Anatomy of mitral annulus insights from non-invasive imaging techniques

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The mitral annulus (MA) is not a continuous ring of connective tissue from which are suspended mitral leaflets. Instead, it is a much more complex structure made up of a mix of fibrous, muscular, and adipose tissues. MA is a key structure in any type of mitral valve repair and recently it has been targeted for transcutaneous devices. Thus, a deep understanding of MA anatomy has never been more important. Traditionally, cardiac anatomy has been described using anatomic specimens. Currently, sophisticated non-invasive techniques allow imaging of MA with a richness of anatomical details unimaginable only two decades ago. The aim of this review is to provide a better understanding of the peculiar aspects of MA as they are revealed through these imaging techniques and discuss clinical implications related to this complex structure.

Keywords

mitral annulus • 2D/3D transthoracic and transesophageal echocardiography • computed tomography and cardiac magnetic resonance

Introduction

The importance of mitral annulus (MA) in mitral valve (MV) repair has been emphasized by Carpentier¹ in their fundamental study in 1983. Implantation of prosthetic ring on MA (annuloplasty) ensures stability of repair preventing recurrence of mitral regurgitation (MR).^{1–3} More recently, MA has been targeted for at least two transcutaneous devices: The CardiobandTM (Edwards Lifesciences), which functions as a percutaneous annuloplasty⁴ and the Carillon Mitral Contour System (Cardiac Dimensions Pty. Ltd. Sydney, Australia), which, implanted in the coronary sinus (CS), exerts a cinching force on the MA with the aim of reducing functional MR.⁵ Thus, a deep understanding of the anatomical structure of MA and surrounding structures has never been more important.

Today, sophisticated non-invasive imaging techniques such as 2D, 3D transthoracic (TTE) and transesophageal (TEE) echocardiography, computed tomography (CT) and cardiac magnetic resonance (CMR), provide images of the beating heart of unprecedented quality which have greatly improved our capabilities of discovering fine details of morphological abnormalities in diseased hearts. Though these techniques have been used on clinical ground exclusively to solve specific clinical problems, a 'collateral benefit' is that they can illustrate the normal anatomical aspects of those cardiac structures which are not involved in the pathological processes.

The aim of this review is to provide a better understanding of the peculiar aspects of MA as they appear through these imaging techniques and discuss clinical implications related to this complex structure.

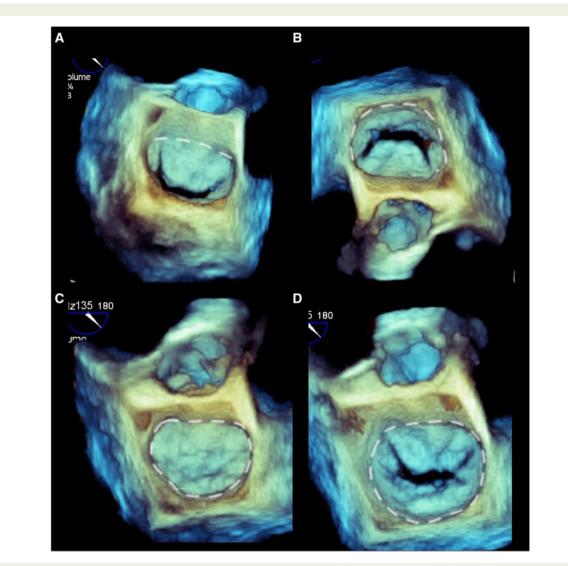
Anatomy of MA

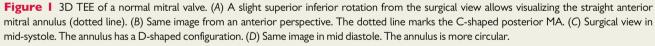
Definition

The term 'annulus' derives from a misspelling Medieval Latin language 'anulus'. Anulus is a Latin diminutive word for 'anus', which means 'ring'. Thus, anulus can be translated in English as 'small ring'. The 'traditional' perception of the MA as a circular ring of dense connective tissue serving as a suspension line for the two leaflets, is rather incorrect. Indeed, such a well-defined and complete connective tissue ring *does not exist*. In this sense, the term left 'atrioventricular junction' (AVJ) should be more appropriate. However, for consistency with previous literature, we will continue to label this component of MV apparatus as MA.

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Shape of the MA

In anatomic studies, MA has described as having a 'D-shaped' aspect: the straight component is conventionally named anterior MA, though in correct anatomical attitudinal orientation it is anterior-medial, while the curved component takes the name of posterior MA (actually posterior-lateral)³ (*Figure 1A, B*). For imaging the shape of MA, 3D TEE is probably the ideal modality. 3D TEE, in fact, has the unique capability of showing the entire MV and the MA from an overhead perspective. Moreover, the multi-beat electrocardiogram gated acquisition allows an elevated temporal resolution capturing even fine changes in MA shape. Thus, the D-shape aspect of MA occurs mainly in mid-systole, while in early diastole the MA takes a more circular shape (*Figure 1C, D*; Supplementary data online, *Video S1*).

Since the anterior and posterior components of MA have different anatomical structures, they will be described separately.

The posterior MA

The posterior MA covers the posterior-lateral aspect of the AVJ from the left to the right commissures sustaining scallops of the posterior leaflet (*Figure 1B*). Interestingly, posterior MA is described in different manners depending on whether the observer is an anatomist, surgeon, or imager.

The anatomical MA

Anatomists describe the posterior MA as the convergence of four components: the atrial wall, the leaflet hinge line (i.e. the fulcrum upon which the posterior leaflet opens and closes), the crest of free wall of left ventricle (LV) and the epicardial adipose tissue (EAT). A string of connective tissue around the posterior mitral orifice is supposed to 'glue' these components together. This fibrous string

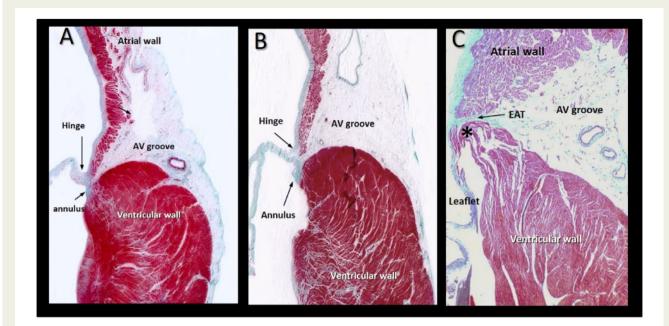


Figure 2 Histologic sections through the posterior leaflet stained in Masson's trichrome showing myocardium in red, fibrous tissue in green. (A) The leaflet is hinged to a discrete annulus that separates atrial from ventricular wall. (B) The annulus and the hinge line are not coincident. (C) The annulus is not discernable. The leaflet is hinged to the muscular crest of the ventricular wall (asterisk). EAT, epicardial adipose tissue.

(Figure 2A), however, is often discontinuous and, when present, may vary in thickness and density along different part of the same posterior annulus.³ Moreover, quite often it is located 1–2 mm inferiorly from the site of the leaflet hinge line (*Figure 2B*). Notably, in those parts in which this fibrous string is absent the posterior leaflet is inserted directly on the crest of ventricular myocardium (*Figure 2C*). EAT fills the posterior atrioventricular groove from right to the left commissures. Remarkably, EAT penetrates deeply on the crest of ventricular myocardium and extends up to the base of posterior leaflet to form the hinge line. This arrangement contributes to the electrical insulation between left atrium and ventricle.

The surgeon's MA

In the operating room, cardiac surgeons have a limited view when exposing MV; the MA can be seen only from the left atrial (LA) side. Not surprisingly, the discontinuous fibrous string described by anatomists is not visible. Visually, the surgeon recognizes the atrial wall for its slightly pink colour and the posterior leaflet for its yellowish colour. Thus, for the surgeon the posterior MA refers to the so-called 'transition zone' a virtual line that separates the atrial wall from the posterior leaflet (*Figure 3*). However, although not visible, the presence of segments of fibrous string is perceived by the surgeon because of the resistance to the needle when surgeons sew and secure the sutures.

The imager's MA

The different imaging modalities have different capabilities to image the posterior MA, emphasizing different aspects of its anatomical structure. Either 2D TTE/TEE or CT and CMR share the same cross-sectional views. Thus, when the posterior MA is transected

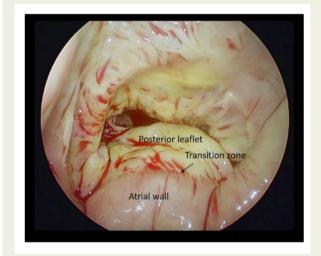
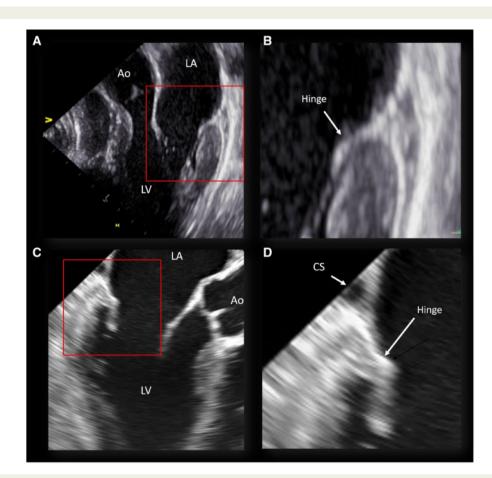
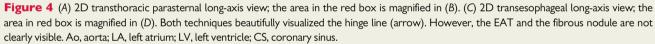


Figure 3 Surgical vision of the MV. Atrial wall and leaflets are visually recognizable because a slightly different shades of colours (pink vs. yellowish, respectively).

cross-sectionally, the string of fibrous tissue appears as a fibrous nodule.

Both 2D TTE and TEE show beautiful images of the hinge line of the posterior leaflet and the atrial and ventricular myocardium. However, likely due to the small difference in acoustic impendence and small size, neither 2D TTE nor TEE can distinguish clearly the fibrous nodule from the EAT or from muscular tissue (*Figure 4*). From several aspects CT is more informative than 2D TTE/TEE.





Indeed, like TTE and TEE, CT clearly shows the hinge line and the atrial and ventricular myocardium. In addition, CT is able to distinguish EAT from surrounding structures on the basis of different attenuation (i.e. EAT, being more hypodense, appears darker). Moreover, CT has the unique ability to display coronary arteries and CS (if the latter is adequately opacified). But, despite its high spatial resolution (voxel as small as 0.6 mm), the technique is unable to display any well-defined fibrous nodule likely due the slight difference in attenuation between fibrous tissue and surrounding structures (*Figure 5*).

As with 2D TEE and CT, CMR is able to visualize the hinge line of posterior leaflet, ventricular and atrial myocardium, but not a fibrous nodule. However, receiving strong signals from EAT and weak signal from the myocardium, CMR provides unique and well-defined images of the EAT's 'intrusiveness' in the atrioventricular groove. This tissue, in fact, is seen penetrating deeply onto the crest of ventricular myocardium up to the leaflet's attachment (*Figure 6*).

In summary, neither 2D/3D TTE/TEE nor CT or CMR are able to visualize the fibrous nodule corresponding to the posterior MA. *Table 1* lists the peculiar abilities of each technique in imaging posterior MA.

The anterior MA

The attachment of the anterior mitral leaflet (AML) shows a different anatomical aspect depending on whether it is observed from the ventricular or from the atrial perspective. Seen from the atrial perspective the hinge line of AML is in continuity with the atrial wall and lies in a more apical position than the hinge line of the aortic leaflet. On the contrary, seen from a ventricular perspective, the hinge line of the anterior leaflet is clearly in continuity with a strip of fibrous tissue which in literature is called mitral-aortic curtain. This fibrous sheet is more or less rectangular in shape, delimited medially and laterally by bumps of dense connective tissue (right and left fibrous trigones). This band gradually continues into the left interleaflet triangle (ILT) located between the non-coronary and left coronary sinus. Thus, on the ventricular aspect of AML, the mitral-aortic curtain and the aortic ILT do not have well-defined boundaries. Cross-sectional planes 2D TEE, CT scan, and CMR have different abilities in visualizing this area (Figure 7). The ability of 3D TEE of visualizing cardiac structures 'en face' permits display of the mitral-aortic curtain from a unique ventricular perspective very similar to the corresponding anatomic cut. This point of view shows as the base of AML, its hinge line, the

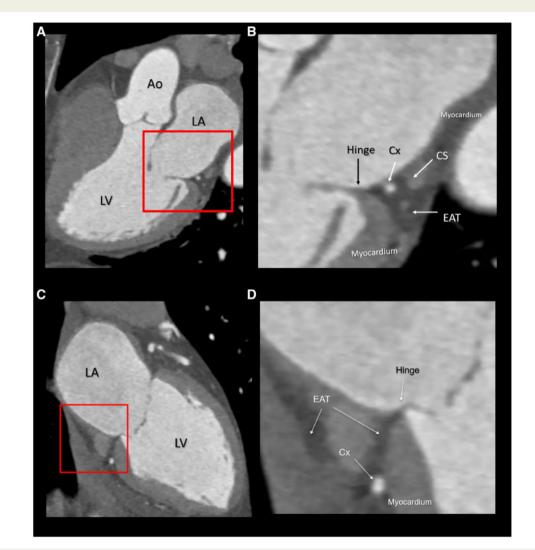


Figure 5 (A) Multiplanar CT reconstruction in long-axis view. The area in red box is magnified in (B). (C) Multiplanar CT reconstruction in twochamber view. The area in red box is magnified in (D). This technique clearly shows the hinge line (arrows), and the atrial and ventricular myocardium. The darker area surrounding the circumflex artery (Cx) and the coronary sinus (CS) corresponds to the EAT. Ao, aorta; LA, left atrium; LV, left ventricle.

mitral-aortic curtain and the ILT appear as a sole structure (*Figure 8* and Supplementary data online, *Video S2*).

The saddle-shaped configuration of the MA

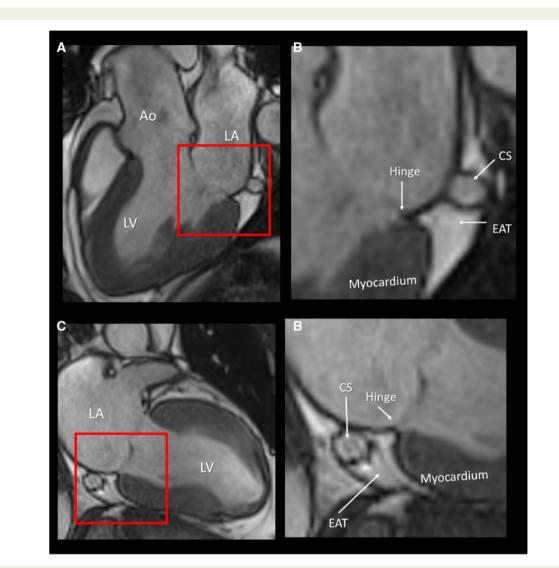
The three-dimensional saddle-shaped configuration of the annulus was first described by Robert Levine and colleagues in 1987.⁶ These authors had the merit to generate a profound conceptual reconsideration of the echocardiographic criteria of MV prolapse. However, it must be noted that neither in their original paper, nor currently using dedicated software, the contour traced to reconstruct the saddle-shaped configuration follows the anatomical annulus but rather the hinge line of leaflets. Indeed, as above-mentioned, the anatomical annulus, when present, is 1–2mm inferiorly laterally displaced from the hinge line. Thus, the saddle-shaped configuration of 'mitral annulus' is

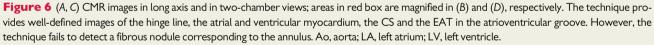
a misnomer, since the three-dimensional saddle-shaped architecture refers to the hinge line of mitral leaflets, rather than to the MA (*Figure 9*). Because a complete fibrous ring does not exist and the anatomical fibrous annulus consists of sparse fragments of fibrous string on the posterior part of the atrioventricular junction, its shape cannot be determined.

Annular motion

During the cardiac cycle the MA has three types of motion: a sphincteric-like contraction, a translation motion and an annular folding. 7

The sphincteric-like contraction depends exclusively on the dynamic motion of the posterior MA. This type of motion is facilitated by the absence of a rigid C-shaped ring of connective tissues. Indeed, since part of posterior leaflet is attached on ventricular myocardium, the hinge line follows contraction and relaxation of ventricular basal





Techniques	Anatomical annulus (fibrous string or nodule)	Hinge line (attachment of leaflet)	Coronary vessels and coronary sinus	Epicardial adipose tissue
ANATOMY (gold standard)	++++	++++	++++	++++
2D TTE/TEE	-	+++	++	+
3D TEE	-	+	+	+
СТ	-	++++	++++	++
CMR	_	++	+++	++++

Table I Peculiar abilities of 2DTTE/TEE/CT/CMR in visualizing posterior MA

helical fibres. The largest area and the maximum diameter are seen in the isovolumetric relaxation, anticipating the torrential early filling, and continues up to early diastole (rapid filling). The smallest area and the minimum diameter occur in isovolumetric contraction, preparing for effective leaflet co-aptation during systole, and continues up to early systole. The substantial reduction occurring in this 'pre-systolic'

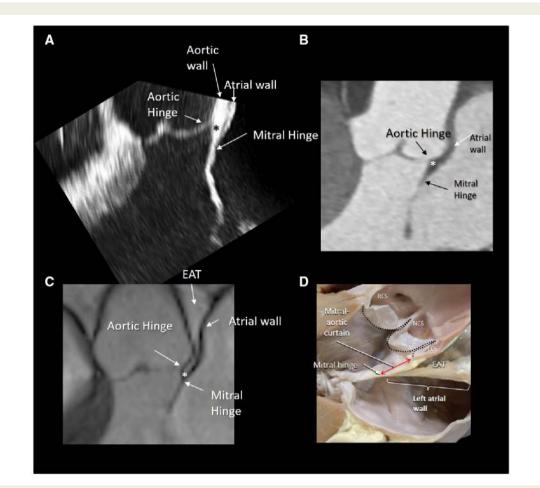


Figure 7 Cross-sectional long-axis view of (A) 2D TEE, (B) CT, and (C) CMR, in a correct anatomical attitudinal orientation, showing the mitralaortic curtain (asterisk). (A) 2D TEE; the good image quality allows distinguishing the aortic from the atrial wall, in between the virtual space of the sinus transversus. (B) CT; the similar attenuation to X-ray does not permit a clear distinction between aortic and atrial wall. (C) CMR; interesting to note as CMR is capable of visualizing even a thin leaf of EAT in between the two walls. (*D*) The anatomic specimen in a corresponding long-axis view; the red double-head arrow marks the mitral-aortic curtain. The black dotted line marks the aortic leaflets hinge line. LCS, left coronary sinus; NCS, non-coronary sinus; RCS, right coronary sinus.

phase is also influenced by atrial contraction, confirming the complex annular architecture made up of both ventricular and atrial myocardium.⁸ The sphincteric-like contraction reduces the MA area by 20– 30%.⁷ In particular, the reduction of anterior-posterior diameter facilitates leaflet coaptation, assuring an effective valve competence. The annular motion can be best appreciated using 3D TEE from an overhead perspective (*Figure 10* and Supplementary data online, *Video S1*).

The translation motion is a consequence of reduction of the long axis of the LV, reflecting the contraction of sub-endocardial and subepicardial myofibres which are prevalently longitudinally/obliquely orientated. In diastole, the MA moves away from the LV apex. This diastolic translation promotes LV filling by displacing a column of blood initially present in the left atrium to underneath the mitral leaflets. Conversely, in systole, the MA moves towards the apex. This motion displaces the column of blood from the outflow tract to the aorta and at the same time enlarges the left atrium. A consequent drop in atrial pressure facilitates the pulmonary venous return. The degree of displacement of the anterior and posterior portion of MA is not equal: the anterior annulus is tethered by the aortic root and translates less than the posterior annulus. The excursion of the annulus is best appreciated in CMR cine sequences (*Figure 11*).

The annular infolding is an accentuation of the saddle-shaped configuration that occurs during the systole. This conformational change avoids leaflets distortion along the hinge line, a potential consequence of annular contraction, and blunts the systolic stress on leaflets by increasing their curvature.⁹ Dedicated software tracking the hinge line automatically or semi-automatically displays the threedimensional changes of MA during the cardiac cycle (*Figure 12*).

Clinical implications related of MA anatomy

Surgical and percutaneous procedure

In surgical MV repair or replacement, the needle should penetrate the atriovalvular junction $1-2\,\text{mm}$ peripheral to the visible leaflet

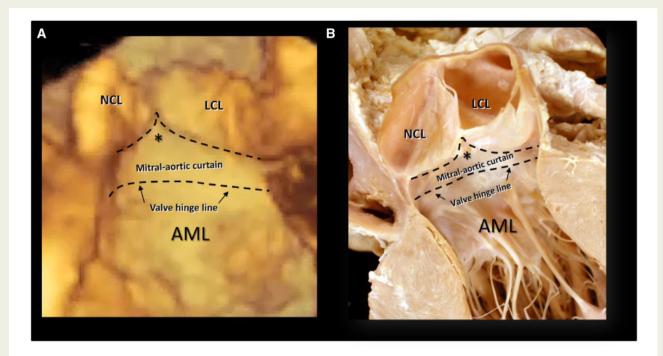


Figure 8 (A) 3D TEE from a ventricular perspective showing the anatomical relationship between the hinge line AML, the mitral-aortic curtain and the ILT (asterisk). (B) The anatomic specimen in a similar perspective. NCL, non-coronary leaflet; LCL, left coronary leaflet.

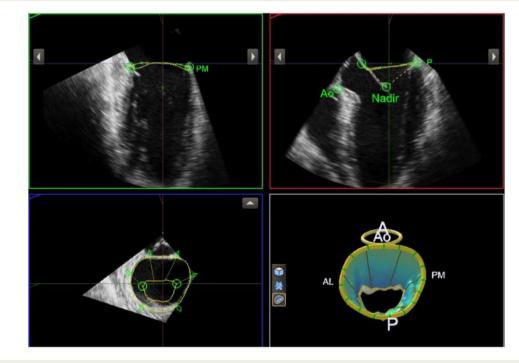
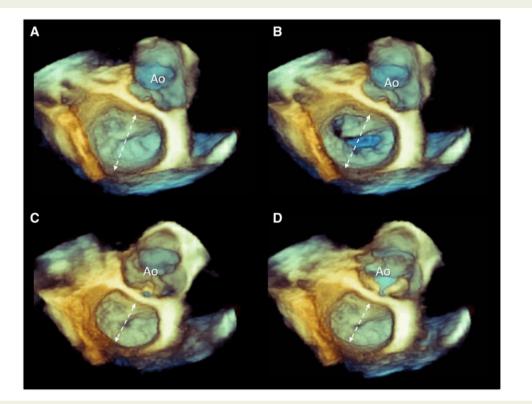
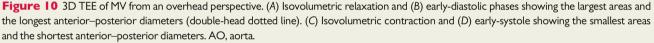


Figure 9 One of the available software designed to automatically or semi-automatically determine the shape and dimension of the MA. The contour traced follows the hinge line of the leaflets and not the 'invisible' MA. A, anterior leaflet; AO, aorta; AL, anterior-lateral commissure; P, posterior leaflet; PM, posterior-medial commissure.





hinge line, in order to preserve the motion of the leaflet, and directed towards the LV to include the sparse segments of fibrous string and, at the same time, avoid circumflex artery.¹⁰ As mentioned above the posterior annulus comprises of 'soft' tissue (muscular and adipose) sparsely reinforced by a fibrous string. Elderly patients who undergo MV replacement may have weaker myocardial tissue putting them at risk of rupture at the level of the atrioventricular junction or surrounding left ventricular free wall.¹¹ Although rare, this complication may be lethal and need to be recognized and repaired immediately. Preserving the posterior leaflet as a buttress for the sutures may prevent this complication.¹¹

In transfemoral direct annuloplasty, anchors are supposed to be hooked along the 'posterior annulus'.¹² However, in those segments without this fibrous string, anchors are inserted directly onto the crest of ventricular myocardium (*Figure 13*). Given the proximity of the circumflex artery, particular care must be taken during the cinching of the band since excessive cinching may cause kinking and obstruction of circumflex artery.¹³

Any device inserted into the CS is designed for cinching the MA in order to reduce the amount of insufficiency in functional MV regurgitation. Conceptually, these devices are effective if the CS is running into the atrioventricular groove close to leaflet hinge line. This is not always the case. In a significant number of individuals, the CS is located adjacent to the atrial wall 1 to 1.5 cm superiorly to the plane of the posterior leaflet hinge line. The device placed inside the CS may result in traction on the LA wall rather than on the hinge line of mitral leaflets with little or no impact on annular area reduction (*Figure 14*).

MA calcifications

Mitral annular calcification (MAC) is a chronic multifactorial degenerative/inflammatory process of the MA which significantly increases with the age (up to 15% of population > 8th decade) and in patients with multiple cardiovascular risk factors or chronic kidney disease.¹⁴ The fact that MAC affects more frequently and extensively the posterior than the anterior MA, might depend on differences in their anatomical structure. The anterior leaflet is directly attached to a mitral-aortic curtain which being an avascular band of connective tissue, rarely may undergo a calcific process. Indeed, when the anterior MA presents with calcifications, these are usually extensions from the aortic leaflets. Conversely, the absence of a continuous dense string of connective tissue at posterior MA might facilitate microinjuries during contraction and relaxation at the junction between leaflet's hinge and the crest of ventricular myocardium, initiating the process of calcific deposition. These micro-sized calcifications may then coalesce over decades into the dense, fibrotic, rigid band macroscopically evident at the base of leaflet. Increased haemodynamic stress in the region caused by hypertension, aortic stenosis, hypertrophic cardiomyopathies, or MV prolapse may exacerbate and accelerate the process.¹⁴ The best imaging techniques to visualize MA

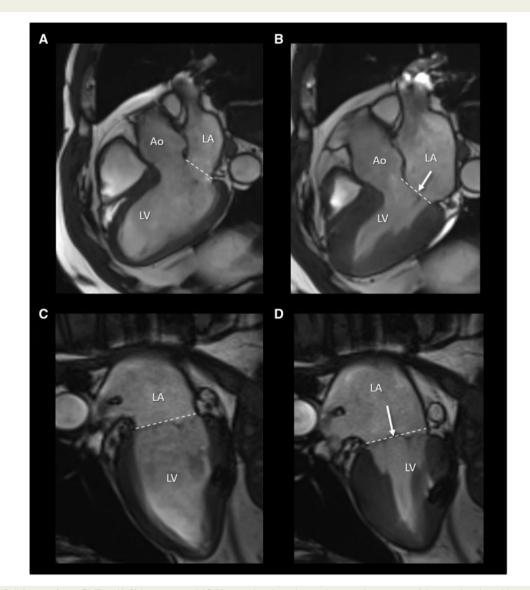


Figure 11 Still frame of cine CMR in (*A*, *B*) long-axis and (*C*, *D*) two-chamber planes, showing the motion of the annular plane (dotted line) towards the ventricular apex (arrow). Ao, aorta; LA, left atrium; LV, left ventricle.

calcification is undoubtedly CT (*Figure 15*). Contrary to echocardiography, in fact, CT is more accurate for differentiating dense fibrosis from calcification and for assessing the extension of calcification in different planes. MV repair or replacement in patients with extensive MAC can be a challenge for the surgeon. Although an 'en bloc' decalcification has been described, this technique remains technically challenging and especially when calcifications invade leaflets or ventricular myocardium, surgical intervention may be complicated by thromboembolic events, atrioventricular block, and paravalvular leak.¹⁵ Because of these technical difficulties and the fact that most affects patients had other several comorbidities, patients with extensive MAC are left untreated despite the presence of concomitant severe MV disease.

An alternative treatment of these patients is positioning a balloonexpandable valve designed for aortic position in the mitral position (valve in MAC). The same calcifications act as an anchor for the valve.¹⁶ In this procedure, echocardiography remains essential for patient selection, detailed anatomic imaging, complete hemodynamic characterization, real-time guidance, and evaluation of procedural success. CT is indispensable for MAC distribution and in predicting left ventricular outflow tract obstruction.

MA dilation

Given the difference in anatomical structure between anterior and posterior segments, MA dilation, in either functional or organic MR, is *asymmetric*, involving the posterior segment more than the anterior. Being supported by two fibrous trigones and by the rigid mitral-aortic curtain, the anterior MA is more resilient, whereas the posterior C-shaped fibrous string partially substituted by muscular and adipose tissue leaves the posterior MA more predisposed to dilated.

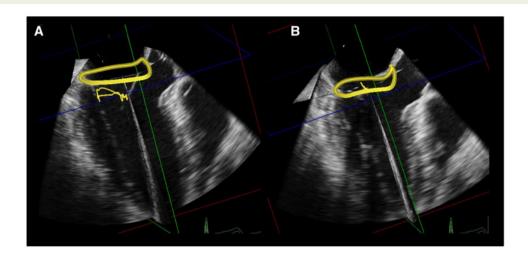


Figure 12 Dedicated software tracing the MA in (A) diastole and (B) systole. The reduction of annular area and accentuation of the saddle-shaped configuration are clearly visible.

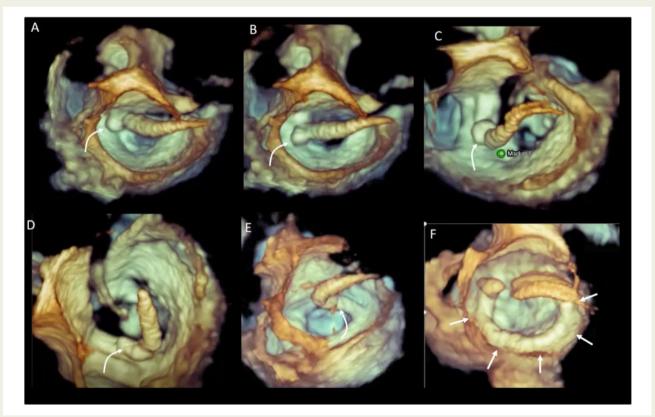


Figure 13 3D TEE from overhead perspective showing steps of Cardioband procedure. The curved arrow point at the tip of catheter in (A) antero-lateral commissure (the site of first implant) and (B-D) then along the posterior annulus up to the medial commissure (E), the last anchoring point. (F) The contraction of the implant (arrows).

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Consequently, the asymmetric dilation increases septal-lateral more than inter-commissural diameter, impairing leaflets coaptation and exacerbating the degree of MR.¹⁷ Moreover, MA dilatation leads to a

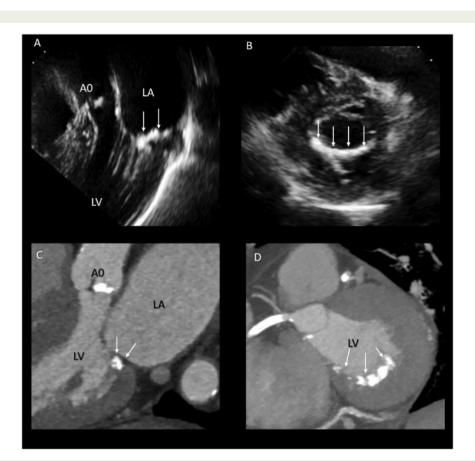
distortion of the saddle-shaped configuration making the annulus larger and flatter (*Figure 16*). Particularly interesting is the MA dilation in long-standing atrial fibrillation and LA enlargement. These patients



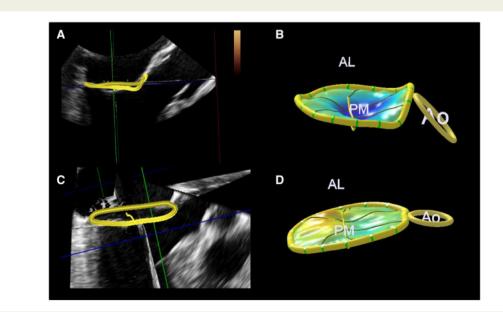
Figure 14 (*A*, *B*) CT volume rendering format, (*C*, *D*) CMR cine long-axis view and (*E*, *F*) 2D TEE two-chamber view. Areas in red box of (A, C, and E) are magnified in (B, D, and F), respectively. Images of all three techniques clearly show as the CS is located superiorly to the hinge line of the leaflet. The dotted line marks the distance between the hinge line and CS. Ao, aorta; LV, left ventricle; LA, left atrium.

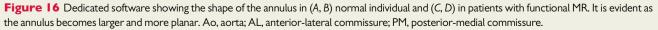
often present with variable degrees of MR.¹⁸ Since the LV is normal and leaflets are not tethered, the only mechanism causing MR must be the annular dilation. From an anatomical point of view, this is perfectly understandable since the LA wall is an integral component of the posterior MA. Displacement of the posterior MA onto the crest

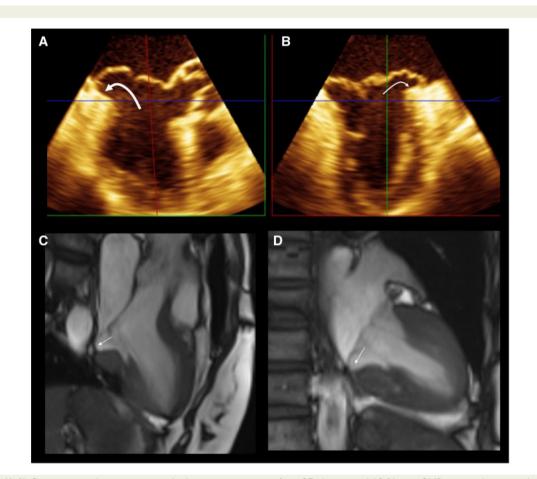
of LV causing a relative reduction of the posterior leaflet's area available for coaptation¹⁹ and insufficient leaflets remodelling relative to MA dilation may contribute to MR.²⁰ Probably one of best methods for visualizing and measuring MA dilation is 3D TEE using dedicated software (*Figure 16*).

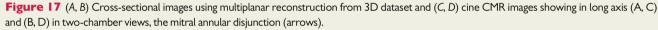












MA disjunction

In a pathological study published in the NEJM in 1986 based on the analysis of 900 hearts, Hutchins et al.²¹ described an anomalous attachment of the posterior leaflet directly on the atrial wall in 23 out of 25 patients with bi-leaflet mitral valve prolapse (MVP) and leaflet's redundancy. They called this anatomical variation mitral annulus disjunction (MAD). In this particular anatomical arrangement, the normal structure of MA comprising of the atrial-valvular-ventricular junction is lost and the posterior leaflet is attached directly on the atrial wall (atrial-valvular junction). The space between the hinge line of the posterior leaflet and the crest of the ventricular wall is replaced by a curtain-like fibrotic tissue. In the same period, Angelini et $al.^{22}$ described a MAD arrangement not only in MVP but also in normal individuals. So, although MAD is more common in cases of floppy MV, it may also occur in isolation. Interestingly, in a recent 3D TEE study Lee et al.²³ demonstrated that MAD is more pronounced at the lateral and central segments of the annulus, leading to a paradoxical annular expansion in late systole (Figure 17). Particularly interesting is the cause/effect relationship between MVP, MAD, complex arrhythmias and sudden cardiac death. Perazzolo Marra et al.²⁴ provided evidence that MAD is a constant feature in patients with arrhythmic MVP. They hypothesized that this peculiar morphology

might contribute to the systolic stretch of the myocardium close to the valve (in particular at the tip of papillary muscles and the basal posterior segment of LV) and result in the propensity to develop regional LV fibrosis and electrical instability. Interestingly, a recent paper hypothesized that the MAD in itself is an arrhythmogenic entity since arrhythmic events are more related to MAD than to valve prolapse.²⁵

Conclusion

This review emphasized the role of non-invasive imaging techniques in describing the anatomy of MA. We highlighted that the concept of the MA as a continuous fibrous ring that anchors the mitral leaflets is unsubstantiated; the ring *does not exist*. Furthermore, the posterior annulus is described differently by the anatomist, the surgeon or the imager and, likewise, the non-invasive imaging techniques have different capabilities in visualizing the complex structure of MA, each of them excelling in visualizing one of the various aspects. Moreover, we described some clinical implications linked to a peculiar structure of MA: the saddle-shaped configuration, for instance, refers to the hinge line and not to the anatomical annuls. Surgical and percutaneous procedures on MA must take into consideration the peculiar anatomy of this structure. Finally, the different structures of anterior and posterior MA might explain their different vulnerability to some pathological conditions such as calcifications and dilation.

Supplementary data

Supplementary data are available at European Heart Journal - Cardiovascular Imaging online.

Conflict of interest: F.F.F. reports several talks supported by Philips. No others financial relation to be disclosed by the other authors.

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