Mitral Valvular Regurgitation
Etiology, Pathophysiologic Mechanisms, Clinical Manifestations

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Abstract
The etiology of mitral valvular regurgitation (MVR) has changed in the last 40–50 years in the industrialized countries. A significant reduction in the incidence of rheumatic fever and its sequelae, increase in life expectancy, recognition of new causes of MVR, and advancement in technology are responsible for the metamorphosis of the etiology of MVR. It should be mentioned that MVR still constitutes a major health problem which will increase with the aging population. Recent advances in imaging techniques and hemodynamic studies allow clinicians to better define valvular structure and the pathophysiologic mechanisms of valvular heart disease in clinical practice. When combined with careful clinical history taking and thoughtful clinical examination, the correlation of laboratory studies with the clinical picture should permit definition of the etiology of valvular heart disease in the majority of the patients.

Key Words:
Mitral regurgitation, chronic, acute · Pathophysiology · Floppy mitral valve

Introduction
Structural abnormalities and disorders of mitral valve result in valvular dysfunction and mitral valve disease. This general term includes a number of etiologic entities, each one with its own pathophysiology, presentation and natural history. The etiology of valvular heart disease in general and mitral valvular disease in particular has changed dramatically over the last 40–50 years. The recognition of non-rheumatic causes of valvular heart disease, a significant reduction in the incidence of acute rheumatic fever and its sequelae, and the recognition of new or evolving diseases are responsible for the metamorphosis in the etiology and pathogenesis of valvular disorders. It should be mentioned, however, that statistics from cardiac surgery may underestimate the true incidence of certain valvular disease by virtue of selection bias, because only surgical candidates are included in the analysis [1–3].

Disruption of the anatomic integrity of cardiac valves may result in valvular regurgitation, valvular stenosis, or mixed disease and in disorders of the valve surface. Mitral valvular regurgitation (MVR) may be chronic or acute. The clinical presentation and pathophysiologic mechanisms are quite different in chronic compared to acute MVR. For this reason, chronic and acute MVR are described separately. Clinical entities which are associated with mitral regurgitation are shown in Table 1 [1–5].

It should be mentioned that the most common diseases that cause MVR in daily clinical
practice are ischemic heart disease, dilated cardiomyopathy, floppy mitral valve (FMV)/mitral valve prolapse (MVP), and mitral annular calcification. Patients with multivalvular involvement require consideration of the etiologies of the underlying cause. For example, cardiomyopathy is a common etiology in patients with combined mitral and tricuspid regurgitation. Heritable connective tissue disorders also cause mitral and tricuspid regurgitation, as well as aortic and mitral regurgitation. Combination of mitral stenosis with MVR most likely is of rheumatic etiology [3].

Recent advances in imaging techniques and hemodynamic studies allow clinicians to better define valvular structure and the pathophysiological mechanism of valvular heart disease in clinical practice. When combined with careful clinical history taking and thoughtful clinical examination, the correlation of laboratory studies with the clinical picture should permit definition of the etiology of valvular heart disease in the majority of the patients [3–5].

**Chronic Mitral Valvular Regurgitation**

Several pathologic conditions may produce chronic MVR (Table 1). The effect of MVR in the cardiovascular system is similar, regardless of the etiology. Pathophysiologic mechanisms and clinical manifestations, however, in MVR may be related to underlying diseases responsible for the valvular abnormality.

**Floppy Mitral Valve (FMV) – Mitral Valve Prolapse (MVP) – Mitral Valvular Regurgitation (MVR)**

Pathophysiology and clinical manifestations in MVR due to FMV/MVP may be unique compared to other cases of MVR, and for this reason FMV-MVP is discussed in more details.

FMV-MVP comprises a heterogeneous genetic group, in which the degeneration of the mitral valve may be the final pathway for several protein defects. At present, it appears that several forms of inheritance exist [6–8]. The definition of generic defects will allow better classification of this complex valvular abnormality.

The FMV-MVP-MVR classification includes patients with a wide spectrum of mitral valve abnormalities from mild to severe. The term “floppy mitral valve” comes from surgical and pathologic observations and refers to the expansion of the mitral valve leaflets, elongated chordae tendineae, dilated mitral annulus and characteristic histological changes of the leaflets and chordae tendineae. Symptoms and findings in these patients are directly related to mitral valve dysfunction. Histopathologic studies have shown that there is a replacement of the dense collagenous fibrosa by loose myxomatous connective tissue with high-acid mucopolysaccharide content in the mitral valve leaflets. The most specific and characteristic change is collagen dissolution and disruption in the mitral valve leaflets and chordae tendineae [1]. Scanning electron photomicrographs demonstrate surface folds and focal loss of endothelial cells. These surface abnormalities may predispose to thromboembolic complications and infective endocarditis [1–3]. Thus, the FMV should be considered the basic abnormality for the diagnosis of MVP. Auscultatory findings and imaging characteristics are directly related to the basic pathology and function of the mitral valve apparatus. The diagnosis of FMV-MVP is generally reliable when based on the auscultatory postural complex with confirmatory echocardiographic findings. In cases where mitral valve involvement is minimal, there may be a systolic click or characteristic late systolic murmur, but no definite echocardiographic abnormality. Conversely, echocardiographic and cineangiographic studies have shown that FMV-MVP may occur without auscultatory phenomena. New develop-