Mitral Annular Disjunction—A New Disease Spectrum

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KEYWORDS

• Mitral annular disjunction • Mitral valve prolapse • Arrhythmia • Echocardiography

KEY POINTS

- Mitral annular disjunction is a structural abnormality of the mitral annulus fibrosus. It refers to a separation between the atrial wall-mitral valve junction and the left ventricular attachment defined by pathologist.
- Mitral annular disjunction is a common finding in patients with myxomatous mitral valve diseases, such as Barlow syndrome.
- Mitral annular disjunction has been recognized in relation to ventricular arrhythmia and sudden death. The width of mitral annular disjunction correlates with the incidence of nonsustained ventricular tachycardia in patients with myxomatous mitral valve diseases.
- Mitral annular disjunction itself possibly concerns to ventricular arrhythmia because of mechanical stretch. We need to perform prospective studies to reveal the meanings of mitral annular disjunction in arrhythmic mitral valve prolapse.

INTRODUCTION

Mitral annular disjunction is a structural abnormality of the mitral annulus fibrosus, which has been described by pathologists to be associated with mitral leaflet prolapse (**Fig. 1**).[1–3] Hutchins and colleagues,[1] in their study of 900 autopsied hearts, observed disjunction of the mitral annulus in hearts with mitral valve prolapse (MVP). They defined disjunction as a separation of the atrial wall-mitral valve (MV) junction and the attachment of the left ventricle (LV). They revealed that disjunction was an anatomic variation of the normal morphologic characteristics of the mitral annulus fibrosus, because it was present in approximately 6% of human hearts.[1] During the cardiac cycle, the region of disjunction permits the atrium-valve leaflet junction of the mitral apparatus to move outwardly in relation to the atrial aspect of the ventricular wall during ventricular systole and inwardly during ventricular diastole. Mitral annular disjunctions are also of varying degrees.

PATHOLOGY OF MITRAL ANNULAR DISJUNCTION

The histopathologic abnormality of mitral annular disjunction was first reported by Hutchins and colleagues in 1986.[1] Among 900 autopsied hearts, floppy MVs were detected in 25 hearts (2.8%). About 92% of these 25 hearts had mitral annular disjunction. In 42 other hearts (5%) from significantly younger patients, there were mitral annular disjunctions without floppy MVs. They defined

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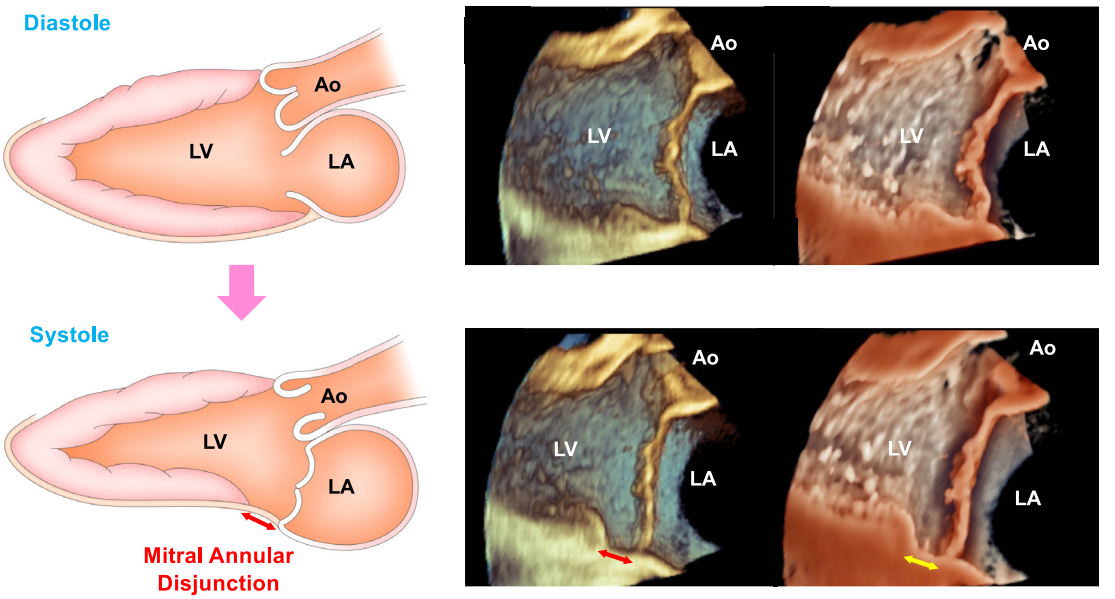

Fig. 1. Mitral annular disjunction (*arrow*). Measurement of mitral annular disjunction is recommended to be performed at end-systolic phase. Ao, aorta; LA, left atrium; LV, left ventricle.

mitral annular disjunction as a separation of the atrial wall-MV junction and the LV attachment.[1] In 1988, Angelini and Becker reported that there was no significant difference in the number of segments around the left atrioventricular junction, which showed disjunction in hearts with normal or prolapsing leaflets.[2] They also pointed out that mitral annular disjunction is an anatomic variation of the normal morphologic characteristics of the mitral annulus, seen in floppy valves, as reported by Hutchins.[2] In addition, they suggested that if hypermobility of the mitral apparatus is important in producing prolapse, it is probably produced by other abnormalities over and above so-called disjunction.[2]

ANATOMY AND PHYSIOLOGY OF THE MITRAL ANNULUS AND MITRAL ANNULAR DISJUNCTION

The aortic valve continues fibrously with the anterior leaflet of the MV and the right and left fibrous trigones. This region of the annulus is fibrous and less prone to dilatation. The remaining two-thirds of the annulus is composed of muscle and dilate easily in patients with mitral regurgitation (MR). Therefore, we can detect mitral annular displacement mainly in the posterior leaflet. This part of the mitral annulus may represent an area weakened by mechanical stress.

Normally, the posterior mitral ring and its adjacent myocardium moves synchronously with the LV. On the contrary, when the mitral annulus is disjunctive, annuloventricular coupling is not preserved and the mitral annulus moves abnormally. Left ventricular wall curling has been defined as an unusual systolic motion of the posterior mitral ring on the adjacent myocardium.[4]

The quantitative assessment of curling by cardiac magnetic resonance imaging (CMR) was defined as a perpendicular distance from a line between the top of LV inferobasal wall and the LA wall-posterior MV leaflet junction to the lower limit of the mitral annulus during end-systole. Perazzolo Marra and colleagues reported that curling of the mitral annulus is associated with mitral annular disjunction. There was a linear correlation between the length of mitral annular disjunction and the severity of curling.[4]

DIAGNOSIS OF MITRAL ANNULAR DISJUNCTION

Usually, we can detect mitral annular disjunction on parasternal long-axis view by transthoracic echocardiography. During the cardiac cycle, this region of disjunction permits the atrium-valve leaflet junction of the mitral apparatus to move outwardly in relation to the atrial aspect of the ventricular wall during ventricular systole and inwardly during ventricular diastole. The mitral annular disjunction distance was usually measured during the end-systolic phase in the parasternal long-axis view. We previously reported 2.0 mm as the minimum value of mitral annular disjunction by which measurement is possible.[5] When multiple sonographers

measured the same cases with mitral annular disjunction, all sonographers could recognize the presence of mitral annular disjunction and could measure the distance when it was greater than 2 mm.[5] Lee and colleagues[6] reported that mitral annular disjunction was located adjacent to the prolapsed segments, circumferentially spanning over average 87° of the annulus on 3-dimensional (3D) transesophageal echocardiography.

CMR is also useful in detecting mitral annular disjunction. Mitral annular disjunction can be detected on the apical 4 chamber in midventricular systole. Dejgaard and colleagues[7] reported that a complete assessment of the mitral annulus circumference can be made by using 6 LV long-axis cine sequences with an interslice rotation of 30°. In that study, the longitudinal mitral annular disjunction distance was 3.0 mm and the circumferential mitral annular disjunction was 150°. They showed that mitral annular disjunction could be detected in up to two-thirds of the mitral ring circumference.[7] An advantage of CMR is that it can be used to evaluate arrhythmogenic left ventricular walls with the aid of late gadolinium enhancement (LGE) in contrast-enhanced CMR (CE-CMR). They also identified the presence of basolateral left ventricular wall curling motion by visual assessment in parasternal long-axis view, apical long-axis view, and apical 4-chamber view by echocardiography.[7] Recently, Putnam and colleagues[8] reported that cardiac computed tomography (CCT) can be used to detect mitral annular disjunction. In that study, a 256-slice multidetector CT scanner was used and then multiplanar reconstruction (MPR) was performed. Using MPR, they could determine the presence and measure the distance of mitral annular disjunction. Future research of CT is expected.[8]

MITRAL VALVE PROLAPSE AND MITRAL ANNULAR DISJUNCTION

We previously reported that mitral annular disjunction was detected not only in patients with a myxomatous MV but also in normal cases, and the frequency of MVP was significantly larger in patients with mitral annular disjunction than in those without it. Mitral annular disjunction was detected in 28% of patients with MVP.[5]

There were 8 reports that investigated the prevalence and clinical outcomes among patients with mitral annular disjunction (**Table 1**). Firstly, Eriksson and colleagues performed a retrospective analysis of the intraoperative transesophageal echocardiography in 67 patients with advanced mitral valvular degeneration. They also analyzed a subgroup of 32 patients with mild/moderate mitral valvular degeneration.[9] They reported that mitral annular disjunction was detected at the base of the posterior leaflet in 98% of patients with advanced and in 9% of patients with mild/moderate mitral valvular degeneration.[9] Lee and colleagues studied 101 patients with MVP, 30 subjects with normal MV, and 25 heart failure patients with functional MR using real-time 3D transesophageal echocardiography and detected mitral annular disjunction in 42 patients with mVP (42%).[6] They also evaluated mitral annular motion and observed that when the annulus was disjunctive, its motion no longer followed LV contraction, but it exhibited paradoxic dynamics, conforming to atrial wall motion. They concluded that the disjunctive annulus was decoupled functionally from the ventricle, leading to paradoxic annular dynamics with systolic expansion and flattening, that may require specific intervention.[6] Recently, Putnam and colleagues studied 90 patients with MVP and severe MR, who had preoperative CCT.[8] The presence of mitral annular disjunction was associated with female gender, smaller annulus size, and greater posterior leaflet length.[8] Mategazza and colleagues concluded that mitral annular disjunction could be detected in a minority of patients with fibroelastic deficiency and not only patients with Barlow disease. The feasibility of MV repair was no different between these groups.[10]

ARRHYTHMIC MITRAL VALVE PROLAPSE AND MITRAL ANNULAR DISJUNCTION

Basso and colleagues[11] reported the autopsy findings of 43 sudden cardiac death patients with isolated MVP and observed bileaflet involvement in 70% of them. Fibrosis of the papillary muscles and inferobasal LV wall correlates with the origins of ventricular arrhythmias.[11] Arrhythmic MVP should be clearly distinguished from echocardiographic MVP. There are various opinions of mechanism. Excessive mobility of leaflets causes mechanical stretching of the mitral annulus.[12] It concerns left ventricular fibrosis.[13] Miller reported that bileaflet MVP is a high-risk feature for sudden cardiac death. Mitral annular disjunction was considered to be a constant feature of arrhythmic MVP with LV fibrosis.[14] Parazzollo Marra and colleagues reported that mitral annular disjunction was significantly longer in MVP patients with LGE on CE-CMR than in those without it. Longer mitral annular disjunction was detected in 50 sudden death patients with MVP and fibrosis than in 20 patients without MVP. Mitral annular disjunction was detected in both patients with arrhythmic MVP with LV LGE and sudden cardiac death cases with LV fibrosis. Mitral annular disjunction and curling were confirmed by histology in sudden cardiac

Table 1
Prevalence of mitral annular disjunction in some studies

First Author	Study Design	Year	Imaging	Diagnosis	Characteristics of Population	Rate of Mitral Annular Disjunction
Erikisson et al,[9] 2005	Retrospective cohort study	1991–1995	TEE	Myxomatous mitral valve disease	n: 67 Mean age: 52 y Female 34%	Advanced MVD: 31/32 (97%) Mild/moderate MVD: 3/32 (9%)
Carmo et al,[15] 2010	Retrospective cohort study	2003–2006	TTE	Myxomatous mitral valve disease	n: 38 Mean age: 57 y Female 47%	21/38 (55%)
Perazzolo Marra et al,[4] 2016	Retrospective cohort study	2010–2014	CE-CMR	MVP	n: 52 Mean age: 44 y Female 63%	37/52 (71%)
Lee et al,[6] 2017	Retrospective cohort study		TEE	MVP, FMR, and normal control	n: 156 Mean age: 58 y Female 33%	42/156 (27%)
Konda et al,[5] 2017	Retrospective cohort study	2014	TTE	Refferred TTE	n: 1439 Mean age: 65 y Female 42%	125/1439 (9%)
Dejgaard et al,[7] 2018	Cross-sectional study	2015–2017	TTE and CE-CMR	Patients with mitral annular disjunction	n:116 Mean age: 49 y Female 70%	
Mantegazza et al,[10] 2019			TTE	MVP and severe MR	n: 979 Mean age: 63 y	103/979 (16.2%)
Putnam et al,[8] 2020	Retrospective cohort study	2013–2019	Cardiac CT	MVP and severe MR	n: 90 Mean age: 63 y Female 26%	18/90 (20%)
Konda et al,[17] 2020	Retrospective cohort study	2009–2010	TTE	MVP and severe MR	n: 185 Mean age: 62 y Female 40%	45/185 (24%)

Abbreviations: CE-CMR, contrast-enhanced cardiac magnetic resonance; FMR, functional mitral regurgitation; MVD, mitral valve disease; MVP, mitral valve prolapse; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

death patients with MVP. Excessive mobility of the leaflets and systolic curling have clinical important implications. They concluded that mitral annular disjunction is associated with arrhythmic MVP.[4] Carmo and colleagues[15] found that the severity of mitral annular disjunction significantly correlated with the occurrence of nonsustained ventricular tachycardia (NSVT), and a disjunction of greater than 8.5 mm was predictive of NSVT. Essayagh and colleagues showed that ventricular arrhythmia were frequent in patients with MVP but rarely severe in those with only MR. They concluded that arrhythmic MVP was strongly associated with specific electrocardiographic (ECG) changes, the presence of mitral annular disjunction, and leaflet redundancy but was independent of MR severity.[16] Dejgaard and colleagues investigated CMR and 24-hour ECG recordings in patients with mitral annular disjunction. About 54% of patients with mitral annular disjunction had MVP. There was no difference in the prevalence of ventricular arrhythmias between those mitral disjunction patients with MVP and those without MVP. They reported that the longitudinal distance of mitral annular disjunction in the posterolateral wall and papillary muscle fibrosis assessed by CMR were predictive of ventricular arrhythmia. They concluded that mitral annular disjunction itself was an arrhythmogenic entity.[7] According to previous studies, the site of mitral annular disjunction may become the origin of arrhythmias. We studied 185 patients with severe MR caused by fibroelastic deficiency and Barlow syndrome. Mitral annular disjunction was detected in 24% patients with severe MR. During a median follow-up of 20.3 years, arrhythmic events and sudden death occurred in 7 patients (3.8%). The number of patients with cardiac events were significantly larger in the group that received medical treatment ($P = .02$). All patients had no mitral annular disjunction. In this study, we investigated for the patients with severe MR limitedly. Therefore, we need to investigate for patients with various MR grade to clarify the significance of mitral annular disjunction.[17]

CLINICAL IMPLICATIONS

The presence of mitral annular disjunction means with hypermobility of the mitral apparatus. Loose connection between the junction of the MV and the LV results in hypermobility of the posterior mitral annulus and may be associated with MVP. Flameng and colleagues[18] reported the importance of using sliding plasty in MV surgery for posterior displacement of the mitral annulus. Newcomb and colleagues concluded that correction of the annular dilation and posterior displacement, shortening of the height of the posterior leaflet, and correction of valvular prolapse provided excellent functional results. They reported that advanced myxomatous degeneration is an independent predictor of repair failure due to inadequate annuloplasty. Posterior annular displacement, which means mitral annular disjunction, may be another cause of repair failure[19] Fixation of the hyperenhanced annular dynamics using ring annuloplasty may be sufficient to restore MV competence.

Mitral annular disjunction has been reported to be associated with ventricular arrhythmia and sudden cardiac death. If mitral annular disjunction is incidentally detected in patients during echocardiography, we have to evaluate for features and a history of arrhythmia. If necessary, a Holter ECG should be performed. The presence and importance of mitral annular disjunction should be spread. The clinical and physiologic meanings of mitral annular disjunction and MVP is an important work in progress. The molecular mechanism should be investigated.[20]

SUMMARY

Mitral annular disjunction is a structural abnormality that is seen not only in patients with myxomatous MVs but also is in patients with MVP. The prevalence of mitral annular disjunction should be checked routinely during presurgical imaging. Otherwise, mitral annular disjunction itself might be an arrhythmogenic entity, irrespective of the presence of MVP. Therefore, we should check echocardiography keeping in mind mitral annular disjunction. Further prospective studies are needed to address whether a causative mechanistic link exists between mitral annular disjunction and arrhythmic MVP or severe MR.

CLINICS CARE POINTS

- Check the presence of mitral annular disjunction in every patient particularly with mitral valve disease because mitral annular disjunction itself is arrhythmogenic.

DISCLOSURE

All authors have nothing to disclose.

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