REVIEW ARTICLE

Mitral Annulus Disjunction: Current Status

Disyunción del anillo mitral: estado actual

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INTRODUCTION

Mitral annulus disjunction (MAD) is the abnormal insertion of the posterior leaflet of the mitral valve outside the atrioventricular (AV) junction.

The anterior leaflet is continuous with the mitral-aortic intervalvular fibrosa, where there can be no disjunction.

The posterior annulus is fibrous in the approaches to the trigones, but it is discontinuous in the remaining segments, with areas of fatty infiltration. It is particularly in those areas that posterior leaflet insertion can vary, and not necessarily in the AV junction area (Figure 1).

Why is it not fibrous in its entire circumference?

Because it contracts, changes shape, and increases height during systole, facilitating coaptation and reducing stress on the leaflets. This would not occur if the entire annulus was fibrous.

Hemle was the first to describe MAD and this feature of the annulus, in 1876. (1) With wonderful drawings, Hemle described the annulus disjunction zones in normal subjects.

In a pathology study, Angelini described areas of annulus disjunction in a very variable extension in all the hearts studied from a small group of normal subjects and patients with mitral prolapse, suggesting that MAD would be a variant of normal hearts (Figure 2). (2) Similar descriptions are found in Mc Alpine's atlas on heart and coronary anatomy. (3)

Recently, Toh H. et al. published a study on tomography and 30-degree slices of the mitral annulus in 98 normal subjects. The study showed that disjunction zones are common, occurring in 98% of normal subjects, with a height of 1.5-7 mm (mean 3 mm) and in 39 + 18 % of the annulus circumference. (4) Interestingly, increased disjunction was found in segments P1 and P3 areas (Figure 3).

Since the first case described by Bharati, (5) in 1981, countless publications have associated MAD with severe arrhythmias (especially in patients with or without myxomatous degeneration valves), and the concept of arrhythmic prolapse is described in association (6-8), which is incongruent with the pathology and CT scan findings, describing it as a normal anatomical variety.

A literature review compiling 19 publications was

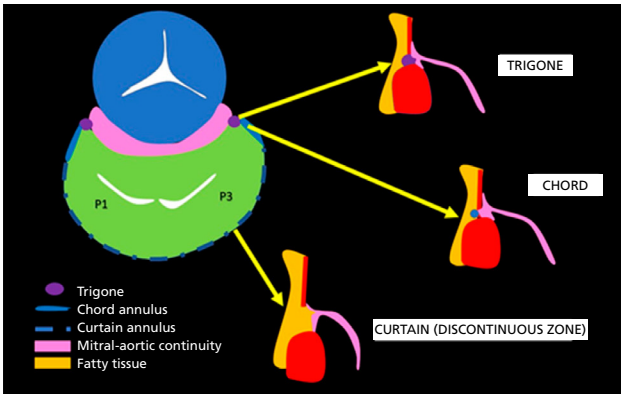

Fig. 1. Position of the mitral annulus; fibrous areas in the approaches to the trigones; discontinuous in the remaining segments, and possible disjunction (modified from European Heart Journal - Cardiovascular Imaging, Volume 22, Issue 6, June 2021, Pages 623–625).

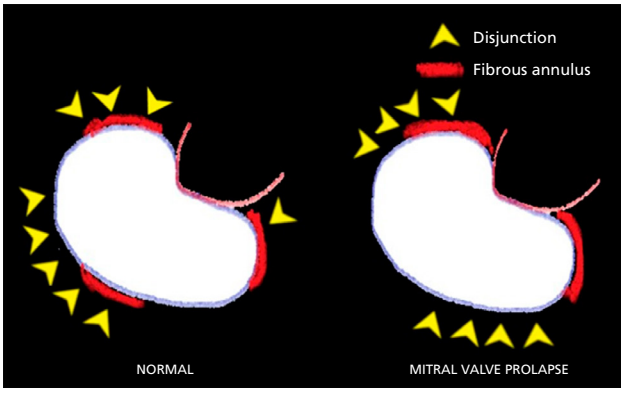

Fig. 2. From the pathology study by Dr. Angelini, examples of the extension of the fibrous annulus and of disjunction areas in a normal and a prolapsed case; disjunction was found in all patients, normal and with prolapse. (modified from Br Heart J 1988; 59: 712-6).

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published in 2019. The reviewers concluded that MAD is usually associated with mitral prolapse and floppy valves, that its origin is unknown, and that there is growing evidence that MAD is associated with ventricular arrhythmias and sudden cardiac death; however, further research and better designed studies are necessary. (9)

Fortunately —and dampening down the fever that had been broken out—, Essayagh et al published in November 2021 a 10-year follow-up study of 595 patients with mitral valve prolapse (MVP), with or without MAD, showing that, while the MAD group had more arrhythmic events, 10-year survival was similar (97% in patients with MVP and MAD, versus 93% in patients with isolated MVP without MAD). (10) This confirms that arrhythmic death events are rare, even if MAD is associated with MVP.

If MAD is so common in normal subjects, how can it be associated with arrhythmias or arrhythmic prolapse? Or are there misconceptions?

Until 2022, all authors agreed that MAD could occur only in systole. Let's discuss three descriptions from different authors:

Enriquez-Sarano states that "disjunction is unnoticeable in diastole"; he considers that the annulus in diastole may be detached, but as it is relaxed, disjunction is unnoticed, whereas over systole, as the posterolateral myocardium contracts, the line of insertion slides and enables disjunction to be observed. (11)

Bennett et al. argue that "MAD is detectable during ventricular systole only when the mitral annulus slides and detaches from the ventricular myocardium by a variable distance ranging from a few millimeters to more than 10 mm in distance". (9)

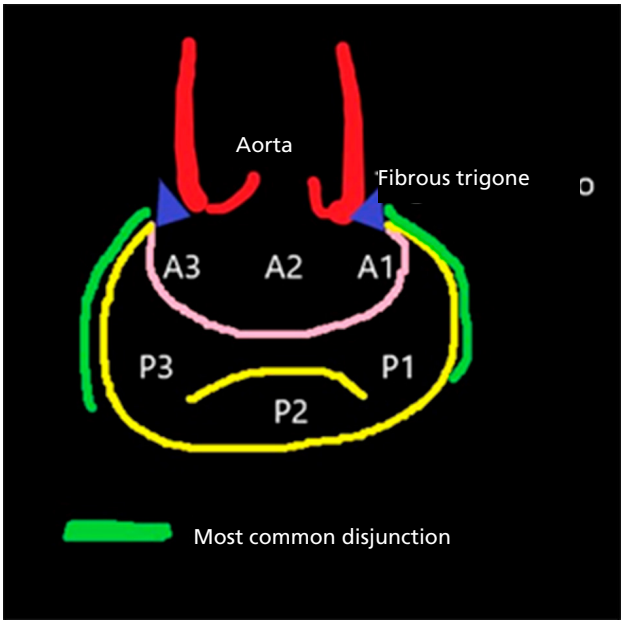

Fig. 3. From the study of Toh H. et al, the areas with the highest frequency of disjunction were found in P1 and P3 segments.

Finally, in a 2021 review, Wunderlich points out that "The diagnosis of a MAD is made in systole. It cannot be made in diastole, because the myocardium of the LV is then appropriately positioned under the mitral valve annulus". (12)

None of these three concepts explains why it is possible to detect disjunction in pathology, where there is no systole. It is very unlikely that there could be 8 or 10 mm of curtain- or cord-like tissue only noticed in systole when the annulus moves towards the apex.

The following image (Figure 4) is a typical example of annulus disjunction as per the definition stating that it is only noticeable in systole. The arrow shows a large detachment area between the possible insertion of the valve and the atrioventricular junction.

Now, the diastolic image of this same patient (Figure 5) clearly shows that mitral valve insertion is detached from the atrioventricular junction, demon-

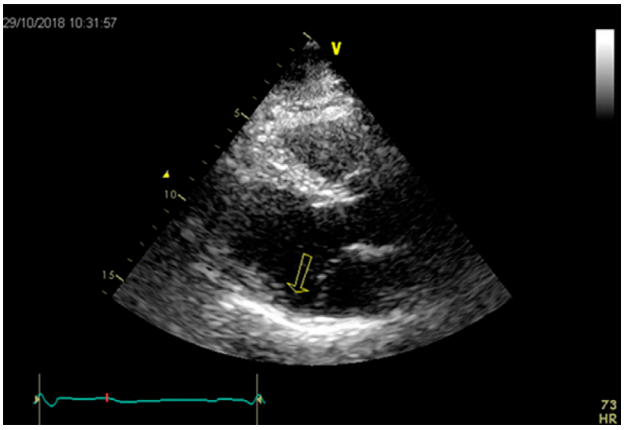

Fig. 4. Parasternal long-axis image showing marked detachment between the posterior mitral valve leaflet and the atrioventricular junction in a patient with mitral valve prolapse.

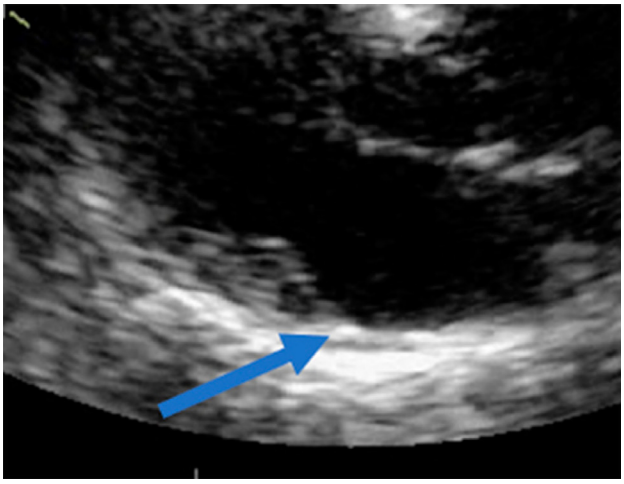

Fig. 5. Diastolic image of the same patient in Figure 2 showing that the posterior leaflet insertion is in the atrial wall and the area of disjunction in diastole.

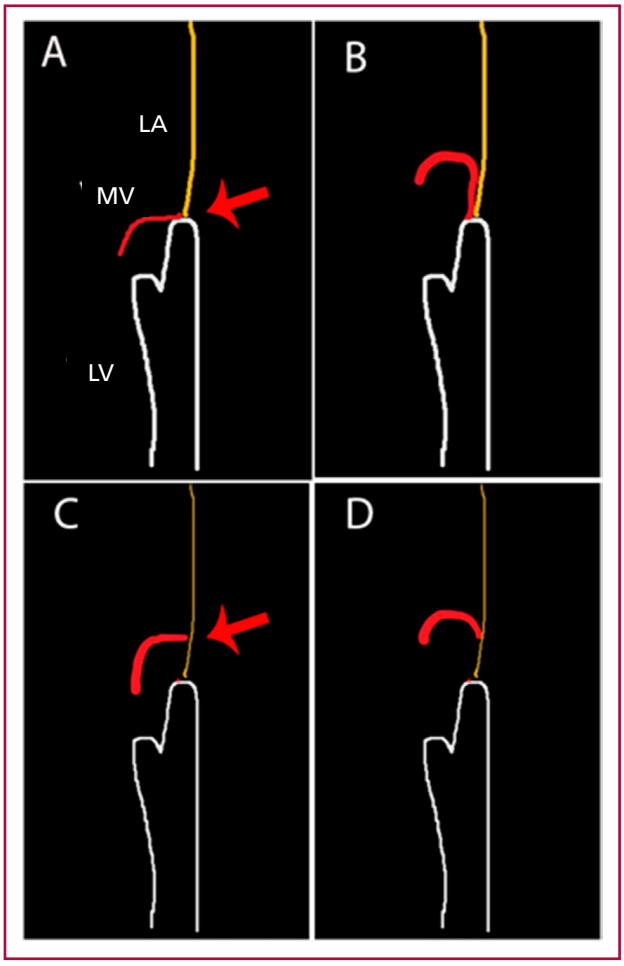

Fig. 6. Images A and B correspond to the pseudo-disjunction phenotype; the posterior leaflet, when prolapsing, is attached to the posterior wall and creates the false image of disjunction, while in diastole, (A) the insertion is at the AV junction. Drawings C and D correspond to the true disjunction phenotype with diastolic insertion in the left atrium.
LA: left atrium; MV: mitral valve; LV: left ventricle

strating that annulus disjunction in diastole can be observed

Dr. Faletra (13) studied mitral valve prolapse patients with cardiac MRI, and described two phenotypes:

True disjunction, when abnormal insertion in diastole (as in the patient in Figure 5) can be visible (Figure 6, drawings C and D).

Pseudo disjunction, when the disjunction space is noticed only in systole, which would only represent marked prolapse with adherence of the posterior leaflet on the atrial wall, creating the appearance of significant disjunction (Figure 6, drawings A and B).

Unfortunately, Dr. Faletra does not explain how frequently each type occurs; he just tells us that true disjunctions are in the minority. At present, it is difficult to estimate how many are true and how many are pseudo disjunctions.

Mantegazza et al. published in 2020 a study on multimodality assessment of MAD with transthoracic and transesophageal echocardiography, and magnetic resonance in patients with mitral valve prolapse. (14) The same criteria for evaluating disjunction in systole was followed. Of the 131 participants, 55 showed disjunction by magnetic resonance; MAD could be visualized in diastole in 22 of them (40% of cases), again, contradicting the concept that disjunction can only be noticed in systole. The authors do not question the implication of observing MAD in diastole.

The papers published this year continue to follow this image-in-systole approach to determine the presence of disjunction.

This year, Essayagh et al. have published another study with three-dimensional transesophageal and transthoracic echocardiography in patients with prolapse and severe mitral regurgitation undergoing valve surgery. (15) They followed the MAD systole approach. MAD was diagnosed in 27/61 patients (44%); diastole disjunction was found only in 4 (almost 15%); this finding is not questioned. Larger prolapses and larger annulus area and diameter were also found in this group. Unlike Dr. Faletra, they persist in the concept of annulus sliding in systole as the cause of disjunction.

Why do patients with disjunction described in previous series have more arrhythmic events?

First, because prolapses are more severe; and second, because of the significant dysfunction of the mitral valve annulus, with larger annuli, less change in their area and less height, resulting in increased stress on the subvalvular apparatus and fibrosis of the papillary muscles and the posterior wall. (16)

The information available is summarized in table 1.

In conclusion, at present:

We know that annulus disjunction is very common in normal patients, due to the anatomy of the annulus itself, which is discontinuous in its posterior segment.

There are two phenotypes: true disjunction (abnormal insertion is observed in diastole and systole) and pseudo disjunction (abnormal insertion is observed only in systole), associated with more arrhythmias; both present similar 10-year mortality rate.

Only two papers describe true disjunction with an incidence of 15-40% of all disjunctions with the systole approach.

Clinical implication of true disjunction is unknown.

Annulus disjunction (following the systole approach) in patients with prolapse is associated with larger annulus, with larger diameters and prolapses, resulting in increased stress on the valvular and subvalvular apparatus, which would explain the higher incidence of arrhythmic events in this group.

Further studies are needed to determine the clinical implication of true disjunction in patients with or without mitral prolapse. Publications to date seem to relate mostly to pseudo disjunction, which would be severe prolapse and has created much confusion about the rather benign nature of true disjunction.

Table 1. True disjunction vs. pseudo disjunction

	Pseudo disjunction	True disjunction
Etiology	Posterior leaflet attached to the atrial wall	Unknown
Frequency	60-85% according to the few series available	15-40% according to the few series available
Association	Floppy valves, severe prolapses	Unknown
Functional effect	Annular dysfunction, stress on the coaptation zone and subvalvular apparatus	Unknown
Clinical implication	Arrhythmias, mitral valve regurgitation, arrhythmic prolapse	Unknown
Effect on mortality	Non-demonstrated in large series	Unknown

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material.)

Ethical considerations

Not applicable.

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