiac Dimensions, Kirkland, Washington), Mitral loop cerclage catheter system (Tau-PNU Medical Co., Ltd., Pusan, Korea).

- MV replacement. CardiAQ (Edwards Lifesciences), Tiara (Neovasc Tiara, Inc., Vancouver, British Columbia, Canada), Tendyne (Abbott Vascular), Intrepid TMVR System (Medtronic, Inc., Redwood City, California).

What needs to be imaged and how to select patients with symptomatic severe MR for the most appropriate transcatheter MV intervention and how to guide the procedure are discussed in this section.

**TRANSCATHETER MV THERAPIES TREATING MV LEAFLETS. MitraClip (Abbott) and Pascal (Edwards Lifesciences) TMVR system.** More than 60,000 patients have been treated with the MitraClip device, which consists of a cobalt chromium clip covered by polyester tissue to promote endothelium growth. Three randomized clinical trials have demonstrated that MitraClip is a safe and feasible treatment for primary and secondary MR (19-21). The first-in-human study using the Pascal TMVR system included 23 patients deemed inoperable and in whom a successful MitraClip implantation would be unlikely (22). The Pascal TMVR system consists of a 10-mm central spacer that fills the regurgitant orifice, 2 paddles of 25-mm width, and 2 clasps of 10-mm length that can be operated simultaneously or independently to facilitate leaflet capture.

Echocardiography is the mainstay for selecting patients for MitraClip and or Pascal TMVR system implantation, as well as to guide the procedure. Both devices share a similar imaging check list:

- Mechanism of MR and MV anatomy and geometry. Currently, MitraClip is approved in the United States for patients with severe primary MR. Mitral valve prolapse with a flail gap of  $\leq 10$  mm and a width of  $\leq 15$  mm are amenable for treatment with the MitraClip. However, implantation of more than 1 MitraClip may correct larger defects without causing significant mitral stenosis. Commissural prolapse, Barlow's disease, and leaflet perforation or clefts are considered unsuitable for use of the MitraClip (23). In Europe, MitraClip has been used more frequently in patients with secondary MR (24). In those patients, leaflet coaptation depth should be  $\geq 2$  mm and a tenting height of  $\leq 11$  mm. When the coaptation depth is  $< 2$  mm and the tenting height is  $> 11$  mm, the tethering of the leaflets by a severely dilated LV is significant and may challenge the MitraClip implantation procedure. In addition, a short mobile posterior mitral

**TABLE 3 Anatomic Criteria that Define Suitability for MitraClip Device Implantation**

Optimal	Conditional	Unsuitable
Central pathology A2-P2	Pathology A1-P1 or A3-P3	Perforation of leaflets
No leaflet calcification	Mild calcification outside the grip-zone, ring calcification	Severe calcification in the grip zone
MVA $> 4$ cm <sup>2</sup>	MVA $> 3$ cm <sup>2</sup> with good residual mobility	MVA $< 3$ cm <sup>2</sup> and mean pressure gradient $\geq 5$ mm Hg
Mobile length PML $\geq 10$ mm	Mobile length PML 7-10 mm	Mobile length PML $< 7$ mm
Coaptation depth $< 11$ mm	Coaptation depth $\geq 11$ mm	—
Normal leaflet strength and mobility	Leaflet restriction in systole	Leaflet restriction in systole and diastole (RHD)
Flail width $< 15$ mm and flail gap $< 10$ mm	Flail width $> 15$ mm only with a large ring width and the option for multiple clips	Barlow's syndrome with multiple segment flail leaflets

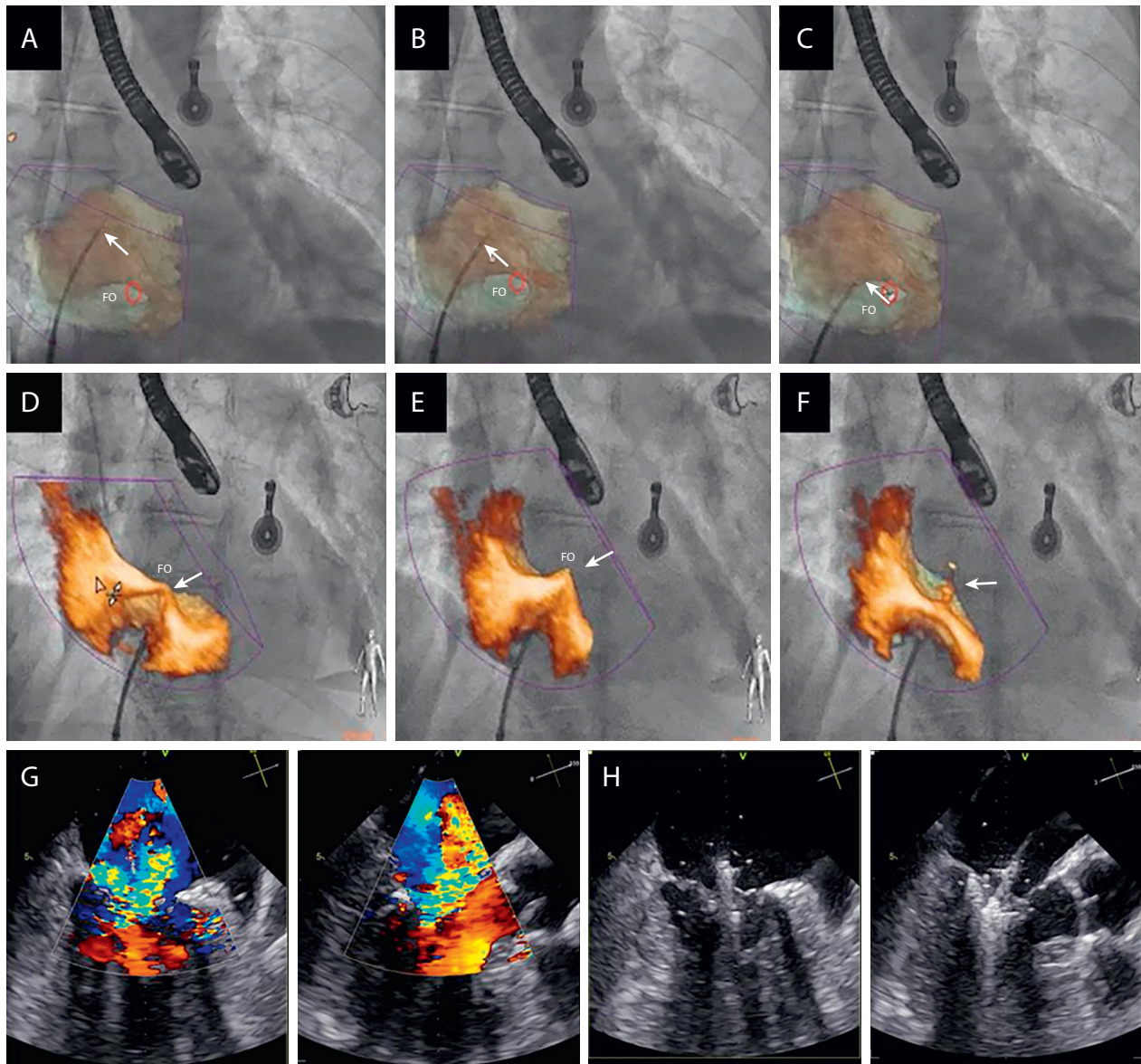
Table was adapted from Boekstegers et al. (23).

A2 = central scallop of the anterior mitral leaflet; A1P1 = lateral scallops of anterior and posterior mitral leaflets; A3 = medial scallop of the anterior mitral leaflet; MVA = mitral valve area; neo-LVOT = neo-left ventricle outflow tract; P2 = central scallop of posterior mitral leaflet; P3 = medial scallop of the posterior mitral leaflet; PML = posterior mitral leaflet; RHD = rheumatic heart disease.

leaflet ( $< 7$  mm) is considered unsuitable for MitraClip implantation. However, the procedure's learning curve is steep, and the possibility of implanting more than 1 device without creating significant obstruction has led to less restrictive criteria of anatomic suitability (Table 3) (23). The Pascal TMVR system may be a suitable alternative in circumstances where the MitraClip may not be successful. Cases of severely calcified leaflets, rheumatic MV disease, and an MV area of  $< 3$  cm<sup>2</sup> or a mean transvalvular gradient of  $\geq 5$  mm Hg are considered contraindications to both devices (23).

- Interatrial septum. The transeptal puncture is a key procedural step. A posterior and superior puncture with a height above the MV annulus between 3.5 and 4 mm is ideal to allow the manipulation of the guiding catheter and deliver the device. During patient selection, the presence of a patent foramen ovale or a floppy septum predict a challenging transeptal puncture in the target zone. During the procedure, the use of 3D TEE and visualization of the interatrial septum with the biplane view helps to define the superior (from the bicaval view) and posterior (from the short-axis view of the aortic valve) location of the puncture. Current fusion imaging systems overlaying the TEE image onto the fluoroscopy have facilitated the transeptal puncture (Figure 6) (25).
- Guiding the delivery of the MitraClip and Pascal TMVR system. Live 3D TEE en face views of the MV and the device are useful to manipulate the catheter, to introduce and position the device without

**FIGURE 6** MitraClip Device Implantation

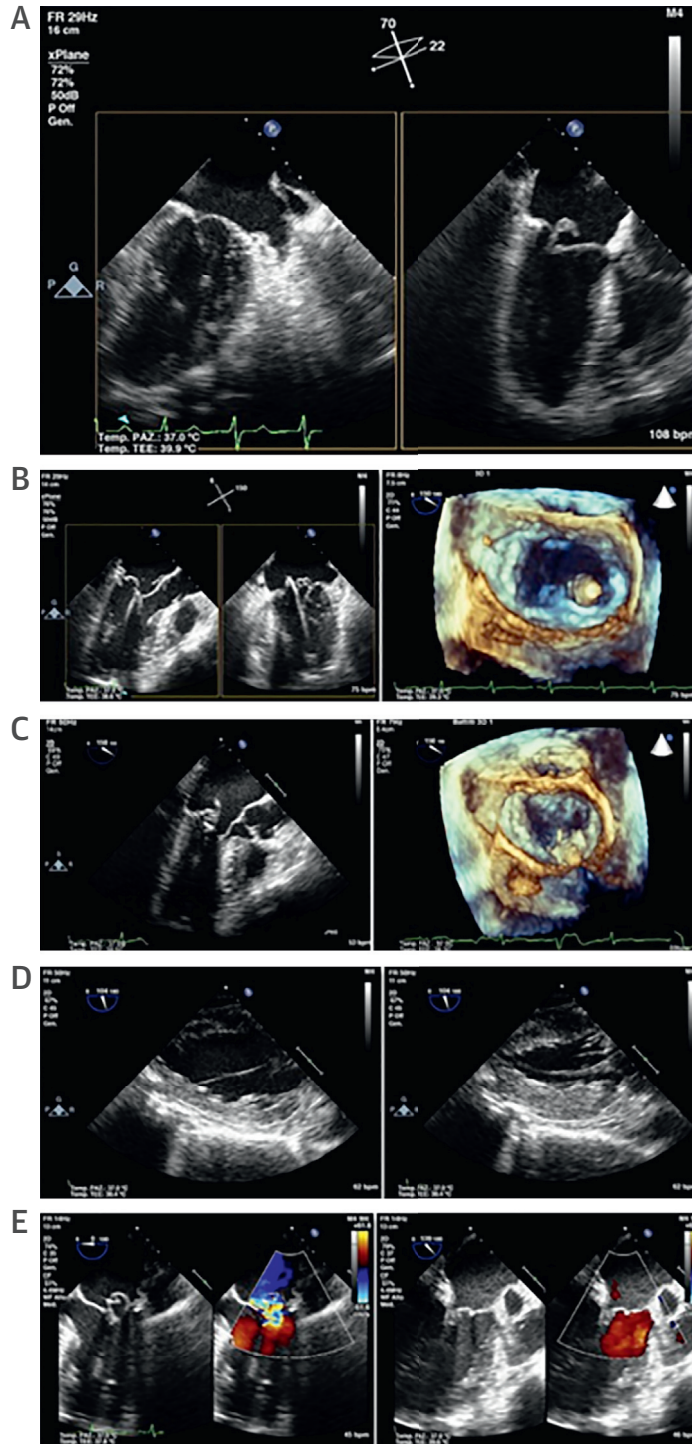


**(A to F)** Fused images of the 3D transesophageal volume rendering of the interatrial septum overlaid onto the fluoroscopic image. The system provides a fiducial landmark to indicate the position of the FO. Panels A to C show how the needle descends from the superior vena cava to the fossa ovalis. **(D to F)** Still frames of the transseptal puncture. **(G, H)** Biplane views (bicommissural and LVOT) of the mitral valve with color Doppler. The largest vena contracta is displayed to indicate the ideal position of the MitraClip device, whereas the images without color are used to grasp the mitral leaflets. Reproduced with permission from Faletra et al. (25). FO = fossa ovalis; other abbreviation as in [Figure 5](#).

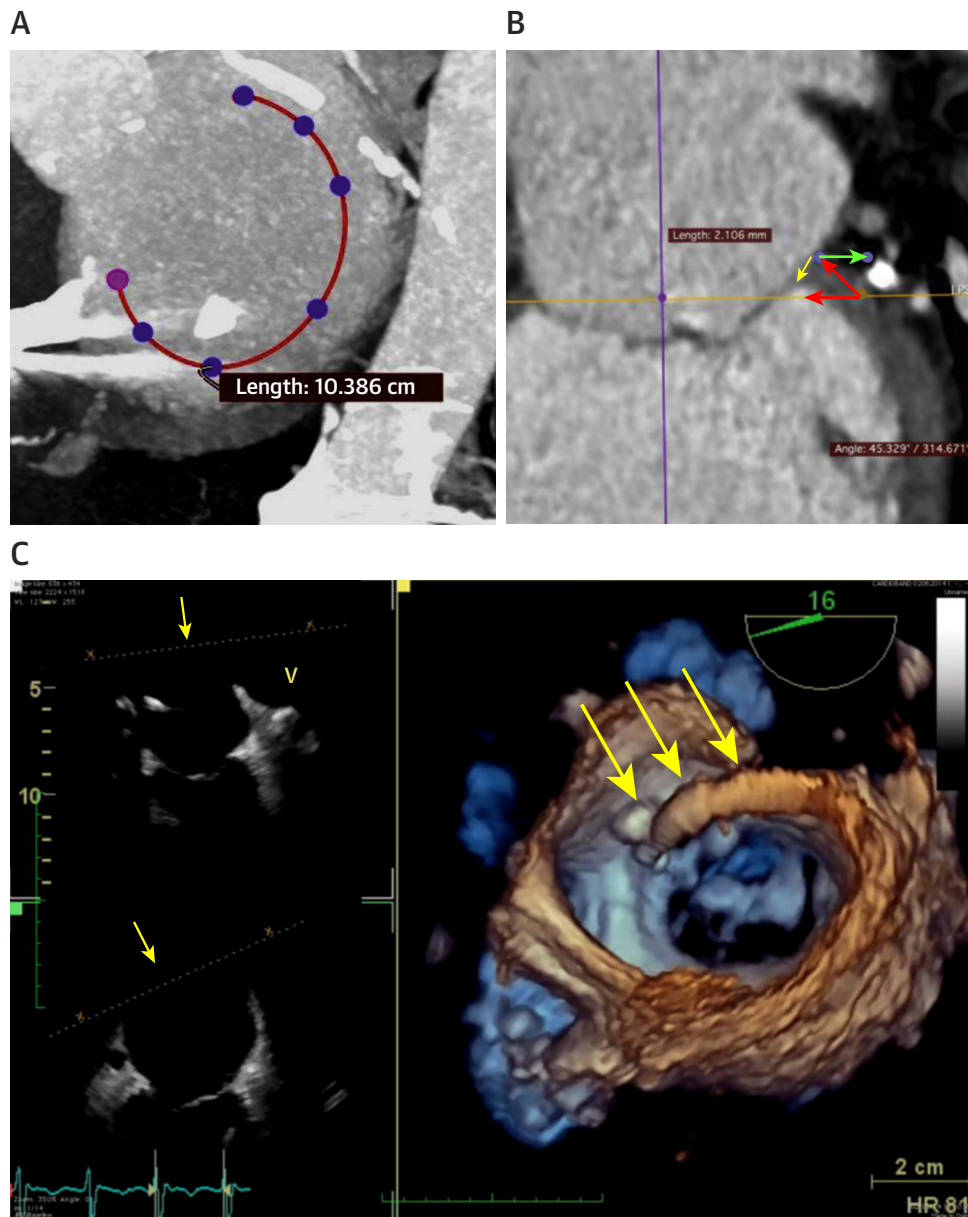
damaging surrounding structures (left atrium, left atrial appendage or pulmonary veins), and to orient the clips and paddles. The biplane view showing simultaneously the bicommissural and the 3-chamber long-axis planes is most frequently used to fine tune the orientation of the device relative to the largest regurgitant orifice area and

perpendicular to the coaptation line ([Figure 6](#)). This 3D TEE visualization mode is also used to capture and grasp the leaflets and detach the device from the guiding catheter. When more than 1 device is needed, a combination of fluoroscopy and TEE is important to ensure that the second device is placed parallel and contiguous to the previous device.

**FIGURE 7** NeoChord Implantation in a Patient With Severe Mitral Regurgitation Due to Prolapse of the Central Scallop of the Posterior Mitral Leaflet



**(A)** Biplane view with the bicommissural view (**left**) and LVOT view (**right**), where the prolapsing scallop can be visualized. **(B, C)** 2D and 3D views of the device approximating (**B**) and grasping the prolapsing scallop (**C**). **(D)** Transgrastic longitudinal view of the left ventricle where the NeoChord can be observed. **(E)** Simultaneous 2D and color Doppler views of the mitral valve before and after the procedure, which resulted in significant reduction in mitral regurgitation. Reproduced with permission from Colli et al. (26).

**FIGURE 8** Multimodal Imaging to Plan and Guide Direct Mitral Valve Annuloplasty Using the Cardioband Device

The length of the mitral valve annulus is measured on the short-axis reconstruction on multidetector row computed tomography (**A**). It is important to assess the thickness of the myocardium forming the mitral annulus (**yellow arrow**), the trajectory of the anchors when implanted in the left ventricular myocardium relative to the annular plane (**red arrows**), and the distance of the circumflex coronary artery (**B, green arrow**). During the procedure, 3D transesophageal echocardiography with simultaneous biplane views (**[C] left**) and en face view of the mitral valve (**C, right**) is pivotal to anchor the device.

**NeoChord and Harpoon.** Both of these systems implant neo-chordae off-pump in the beating heart to correct MR caused by isolated prolapse of the central scallop of the posterior MV leaflet. The DS 1000 (NeoChord) consists of a handle, a needle that is advanced through

the MV leaflet tissue, and a long shaft with a grasping mechanism at the tip. The Harpoon system consists of a 14-F hemostatic introducer and 21-gauge needle to securely anchor the expanded polytetrafluoroethylene chords in the desired position. Both systems

access the LV through a small anterolateral left thoracotomy in the fourth or fifth intercostal space and, under TEE guidance, the targeted MV leaflet segment is grasped by the 2 grippers of the DS 1000 device or by appropriate apposition and stabilization of the shafted device underneath the leaflet with the Harpoon system. The MV leaflet is perforated, and a knot is formed on the atrial surface of the MV leaflet, and multiple polytetrafluoroethylene chords are fixed on the LV apex at a specific length for correction of the prolapse. To ensure a successful procedure with these systems, the following steps in patient selection and procedural guidance should be assessed with echocardiography, although computed tomography (CT) also may help in procedural planning:

- Accurate evaluation of the MR mechanism and anatomy of the MV. Localized, isolated prolapse of the central scallop of the posterior MV leaflet is amenable to treatment with these devices. A short, posterior MV leaflet in relation to the anteroposterior mitral annulus dimensions may reduce the procedural success because the correction of the prolapse will not be sufficient to ensure adequate coaptation between the anterior and posterior MV leaflets. Evaluation of the MV annulus calcification is also important because this may cause shadowing and impaired visualization of the device.
- Determination of the transapical access. Trans-thoracic echocardiography is frequently used to decide the optimal intercostal space and location for the minithoracotomy. For the DS 1000 device, the posterolateral access is considered ideal as different trajectories to reach the posterior MV leaflet arise between the papillary muscles. For the Harpoon system, an anterolateral thoracotomy in the fourth or fifth intercostal space is preferred. The transapical access can also be defined using CT, which permits visualization of the trajectory of the device (Figure 7) (26).

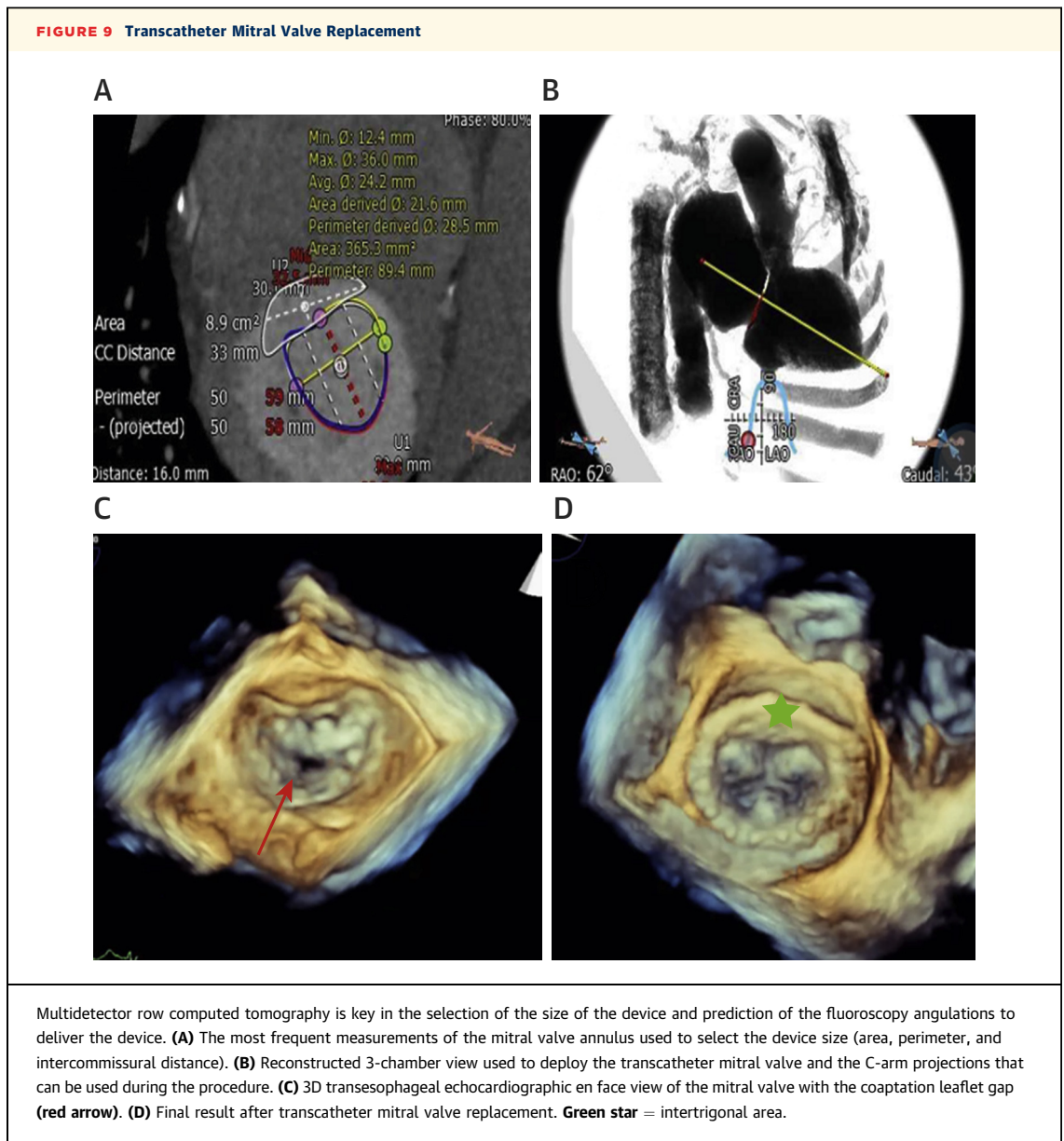
**TRANSCATHETER MV THERAPIES TREATING THE MV ANNULUS.** **Cardioband.** The Cardioband (Edwards Lifesciences) is a percutaneous direct annuloplasty device with supra-annular fixation and transfemoral delivery. The device is composed of a polyester sleeve with radiopaque markers at 8-mm intervals with a contraction wire connected to the end (adjusting spool) which allows shortening of the device. Depending on which of the 6 available sizes of the device is used, 12 to 17 stainless steel anchors 6 mm in length are implanted through the annulus and into the LV myocardium through the sleeve, beginning at

the anterolateral commissure and ending at the posteromedial commissure. The anchors are repositionable and retrievable until deployed. Once all anchors are in place, a stainless steel contraction wire is retracted, resulting in annular reduction. The Cardioband delivery system approach is from the femoral vein, using a mid-septal transseptal puncture site to gain the requisite height above the annular plane. The imaging check list for the selection of patients with MR for this therapy and procedural planning include the following.

- Mitral annulus size. The posterior annular circumference from the left to right trigones during maximum diastolic opening of the MV should be measured (Figure 8A). MDCT is the recommended method to assess this diameter. However, 3D TEE and CMR could be feasible alternatives for patients with contraindications for MDCT (severely impaired renal dysfunction).
- Course of the circumflex coronary artery. MDCT is the preferred imaging modality to assess the course of the circumflex coronary artery (Figure 8B). TEE may also be used to assess the position of the circumflex coronary artery at the level of the anterolateral trigone where the first anchors are implanted.
- Location of the transseptal puncture and fluoroscopic angles. MDCT can help define the location of the transseptal puncture to facilitate the manipulation of the guiding catheter during the procedure. In addition, MDCT can recreate the fluoroscopic views used to implant the device: the short-axis view with the en face view of the MV to set the first anchor at the anterolateral trigone and the 2- and 3-chamber views to implant the medial anchors.

During the procedure, a combination of fluoroscopy and TEE is needed to monitor the implantation of the device. The C-arm is angled to visualize the short-axis view of the MV and, with the help of 3D TEE providing the multiplanar reformation planes, the first anchor is implanted as close as possible to the posterior leaflet hinge targeting the ventricular portion of the annulus and avoiding the circumflex coronary artery (Figure 8C). Subsequently, the following anchors are implanted under fluoroscopy and TEE guidance. The C-arms that project the 2- and 3-chamber views are helpful to implant the medial anchors.

**Mitralign.** The Mitralign device (Mitralign Inc.) provides an alternative direct mitral annuloplasty solution that does not require transseptal puncture. This system consists of a bident catheter that can deliver

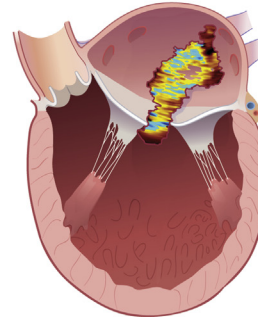
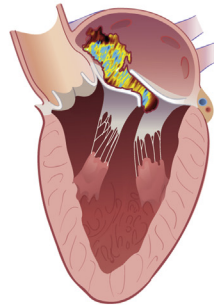


radiofrequency energy and pledgets that are implanted in the ventricular and atrial side of the P1 and P3 regions of the posterior mitral annulus. In the selection process of patients with secondary MR for this procedure the following parameters should be assessed.

- Severity and mechanism of MR. Only patients with severe secondary MR are candidates for this device. This procedure is not suitable for patients with primary MR with significant calcification of the mitral annulus.
- Left ventricular dimensions. The LV end-diastolic dimension should be within 5.0 to 7.5 cm, and the distance between the mitral annulus plane and the LV apex should be  $\geq 5.0$  cm to allow proper catheter manipulation.
- Left ventricular or atrial thrombus. The presence of LV or atrial thrombus is a contraindication. Trans-thoracic echocardiography with contrast permits accurate assessment of the presence of LV thrombus. LA (appendage) thrombus is best assessed using TEE or CT.



**CENTRAL ILLUSTRATION Transcatheter Techniques Used to Treat Mitral Regurgitation and Imaging Needs**



	Primary MR			Secondary MR		
Target Structure	Device	What to look for?	Imaging Technique	Device	What to look for?	Imaging Technique
Leaflets	MitraClip/ Pascal	<ul style="list-style-type: none"> <li>Length of leaflets</li> <li>Prolapse width</li> <li>Flail gap</li> <li>Procedural guidance</li> </ul>	2D/3D TTE/TEE  2D/3D TEE Fluoroscopy Fusion	MitraClip/ Pascal	<ul style="list-style-type: none"> <li>Length of leaflets</li> <li>Coaptation depth</li> <li>Coaptation length</li> <li>Procedural guidance</li> </ul>	2D/3D TTE/TEE  2D/3D TEE Fluoroscopy Fusion
	Neochoord/ Harpoon	<ul style="list-style-type: none"> <li>PML segments prolapsing</li> <li>AML and PML length</li> <li>AP annulus diameter</li> <li>Chest incision</li> <li>Procedural guidance</li> </ul>	2D/3D TTE/TEE  TTE/CT  2D/3D TEE			
Annulus				Cardioband Mitralign Carillon MCS	<ul style="list-style-type: none"> <li>AML and PML length</li> <li>Course of the coronary sinus</li> <li>Course of the LCx</li> <li>Procedural guidance</li> </ul>	CT  2D/3D TEE Fluoroscopy
Valve	TMVR Systems	<ul style="list-style-type: none"> <li>Annulus perimeter</li> <li>Annulus calcification</li> <li>Length of leaflets</li> <li>Neo-LVOT</li> <li>Procedural guidance</li> </ul>	CT/3D TEE  3D TEE Fluoroscopy	TMVR Systems	<ul style="list-style-type: none"> <li>Annulus perimeter</li> <li>Annulus calcification</li> <li>Length of leaflets</li> <li>Neo-LVOT</li> <li>Procedural guidance</li> </ul>	CT/3D TEE  3D TEE Fluoroscopy

Bax, J.J. et al. *J Am Coll Cardiol Img.* 2019;12(10):2029-48.

CT = computed tomography; LVOT = left ventricular outflow tract; MCS = mitral contour system; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

- Aortic valve function. Moderate to severe aortic stenosis or regurgitation is a contraindication (because access is performed retrograde through the aorta).
- Femoral artery dimensions. Patients with a narrow and tortuous iliofemoral arterial system that cannot hold a 14-F introducer sheath are not candidates. CT angiography of the iliofemoral arterial system provides the most accurate assessment.

The procedure is guided with TEE and fluoroscopy. The guiding catheter is introduced in the LV retrograde through transfemoral arterial access. The bident catheter is introduced in the LV and directed toward the posterior mitral annulus at the level of P1 and P3, and the crossing wire is advanced into the LA facilitated by radiofrequency energy applied to the annulus. The pledget delivery catheter is introduced over the wire across the mitral annulus. After implantation of the pledgets, tension is applied to the 2 sutures exiting the guiding catheter to plicate the mitral annulus and reduce the anteroposterior diameter. If the MR is not reduced enough, a second pair of pledgets can be implanted at the P1 and P3 levels. Patency of the circumflex coronary artery should be monitored during the procedure by using invasive coronary angiography.

**Carillon mitral contour system.** The proximity of the coronary sinus to the posterior mitral annulus makes this anatomical structure a suitable vehicle to introduce devices such as the Carillon mitral contour system (Cardiac Dimensions), which cinches the mitral annulus, reduces the anteroposterior annulus diameter, and improves mitral leaflet coaptation, thereby reducing MR. The Carillon mitral contour system consists of 2 self-expanding nitinol anchors connected by a nitinol curvilinear segment. Various anchor diameters (distal 7 to 14 mm and proximal 16 to 20 mm) and segment lengths (60, 70, and 80 mm) are available. In the patient selection process for implantation of this device the following anatomical and functional aspects need to be evaluated.

- The dimensions of the coronary sinus and great cardiac vein should be measured with invasive venography. The vein should be at least 9 mm (preferably 10 mm) to host at least a 60-mm device length and pull a minimum of 3 cm of tension to cinch the mitral annulus. CT was proposed as an alternative to invasive venography because it provides information about the dimensions of the coronary sinus and great cardiac vein and the spatial relationships with the mitral annulus and

circumflex coronary artery. However, a substudy of AMADEUS (CARILLON Mitral Annuloplasty Device European Union Study) did not find CT to be a good alternative to invasive measurements (27).

- Mechanism of MR. Only patients with secondary MR are suitable. Patients with severe annular calcification or with primary MR are not candidates.

During the implantation, fluoroscopy is the main imaging technique to guide the procedure and the results can be assessed with transthoracic or TEE. The following steps should be monitored.

- Deployment of the device. The delivery system is introduced through a transfemoral venous access, and, after cannulation of the coronary sinus under fluoroscopic guidance, the system is advanced, and the distal anchor is unsheathed in the target location within the great cardiac vein and locked. Thereafter, tension is applied to the system to approximate the posterior to the anterior annulus to improve mitral leaflet coaptation. The reduction in MR can be checked at this moment with TEE or transthoracic echocardiography. The proximal anchor is then deployed near the coronary sinus ostium. Patency of the circumflex coronary artery is assessed by coronary angiography.

**TRANSCATHETER MV REPLACEMENT.** A number of TMVR devices are currently under investigation, each with different design features to address the primary issues of access, variable native valve morphology, anchoring, and mitral-aortic continuity. It is beyond the scope of this review to discuss the various designs of the rapidly evolving TMVR device fields. However, for all devices, the inherently more complex nature of MV disease and MR requires multimodality imaging for pre-procedural assessment, intraprocedural guidance, and post-procedural follow-up.

For selecting the prosthesis size, MDCT provides high spatial resolution data to assess the MV dimensions and geometry and the structures surrounding the entire landing zone of the TMVR (28,29). Important annular measurements may vary by device but typically include the intercommissural diameter (the major or long-axis) and septal-to-lateral diameter (also known as the A2 to P2 distance, minor or short-axis) (Figure 9). The mitral annulus can be segmented using MDCT to yield the 2D planar mitral annular dimensions, area and perimeter, annular displacement, tenting area and

volume, and area and volume of each leaflet. Blanke et al. (29) proposed using the trigones of the annulus to define a virtual line, beyond which a device may obstruct the LVOT. Thus, the reconstructed and measured annulus would be “D-shaped” with the flat portion of the “D” represented by this trigone-to-trigone line. In addition, the axis perpendicular to the mitral annulus plane, referred to as the “mitral annular trajectory,” can be assessed. Dynamic changes in annular size and shape may affect sizing and the location of the intended landing zone. Sizing of the mitral annulus is performed in both end-systole and end-diastole.

Depending how the valve anchors in the MV landing zone, the measurements of the MV apparatus may vary. If the device anchors by grasping leaflets, chordal and leaflet anatomy must be defined. If the anchoring occurs behind the leaflets or trigones, the distance to the papillary muscle tips may be important to predict potential obstruction to anchor positioning. Mitral annular calcification can impede anchoring and should be characterized.

Intraprocedural imaging using fluoroscopy requires a co-planar view of the mitral annulus, which can be determined pre-procedurally by MDCT (30). Both long-axis views (extreme right anterior oblique and caudal orientation) as well as commissural views (right anterior oblique and cranial orientation) can be obtained for implantation of the device. Frequently a coronary sinus wire is used to help locate the annular plane on fluoroscopy. CT allows for prediction of optimal fluoroscopic angulations to achieve a co-planar view of the mitral annulus but also may allow for a more patient-specific approach to the use of a coronary sinus guide wire as a fluoroscopic landmark (31). Real-time assessment of MV morphology and function is performed by preferably 3D TEE, which allows simultaneous visualization of orthogonal planes with high frame rates and good axial resolution for rapid and accurate assessment of device positioning (9,32).

## HIGHLIGHTS

- Transcatheter interventions for mitral regurgitation are a therapeutic breakthrough for patients with contraindications for surgery.
- Multimodality imaging is key to select the patients for each transcatheter device.
- Echocardiography and computed tomography are the imaging techniques that can answer all the preprocedural questions.
- Echocardiography is the main imaging technique for procedural guidance and important aid to fluoroscopy.

## CONCLUSIONS

Treatment of patients who have severe MR is changing with the development of new transcatheter treatments. Accurate characterization of the MV apparatus, MV function, and LV and atrial dimensions are key to select the patients who can be treated with these therapies. Each transcatheter treatment has a different target (leaflets, mitral annulus) but a common objective, to reduce MR (Central Illustration). The anatomical characteristics of the MV and surrounding structures will partially determine which transcatheter treatment may be more appropriate. A combination of transesophageal or transthoracic echocardiography, MDCT, fluoroscopy (and specific situations CMR) is important to select the patients for the most appropriate therapy and to guide the procedure and check the results.

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**KEY WORDS** cardiac magnetic resonance, computed tomography, mitral regurgitation, transesophageal echocardiography



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