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Review

Basic Mechanisms of Mitral Regurgitation

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ABSTRACT

Any structural or functional impairment of the mitral valve (MV) apparatus that exhausts MV tissue redundancy available for leaflet coaptation will result in mitral regurgitation (MR). The mechanism responsible for MV malcoaptation and MR can be dysfunction or structural change of the left ventricle, the papillary muscles, the chordae tendineae, the mitral annulus, and the MV leaflets. The rationale for MV treatment depends on the MR mechanism and therefore it is essential to identify and understand normal and abnormal MV and MV apparatus function.

RÉSUMÉ

Toute détérioration structurelle ou fonctionnelle de l'appareil valvulaire mitral (VM) qui épuise l'excès tissulaire de la VM disponible pour la coaptation des feuillets entraînera la régurgitation mitrale (RM). Le mécanisme responsable de la mauvaise coaptation de la VM et de la RM peut être la dysfonction ou la modification structurelle du ventricule gauche, des muscles papillaires, des cordages tendineux, de l'anneau mitral et des feuillets de la VM. La justification du traitement de la VM repose sur le mécanisme de RM. Il est donc essentiel de cerner et de comprendre le fonctionnement normal et anormal de la VM et de l'appareil VM.

Normal mitral valve (MV) function is dependent on the integrity of the MV apparatus and the harmonious interplay of its main components—the mitral annulus (MA), the MV leaflets, the chordae tendineae, and the left ventricle (LV) wall with its attached papillary muscles (PMs) (Fig. 1, A and B). This spatially and temporally finely tuned system maintains the MV leaflets within the LV, preventing prolapse, and maintains them beneath the LV outflow tract (LVOT) flow and taut, preventing systolic anterior motion (SAM). Adequate MV leaflet closure and coaptation depend on the balance of systolic leaflet tethering vs LV closing forces and leaflet size.[3] Tethering forces are dependent on and transmitted via the LV wall-PM-chordae system, and closing forces reflect the pressure generated by the contracting LV (Fig. 1A).[4-6] MV dysfunction is relatively uncommon in patients younger than 65 years,[7] but structural and/or functional impairment of any MV apparatus components can unsettle the tethering force-closing force balance and result in mitral regurgitation (MR).[4-6]

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MV Apparatus

The MV has anterior and posterior leaflets and variable commissural scallops. The leaflet bases circumferentially insert into the MA, and the ventricular leaflet bodies and edges are connected to the PMs and LV wall via chordae (Fig. 1B and C). The leaflet cross-sectional structure is trilaminar and each layer's extracellular matrix (ECM) has unique characteristics and biomechanical properties important to the normal function of the MV. On the atrial side, the atrialis layer is rich in subendothelial elastic proteins that buffer leaflet stretch during systole. The atrialis is covered by endothelium in continuum with the left atrium (LA). Toward the leaflet core, the spongiosa layer contains hydrophilic proteins that act as cushion-like coaptation zone shock absorbers and therefore promote a tight MV seal. Facing the ventricular side, the fibrosa/ventricularis layer is characterized by a subendothelial collagen fibre network aligned to transmit and spread the LV closure/chordal force optimally toward the MA. Valve interstitial cells can be found in all layers and have an important role in maintaining leaflet homeostasis. Mostly quiescent in the normal adult leaflets, these interstitial cells can become activated in response to mechanical stress or injury to promote ECM remodelling.[8] The anterior leaflet is larger (4-7 cm^2 vs 2-3 cm^2), longer (18-24 mm vs 11-14 mm) and usually thicker than the posterior leaflet and is trapezoid/dome-shaped.[9-14] It shares a rigid fibrous tissue continuity with the noncoronary cusp of the aortic valve (Fig. 1, B and C). The posterior leaflet is crescent-shaped with a short radial length[14] and a long

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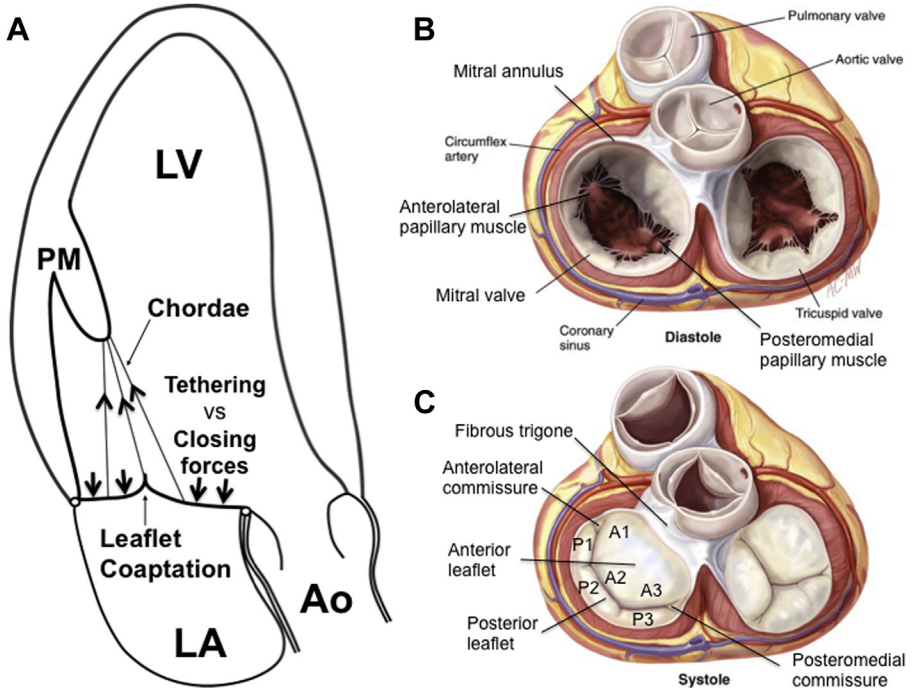

Figure 1. (**A**) Schematic apical long-axis view of the heart in systole (apex on top). There is normal function and spatial relationship of the left ventricular myocardium, the PMs, chordae, leaflets, and mitral annulus. The tethering force—closing force relationship is balanced, both leaflets normally configured, and concave toward the LV, and leaflet tissue coaptation sufficient to prevent mitral regurgitation. (**B**) Surgical view of the open mitral valve in diastole. (**C**) Surgical view of the closed mitral valve in systole. Ao, aorta; LA, left atrium; LV, left ventricle; PM, papillary muscle. (**A**) Modified from Dal-Bianco and Levine[1] with permission from Elsevier. (**B**, **C**) Modified from Carpentier et al.[2] with permission from Elsevier. © 2010 by Saunders, an imprint of Elsevier Inc.

circumferential base that is attached to the posterior MA (Fig. 1, B and C). The MA is a nonplanar saddle-shaped tissue structure that interconnects the LA, the LV, and the mitral leaflets (Fig. 1, B and C; Fig. 2A).[15,16] The MA is innervated and supplies blood vessels and nerve fibres to the attached leaflet bases.[17,18] The anterior portion of the MA is continuous with the rigid aortic annulus and is the elevated (most atrial) "horn" of the saddle shape (Fig. 2A).[15,19] The posterior MA includes the low points of the saddle (most ventricular), close to the lateral and medial commissures and the posterior saddle horn (Fig. 2A). The average MA area in healthy subjects is approximately 10 cm^2.[12,20-23] The flexible posterior MA allows for systolic apical bending along a commissural axis.[19,24] This mechanism, in combination with the planar kidney bean and horizontal saddle shape configuration allows the MA to sphincter-like shrink in area by approximately 20%-42% from diastole to systole,[21-23,25,26] which reduces leaflet tissue stress and is important to maintain coaptation (Fig. 2, B and C).[27-32] The chordae tendineae originate from the PM heads and are fibrous strings composed of an interfacing, tightly linked collagen and elastin network. They insert fan-like into the anterior, posterior, and commissural leaflets and dampen the PM-leaflet force transmission (Fig. 1B).[33,34] Chordae can be distinguished by leaflet location insertion as primary and secondary. Primary (marginal) chordae attach to the leaflet free edges, are thinner, and have limited extensibility because of greater collagen fibril density and reduced crimping.[35] These characteristics ensure a stable systolic coaptation location. Secondary (basal) chordae insert into the central anterior and posterior leaflet bodies,[36] are thicker, and have more tightly crimped collagen that makes them more extensible.[35] The PMs are labelled by their projected relationship to the mitral commissures as lateral and medial (Fig. 1, B and C).[13] Their bodies originate from the apical third of the LV and protrude finger-like into the cavity (Fig. 1, A and B; Fig. 3).[37] In most cases, the lateral PM has a single head and dual blood supply from the left circumflex and left anterior descending coronary arteries. The medial PM has commonly 2 heads and is either supplied by the right or circumflex coronary artery based on dominance.[10,13,38] PM contraction maintains the spatial relationship between the MA and the PM heads during systole and prevents leaflet prolapse.[39-41]

MR Mechanism

MR develops if the MV leaflets do not sufficiently cover the MA orifice throughout LV systole, and is commonly classified as primary MR—indicating leaflet pathology—or secondary MR in the setting of LV myocardial pathology. MR can also be functionally classified based on MV leaflet pliability and motion (Carpentier classification).[42,43] To facilitate medical communication, MV leaflet malcoaptation and MR jet origin are commonly indicated by anterior (A) or posterior (P) leaflet and lateral (A1/P1), central (A2/P2), or medial scallop location (A3/P3) (Fig. 1C).[33]

It is important to understand that significant MR regardless of etiology can prompt independent and ongoing LV and MV apparatus remodelling and start a vicious cycle in which reactive remodelling contributes to MR.[6,12,44] An example is MA dilatation and dysfunction, which is rarely a primary cause for MR,