Calcific Mitral Stenosis

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KEYWORDS

• Calcific mitral stenosis • Mitral annular calcification • Mitral stenosis • Mitral valve
• Echocardiography

KEY POINTS

- Key risk factors for mitral annular calcification (MAC) include advanced age, female gender, and end-stage renal disease.
- MAC is associated with an increased risk of atrial fibrillation, coronary artery disease, stroke, and cardiovascular morbidity and mortality.
- Severe MAC can extend onto the base of the mitral valve leaflets, particularly the posterior leaflet, and cause a calcific, degenerative form of mitral stenosis (MS).
- The morphologic features of calcific versus rheumatic MS are different. Therefore, the echo approach to quantifying MS severity is different for these two disease entities.
- 3-dimensional transthoracic and transesophageal echo are valuable adjunctive methods for evaluating calcific MS and determining stenosis severity.

INTRODUCTION

The mitral valve annulus is a complex structure that forms an integral part of the mitral valve apparatus. The saddle-shaped annulus plays an active role in mitral valve leaflet coaptation and in left atrial and left ventricular (LV) systole and diastole.[1] Situated in continuity with the aortomitral curtain anteriorly and the posterior mitral valve leaflet posteriorly, the annulus is susceptible to disease processes that are distinct from those that affect the mitral valve leaflets. In addition, advanced annular calcification may extend onto the mitral valve leaflets, particularly the posterior leaflet, thereby by causing increased diastolic gradients across the mitral valve. This form of mitral stenosis (MS) is often referred to as calcific, or degenerative, MS and must be distinguished from the disease process and valve morphology inherent to rheumatic MS. The following review highlights risk factors for mitral annular calcification (MAC), features of calcific MS, and the echo approach to this unique form of valvular heart disease.

MITRAL ANNULAR CALCIFICATION

Description

Annular calcification, one of the most common cardiac findings at autopsy, occurs when calcium is deposited in the region between the posterior LV wall and the posterior mitral valve leaflet.[2] Surgical and autopsy studies suggest that calcium may also extend into the LV myocardium and beneath the endocardial surface of the posterior leaflet.[1] MAC is typically appreciated by transthoracic echo (TTE) in the parasternal long-axis and short-axis views as an echogenic structure in this region (**Fig. 1**). Anterior involvement is less common but may occur in advanced cases. Calcification of the aortic valve, papillary muscles, and chordae tendinae frequently coexist with MAC and, if present, will also be appreciated by echo.[1]

Caseous calcification of the mitral annulus (CCMA) is a rare variant of MAC that may be misinterpreted as tumor, abscess, or thrombus on echo. This finding is sometimes described as soft annular calcification that consists of a combination

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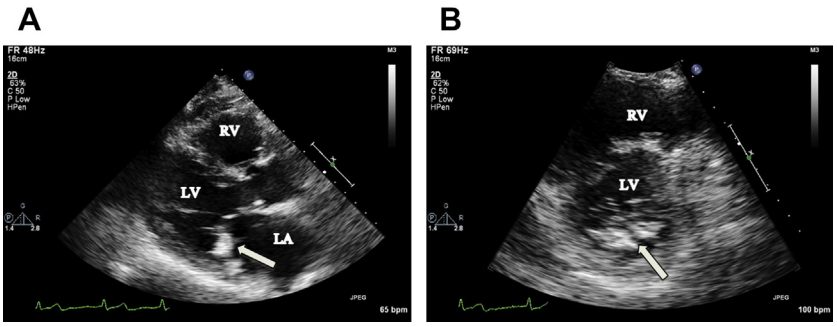

Fig. 1. MAC. MAC is best appreciated in the parasternal long axis (*A*) and short axis (*B*) views as a bright echodensity along the posterior mitral annular plane (*arrow*). LA, left atrium; LV, left ventricle; RV, right ventricle.

of calcium, fatty acids, and cholesterol.[2,3] These components, which form a white, caseous, toothpastelike material, are surrounded by a calcified shell.[2,3] Microscopic analysis of the caseous material demonstrates amorphous eosinophils, macrophages, and lymphocytes with scattered areas of calcification and necrosis.[2] By TTE, CCMA appears as a round, echo-dense mass with smooth borders that is typically located in the posterior periannular region. A central area of echolucency, which represents liquification necrosis, and the absence of acoustic shadowing help distinguish this entity from true MAC.[2]

The cause of CCMA is unknown, and serial echo studies may demonstrate progression or spontaneous resolution, reflecting the dynamic nature of this entity.[1,3] No clinical differences have been show to exist between patients with MAC and those with CCMA; thus, appropriate diagnosis rests on a detailed echo evaluation. Although the clinical course is typically benign, CCMA has, in rare cases, been reported to cause MS or regurgitation by mass effect, erosion into the left atrium, and erosion into the left circumflex artery.[1]

CCMA may also be misinterpreted by echo as tumor, abscess, or even thrombus. Appropriate diagnosis is critical becauasae misdiagnosis in this context may lead to unnecessary and invasive management strategies. Clinical correlation with features that support malignancy, infection, or hypercoaguability will distinguish these entities from CCMA and additional imaging modalities, such as transesophageal echo (TEE) and cardiac magnetic resonance imaging, may be required.

Demographics

MAC is associated with female gender, advanced age, diabetes, hypertension, and coronary artery disease (CAD).[4] MAC has also been found in patients with mitral valve prolapse. In this disorder, dystrophic calcification at sites of annular trauma is thought to result from excess tension exerted by the redundant leaflets.[1] It is estimated that MAC is present in approximately 9% of women and 3% of men who are more than 60 years of age.[1] Annular calcification is also common among patients with chronic renal disease, particularly those with end-stage renal disease (ESRD) requiring dialysis (**Fig. 2**). Prior studies suggest MAC is present in greater than 40% of patients with ESRD and that it tends to develop in younger patients and at a more rapid rate compared with patients without advanced renal disease.[5,6] Studies also show that even mild forms of chronic kidney disease (CKD) confer an increased risk for MAC. A subgroup analysis from the Framingham Heart Study, for example, demonstrated that individuals with chronic kidney disease (defined as a glomerular filtration rate <60 mL/min per 1.73 m^2) were 1.9 times more likely to have MAC compared to those without chronic kidney disease even after adjusting for age and gender.[7]

The major contributor to MAC in patients with renal disease is deranged calcium and phosphorus metabolism caused by secondary hyperparathyroidism. This condition results in a high systemic burden of calcium-phosphorus products, with subsequent calcification of soft tissue structures like the annulus. The presence of MAC in this population bears relevance to the increased cardiovascular risk associated with CKD because MAC is a marker for atherosclerotic burden and is associated with an increased risk of atrial arrhythmias, stroke, and cardiovascular morbidity and mortality.[7]

Clinical Manifestations

MAC is associated with an increased risk of atrial fibrillation, CAD, stroke, and cardiovascular mortality in patients with and without renal disease. Studies have demonstrated the association between MAC and the presence of CAD in younger (<65 years old) and older patients.[8,9] The association between MAC and the risk of cardiovascular