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Editorial

The mitral valve is still playing tricks on us

Mitral annular disjunction (MAD) is a detachment of the mitral annulus from its normal myocardial attachment, which becomes detectable during ventricular systole [1–3]. The normal mitral annulus anatomy involves different attachments for anterior and posterior leaflets. The annulus supporting the anterior leaflet is part of the heart's fibrous core in continuity with the fibrous trigones and the aortic annulus, which is highly fibrous and not prone to disjunction. Conversely, the annulus portion supporting the posterior leaflet while occupying two-thirds of the circumference is much thinner, less dense, and is located at the convergence of three structures. The annulus is implanted in the ventricular myocardium, forms the base of the posterior mitral leaflet, and is also at the fibrous end of the left atrial wall [4]. Thus, the mitral annulus ensures electric isolation of atrium/ventricle, provides mechanical support for the posterior leaflet, and allows appropriate coupling of left atrium (LA) to ventricular systole [5].

Due to the difficulty in imaging such an evanescent structure, MAD diagnosis was almost universally ignored for many years by echocardiography. Furthermore, confusion arises from variable definitions of annular disjunction, alternatively reported as microscopic, of limited extent and present in almost all patients including normal individuals [2,6] to macroscopic and part of the slippage associated with myxomatous degeneration of valvular/annular tissue [7,8]. However, the major issue is the precise definition of the mitral annulus position throughout the cardiac cycle, which requires high spatial resolution and high frame rate to accurately evaluate not only the annular position but its maintained attachment to the ventricular myocardium throughout systole by perfectly orthogonal imaging. This difficult imaging diagnosis explains a considerable confusion in the current literature.

MAD, in the clinical setting, is characterized by visible detachment of mitral annulus supporting the posterior mitral leaflet from adjacent ventricular myocardium, as part of myxomatous mitral valve disease [4,9]. Since the description of MAD in subjects without mitral valve prolapse (MVP), we have incessantly attempted to demonstrate such a "clinical" entity and have been unsuccessful. MAD is not uniformly observed in MVP, detectable by echocardiography in approximately one of three patients [7]. Diagnosis requires high spatial/temporal resolution imaging in long-axis views by transthoracic-echocardiography [10–13] or cardiovascular magnetic resonance (CMR) [8,13,14] through dynamic frame-by-frame analysis with careful examination of mitral annulus position (Fig. 1) [15,16]. Clinical macroscopic MAD is associated with partial loss of mechanical annular function with late systolic expansion, while electrical isolation of LA/ventricle is maintained and the impact on atrial function remains undefined, although the LA is generally notably dilated with MAD [7,17]. MAD is predominantly observed at insertion of the posterior leaflet, extending laterally variably under all scallops but preferentially under the P2 scallop.

1. The present report

The article by Figliozzi et al. [18] aims at reporting, in a single-center retrospective cohort, the prevalence of MAD in consecutive unselected patients undergoing CMR, and its association with MVP and ventricular arrhythmias. In a registry of 441 patients with CMR, the prevalence of MAD ≥1 mm was common 49% (49/100), with higher prevalence and greater extent in patients with MVP (up to 90% (90/100) ≥1 mm). MAD ≥4 mm was rare, showing association with higher burden of ventricular ectopy but not with sudden cardiac death, unexplained syncope, and sustained ventricular arrhythmia at 12 months.

The study is interesting in reporting MAD prevalence by CMR among healthy individuals but remains limited by the small number of MVP patients included, meager number of events, and inconsistent arrhythmia surveillance, profoundly hindering the analysis of the MVP phenotype associated with MAD and sudden cardiac death. Additionally, the question of the high MAD prevalence with and without MVP remains puzzling, contrasting with previous reports. Irrespective, the inconsistent MAD definition and prevalence in the literature clearly pose the question of MAD diagnostic criteria.

2. Is MAD that common?

Our knowledge of the mitral valve has considerably improved over the past 30 years, from MVP diagnosis criteria, to better understanding of the mitral annulus saddle shape, MVP long-term prognosis and, more recently, the arrhythmic MVP phenotype. In the early 1980s, MVP was diagnosed in so many subjects that were otherwise normal that its prevalence was clearly overestimated, and we created a medical "condition" in perfectly normal subjects. It is essential that we do not reiterate such a mistake with MAD. Despite uncertainties regarding MAD prevalence, it is most commonly observed in advanced myxomatous degeneration with bi-leaflet MVP, abnormal annular movement, and LV excess remodeling in Degenerative Mitral Regurgitation. MAD existence, physiopathology, and clinical consequences without MVP, if confirmed by appropriate large imaging cohorts, remain undefined. In patients with MVP, the clinical link between macroscopic MAD and progressive development of ventricular arrhythmias is now

Abbreviations: CMR, cardiac magnetic resonance; LA, left atrium; MAD, mitral annular disjunction; MVP, mitral valve prolapse

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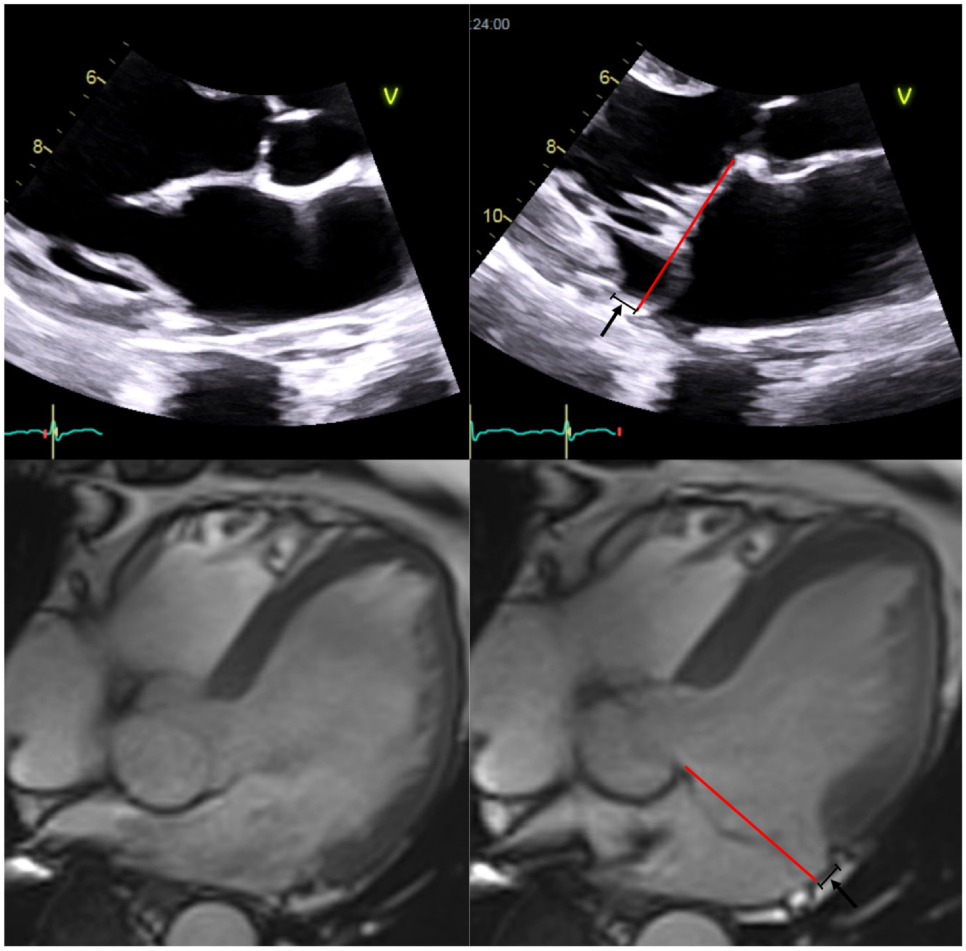

Fig. 1. Mitral valve prolapse and mitral annulus disjunction by transthoracic-echocardiography and cardiovascular magnetic resonance (CMR). Transthoracic-echocardiographic long-axis view in end-diastole displaying the mitral valve without MAD (upper left), and in end-systole with myxomatous posterior leaflet prolapse and MAD of 5 mm length (upper right). CMR three-chamber view in mid-diastole displaying the mitral valve without MAD (lower left), and in end-systole with bi-leaflet mitral valve prolapse and MAD of 4 mm length (lower right). *MAD* mitral annular disjunction

well-established [7]. Patients with MAD at MVP diagnosis have a two-fold increase in the cumulative probability of arrhythmic events, and, particularly ventricular tachycardia, compared to those without MAD. Arrhythmic events incidence tends to be progressive, affecting close to one in three patients 5 years after diagnosis and two in three at 10 years after diagnosis but is much higher than in patients without MAD.

Thus, even if most healthy individuals present with *microscopic* MAD or discontinuous mitral annulus, such findings become meaningless, if most normal subjects are diagnosed with it or even if present in 50% (50/100) of the normal adult population. On the other hand, the *macroscopic* definition of MAD as applied at MVP diagnosis is physiologically and outcome-wise clinically meaningful through its association with ventricular arrhythmias [7,19]. The position of the mitral valve is paramount for defining MAD and MVP. Dynamic evaluation is mandatory to avoid confusion between MVP and MAD based on the positioning of the insertion of the posterior mitral valve leaflet. While CMR has greater temporo-spatial resolution, it remains operator- and imaging protocol-dependent. CMR scanning protocol should include a contiguous stack centered at the left ventricular outflow track perpendicular to the mitral annulus covering all the MV scallops and the mitral annulus. This obviously increases the number of breath-holds, cine acquisitions and prolongs the CMR study.

Since there are significant challenges in defining MAD, a consensus document by numerous experts regarding appropriate imaging is necessary. Indeed, as our knowledge regarding MVP diagnosis was crucially redefined 30 years ago, based on the saddle shape of the mitral annulus, leading to a profound reconsideration of echocardiographic standards for MVP diagnosis [20], it is reasonable to question MAD diagnosis standards. The mitral valve is still playing tricks on us, and unified criteria for MAD diagnosis are required to ultimately uncover its prevalence and outcome impact with and without MVP.

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Declaration of competing interests

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