Anatomy of the Mitral Valvular Complex and Its Implications for Transcatheter Interventions for Mitral Regurgitation

Nicolas M. van Mieghem, Nicolo Piazza, Robert H. Anderson, Apostolos Tzikas, Koen Nieman, Lotte E. de Laat, Jackie S. McGhie, Marcel L. Geleijnse, Ted Feldman, Patrick W. Serruys, Peter P. de Jaegere.

J Am Coll Cardiol 2010;56(8):617-26

ABSTRACT

Mitral regurgitation (MR) poses a significant clinical burden in the adult population, which is expected to increase even more with the ever prolonging life expectancies in developed countries. New technology has brought MR, once exclusively the arena of cardiac surgeons, to the attention of interventional cardiologists. A variety of device-oriented transcatheter strategies have evolved in recent years. A comprehensive understanding of mitral valvular anatomy is crucial for the selection of patients, the implementation of devices, and further refinements of these transcatheter techniques if they are eventually to produce procedural and clinical success. The aim of this review is to elucidate the morphology of the mitral valvular complex, integrating key anatomical features into the developing transcatheter options for the treatment of MR.

INTRODUCTION

Valvular heart disease frequently affects the adult population in developed countries [1]. Because age is the dominant risk factor and is uncontrollable, the incidence of such problems will rise. In the U.S., 0.7% of young adults below the age of 45 years have moderate to severe valvular heart disease, a proportion increasing to one-sixth of those over 75 years of age. In every age group, mitral regurgitation (MR) is the most common valvular disorder, with a global prevalence of 1.7%, increasing to 10% in those age >75 years.

The mitral valvular apparatus is a complex anatomical and functional entity [2]. One or more flaws in its components can result in MR. According to etiology and pathophysiology, MR can be divided somewhat artificially into primary or organic and secondary or functional categories [3,4]. In primary lesions, 1 or more of the components of the mitral valve (MV) itself is deranged, whereas in secondary lesions, geometric and/or functional changes of the left ventricle (LV) are the core of the problem.

Despite guidelines for the management of patients with severe MR, a recent European survey established that one-half of these patients are not referred for surgery, largely because of their advanced age, the presence of comorbidities, or impaired LV function [5–7]. Even more notably, repair as opposed to valvular replacement was performed in only one-half of those who underwent surgery, mostly because of a lack of institutional expertise in this particular technique. The surgical treatment of functional MR remains a subject of debate [8].

This underserved population of patients with severe MR opens the door for several innovative transcatheter concepts, which are comparable with various aspects of surgical repair [9]. To take full advantage of these new technologies, it is axiomatic that those attempting treatment should have comprehensive knowledge of the anatomy of the mitral valvular apparatus and its relationship to the LV. Our aim in this review, therefore, is to address the anatomy of the mitral valvular complex with catheter-based techniques for valvular repair in mind.

HISTORY

It was the Belgian anatomist and physician Andreas Vesalius, while working in Padua, Italy, who likened the bifoliate left atrioventricular valve to a bishop's mitre, hence the term "mitral valve" [10]. The physiology of the working components of the valve, its 2 leaflets, can be understood only when note is taken of their crucial relationships to the adjacent anatomical structures, namely, the left atrium (LA), the LV, the aortic valve, the papillary muscles, the tendinous cords, and the cardiac central fibrous body. In 1972, Perloff and Roberts put forward the concept of a mitral valvular complex to underscore this essential and harmonious structural relationship [2]. From a clinical perspective, the French surgeon Alain Carpentier introduced the paradigm of the pathophysiologic triad to better define

regurgitation across the valve, pointing out that the underlying disease, the first leg of the triad, creates structural or geometric changes in the valvular apparatus, this being the second leg, which may lead to valvular dysfunction as the third leg [3,4].

More recently, the extraordinary revolution in cardiac imaging has contributed to better understanding and integration of the anatomy, physiology, and pathophysiology of the MV, with 3-dimensional echocardiography, multislice computed tomography, and cardiac magnetic resonance imaging all proving invaluable in evaluating valvular regurgitation and playing a defining role in the development and execution of transcatheter valvular therapies [11–16].

THE MITRAL VALVULAR COMPLEX

For normal closure of the MV, both leaflets must align in the same plane as they coapt along their solitary zone of apposition. To achieve such apposition, it is necessary to have an optimal size of the so-called valvular annulus, a geometrically correct orientation of the papillary muscles giving rise to the tendinous cords, and appropriate closing forces generated by muscular contraction of the LV. Thus, it is necessary to take account not only of the mitral valvular apparatus when considering the salient anatomy but also of the relationship between its components and surrounding structures, such as the atrioventricular conduction axis, the aortic valve, the coronary sinus, and the circumflex coronary artery.

The left atrioventricular junction

From an anatomical perspective, the term “mitral annulus” is a misnomer. The essential structure supporting the valvular leaflets is the left atrioventricular junction, this being the D-shaped orifice formed at the confluence between the LA walls and the supporting LV structures [2,10,17,18]. On the ventricular aspect, these supporting structures are not exclusively myocardial, because there is an extensive area of fibrous continuity (the so-called aortic-mitral curtain) between the anterior leaflet of the MV and the aortic valve in the roof of the LV (Figure 1). When considered 3-dimensionally, the overall atrioventricular junction is nonplanar, with elevated septal and lateral segments at the ends of the solitary zone of apposition between the leaflets and complementary depressed medial segments along the central component of the zone of apposition, giving a characteristic saddle-shaped overall appearance (Figure 2) [19]. It is along the depressed anterior segment of the junction that 1 of the leaflets of the valve is in fibrous continuity with the noncoronary and left coronary leaflets of the aortic valve, this extensive area being well described as the aortic-mitral curtain (Figure 1). At either end, the central part of the fibrous curtain, which represents the annulus of the aortic or anterior leaflet of the valve, is attached by fibrous expansions, the left and right fibrous trigones, to the ventricular myocardium (Figures 3 and 4). The right trigone is itself continuous with the membranous septum, the combined entity forming the

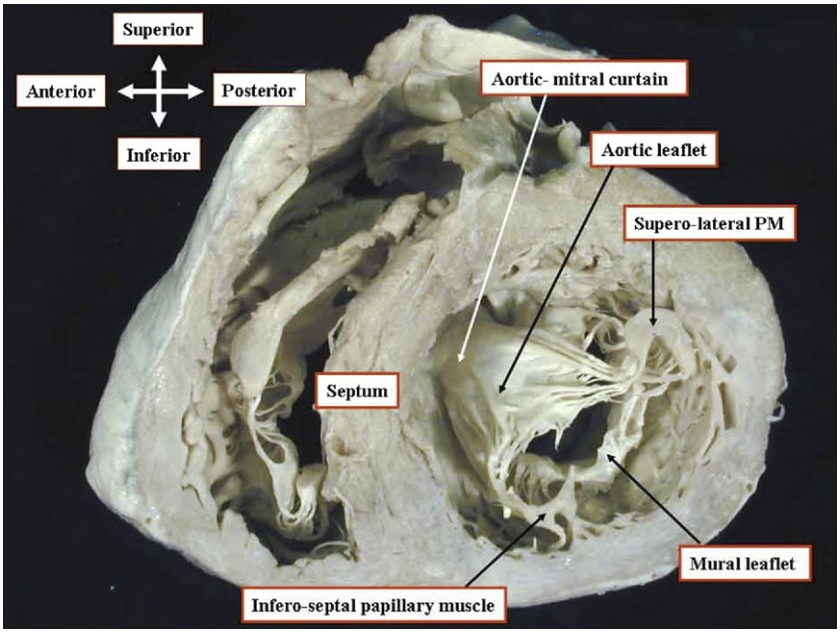

Figure 1. Anatomical Orientation of the Left Atrioventricular Junction. The ventricular mass has been sectioned along its short axis and photographed from the cardiac apex; the heart is presented in the location it occupies in the thorax. Note that the septum is anteriorly located, and the papillary muscles (PM) supporting the leaflets of the mitral valve, when assessed in attitudinally appropriate location, are positioned inferoseptally and superolaterally. Note also that 1 of the leaflets of the mitral valve is in fibrous continuity with the leaflets of the aortic valve, the fibrous aortic-mitral curtain formed by the area of their continuity creating the roof of the left ventricle.

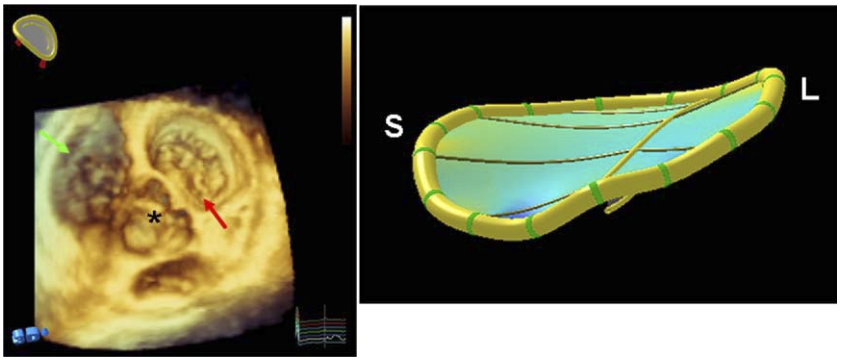

Figure 2. 3-Dimensional Echocardiographic Reconstruction of the Left Atrioventricular Junction. (Left) Three-dimensional echocardiographic reconstruction of the left atrioventricular junction, demonstrating the location of the mitral valve (red arrow) relative to the aortic valve (*). The green arrow indicates the right ventricle. (Right) Saddle-shaped appearance of the mitral atrioventricular junction or "annulus." Note the elevated septal (S) and lateral (L) segments and complementary depressed segments along the central zone of apposition.

central fibrous body, and with the penetrating part of the atrioventricular conduction axis passing through the atrioventricular component of the membranous septum [18]. Fibroelastic cords of various firmness and structure extend from the fibrous trigones through the mural part of the left atrioventricular junction. It is rare for the cords to form a complete ring to support the mural, or posterior, leaflet of the valve. The so-called annulus, therefore, is much more resistant to pathologic dilation along the aortic as opposed to the mural leaflet. Especially in its posterior aspects, several deficiencies in the annular structure are filled with adipose tissue. The absence of a well-formed fibrous cord in this particular position opposite the aortic-mitral curtain explains its predilection for annular dilation and calcification, which result in a disproportional increase in the aortic-to-mural, or septal-to-lateral, diameter of the valvular orifice, potentially precluding adequate leaflet coaptation.

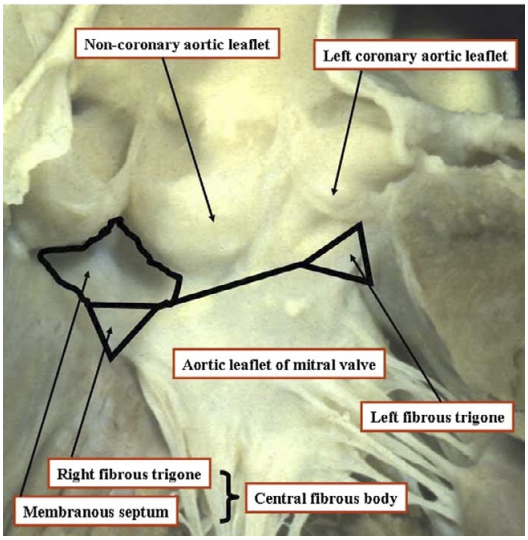

Figure 3. The Aortic-Mitral Curtain and Fibrous Continuity. The heart has been opened through the outflow tract of the left ventricle, showing the ventricular surface of the aortic leaflet of the mitral valve. Note how the ends of the area of fibrous continuity between the aortic leaflet of the mitral valve and the noncoronary and left coronary leaflets of the aortic valve anchor the aortic-mitral curtain in the roof of the left ventricle. The ends of the area of fibrous continuity are the left and right fibrous trigones. As can be seen, the right fibrous trigone is itself continuous with the membranous septum, the conjoined are being known as the central fibrous body.

The goal of surgical annuloplasty when the atrioventricular junction is dilated is to decrease the circumference of the valvular orifice, the aim being to reduce the septal-to-lateral diameter by at least 8 mm [20]. Transcatheter strategies now exist to achieve this same goal (Figures 5A and 5B). Key anatomical features for success are the patency of the coronary sinus and the anatomical relationship between the myocardial components of the mural junction, the sinus itself, and the circumflex coronary artery. The potential to produce damage to the atrioventricular conduction axis should also be remembered (Figure 4).

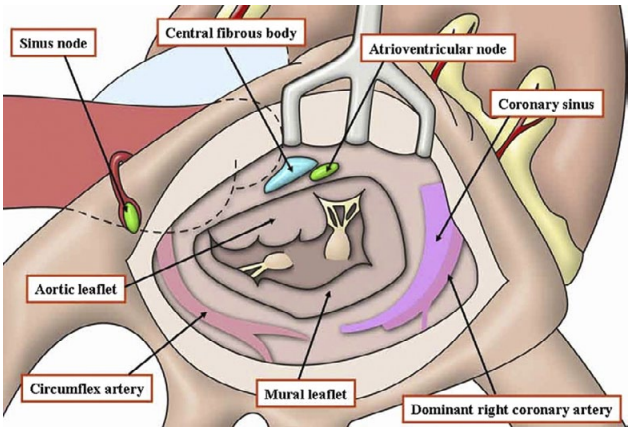

Figure 4. Anatomical Structures Surrounding the Left Atrioventricular Junction. Relationships of the mitral valve as seen by the surgeon operating through the roof of the left atrium.

Transcatheter annuloplasty can be performed indirectly by reshaping and restraining the valvular orifice via the coronary sinus (see the following discussion) or by approaching the junction directly via the LA or LV [9]. The Mitralign system (Mitralign, Inc., Tewksbury, Massachusetts) and Accucinch (Guided Delivery Systems, Inc., Santa Clara, California) are both direct annuloplasty devices. Dedicated catheters are advanced retrogradely into the LV to position anchors to the ventricular side of the posterior segment of the left atrioventricular junction. By pulling the anchors together with sutures, the circumference of the atrioventricular junction is reduced. Mitral cerclage annuloplasty is a circumferential suture-based concept that combines the indirect and direct techniques [21]. A guidewire is advanced through the coronary sinus into the first septal perforating branch of the great cardiac vein and subsequently directed across a short segment of myocardium to establish a right ventricular or right atrial re-entry. The guidewire is then ensnared and exchanged for a suture and tension fixation device. A rigid arch protects the suture at the site where the coronary sinus crosses the circumflex artery. Annuloplasty can also be achieved by applying thermal radiofrequency to the fibroadipose tissue of the left atrioventricular junction, producing shrinkage without jeopardizing the cardiac vessels or mitral valvular leaflets (QuantumCor system, QuantumCor, Inc., Bothell, Washington) [22].

The valvular leaflets

The MV is bifoliate. The leaflet classically described as being anterior is in fibrous continuity with 2 of the leaflets of the aortic valve, hence the alternative term “aortic leaflet.” The opposing posterior leaflet is also appropriately described as the mural leaflet [10,18]. The aortic leaflet has a wider surface with a shorter base and guards one-third of the left atrioventricular junction. It separates the LV inflow and outflow tracts. The mural leaflet is shallower but wider, guarding two-thirds of the junctional circumference. The surface area of both

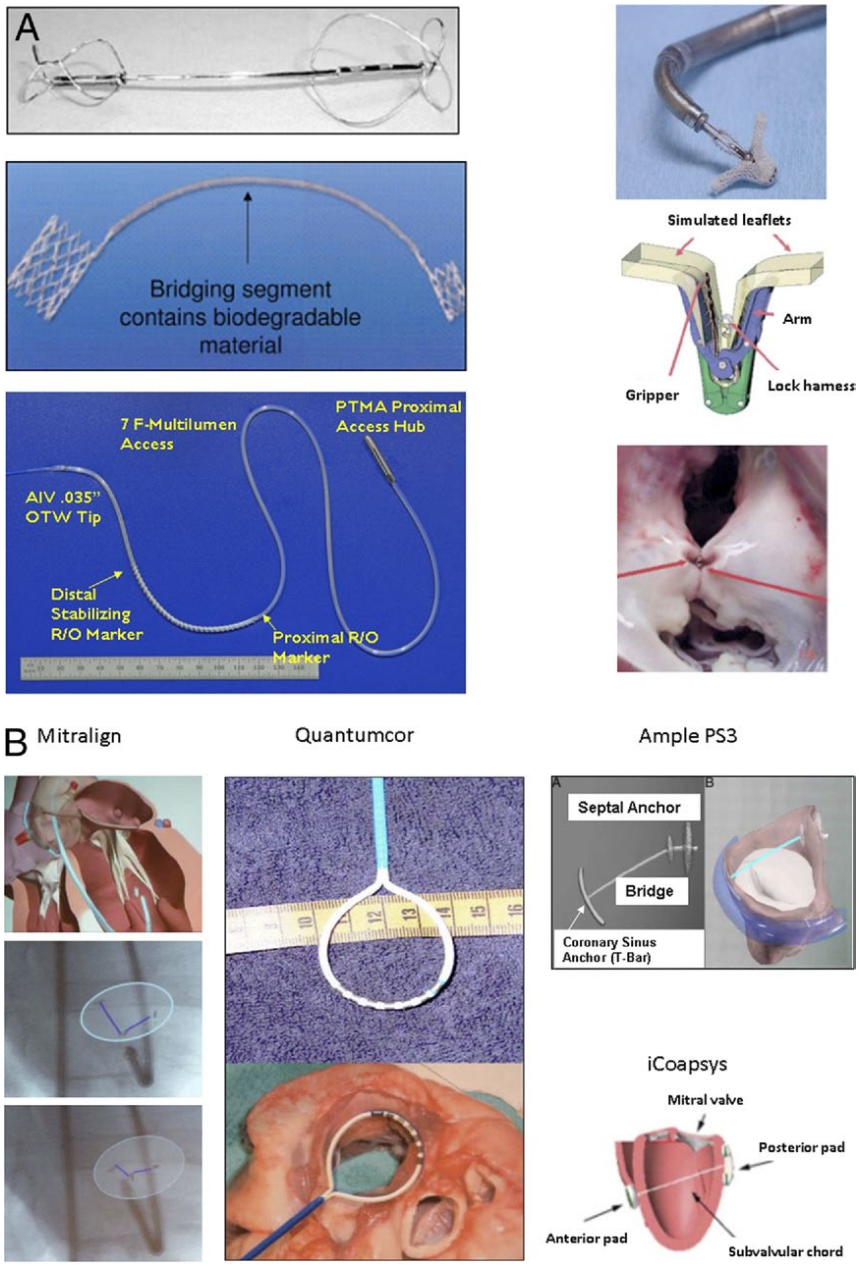

Figure 5. Devices for Indirect Transcatheter Mitral Annuloplasty and MitraClip and Devices to Reduce Mitral Regurgitation. (A) Devices available for indirect transcatheter mitral annuloplasty. (Left) From top to bottom, the Carillon (Cardiac Dimensions, Inc., Kirkland, Washington), Edwards MONARC (Edwards Lifesciences, Irvine, California), and Percutaneous Transvenous Mitral Annuloplasty (PTMA) (Viacor, Inc., Wilmington, Massachusetts) devices. (Right) The MitraClip (Evalve, Inc., Menlo Park, California). (B) Devices to reduce mitral regurgitation through transcatheter repair of the mitral valve. AIV = anterior interventricular vein; OTW = over-the-wire; R/O = radio-opaque.

leaflets taken together is 2.5 times the area of the valvular orifice. In systole, the leaflets coapt over a height of, on average, 8 mm, giving an "overlapping reserve" or "coaptation reserve" in case of annular dilation (Figure 6). The zone of apposition between the leaflets is obliquely oriented relative to the orthogonal planes of the body but is recognized as the "mitral smile" on short-axis echocardiography. Its 2 ends are positioned inferoseptally and superolaterally (Figure 1), although these positions are currently incorrectly described as being posteromedial and anterolateral [17]. Slits in the mural leaflet create 3 scallops, while further segments of leaflet tissue are found at the ends of the solitary zone of apposition, this zone representing the true valvular commissure. These various components of the mural leaflet produce a more flexible structure compared with the more rigid aortic leaflet and combine with the dynamic motions of the junction to produce the so-called sphincter mechanism.

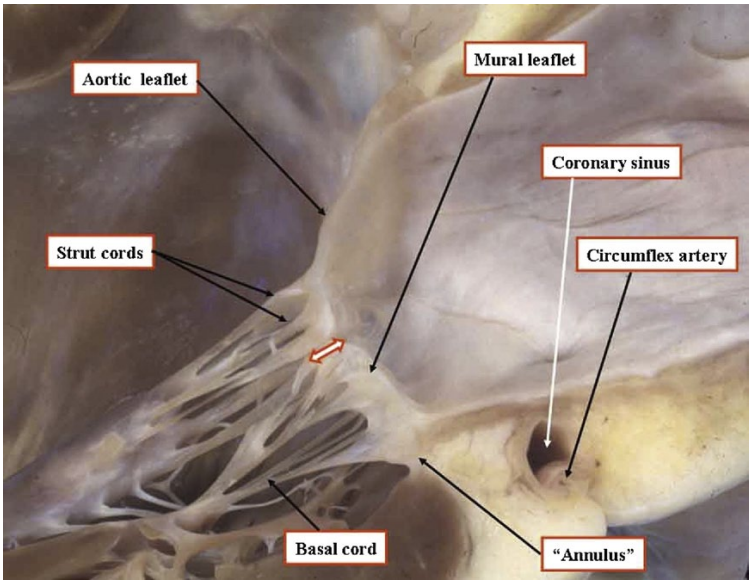

Figure 6. Mitral Leaflet Coaptation. The heart has been sectioned along the long axis of the left ventricle, having fixed the heart with the leaflets of the mitral valve in closed position. The double-headed arrow indicates the coapting surfaces of the leaflets. Note the strut cords supporting the ventricular aspect of the aortic leaflet of the valve and the basal cord supporting the ventricular aspect of the mural leaflet. Note also the relationships of the coronary sinus and the circumflex artery to the mural leaflet of the valve.

When regurgitation across the valve is the consequence of inappropriate coaptation of the leaflets, one approach to surgical treatment is to create a double orifice by suturing together the free edges of the middle segments of the anterior and posterior leaflets, the edge-to-edge or Alfieri stitch [23]. This technique has now been adapted for transcatheter use, and has received Conformité Européenne mark approval as the MitraClip (Evalve, Inc., Menlo Park, California). Unlike the surgical approach, however, the transcatheter technique does

not currently involve an annuloplasty, although the clinical value of a combined approach remains debatable [24].

The Alfieri stitch is used for organic as well as functional MR [25]. A transseptal puncture is required to advance the catheter to the LA. The MitraClip uses 1 or 2 clips to join the 2 leaflets at the level of the middle scallop of the mural leaflet. After implantation, a tissue bridge forms across the clip between the leaflets, providing additional support for the repair and preventing septal-to-lateral dilation. Importantly, the contractile function of the atrioventricular junction is preserved. For MitraClip trial inclusion, several anatomical premises must be fulfilled. First, the regurgitant jet must be centered at the level of the zone of coaptation in the central two-thirds of the line of coaptation. Second, coaptation length of at least 2 mm, and a depth below the mitral annular plane of no more than 11 mm, must be available for coaptation between the leaflets, although the coaptation depth may be less important. Should one of the leaflets be flail, the gap and the width of the flail segment can be no more than 10 and 15 mm, respectively (Figure 7).

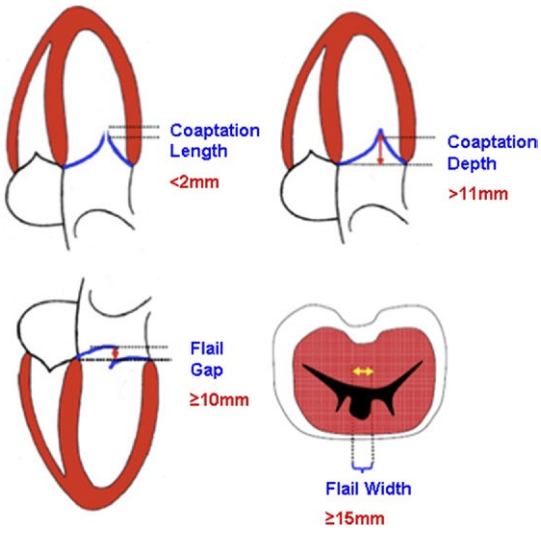

Figure 7. Key Anatomical Dimensions for the MitraClip. Anatomical measurements less favorable for the MitraClip device (Evalve, Inc., Menlo Park, California).

Tendinous cords and papillary muscles

The mitral valvular leaflets, via the tendinous cords and papillary muscles, are connected to the LV free wall like the shrouds of a parachute [2,10,18]. The fibrocollagenous tendinous cord, or chordae tendineae, take origin from the papillary muscles, bifurcate several times, and attach to the free edges and ventricular aspects of both leaflets. The cords are thinnest at their sites of insertion on the leaflets, and this is the site of predilection for chordal rupture.

Most of the cords insert uniformly along the free margins of the leaflets, thus preventing marginal prolapse and aligning the zone of coaptation. Strut cords attach to the ventricular aspect of the aortic mitral leaflet (Figure 1), precluding billowing and serving to distribute load throughout the leaflet. The basal cords originate directly from the ventricular wall and attach exclusively to the ventricular surface of the mural leaflet, contributing to ventricular geometry and fortifying the ventricular aspect of the atrioventricular junction.

The cords arise from the paired papillary muscles, which arise from the apical to middle thirds of the LV free wall, with each muscle made up of a variable number of heads. It is conventional wisdom to state that the superolateral muscle is supplied by 1 or more branches of the circumflex artery, or by diagonal branches, whereas the inferoseptal papillary muscle is supplied by a single branch of the circumflex or right coronary artery, depending on coronary artery dominance. Because of its single vascular supply, the inferoseptal muscle in particular is susceptible to coronary ischemia. Organic disease usually involves these components of the mitral valvular complex [26]. Myxomatous degeneration can render the cords inappropriately long and abolish their specific elastic properties, thus inducing prolapse. Fibroelastic deficiency produces the exact opposite phenomenon. There will be retraction of tissue, making the cords vulnerable to rupture and resulting in a partial or total flail leaflet. As already discussed, it is the MitraClip that represents the transcatheter approach targeting degenerative regurgitation.

Integration of the LA and LV

The myocardium of the LA and LV is intimately connected to support the mural leaflet of the MV. The term "disjunction" refers to the fact that the valvular tissue hinges directly from the myocardium rather than being supported by an anatomical cordlike structure [27]. The insertion of the LA myocardium follows the general contour of the junction, as opposed to the LV myocardium, which has no relationship with the aortic leaflet of the MV. Indeed, the LV outflow tract interposes between the aortic leaflet of the MV and the ventricular septum [10]. The posteroinferior wall of the LV, in contrast, supports directly the mural leaflet through the basal cords. Given the tight interdependence with the ventricular free wall and the unique arrangements of the different components, changes in ventricular geometry can have serious consequences for mitral valvular dynamics [28]. LV mural dyskinesia can change the orientation of the basal cords, producing a tethering effect on the mural leaflet. More global LV dilation can displace the papillary muscles in an apical direction, creating tenting of the leaflets with lack of coaptation and eventual regurgitation.

Catheter techniques have been developed to remodel the LV by introducing a transventricular bridge between anterior and posterior pads, placed through the pericardial space (iCoapsys, Edwards Lifesciences, Irvine, California). By drawing the pads together, it is possible to change the LV geometry, potentially narrowing the atrioventricular junction

and optimizing the orientation of the papillary muscles relative to the leaflets, although this technology is currently in abeyance [29].

Transcatheter replacement of the MV, via either a transapical or a transseptal approach, is a much anticipated technique. Several anatomical hurdles remain. The inherent radial force needed to anchor the stented valve might squeeze the LV outflow tract, while the tendinous cords might impede positioning, expansion, and anchoring of the prosthesis [30,31]. The asymmetry of the mitral orifice is also a technical challenge.

Coronary venous and arterial anatomy

In a venous system known to show marked variability, consistent entities are the great cardiac vein and the coronary sinus (Figure 8) [12,32,33]. In general, the great cardiac vein, also known as the anterior interventricular vein, originates at the lower or middle third of the anterior interventricular groove [32]. It follows the groove toward the base of the heart and then turns inferiorly at the atrioventricular junction, fusing with the oblique vein of the LA, a remnant of the embryonic left superior caval vein, to become the coronary sinus. The middle cardiac vein runs along the inferior interventricular groove to empty into the coronary sinus close to its orifice in the right atrium. At its orifice, the coronary sinus is guarded by a thin semicircular valve, the Thebesian valve. There is significant variability in the morphology and composition of this valve, such that it can become a notorious obstacle to cannulation of the sinus [33]. The location of the coronary sinus changes as it courses through the left atrioventricular junction. In over nine-tenths of cases, the body of the sinus is adjacent to the inferior LA wall, well above and cranial to the deeper atrioventricular junction (Figure 6) [12,16,34]. It is closest to the lateral segment of the atrioventricular junction at the midpoint of the mural leaflet and furthest away at the ends of the solitary zone of apposition. When there is significant regurgitation, particularly in the setting of ischemic cardiomyopathy,

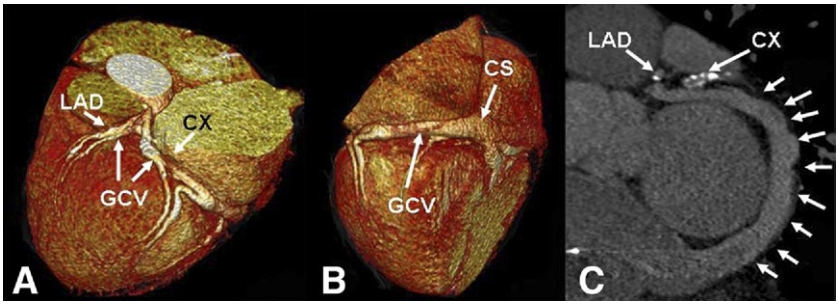

Figure 8. CS and Left CX by Multislice Computed Tomography. Electrocardiographically-gated dual-source 128-slice computed tomographic scan showing the morphology of the coronary sinus (CS). (A, B) 3-dimensional reconstructions showing the great cardiac vein (GCV) originating from the CS and extending into the left atrioventricular groove. (C) Cross-sectional plane taken parallel to the left atrioventricular groove showing the entire circumferential course and diameter of the great vein (arrows), demonstrating its relationship to the coronary arteries. CX = circumflex coronary artery; LAD = left anterior descending coronary artery

the sinus is lifted away from the posterior segment and conversely moves closer to the ends of the solitary zone of apposition between the leaflets [11,12]. This coincides with flattening of the saddle-shaped "annulus" and an increase in the septal-to-lateral annular diameter [35]. As the sinus approaches its right atrial termination and receives several tributaries, its caliber grows. The sinus is always a close neighbor of the circumflex artery, which crosses the venous structure in up to four- fifths of patients. The point of crossing, the length of the overlapping segment, the length of the parallel course, as well as the distance of the crossing point to the atrioventricular junction are all highly variable. The great cardiac vein crosses diagonal or intermediate arterial branches in one-sixth of individuals [33].

Several different devices are in development to provide indirect transcatheter annuloplasty [36–38]. Depending on the anatomical proximity of the coronary sinus to the left atrioventricular junction to accomplish an indirect annuloplasty, however, has obvious limitations. Coronary arteries can be pinched, and the location of the sinus relative to the annulus may be unfavorable, precluding procedural success. Various imaging techniques have been used to identify these spatial interrelationships. To date, however, none has been shown to accurately predict the suitability of the sinus for the purposes of transcatheter annuloplasty, nor could they predict whether the technique would jeopardize the circumflex artery. Cardiac failure, with at least moderate to severe MR, seems the tentative target indication. With this in mind, we briefly review the main devices under investigation.

Transcatheter indirect mitral annuloplasty devices

The Percutaneous Transvenous Mitral Annuloplasty device (Viacor, Inc., Wilmington, Massachusetts) consists of up to 3 straight and rigid nitinol rods seated in a dedicated multilumen polytetrafluoroethylene (Teflon, DuPont, Wilmington, Delaware) catheter, which is introduced in the coronary sinus with its distal atraumatic silicone tip in the great cardiac vein down the interventricular groove 38. The assembly will produce an outward force at its proximal and distal ends, resulting in anterior displacement of the middle scallop of the mural leaflet and a decrease in the septal-to-lateral diameter of the valve. After positioning, the titanium proximal Percutaneous Transvenous Mitral Annuloplasty hub is closed and sutured to the subclavian fascia, as would happen with a permanent pacemaker device.

The Carillon device (Cardiac Dimensions, Inc., Kirkland, Washington) consists of a curved nitinol arc connecting a proximal and a distal anchor [36]. A dedicated delivery catheter is used to position the distal anchor near the point at which the great vein enters the anterior interventricular groove. The device is then passively deployed by retracting the delivery catheter. During the implantation procedure, the functional efficacy on regurgitation, and potential coronary compromise, can be evaluated with ability to recapture the device if needed.

The Edwards MONARC system (Edwards Lifesciences) is a nitinol assembly with a small distal anchor, a larger proximal anchor, and a springlike bridging segment [37]. The

device is introduced through a delivery catheter. Both anchors are self-expandable. By retracting the delivery system, the device is deployed, and both anchors are drawn together, displacing the inferior part of the annulus more superiorly. The bridge contains biodegradable material, causing the system to shrink over the following weeks. Hence, the final result becomes evident only after 4 to 6 weeks. The downside of this system is 2-fold: the impact of the MONARC system on the dimensions of the valvular orifice and flow through the coronary arteries cannot be monitored during the implantation, and the device is not retrievable. The great cardiac vein must be at least 3 mm wide to receive the distal anchor, and the total length of the coronary venous system should be from 14 to 18 mm.

The various indirect coronary sinus annuloplasty devices have suffered fractures after implantation. The mechanical stresses in the coronary sinus are difficult to model and have not been fully appreciated. Also, not only the circumflex artery and its branches but also the diagonal and intermediate branches are at risk for impingement over time. All of these devices have been redesigned and require further study.

Indirect remodeling and concomitant reduction in the circumference of the valvular orifice through transatrial fixture is pursued with the Transcatheter Septal Sinus Shortening or PS3 device (Ample Medical, Inc., Foster City, California) [39]. This system creates a transatrial bridge using an atrial septal occluder and a T-bar element constricting the LA, thus reducing the septal-to-lateral dimension of the atrioventricular junction. Despite promising pre-clinical data and the first human experience, no further investigational efforts are currently scheduled.

CONCLUSION

The MV is a complex anatomical structure. Normal valvular mechanics require a sophisticated interaction of its components, along with the adjacent LV and atrial myocardium. Surgery is currently the standard of care for patients with severe MR [5,6,40,41]. In this respect, repair has a clear advantage over replacement, preserving as it does LV systolic function, obviating the need for oral anticoagulation, and improving survival [8,42]. Unfortunately, surgical repair is not always feasible, and at many cardiothoracic centers, the required surgical expertise is unavailable, and patients end up with MV replacement [43]. In addition, patients do not undergo surgical intervention because of age and comorbidities, while the indications for surgery in the setting of moderate to severe functional regurgitation are highly debated [7,8,44]. This confers a window of opportunity for the creation of new transcatheter technology. Knowledge of the anatomy of the mitral valvular complex is crucial for the clinical implementation and further refinement of these technologies. If their efficacy and safety can be demonstrated in relevant trials, the stage might be set for a paradigm shift whereby these transcatheter interventions could be added to the therapeutic

armamentarium in the heart failure arena and as a potential alternative for surgical valvular repair in selected cases.

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. Perloff JK, Roberts WC. The mitral apparatus. Functional anatomy of mitral regurgitation. Circulation 1972;46:227–39.
3. Carpentier A. Cardiac valve surgery—the "French correction." J Tho- rac Cardiovasc Surg 1983;86:323–37.
4. Carpentier A, Chauvaud S, Fabiani JN, et al. Reconstructive surgery of mitral valve incompetence: ten-year appraisal. J Thorac Cardiovasc Surg 1980;79:338 – 48.
5. Bonow RO, Carabello BA, Chatterjee K, et al. 2008 focused update incorporated into the ACC/AHA 2006 guidelines for the manage- ment of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guide- lines for the Management of Patients With Valvular Heart Disease). J Am Coll Cardiol 2008;52:e1–142.
6. Vahanian A, Baumgartner H, Bax J, et al. Guidelines on the management of valvular heart disease: the Task Force on the Man- agement of Valvular Heart Disease of the European Society of Cardiology. Eur Heart J 2007;28:230 – 68.
7. Mirabel M, Iung B, Baron G, et al. What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery? Eur Heart J 2007;28:1358 – 65.
8. Enriquez-Sarano M, Loulmet DF, Burkhoff D. The conundrum of functional mitral regurgitation in chronic heart failure. J Am Coll Cardiol 2008;51:487
9. Piazza N, Asgar A, Ibrahim R, Bonan R. Transcatheter mitral and pulmonary valve therapy. J Am Coll Cardiol 2009;53:1837–51.
10. Ho SY. Anatomy of the mitral valve. Heart 2002;88 Suppl:iv5–10.
11. Chiribiri A, Kelle S, Kohler U, et al. Magnetic resonance cardiac vein imaging: relation to mitral valve annulus and left circumflex coronary artery. J Am Coll Cardiol Img 2008;1:729 –38.
12. Choure AJ, Garcia MJ, Hesse B, et al. In vivo analysis of the anatomical relationship of coronary sinus to mitral annulus and left circumflex coronary artery using cardiac multidetector computed to- mography: implications for percutaneous coronary sinus mitral annu- loplasty. J Am Coll Cardiol 2006;48:1938 – 45.
13. Grayburn PA. How to measure severity of mitral regurgitation: valvular heart disease. Heart 2008;94:376 – 83.
14. Kwan J, Shiota T, Agler DA, et al. Geometric differences of the mitral apparatus between ischemic and dilated cardiomyopathy with signifi- cant mitral regurgitation: real-time three-dimensional echocardiogra- phy study. Circulation 2003;107:1135– 40.
15. Levine RA, Handschumacher MD, Sanfilippo AJ, et al. Three- dimensional echocardiographic reconstruction of the mitral valve, with implications for the diagnosis of mitral valve prolapse. Circulation 1989;80:589 –98.
16. Tops LF, Van de Veire NR, Schuijf JD, 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.
17. Anderson RH, Loukas M. The importance of attitudinally appropriate description of cardiac anatomy. Clin Anat 2009;22:47–51.
18. Muresian H. The clinical anatomy of the mitral valve. Clin Anat 2009;22:85–98.

19. Anwar AM, Soliman OI, ten Cate FJ, et al. True mitral annulus diameter is underestimated by two-dimensional echocardiography as evidenced by real-time three-dimensional echocardiography and mag- netic resonance imaging. Int J Cardiovasc Imaging 2007;23:541–7.
20. Daimon M, Fukuda S, Adams DH, et al. Mitral valve repair with Carpentier-McCarthy-Adams IMR ETlogix annuloplasty ring for ischemic mitral regurgitation: early echocardiographic results from a multi-center study. Circulation 2006;114:I588 –93.
21. Kim JH, Kocaturk O, Ozturk C, et al. Mitral cerclage annuloplasty, a novel transcatheter treatment for secondary mitral valve regurgitation: initial results in swine. J Am Coll Cardiol 2009;54:638 –51.
22. 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.
23. Fucci C, Sandrelli L, Pardini A, Torracca L, Ferrari M, Alfieri O. Improved results with mitral valve repair using new surgical tech- niques. Eur J Cardiothorac Surg 1995;9:621–7.
24. Maisano F, Vigano G, Blasio A, Colombo A, Calabrese C, Alfieri O. Surgical isolated edge-to-edge mitral valve repair without annulo- plasty: clinical proof of the principle for an endovascular approach. Eurointervention 2006;2:181– 6.
25. Feldman T, Kar S, Rinaldi M, et al. 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.
26. Anyanwu AC, Adams DH. Etiologic classification of degenerative mitral valve disease: Barlow's disease and fibroelastic deficiency. Semin Thorac Cardiovasc Surg 2007;19:90 – 6.
27. Hutchins GM, Moore GW, Skoog DK. The association of floppy mitral valve with disjunction of the mitral annulus fibrosus. N Engl J Med 1986;314:535– 40.
28. Otto CM. Clinical practice. Evaluation and management of chronic mitral regurgitation. N Engl J Med 2001;345:740 – 6.
29. Pedersen WR, Block P, Leon M, et al. iCoapsys mitral valve repair system: percutaneous implantation in an animal model. Catheter Cardiovasc Interv 2008;72:125–31.
30. Cheung A, Webb JG, Wong DR, et al. Transapical transcatheter mitral valve-in-valve implantation in a human. Ann Thorac Surg 2009;87:e18 –20.
31. Lozonschi L, Quaden R, Edwards NM, Cremer J, Lutter G. Transapical mitral valved stent implantation. Ann Thorac Surg 2008; 86:745– 8.
32. Van de Veire NR, Marsan NA, Schuijf JD, et al. Noninvasive imaging of cardiac venous anatomy with 64-slice multi-slice com- puted tomography and noninvasive assessment of LV dyssynchrony by 3-dimensional tissue synchronization imaging in patients with heart failure scheduled for cardiac resynchronization therapy. Am J Cardiol 2008;101:1023–9.
33. Maselli D, Guarracino F, Chiaramonti F, Mangia F, Borelli G, Minzioni G. Percutaneous mitral annuloplasty: an anatomic study of human coronary sinus and its relation with mitral valve annulus and coronary arteries. Circulation 2006;114:377– 80.
34. Shinbane JS, Lesh MD, Stevenson WG, et al. Anatomic and electro- physiologic relation between the coronary sinus and mitral annulus: implications for ablation of left-sided accessory pathways. Am Heart J 1998;135:93– 8.
35. Timek TA, Miller DC. Experimental and clinical assessment of mitral annular area and dynamics: what are we actually measuring? Ann Thorac Surg 2001;72:966 –74.
36. Schofer J, Siminiak T, Haude M, et al. Percutaneous mitral annulo plasty for functional mitral regurgitation: results of the Carillon Mitral Annuloplasty Device European Union Study. Circulation 2009;120:326-33.

37. Webb JG, Harnek J, Munt BI, et al. Percutaneous transvenous mitral annuloplasty: initial human experience with device implantation in the coronary sinus. Circulation 2006;113:851–5.
38. Sack S, Kahlert P, Bilodeau L, et al. Percutaneous transvenous mitral annuloplasty: initial human experience with a novel coronary sinus implant device. Circ Cardiovasc Interv 2009;2:277– 84.
39. Rogers JH, Macoviak JA, Rahdert DA, Takeda PA, Palacios IF, Low RI. Percutaneous septal sinus shortening: a novel procedure for the treatment of functional mitral regurgitation. Circulation 2006;113: 2329 –34.
40. Carabello BA. The current therapy for mitral regurgitation. J Am Coll Cardiol 2008;52:319 –26.
41. Otto CM, Salerno CT. Timing of surgery in asymptomatic mitral regurgitation. N Engl J Med 2005;352:928 –9.
42. Mohty D, Orszulak TA, Schaff HV, Avierinos JF, Tajik JA, Enriquez-Sarano M. Very long-term survival and durability of mitral valve repair for mitral valve prolapse. Circulation 2001;104:I1–I7.
43. Flameng W, Herijgers P, Bogaerts K. Recurrence of mitral valve regurgitation after mitral valve repair in degenerative valve disease. Circulation 2003;107:1609 –13.
44. Mihaljevic T, Lam BK, Rajeswaran J, et al. Impact of mitral valve annuloplasty combined with revascularization in patients with functional ischemic mitral regurgitation. J Am Coll Cardiol 2007;49:2191–201.