Introduction

Mitral annular calcification (MAC) is a chronic degenerative process that affects the fibrous structure supporting the mitral valve. It is present in 8–15% of the general population; however, its prevalence can reach 40% in older people and 50% in patients with chronic kidney disease. Although it was previously classified as a degenerative pathophysiology associated with age or calcium metabolism, other etiological factors have been suggested, such as atherosclerotic disease and its risk factors (hypertension, obesity, dyslipidemia, diabetes mellitus, smoking), exposure to radiation therapy, and conditions that increase mitral valve stress, such as aortic valve stenosis, hypertrophic cardiomyopathy, and mitral valve prolapse.¹⁻⁵

MAC is related to an increased risk of a number of adverse cardiac events, such as acute myocardial infarction, stroke, arrhythmias (conduction disorders and atrial fibrillation), and mitral valve disease (mitral stenosis, mitral regurgitation, and infective endocarditis).⁶⁻⁸ It is also associated with a higher risk of complications and mortality in patients undergoing mitral valve surgery. Although most cases are not associated with mitral valve dysfunction, some may progress with an increased mitral transvalvular gradient.⁴⁻⁹

Normal mitral annulus anatomy and function

The mitral valve apparatus is a complex three-dimensional unit formed by different structures dynamically interacting throughout the cardiac cycle, including the left ventricle (LV), papillary muscles, chordae tendineae, leaflets, and mitral valve annulus. It is not histologically uniform. Its anteromedial portion, called the mitral-aortic curtain, is more rigid and formed by a curved band of connective tissue that connects the aortic annulus at the level of the left and non-coronary leaflet and the junction of the left atrium wall with the anterior leaflet. On the other hand, the posterior portion of the annulus is formed by a semicircle of fibrous tissue connected with the muscular walls (atrial and left ventricular), the mitral leaflets at the level of the hinges, and the epicardial adipose tissue. The mitral annulus is shaped like a bean or a “D”; however, its three-dimensional evaluation appears as a horse saddle, the ideal configuration to minimize leaflet stress and ensure adequate coaptation. In this saddle, the “highest” points correspond to the most anterior portion, visualized on the two-dimensional echocardiogram in the parasternal longitudinal window. Its nadir corresponds to the portion visualized in the apical four-chamber view. The posterior portion of the annulus, which is less fibrotic, shifts during left ventricular systole, increasing the saddle height and decreasing the circumferential area.⁴⁻⁹⁻¹¹

The quantitative analysis of the mitral annulus through linear measurements obtained using tomographic techniques such as two-dimensional echocardiography may not adequately represent its complex non-planar structure, underestimating these measurements; moreover, it is examiner-dependent due to the need for adequate plane alignment for image acquisition.¹²⁻¹³ In contrast, measurements obtained with the three-dimensional method are not dependent on geometric assumptions and can be obtained even using transthoracic echocardiography; however, this method is less available, expensive, and dependent on a software-dedicated analysis.¹⁴ Important measurements for understanding the mitral annulus, such as its anteroposterior and inter-commisural diameters (Figure 1) or even its circumference and height, are easily quantified by three-dimensional echocardiography and should ideally be acquired transesophageally.
**Echocardiographic evaluation of MAC**

MAC can be identified on echocardiography as an irregular hyperechoic structure involving the mitral valve annulus with the formation of a posterior acoustic shadow that most commonly affects its posterior portion (Figure 2).

Calcifications identified on two-dimensional echocardiography are usually already extended beyond the thin portion corresponding to the mitral valve annulus itself; their location must be described in detail as it has prognostic and therapeutic implications. Calcifications involving the base of the valve leaflets can result in calcium mitral stenosis. Unlike rheumatic stenosis, mitral stenosis does not progress with commissural fusion, as it is unresponsive to percutaneous intervention with a balloon catheter. Furthermore, in MAC stenosis, the valve apparatus usually appears more tubular, with the area at the tip of the leaflets closer to the basal portion area; in rheumatic stenosis, the valve apparatus has a funnel-shaped appearance, with the area at the tip of the leaflets smaller than the basal area. On the other hand, involvement of the atrial surface of the leaflets can result in valve failure due to reduced mobility and consequent difficult leaflet coaptation. Some patients with LV basal wall involvement (Figure 3) may have mobile deposits that must be described due to the risk of embolization. Finally, patients with calcifications extending to the right fibrous trigone are at increased risk of atrioventricular conduction disorders.

MAC is subjectively graded according to the extent of mitral annulus surface calcification. It is considered severe when more than 4 mm thick (measured on the short axis in the anteroposterior direction) (Figure 2), when involving more than 50% of the mitral annulus, or if it reaches the LV inlet. Calcium deposition in less than ⅓ of the annulus is considered mild MAC, while that affecting ⅓ to ½ of the annulus is considered moderate.

Three-dimensional echocardiography may be useful in the study of annulus dynamics in MAC patients. The annulus is more extended during diastole; however, it is flatter (i.e. loses its height) with an increased anteroposterior dimension. During systole, there is a reduction in saddle conformation and annular contraction (annulus area variation), mainly...
due to a reduced anteroposterior diameter variation and increased leaflet tenting length and volume without significant inter-commissural diameter variations.\textsuperscript{15,18}

Estimating the mitral valve area in such patients can be challenging. The continuity equation can be used as long as mild mitral or aortic regurgitation is not greater than mild. Even so, the estimate may be less accurate due to difficulties in measuring the diameter of the LV outflow tract (due to associated aortic or mitral-aortic curtain calcification). In addition, the LV outflow tract and mitral valve flows are not obtained simultaneously and temporally in the cardiac cycle, which can be even more challenging in patients with an irregular heart rhythm. On the other hand, Doppler estimation using pressure half-time may overestimate the valve area (underestimating stenosis severity) due to decreased LV compliance and increased LV diastolic pressure, which are common in older patients.\textsuperscript{9,16,19} Planimetry by two- and three-dimensional echocardiography may be inaccurate due to acoustic shadow formation.\textsuperscript{9}

The dimensionless index of the mitral valve can be useful for grading stenosis. It can be obtained by dividing the time-velocity integral value obtained by pulsed-wave Doppler in the LV outflow tract by the time-velocity integral value obtained by continuous-wave Doppler of the mitral inflow. Values lower than 0.35 are correlated with very severe stenosis (mitral valve area < 1 cm\textsuperscript{2}), while those 0.35–0.50 suggest severe stenosis (< 1.5 cm\textsuperscript{2}) (Figure 4).\textsuperscript{9,19}

The mitral transvalvular gradient should also be cautiously interpreted. In rheumatic mitral stenosis, the relationship between the mean gradient (MG) and the mitral valve area (MVA) is predictable, i.e., when the MG is > 10 mmHg, the MVA is < 1.0 cm\textsuperscript{2}. In MAC, this relationship is unpredictable due to a series of confounders. The high flow often present in renal failure and mitral regurgitation may overestimate the MG.\textsuperscript{20}

These are the predictors of a worse one-year prognosis: MG > 8 mmHg, MVA < 1.5 cm\textsuperscript{2}, RV systolic pressure > 50 mmHg, and the presence of atrial fibrillation.\textsuperscript{8}

It is important to remember that the transthoracic echocardiogram may underestimate the degree of mitral regurgitation due to the formation of an acoustic shadow posterior to the valve annulus. The regurgitant jet should be analyzed by color Doppler in multiple views, and the power of the subcostal window for this purpose should not be underestimated since it is complemented by transesophageal echocardiography.

In symptomatic patients, interventional procedures may be indicated when symptom control fails after optimized drug treatment; however, the results are dubious and the perioperative risk is often high. Mitral valve replacement surgery with calcium removal is technically challenging due to difficulty obtaining adequate cleavage planes, especially in patients with calcification extending to the LV wall.\textsuperscript{21} On the other hand, mitral valve replacement with calcium maintenance can result in paravalvular leak and prosthesis–patient mismatch, common complications in this scenario. In recent years, percutaneous intervention with aortic prosthesis implantation in the mitral position (valve in MAC) has become an alternative in selected cases.\textsuperscript{22} The major complications of this procedure involve LV outflow obstruction, atrial embolization of the prosthesis, and paravalvular leak.\textsuperscript{21}

### Conclusion

MAC is a progressive process with several risk factors and related to a series of adverse cardiovascular events such as arrhythmias, valvular heart disease, heart rhythm disorders, and stroke. In the presence of calcium valve stenosis, stenosis degree grading has some particularities related to rheumatic mitral valve stenosis. The complex anatomy of the mitral valve apparatus can be assessed by two- and three-dimensional echocardiography, and its detailed characterization can add prognostic information that aids the cardiologist with clinical decision-making.
Barros Filho et al.
Mitral Annular Calcification: Challenges and Particularities

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Authors’ contributions
Manuscript writing: Barros Filho ACL; Literature review: Barros Filho ACL; Image release agreement and figure preparation: Barros Filho ACL, Romano MMD; Manuscript review: Romano MMD; Critical analysis: Romano MMD

References

Conflict of interest
The authors have declared that they have no conflict of interest.
Barros Filho et al.
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