Pathophysiology of Degenerative Mitral Regurgitation
New 3-Dimensional Imaging Insights

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Abstract—Despite its high prevalence, little is known about mechanisms of mitral regurgitation in degenerative mitral valve disease apart from the leaflet prolapse itself. Mitral valve is a complex structure, including mitral annulus, mitral leaflets, papillary muscles, chords, and left ventricular walls. All these structures are involved in physiological and pathological functioning of this valvuloventricular complex but up to now were difficult to analyze because of inherent limitations of 2-dimensional imaging. The advent of 3-dimensional echocardiography, computed tomography, and cardiac magnetic resonance imaging overcoming these limitations provides new insights into mechanistic analysis of degenerative mitral regurgitation. This review will detail the contribution of quantitative and qualitative dynamic analysis of mitral annulus and mitral leaflets by new imaging methods in the understanding of degenerative mitral regurgitation pathophysiology. **(*Circ Cardiovasc Imaging*. 2018;10:e005971. DOI: 10.1161/CIRCIMAGING.116.005971.)**

Key Words: echocardiography ■ heart ventricles ■ magnetic resonance imaging ■ mitral valve ■ papillary muscles

Degenerative mitral regurgitation (DMR) characterized by mitral valve prolapse is the most frequent type of organic mitral valve disease,[1,2] is highly repairable,[3,4] and is the subject of several guidelines for evaluation[5,6] and treatment.[3,4] Despite this high frequency and volume of clinical description, mechanistic analysis of valve lesions and regurgitation remains mainly descriptive and focuses solely on leaflets' excessive motion.[6] Little attention has been paid to quantitative annular and valvular dynamics and their impact on mitral regurgitation mechanism and severity. Yet, degenerative mitral disease involves the entire mitral apparatus and cannot be confined to excessive leaflet movement. The recognized role of mitral annuloplasty in achieving quality/durability of mitral valve repair[7–9] emphasizes the necessity to understand, measure, and characterize the entire mitral valvuloventricular complex in DMR. This need for enhanced mechanistic understanding of each mitral valvular component dynamic behavior in normal and degenerative valves is compounded by current development of percutaneous interventions for mitral regurgitation,[10,11] which, unlike surgical repair, do not combine procedures addressing all dysfunctional components in 1 intervention. Thus, comprehensive pathophysiologic characterization of all components of DMR is essential in matching patients to specific tools for its correction.

Up to now, DMR mechanistic analysis has remained rudimentary for various reasons. First, there is no standardized DMR animal model. Second, imaging the 3-dimensional (3D) mitral valve structure is imperfect with 2-dimensional echocardiography. Even surgeons observing the entire 3D mitral structure can only focus on those requiring surgery in nonbeating, flaccid hearts that generally preclude detailed measurements and do not allow mitral valve dynamics assessment.

In this context, real-time 3D echocardiography, computed tomographic scan, and cardiac magnetic resonance imaging provide new possibilities of imaging the entire mitral valvular apparatus throughout the cardiac cycle. Combining 3D imaging and specific software allows proper image positioning and measurement of various mitral components. Although 3D surgical en face mitral view display of prolapse location is now widely accepted,[12–14] quantitative analysis of mitral dynamics using 3D echocardiography requires complex measurements and has rarely been reported. Static applications of 3D echocardiographic measurements, generally in systole, allow estimation of mitral annulus and leaflets' dimensions while dynamic, repeated measurements allow quantification of mitral components' changes throughout the cardiac cycle. This review aims to summarize recent advances based on 3D imaging, defining normal mitral function, describing annular and valvular alterations in DMR and dynamic interactions in specific DMR types, outlining valvular patterns/mechanisms affecting valve repair, and examining clinical implications of these recent insights.

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Functional Anatomy of Normal and Degenerative Mitral Valve

Normal Mitral Valve

Mitral valve apparatus is composed of the annulus, 2 leaflets, papillary muscles, and chords.

Mitral annulus (Figure 1) is a saddle-shaped,[15] fibrous structure, with shorter anteroposterior than intercommissural diameter. Its anterior part, between the 2 fibrous trigones of the mitral-aortic junction, central to cardiac skeleton, accounts for 1/3 of annulus perimeter. The posterior annulus occupies 2/3 of the perimeter, inserts into ventricular myocardium, and forms an electric barrier separating ventricular and atrial myocardium. Attached to mitral annulus are anterior and posterior leaflets. Posterior leaflet has wider annulus implantation but shorter height versus anterior leaflet. It is divided in 3 scallops (labeled P1, P2, and P3 from lateral to medial)[16] separated by physiological indentations. Anterior leaflet is labeled A1-A2-A3 in regard to corresponding posterior scallops but is tongue-like nonscalloped. Subvalvular apparatus is composed by papillary muscles (posteromedial and anterolateral) and chords, distributed in primary, secondary, and tertiary chords, respectively, attaching to free edge, body, or mural portion of leaflets.

Degenerative Mitral Regurgitation

DMR is caused by valvular or chordal degeneration with core mechanism of systolic excessive leaflet movement defined by a prolapse in left atrium ≥2 mm, which can affect one or both leaflets and one or multiple scallops.

Two different DMR phenotypes are generally described: fibroelastic deficiency (FED) and diffuse myxomatous disease (DMD, also called Barlow disease). FED is mostly localized to 1 segment and often involves ruptured chords with histologically myxomatous degeneration and macroscopically leaflet redundancy and thickening predominant on the flail segment (usually posterior, especially P2). The valve remainder is usually thin and translucent. Conversely, DMD lesions are generalized with redundancy/thickening of both leaflets, involving multiple segments (Figure 2). In those cases, mitral regurgitation typically predominates in midlate systole, and its severity varies from mild to severe. DMR can be severe in both forms, but in DMD, patients considered for surgery are usually younger (fifth decade) versus FED (sixth decade). Repair is more complex in DMD versus FED although DMR surgical repair generally entails standard techniques. Categorizing anatomically FED versus DMD based on valvular redundancy/thickening can be problematic, and it is uncertain whether these are variants along a single pathophysiologic spectrum. In that regard, presence of distinct physiological differences (detailed later) suggests that FED and DMD are related but separate entities.

Assessment of Mitral Valve Physiology via 3D Imaging

Progress in Quantitative 3D Echocardiography

Owing to the development of dedicated software, quantification of each component of the mitral valvuloventricular complex is now possible using transesophageal and transthoracic 3D echocardiography after acquisition and storage of full-volume images.[17–22] These images are analyzed offline, displayed on orthogonal planes including en face annular view. Echocardiographic markers positioned along mitral annulus and leaflets, manually or by semiautomated software, can be followed along the cardiac cycle. Annular dimensions and shape are quantified as perimeter, area, height, intercommissural, and anteroposterior diameters. From these, annular saddle shape index (height/intercommissural diameter ratio) and eccentricity index (anteroposterior/intercommissural diameter ratio) are derived. Leaflets length/area, prolapse volume/height, and tenting volume/height quantify valvular characteristics (Figure 3).[23] Although these measurements are often obtained in static mode in systole, measurements throughout the cardiac

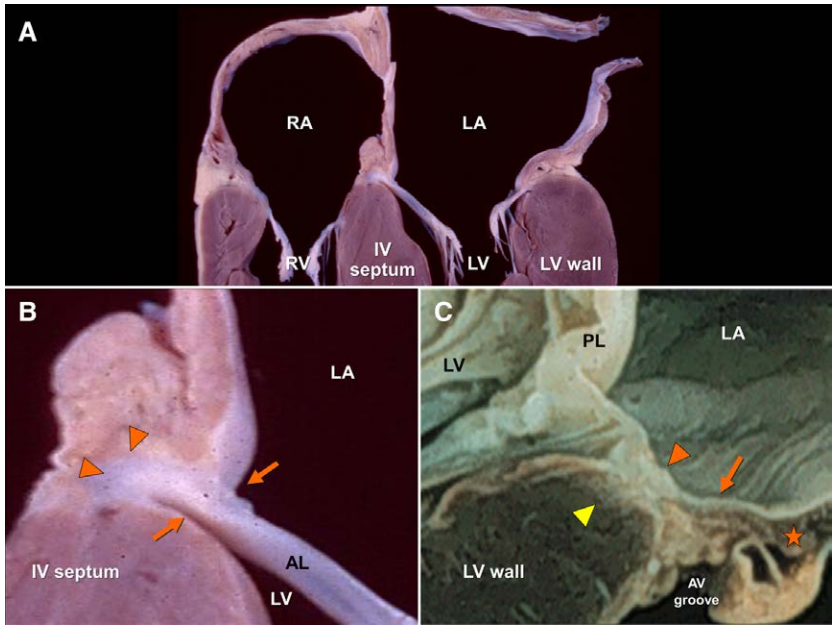

Figure 1. Mitral valve anatomy with focus on mitral annulus insertion. **A**, anatomic section of the heart depicting the mitral (**right**) and tricuspid valve (**left**) in relation to the atrium and ventricles. The insertion of the mitral annulus can be seen at the atrioventricular junction. **B**, The anterior leaflet is attached to the atrioventricular (AV) junction by the mitral annulus (orange arrowheads), with a continuity between the leaflet endothelium and the ventricular and atrial endothelium (orange arrows), (**C**) the posterior leaflet is attached to the posterior annulus (orange arrowhead) which separate the atrial myocardium (orange star) from the ventricular myocardium, orange arrow indicates the continuity between the left atrium endothelium and the posterior leaflet. Yellow arrowheads indicate the insertion of the mitral annulus inside the left ventricular wall. AL indicates anterior leaflet; IV, interventricular; LA, left atrium; LV, left ventricle; PL, posterior leaflet; RA, right atrium; and RV, right ventricle.

Figure 2. Diffuse myxomatous disease vs fibroelastic deficiency. **Left**, En face view of the mitral valve from the left atrium depicting a diffuse myxomatous disease with large excess of tissue and bileaflet prolapse. **Right**, Longitudinal anatomic view of the left ventricle (**left**), left atrium (**right**), and mitral valve depicting an isolated posterior leaflet prolapse consistent with fibroelastic disease.

cycle allow insights into dynamic, pathophysiologic behavior of mitral valvuloventricular complex. Computed tomography and cardiac magnetic resonance imaging by collecting 3D volume data also allow reorienting 2-dimensional views of mitral apparatus and gain 3D insights.

Normal Mitral Annular and Valvular Dynamics

With advent of 3D imaging,[20,21,24–27] detailed and consistent pattern of annular dynamics in normal humans emerged.

Systole

At the beginning of systole, rising left ventricular pressure has not yet apposed anterior and posterior leaflets, and as papillary muscles contraction causes leaflet tethering by increasing distance between papillary muscle heads and leaflet fibrosa,[21] early-systolic regurgitation may ensue. Meanwhile early-systolic annular dynamics is characterized by anteroposterior contraction which decreases anteroposterior diameter and by apical descent of commissures,[20] which accentuates the

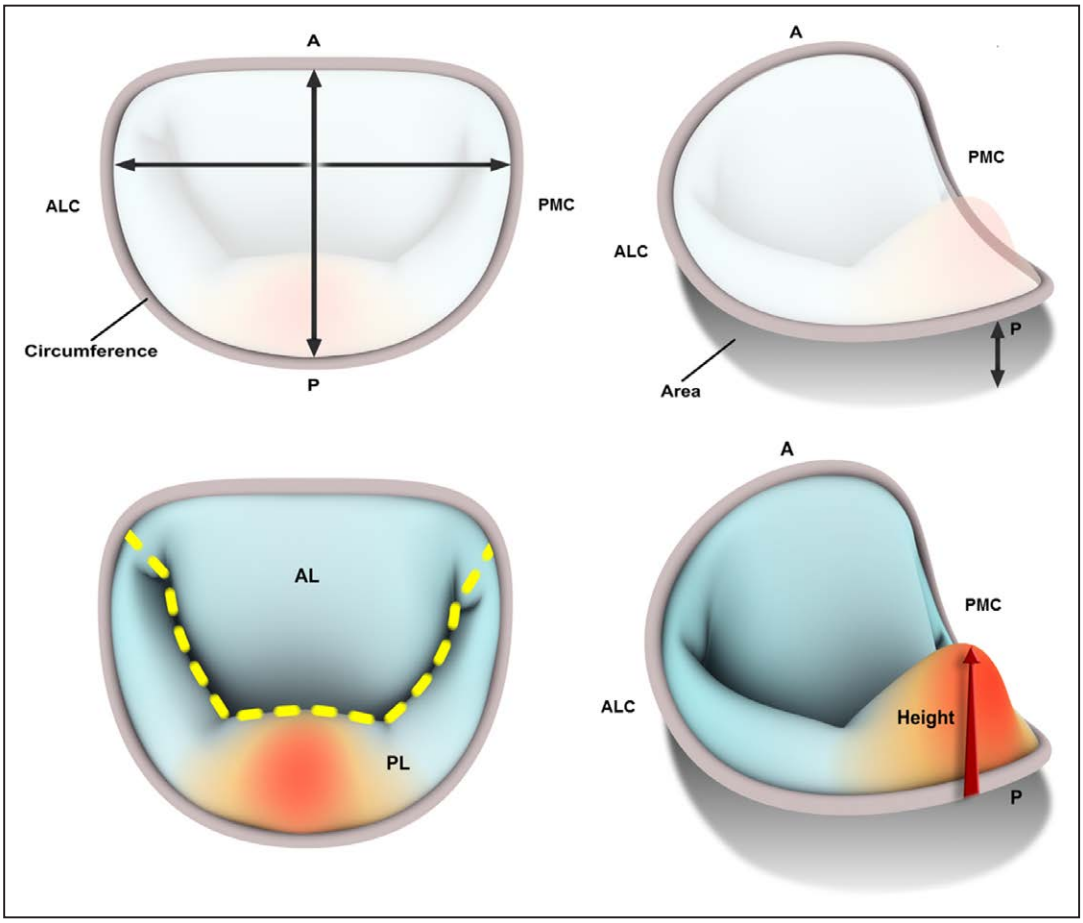

Figure 3. Representation of the different measures of mitral annulus and leaflets. **Top left**, Mitral annulus anteroposterior diameter (vertical arrow), intercommissural diameter (horizontal arrow), and circumference. **Top right**, Mitral annulus projected area (shadow) and height (black arrow). **Bottom left**, Leaflet area, anterior and posterior. **Bottom right**, Prolapse height (red arrow). A indicates anterior; AL, anterior leaflet; ALC, anterolateral commissure; P, posterior; PL, posterior leaflet; and PMC, posteromedial commissure. Reprinted from Clavel et al [23] with permission. Copyright ©2015.

annulus saddle shape. As a result, annular area is reduced,[25–27] and anterior and posterior leaflets are brought closer to each other. Approximation of mitral leaflets, produced by late-diastolic flow-deceleration followed by early-systolic annular contraction, precedes systolic elevation of ventricular pressure. Our interpretation of these changes is that combining leaflet straightening and approximation by normal annular contraction are probably key in preventing early-systolic mitral regurgitation (Figure 4).

After leaflet closure, annular anteroposterior diameter and area return to their diastolic level while intercommissural diameter remains unchanged and while accentuated annulus saddle shape persists,[20,21] possibly contributing to reducing mitral tension.[28] With continued ventricular wall contraction, distance between fibrosa and papillary muscle heads decreases (after its initial lengthening), so leaflet tenting height is maximal in early systole and tends to decrease throughout systole.[21] Hence, progressive systolic reduction of tenting enhances leaflet area available for annular coverage.

Diastole

In early diastole, the annulus stretched by persistent systolic saddle shape accentuation is released and recoils,[20] contributing to prompt opening of leaflets that are now attracted forward by ventricular suction during myocardial relaxation, leading to low inertia, nonobstructive valvular opening.

Mitral Annulus Dynamics in DMR

Annular shape and dynamics have been studied in various subsets of patients presenting DMR (Table 1).[18,20,22,23,25,29–33] Considering static measures, mitral annulus is consistently reported as enlarged, flattened, and more circular, with increased anteroposterior diameter, intercommissural diameter, circumference, and area compared with normal valves while annulus height is close to normal. Annular enlargement is more pronounced with more severe mitral regurgitation.[29,30] Importantly, DMR annular enlargement is different from that of ischemic mitral regurgitation, in which anteroposterior annulus is enlarged exclusively versus DMR marked intercommissural enlargement for similar ventricular/atrial size, suggesting that annular alterations are intrinsic to degenerative disease.[20,21,33]

DMR annular dynamics are more disputed. Some studies[25,34] described DMR annular dynamics close to normal, with early-systolic area reduction and anteroposterior contraction of magnitude barely reduced. Conversely, we and others[20,30] observed abnormal early-systolic dynamics of DMR annulus with reduced anteroposterior contraction and simultaneous enlargement of intercommissural diameter resulting in decreased annular area contraction. In these studies, systolic saddle shape accentuation was markedly delayed and diminutive.[20] DMR early-systolic annular dysfunction, decreased annular contraction, and decreased saddle shape accentuation

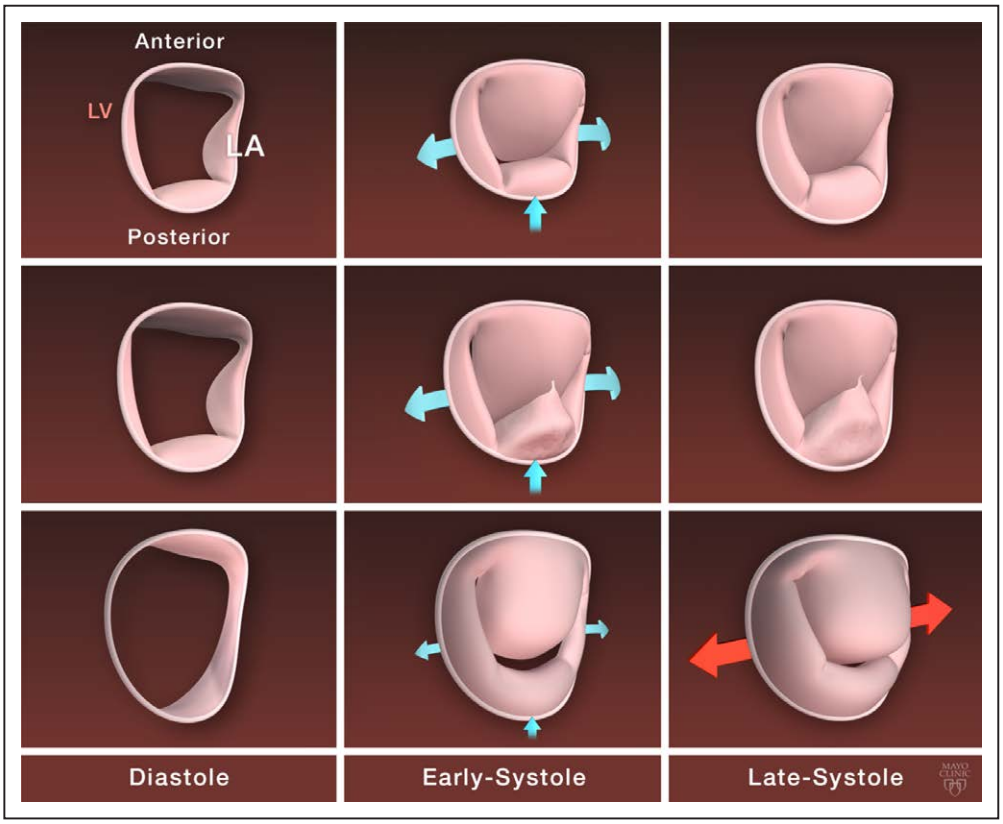

Figure 4. Mitral annulus dynamic in normal mitral valve and by degenerative mitral regurgitation phenotype. **Top row,** Normal mitral annulus dynamic with stretching of the commissure toward the ventricle and anteroposterior contraction in early systole and few modification in late systole. Middle row, Mitral annulus dynamic in fibroelastic deficiency: moderately enlarged dynamic with similar motion in early systole but of decreased magnitude compared with normal annulus. Bottom row, Mitral annulus dynamic in diffuse myxomatous disease with a severely enlarged and flattened mitral annulus, a severe decrease in the anteroposterior contraction in early systole, and an abnormal enlargement of the intercommissural diameter in late systole. LA indicates left atrial; and LV, left ventricle.

Table 1. Main 3D Studies on Mitral Valve Annulus or Leaflets in Degenerative Mitral Regurgitation

Study	Population	Imaging Mode	Main Results
Static analysis			
Ben Zekry et al[32]	15 patients with severe DMR	TEE	Enlarged and flattened mitral annulus among patients with DMR
	15 control patients		
Lee et al[29]	68 DMR,32 with MR ≤2+, 36 with MR ≥3+	TEE	Enlarged and flattened mitral annulus in DMR
	32 control patients		More severe MR associated with more annulus enlargement and flattening
Chandra et al[22]	57 severe surgical DMR (29 FED and 28 MD)	TEE	Enlarged mitral annulus and leaflets area in DMR vs controls
	20 controls patients		Larger mitral annulus and leaflets in DMD vs FED
Maffessanti et al[31]	56 severe surgical degenerative MR (29 FED and 27 MD)	TEE	Enlarged and flattened mitral annulus and larger
	18 controls patients		Leaflets area in DMR vs controls
			Larger mitral annulus and leaflets in DMD vs FED
Static and dynamic analysis			
Mihaila et al[30]	52 mild to severe DMR	TTE	DMR annulus enlarged, more circular and flattened
	52 control patients		Delayed and reduced mitral area contraction
			Larger leaflets area
Clavel et al[23]	49 severe surgical DMR (31 FED and 18 DMD)	TEE	Enlarged, flattened, and more circular annulus, larger leaflets in DMD vs FED
			Abnormal annulus dynamic in DMD
			Highly dynamic increase in leaflet area and prolapse along systole in DMD
Grewal et al[20]	32 severe surgical DMR, 15 control patients	TEE	Larger and flattened annulus in DMR
			Abnormal annulus dynamic with early-systolic intercommissural enlargement, delayed saddle shape deepening, exaggerated late-systolic annular enlargement
Little et al[25]	28 ≥moderate MR (13 functional MR, 15 DMR)	TTE	Larger annulus in DMR
	15 control patients		Preserved annular dynamic, close to normal with early-systolic area contraction

3D indicates 3 dimensional; DMD, diffuse myxomatous disease; DMR, degenerative mitral regurgitation; FED, fibroelastic disease; MR, mitral regurgitation; TEE, transesophageal echocardiography; and TTE, transthoracic echocardiography.

may cause early-systolic regurgitation when mitral prolapse has not yet fully developed and may lead to more severe holosystolic regurgitation.[29]

Later is systole, DMR annulus remains abnormal with exaggerated increase of annular area,[20,23] which may contribute to further separation of mitral leaflets and accentuate late-systolic predominance of DMR.[35,36]

Some divergences in DMR annular dynamics depictions raise the question of whether DMR should be seen as a single entity or whether different dynamic phenotypes and pathophysiology would match classic FED versus DMD types defined by functional anatomy.[22] Annular shape[22,23,31] and dynamics[23] have been analyzed according to FED or DMD phenotype in patients with severe DMR referred for surgery. For similar DMR severity and left ventricle/atrium dimensions, DMD annulus was larger, flatter, and with more intercommissural enlargement than in FED. Annular excess enlargement in DMD unexplained by cavities remodeling or regurgitation severity suggests intrinsically diseased annulus in DMD. Annular dynamics reinforce this hypothesis.[23] FED annular motion is close to normal with early-systolic anteroposterior contraction and saddle shape accentuation without change in intercommissural diameter (Figure 4). Hence, in FED, the annular enlargement is modest, most probably

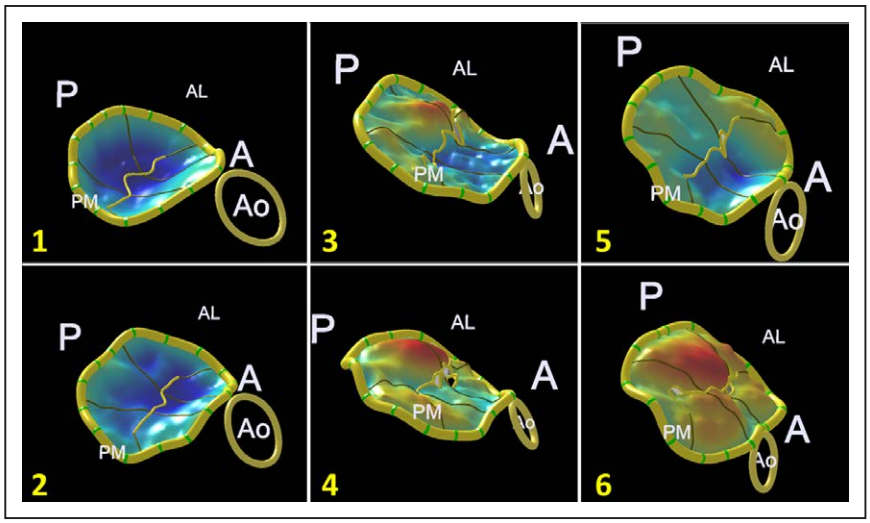

Figure 5. Mitral valve analysis in normal, fibroelastic deficiency and diffuse myxomatous disease. Early- **(1)** and late-systole **(2)** normal mitral valve, early- **(3)** and late-systole **(4)** fibroelastic deficiency with preserved saddle shape of the annulus and holosystolic posterior prolapse, early- **(5)** and late-systole **(6)** diffuse myxomatous disease with flattened and enlarged mitral annulus in early systole and worsening of the prolapse in late systole. A indicates anterior; Ao, aortic valve; AL, anterolateral commissure; P, posterior; and PM, posteromedial commissure.

secondary to DMR severity and cavity enlargement, while its function and dynamics remain close to normal. Conversely, DMD annular dynamics are profoundly altered with severely decreased early-systolic anteroposterior contraction followed by late-systolic increase in intercommissural diameter. Consequently, there is neither early-systolic decrease in annulus area nor saddle shape accentuation and in late-systole annular area increases, further separating leaflets and worsening regurgitation (Figures 4 and 5).[23] DMD annulus enlargement exceeds what DMR and cardiac remodeling would impart and, while annulus remains dynamic, it is profoundly dysfunctional, demonstrating that in DMD, annulus is an integral part of mitral degeneration.

Leaflet Redundancy: A Marker of Severe DMR?

Leaflet redundancy is defined as an excess of leaflet tissue qualitatively observed in DMR but could not be quantified until 3D echocardiography allowed direct measurement of leaflets' areas. Mitral leaflet's characteristics (area and length, prolapse height and volume), static, and dynamic have been studied in DMR accounting for mitral regurgitation severity[29,30] and for the mitral phenotype (FED versus DMD; Table 1).[22,23,31] Leaflet tissue area is increased in DMR versus controls,[22,29,30] and in those with severe DMR, prolapse volume and height are larger.[22,29] Redundancy is more pronounced when DMR is severe[29,30] and affects both anterior and posterior leaflets. Interpretation of redundancy reaches significance when analyzed according to mitral phenotypes, FED versus DMD. For similar DMR severity, redundancy is larger in DMD versus FED with larger leaflets' area and prolapse volume.[22,23,31] Dynamic differences between DMD and FED are even more striking: while both types present with dynamic DMR,[35,36] related to prolapse predominance in late systole, DMD is associated with considerably larger dynamic increase of prolapse volume than FED.[23] From early- to late-systole, leaflets' areas remain stable in FED while in DMD it considerably increases in late systole (Figure 6), demonstrating little valvular tissue reserve in FED versus considerable tissue reserve available to unfurl during systole in DMD.[23]

In DMD, larger prolapse volume and annulus area, both increasing more through systole than in FED, are expected to lead to more severe DMR among patients with DMD

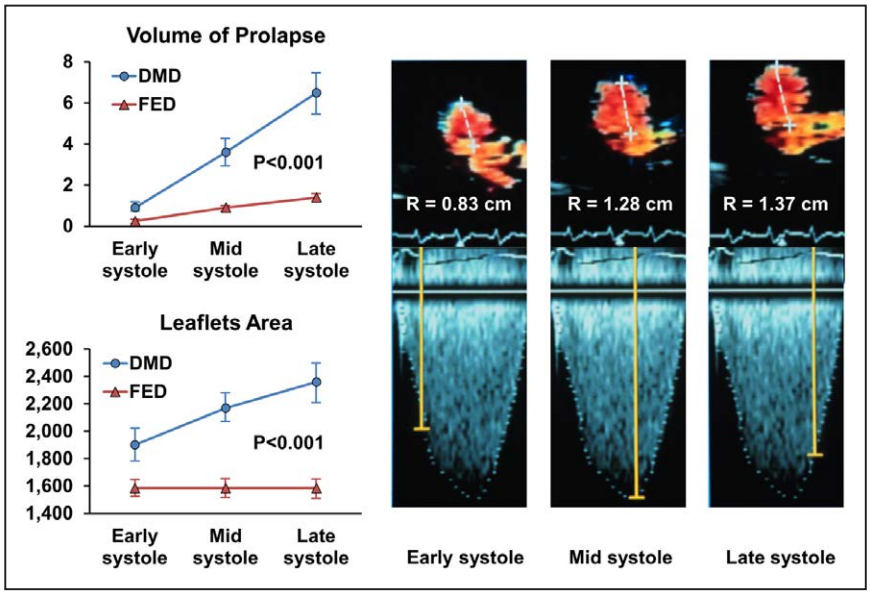

Figure 6. Dynamic of mitral leaflets and prolapse by degenerative mitral regurgitation phenotype. Dynamic evolution of leaflet area (**bottom left**) and prolapse volume (**top left**) in diffuse myxomatous disease (DMD) vs fibroelastic deficiency (FED), related with a dynamic flow convergence during the systole (**right**). Reprinted from Clavel et al[23], Copyright ©2015, and Enriquez-Sarano, Copyright ©1995, with permission.

compared with those presenting with FED. However, among patients with severe DMR, DMD phenotype is not associated with larger regurgitant orifice or regurgitant volume than FED whereas it is associated with larger annulus area and larger prolapse volume. These factors of excess regurgitation are, therefore, compensated. An obvious candidate to counteract excess prolapse and annular enlargement in DMD is excess tissue redundancy allowing coverage of prolapsing segments and annular enlargement. Conversely in FED, relative tissue paucity prevents coverage of smaller prolapse volume and smaller annulus. Valve redundancy, while abnormal, probably helps covering annular area in systole, potentially minimizing regurgitation because of prolapse in DMD (Table 2). Figures 4 and 5 highlight the differences between FED and DMD phenotypes of DMR from static and dynamic pathophysiologic perspectives.

Associated Abnormalities and Valvular Physiology

A frequent association with DMR is mitral annular calcification, which reduces annular dynamics and the more severe the calcification the worse the annular function.[24]

Unlike congenital cleft leaflets that are generally not associated with mitral prolapse,[37] cleft-like indentations in DMR can be deep, frequent,[38] and are potential cause for postrepair residual regurgitation.[39] The 3D transesophageal echocardiography is crucial because these deep indentations cannot be visualized by 2-dimensional echocardiography. Mitral valve en face 3D view is key to their diagnosis[40] by showing the exaggerated form of physiological indentations, extending >50% from free edge into leaflet depth. Initial suspicion of excessively enlarged annulus or excess regurgitation severity associated with cleft-like indentations[38] was not confirmed.[40] DMR with cleft-like indentation display mildly dilated annulus (smaller than without indentation), single segment of posterior leaflet prolapsing, and relative paucity of leaflet tissue compared with absent cleft-like indentation.[40] Besides the importance of cleft-like indentation diagnosis for valve repair, these features reinforce redundancy's role in valvular coverage, whereby excess valvular tissue is associated with less cleft-like indentations and with less regurgitation than annular dilation and prolapse volume would imply.

Other Imaging Modes and Valvular Physiology

In addition to potential prognostic role of left ventricular global strain in DMR,[41] strain analysis of mitral apparatus may provide insights into DMR pathophysiology. Recent work[30] suggested that left atrial strain (reflecting atrial function?) may be linked to annular dysfunction. Preliminary data[32] suggesting higher leaflet strain among DMR versus controls (posterior>anterior), and higher annular strain at commissures will need further confirmation.

Computed tomographic analysis of annular dimensions (Figure 7) in DMR emulates 3D echocardiographic analysis[33] and is important in preparing percutaneous mitral prosthesis implantation, relating mitral annulus to left ventricular outflow tract[33,42,43] to prevent left ventricular outflow tract obstruction and detecting calcifications.

Cardiac magnetic resonance imaging can detect mitral prolapse (Figure 8) and valve features associated with regurgitation severity,[44,45] consistently with echocardiography. Anterior leaflet length, posterior leaflet displacement, flail presence, and posterior leaflet thickness may be linked with regurgitation severity. Cardiac magnetic resonance imaging contributes particularly in identifying myocardial fibrosis[44,46,47] and mitral annulus disjunction,[48] that is, separation of annular base from ventricular myocardium (Figure 8), especially important for risk of sudden cardiac death because of ventricular arrhythmias. Papillary muscles analysis shows often increased excursion, but most importantly papillary muscles myocardial fibrosis that may extend to ventricular wall and correlate to ventricular arrhythmias and annular disjunction,[44,46,48] potentially playing a role in rhythmic risk stratification among patients with DMR, mostly DMD phenotype.

Perspectives

Valvular function normally ensured by a delicate balance of support by the chordae and papillary muscle displacement and is altered in a complex manner in DMR. The 3D echocardiography allows in vivo analysis of each mitral valvuloventricular complex component throughout the cardiac cycle, providing unprecedented insights into DMR mechanisms. This review highlights the heterogeneous nature of DMR with varying degrees of dysfunction of each element of the

Table 2. Summary of Annulus and Leaflet Abnormalities Depending on the Degenerative Mitral Regurgitation Phenotype

		Fibroelastic Disease	Diffuse Myxomatous Disease
Mitral annulus	Static	Moderately enlarged	Severely enlarged and flattened
	Dynamic	Close to normal	Absence of anteroposterior contraction in early systole
			No deepening of the saddle shape
			Abnormal enlargement in mid-late systole
Leaflets	Static	Moderately increased length and area	Severely increased length and area
	Dynamic	Stable size during systole	Increase in both leaflets area in mid and late systole
			More pronounced area increase in posterior leaflet
Prolapse	Static		Height and volume larger than in FED
	Dynamic	Minimal increase during the systole	Important increase in both height (+250%) and volume (+650%) of prolapse in mid and late systole

FED indicates fibroelastic disease.

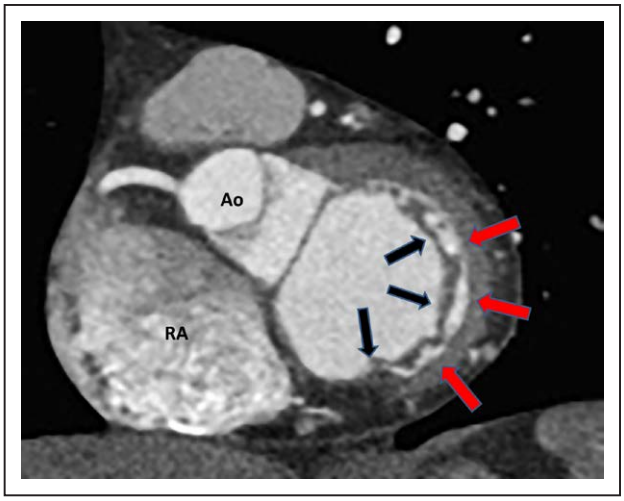

Figure 7. Computed tomographic analysis of mitral annulus. En face view (obtained by reorientation of the 3-dimensional imaging plane) of the mitral annulus and the valvular line of coaptation. Black arrows indicate mitral leaflets coaptation line, and red arrows indicate mitral annulus. Ao indicates aortic valve; and RA, right artery.

valvuloventricular complex within 2 main phenotypes: DMD and FED (Figures 4 and 5). Annular dysfunction is frequent in DMR, particularly DMD, where it fails to ensure early-systolic mitral continence but also yields late-systolic regurgitation by unduly enlarging. Mitral leaflets dynamics shows in DMD considerable redundancy with valvular reserve allowing systolic unfurling that does not increase DMR severity but rather compensates the prolapse and somewhat minimizes regurgitation. Conversely, FED tissue paucity probably leaves some valvular areas uncovered.

These findings have important clinical implications for valve repair. Annuloplasty is essential for support, particularly reattaching ventricular myocardium and annulus but at the expense of losing the annulus dynamic.[16] Achievement of a perfect annuloplasty device, restoring annular function, is uncertain, and it is unclear whether there is benefit in restoring annular saddle shape and systolic accentuation.[27,49] Leaflet tissue amount also is an essential component of mitral function, and its quantification seems promising about choices made for valve repair, specifically to balance valve resection extent[50] exemplified by the concept of resect versus respect.[51] With relative tissue paucity, such as FED, excess resection may leave insufficient valvular coverage, even after annular area normalization by annuloplasty, and may reveal or worsen cleft-like indentations. Conversely, with tissue excessive redundancy, such as DMD, resection of posterior leaflet tissue may be indispensable in rebalancing coaptation and ensuring stable, durable repair.

Implication for Future Clinical Management and Research

DMR reference treatment remains surgical, preferably repair whenever possible.[3] Surgical decisions during mitral repair about leaflet resection, subvalvular support, and annuloplasty type and size are based on qualitative visual inspection of valvular elements by the surgeon. Although experts in valve repair with high surgical volume provide high-quality results and good outcomes with this qualitative inspection, it is uncertain whether such evaluation conducted by surgeons with less expertise is sufficient or may lead to lower rates, quality, and durability of valve repair. Hence, it is essential to develop a standardized set of measurements allowing evaluation of mitral valvuloventricular complex before entering operating theater. Knowledge of quantitative degree of annular enlargement and dysfunction, of valvular redundancy or paucity, of prolapse characteristics (volume and height), and of cleft-like indentations presence may allow better and standardized definitions of surgical procedures to be performed.

New developments of interventional procedures to treat DMR[10] require even more systematic measurements using

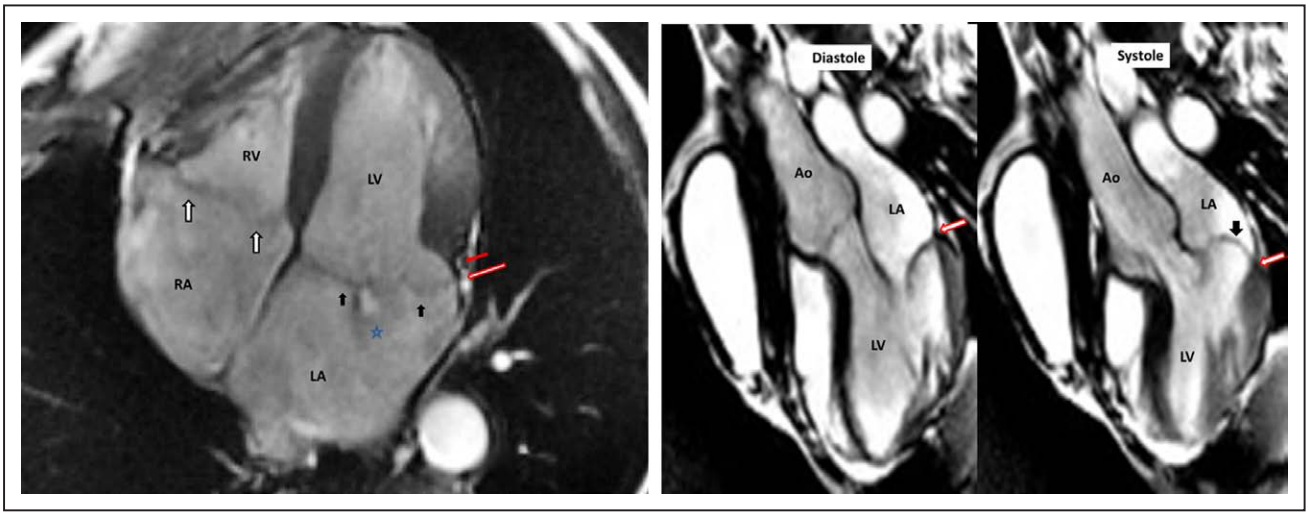

Figure 8. Magnetic resonance imaging of mitral valve prolapse with or without annular disjunction. **A** (**left**), Bileaflet prolapse with annular disjunction in systole: solid red arrow indicates the left ventricle (LV) wall tip, and the annular disjunction is measured by the distance to the red/white arrow located at the actual annulus position, solid black arrows indicate mitral prolapse, blue star indicates regurgitant jet, and white arrows indicate associated tricuspid prolapse. **B** (**right**), Mitral posterior prolapse without annular disjunction. The red/white arrow is located at the annulus level and is on top of left ventricular myocardium both in diastole and systole. Solid black arrows indicate the mitral prolapse. Ao indicates aorta; LA, left atrium; RA, right atrium; and RV, right ventricle.

dynamic 3D echocardiography. Although ≈50 000 mitral clips have been implanted worldwide, it remains uncertain whether and how mitral valve characteristics quantitatively measured influence implantation success and absence of residual mitral regurgitation. Other procedures, percutaneous annuloplasty, or implantation of artificial chordae will soon become clinically available, but short of knowledge of mitral characteristics in successful and unsuccessful cases, clinical indications for these procedures will remain uncertain. However, measurements of 3D echocardiographic dynamic characteristics of the mitral valvuloventricular complex are time consuming and are unlikely to enter clinical practice if not rendered at least semiautomatic. Such developments will require collaboration of imagers and engineers in academic and commercial contexts. We, therefore, make a plea for developing improved software analyzing mitral characteristics and generalizing their application in centers that will treat patients with mitral valve diseases in general and DMR in particular.

Finally, little is known about progressivity of DMR. Mitral prolapse is rare in young patients, and most cases develop with aging. It remains uncertain to predict progression for individual patients. Finite element analysis reporting conditions of tension on mitral apparatus has been rarely conducted and links to genetic characteristics are not established. Analyzing mitral valve dynamic characteristics with extended and automatic armamentarium of measures will undoubtedly allow better comprehension of this frequent disease and of its treatment.

Conclusions

Development of real-time 3D imaging and quantitative software has allowed for the study of dynamic mitral apparatus 3D physiology. Resulting findings reveal normal mitral annulus dynamic function and its role in avoiding mitral regurgitation. Two distinct phenotypes of DMR, matching the historical FED versus DMD classification, are depicted, with considerable mechanistic differences despite common presence of prolapsing leaflets. This should guide future studies on fundamental molecular mechanisms causing DMR. Future directions are for new developments in 3D imaging and software which will simplify analyses of quantitative measures to apply widely these approaches in clinical practice and guide treatment of patients affected by DMR.

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Disclosures

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