Dynamic Changes of the Mitral Valve Annulus
New Look at Mitral Valve Diseases
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The appreciation of mitral valve prolapse (MVP) has evolved from clinical recognition to surgical classification to guide repair, echocardiographic analysis, and specificity with 3-dimensional (3D) depiction and most recently genetic and molecular studies. Two manifestations of degenerative mitral valve disease (DMVD), the main cause of MVP, have been recognized: diffuse myxomatous degeneration (DMD) with involvement of multiple scallops of both leaflets and fibroelastic deficiency (FED), with generally thin leaflets except for myxoid degeneration of one or a few scallops of a single leaflet, generally the posterior. From both mechanistic and surgical perspectives, it remains unresolved whether these are 2 distinct phenotypes or a spectrum, and whether the localized thickening in FED is primary or secondary to the adjacent turbulent blood flow emerging from a scallop with deficient chordal restraint.

See Article by Clavel et al

Clavel et al, in this issue of Circulation: Cardiovascular Imaging, have now contributed information from dynamic quantitative 3D echocardiography relevant to this question in patients undergoing reconstructive surgery that allows visual classification. Despite comparable mitral regurgitation (MR) severity consistent with surgical selection, in addition to previously described static anatomic characteristics, namely enlarged annulus and excess valvular tissue, cyclic annular dynamics are blunted in DMD and systolic leaflet area changes are reduced in FED. These findings raise the possibility of primary alterations of the mitral annulus and biomechanical differences in the leaflet tissue with excess distensible tissue in DMD versus relatively deficient and less extensible tissue in FED. These variations could reveal differences in mechanism and require differences in surgical approach.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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Do Primary Alterations of the Mitral Annulus Exist?

DMVD can affect any of the mitral apparatus components: the leaflets, chordae tendineae, papillary muscles, and annulus. Whether primary changes in the annulus occur has been a long-standing question. The annulus is complex and irregular with both structural and sphincteric roles and changes in shape, size, and force distribution throughout the cardiac cycle. Histologically, the annulus is a noncontinuous structure varying from chord-like to curtain-like, with stiffness correlating with dense collagen content. Static abnormalities of the annulus have previously been shown in DMVD by 3D echocardiography, with a larger, flatter annulus associated with more severe MR and chordal rupture. Annular flattening, expressed as height relative to dimension within the average plane, might simply be secondary to annular dilatation, but in the current study FED and DMD patients interestingly had similar ventricular and atrial remodeling. Annular flattening also exerts increased out-of-plane tension on the annulus, leaflets, and chords, which can elongate biomechanically weakened leaflets, promoting prolapse and increasing the likelihood of chordal rupture. In patients with MVP and no or mild MR, annular flattening likely might suggest primary annular pathology in DMD. However, annular enlargement (with consequent flattening) may reflect the multisegmental extent of prolapse in DMD compared with the limited segment in FED: prolapse can cause annular dilatation by exerting increased outward forces on the annulus, creating an imbalance in annular tension and myocardial force. Confirming primary annular changes may benefit from familial genetic studies of whether annular abnormalities precede or segregate with MVP.

Valve Tissue Reserve: A Passive or Active Process?

In FED, valve tissue area (including that of prolapsing leaflet) is smaller than in DMD and does not increase during systole, whereas in DMD valve tissue area and prolapse volume increase markedly throughout systole. This has led the authors to the concept of valve reserve, consistent with reduced valve stiffness of myxomatous valves. Mitral valve reserve then corresponds to the ability of stressed leaflets to be stretched by ventricular forces in systole, a passive phenomenon, a process in which the valve cells themselves would be passive.

Abnormal mechanical forces exerted on the leaflets, although also strongly influence valve cell behavior. Increased leaflet stretch, set in motion by prolapse, can in turn induce myofibroblast activation of valvular interstitial cells. Quiescent valvular interstitial...
cells contribute to normal valve matrix homeostasis with low turn- 
over. During embryonic development and myxomatous degenera-
tion, valvular interstitial cells are activated to myofibroblasts that 
expressing smooth muscle–associated contractile proteins, metal-
lopainases, and inflammatory cytokines that rapidly remodel 
the extracellular matrix, produce collagens, proteoglycans, and 
growth factors such as transforming growth factor-β, and lead to 
broader, more extensible valves.20 Therefore, leaflet stretch caused 
by initial prolapse and accentuated by annular flattening, may 
lead to cellular activation that potentially increases prolapse. 
This may also explain why myxomatous degeneration is usu-
ally limited to the prolapsing leaflet scallop in FED.

Valvular redundancy in DMD versus paucity in FED may 
affect degree of regurgitation: excess but nonflail leaflet tis-
ue may increase the leaflet coaptation zone, actually reduc-

ing MR, whereas limited leaflet tissue and extensibility may 
limit coaptation. Factors that determine whether leaflets are 
too long or small in relation to the left ventricular remodeling 
need to be considered,21 as in functional MR, with decreased 
valve reserve because of leaflet thickening with restricted motion,22,23 and hypertrophic cardiomyopathy, with elongated 
leaflets disproportionate to the reduced cavity size that can 
explain the coexistence of MVP.

Should Mitral Annulus Dynamics Help 
for Redefine DMVD Phenotypes?
Barlow disease is characterized by excess connective tissue, 
with redundant, thickened and yellowish leaflets, marked 
annulus dilatation, elongated chordae, disrupted collagen 
and elastic layers, and excess acid mucopolysaccharides. FED 
is characterized by decreased connective tissue, deficient in 
collagen, elastin and proteoglycans, thin, smooth and trans-
lucent leaflets without excess tissue and only moderate an-
ulus dilatation and thin, slightly elongated chordae; localized 
myxomatous degeneration and thickening occur within the 
flail scallop, mainly the posterior leaflet. To date, however, 
clear echocardiographic definitions of those entities have not 
been standardized or validated; moreover, histopathologic fea-
tures are not always conclusive; finally, the surgical classifica-
tion remains difficult or impossible in some patients. Thus, 
dynamic changes of the mitral annulus might be helpful in 
the near future (when semiautomatic analysis available) to 
approach the differential diagnosis between DMD and FED, 
suturing or clipping? What is the best technique of commissural 
repair for all patients with DMVD.

Future Directions
This new functional approach based on 3D transesophageal 
ehocardiography complements the functional approach intro-
duced in the beginning of reconstructive valve surgery.2 It 
should open a new era in valve surgical analysis and repair, 
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