JACC: CASE REPORTS VOL. 3, NO. 10, 2021

CASE REPORT

ADVANCED

CLINICAL CASE SERIES

Varied Extent of Mitral Annular Disjunction Among Cases With Different Phenotypes of Mitral Valve Prolapse

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ABSTRACT

Detailed 3-dimensional analysis of mitral annular disjunction was undertaken in 3 comparative cases of mitral valve prolapse. A case of Barlow disease showed extensive disjunction, whereas cases of fibroelastic deficiency and forme fruste demonstrated less extensive disjunction. Considering the current controversies surrounding disjunction, these observations call for detailed research in the future. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2021;3:1251–1257)

Mitral valve prolapse (MVP) involves various underlying processes affecting the papillary muscles, tendinous cords, mitral valve leaflets, and attachment of the mitral valve (1). MVP is the main functional feature of degenerative mitral valve disease (2), which involves the following phenotypes (**Central Illustration**). Barlow disease is characterized by billowing of both mitral leaflets with diffuse myxomatous changes, combined with severe dilatation of the annulus. By contrast, fibroelastic deficiency is characterized by focal prolapse. Myxomatous thickening of the leaflet is generally restricted to the prolapsed segments, with the rest of the leaflet remaining rather thin and transparent without annular dilatation. The intermediate state between Barlow disease and fibroelastic deficiency disease is called forme fruste (2,3).

LEARNING OBJECTIVES

- To recognize the utility of cardiac CT for accurate 3-dimensional evaluation of the extent of disjunction.
- To highlight the feasibility of cardiac CT for identification of subtle morphologic differences between different phenotypes of MVP.

Thus, overall, MVP involves diverse conditions. Recent clinical studies have shown potential relationships between mitral annular disjunction and MVP and/or left ventricular tachyarrhythmia (4-9). However, only a few studies have focused on the underlying diversity in the phenotypes (6,9). Furthermore, disjunction was most commonly evaluated by a single plane or several discontinuous sections, failing to assess its 3-dimensional extent. On the basis of accumulated insights into both prolapse and disjunction, we present cases of MVP with a 3-dimensional mitral valve morphology and the extent of disjunction analyzed by cardiac computed tomography (CT) (4). The aim of this

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received May 7, 2021; accepted June 1, 2021.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2021.06.038

ABBREVIATIONS AND ACRONYMS

CT = computed tomography

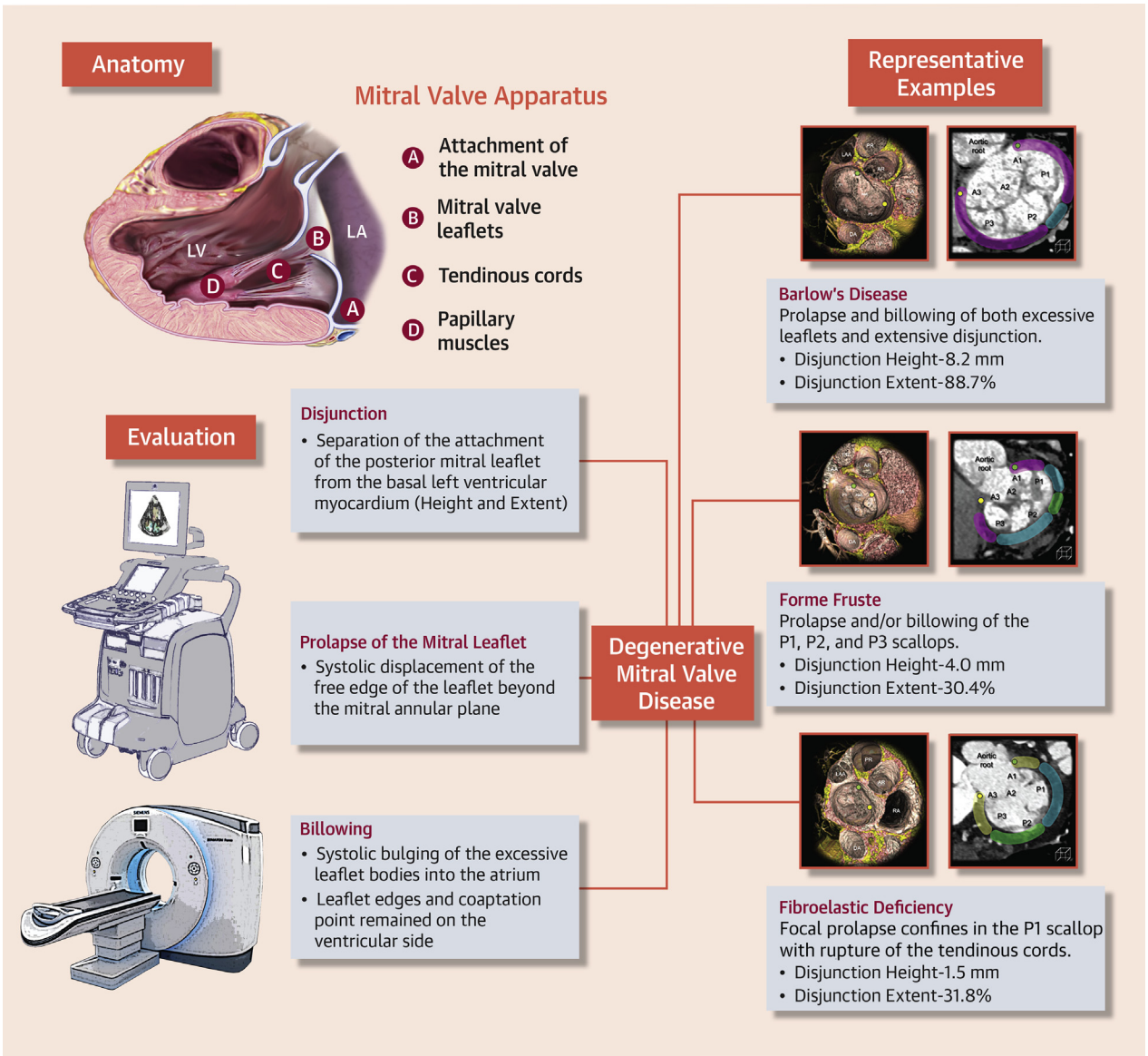
MVP = mitral valve prolapse

presentation is to describe differences in the 3-dimensional extent of disjunction between different phenotypes of MVP.

REPRESENTATIVE COMPARATIVE CASES

We retrospectively evaluated 3 patients with symptomatic severe primary mitral regurgitation caused by degenerative mitral valve disease. Prolapse of the mitral leaflet was defined as systolic displacement of the free edge of the leaflet beyond the mitral annular plane (Figure 1) (1). Billowing was defined as systolic bulging of the excessive leaflet bodies into the atrium while the leaflet edges and coaptation point remained on the ventricular side (1). Prolapse may coexist with billowing (1). Disjunction was defined as separation of the attachment of the posterior mitral leaflet from the

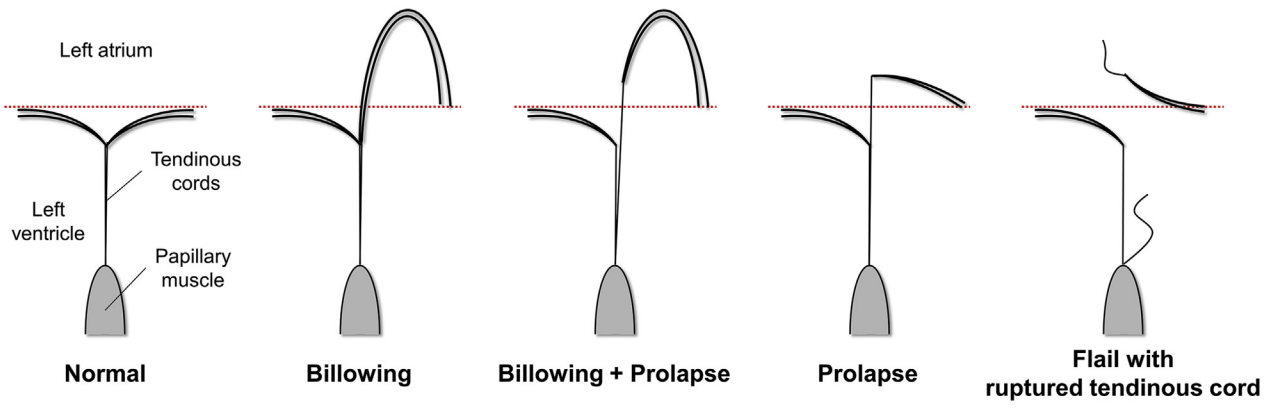
CENTRAL ILLUSTRATION **Comprehensive Assessment of the Degenerative Mitral Valve Disease**



Toh, H. et al. J Am Coll Cardiol Case Rep. 2021;3(10):1251–1257.

Detailed 3-dimensional analysis of the mitral valve using cardiac computed tomography identifies subtle morphological differences between different phenotypes of mitral valve prolapse.

FIGURE 1 Schematic Diagram of Prolapse, Billowing, and Flail



Red dotted lines indicate the mitral annular plane. In addition to this simple scheme, function and morphology of papillary muscle and left ventricle need to be taken into account. Whereas this definition of prolapse appears to be well accepted among cardiac surgeons, mitral valve prolapse is also generally recognized as the wide concept involving diverse phenotypes of degenerative mitral valve diseases, including both prolapse and billowing, especially by cardiologists or sonographers (10).

basal left ventricular myocardium (4,7). The circumferential extent and maximal height of disjunction were determined by a verified method using continuous multiplanar reconstruction images (4). All acquisitions were performed with a dual-source CT scanner (SOMATOM Force, Siemens Healthcare). The images were analyzed with a commercially available workstation (Ziostation2 version 2.4.2.3, Ziosoft Inc). Table 1 shows a comparison of the CT measurements.

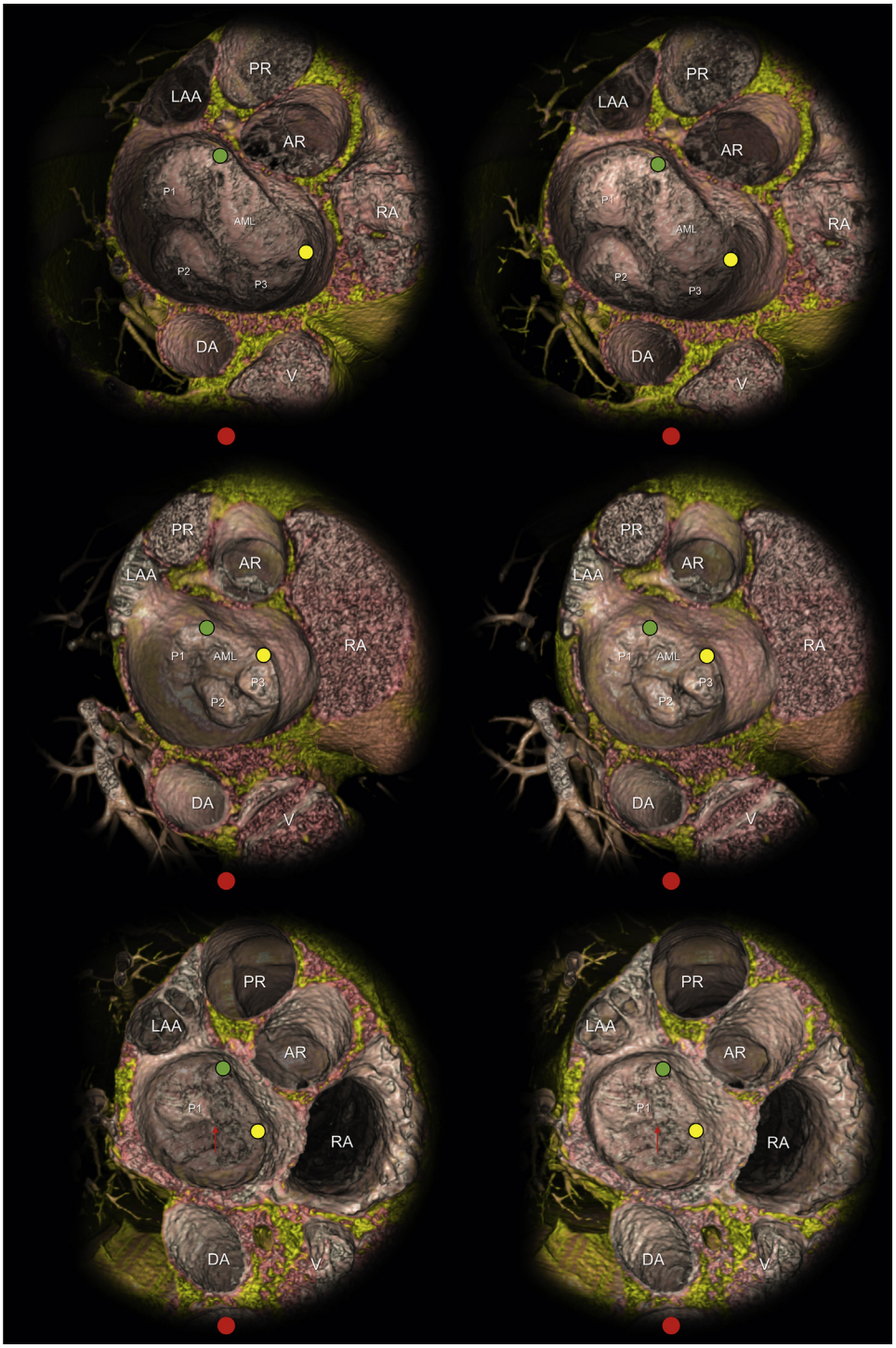
PATIENT 1: BARLOW DISEASE. The patient had received a diagnosis of moderate mitral regurgitation 3 years earlier, which had progressed to a severe category at the latest evaluation. Cardiac CT (Figures 2 and 3) revealed prolapse and billowing of both excessive leaflets, with extensive disjunction. The maximal height of disjunction was 8.2 mm, and the disjunction encircled almost the entire attachment of the posterior mitral leaflet, found in 88.7% of the region. Marked annular dilatation was also noted, with paradoxical systolic expansion of the mitral annulus. Barlow disease was diagnosed, and the patient was scheduled for surgery.

PATIENT 2: FORME FRUSTE. Severe mitral regurgitation was accidentally detected during the patient's treatment for endophthalmitis. Cardiac CT (Figures 2 and 3) revealed prolapse and/or billowing of the P1,

TABLE 1 Computed Tomographic Measurements

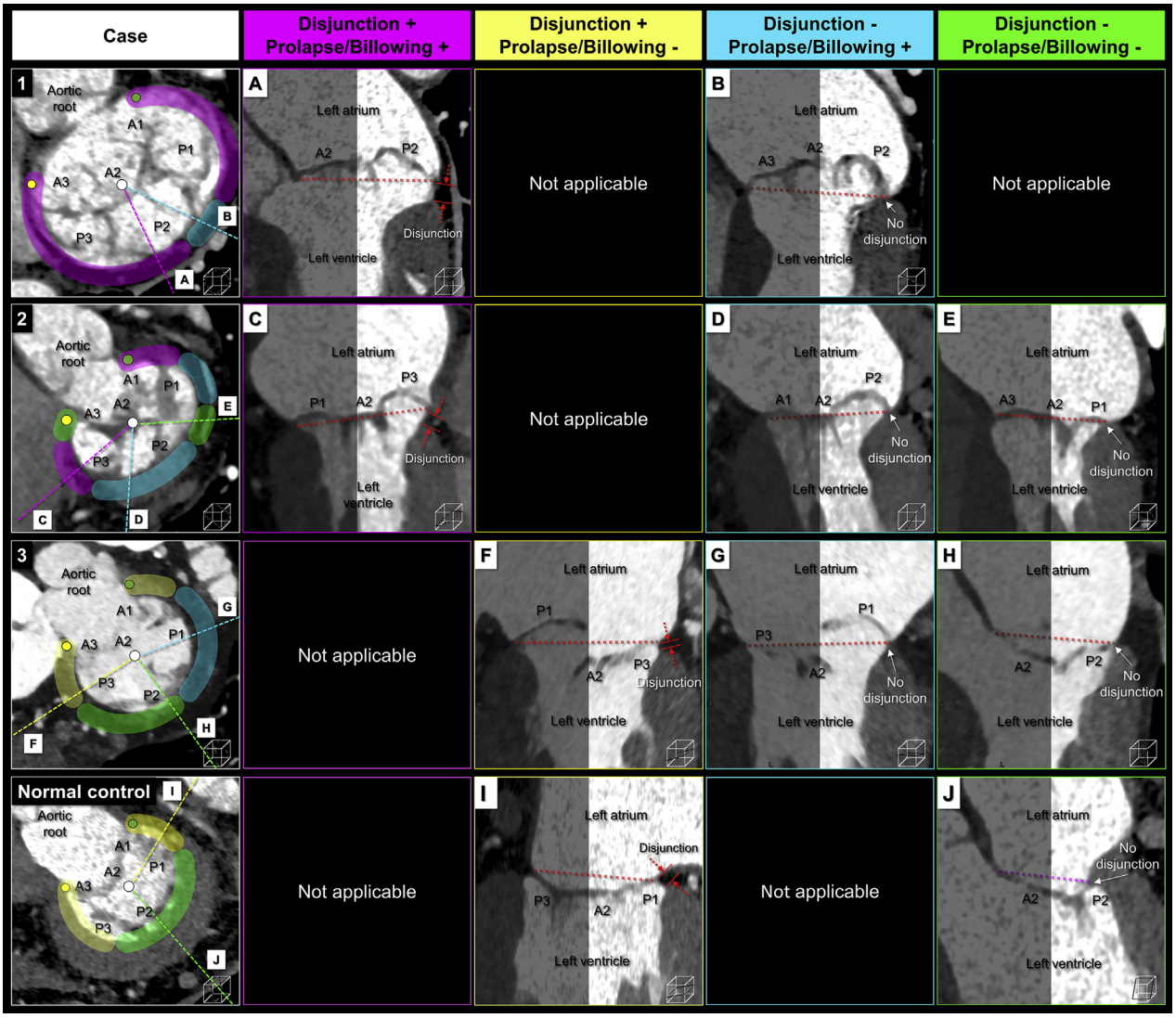
	Patient 1	Patient 2	Patient 3
Age, y	53	77	70
Sex	F	F	F
Body height, cm	162	155	152
Body weight, kg	42.9	48.1	52.3
Body mass index, kg/m^2	16.3	20.6	22.6
Body surface area, m^2	1.4	1.4	1.5
Mitral annular diameter (diastole), mm			
Major	55.0	44.6	37.2
Minor	44.0	31.6	30.8
Mitral annular diameter (systole), mm			
Major	63.6	42.8	39.8
Minor	48.0	32.0	29.8
Mitral annular area (diastole), cm^2	19.0	11.1	9.0
Mitral annular area (systole), cm^2	24.0	10.8	9.3
Rate of systolic expansion of the mitral annular area	1.3	1.0	1.0
Left ventricular diastolic dimension, mm (a)	62.5	45.5	49.6
Left ventricular systolic dimension, mm	40.1	23.0	24.1
Left ventricular diastolic dimension (long axis), mm (b)	88.7	71.4	76.5
Left ventricular sphericity index (a/b)	0.70	0.64	0.65
Left ventricular volume (diastole), mL (index)	148.2 (105.9)	93.4 (66.7)	127.1 (84.7)
Left ventricular volume (systole), mL (index)	71.4 (51.0)	25.3 (18.1)	40.4 (26.9)
Left atrial dimension (systole), mm	48.3	43.3	40.9
Left atrial volume (systole), mL (index)	208.8 (149.1)	122.4 (87.4)	118.2 (78.8)
Disjunction			
Maximal height, mm	8.2	4.0	1.5
Distribution angle, degrees	235.0	85.0	91.0
Proportion relative to distal height attachment	88.7	30.4	31.8

FIGURE 2 Virtual Surgical View of the Mitral Valves With Stereoscopic Displays for Cross-Eyed Method



Atrial aspect of the systolic mitral valve is reconstructed to show surgical view. **Top, middle, and bottom panels** represent patients 1, 2, and 3, respectively. In patient 1, mitral annular dilatation with extensive billowing/prolapse of both mitral leaflets is evident, consistent with Barlow disease. Patient 3 shows localized prolapse of P1 scallop with rupture of the tendinous cords **(red arrows)** without annular dilatation, consistent with fibroelastic deficiency. Patient 2 shows prolapse and/or billowing of P1, P2, and P3 scallops without evident rupture of the tendinous cords and annular dilatation. This intermediate phenotype is consistent with forme fruste. **Green and yellow circles** indicate superolateral and inferomedial commissures, respectively. Red circles can be used to help fuse both panels using cross-eyed method (11). AML = anterior mitral leaflet; AR = aortic root; DA = descending aorta; LAA = left atrial appendage; PR = pulmonary root; RA = right atrium; V = vertebra.

FIGURE 3 **3-Dimensional Extent of the Mitral Annular Disjunction**



Extent of disjunction in relation to segments with prolapse and/or billowing is visualized by color code on the images of mitral orifices viewed from the apical direction **(left column)**. **A to J** correspond to the representative sections orthogonal to the mitral orifice plane rotated along the central longitudinal axis **(white circles)**. In patient 1, disjunction is pathologically extensive **(purple)**, encircling substantial part of the attachment of the posterior mitral leaflet. In patients 2 and 3, extent of disjunction is less extensive **(purple and yellow)**. The extent of disjunction is not associated with the distribution of scallops showing prolapse or billowing, as supported by the observation of extensive **yellow and/or sky-blue** regions. **Red dotted lines** denote mitral annular plane. **Green and yellow circles** indicate supero-lateral and infero-medial commissures, respectively.

P2, and P3 scallops. The maximal height of disjunction was 4.0 mm, and it was found in 30.4% of the attachment of the posterior mitral leaflet. The disjunction exhibited a characteristic bimodal distribution pattern (4), and annular dilatation was less marked than in patient 1, with a loss of physiological systolic contraction of the mitral annulus. Her morphologic assessment was consistent with forme fruste. The patient was scheduled for surgery.

PATIENT 3: FIBROELASTIC DEFICIENCY. Severe mitral regurgitation due to MVP was diagnosed

during initial admission, with heart failure. Cardiac CT (**Figures 2 and 3**) showed prolapse confined to the P1 scallop with rupture of the tendinous chords. The maximal height of the disjunction was 1.5 mm, and it was found in 31.8% of attachment of the posterior mitral leaflet with a characteristic bimodal distribution pattern (4). Annular dilatation was less marked than in patients 1 and 2, with a loss of physiological systolic contraction of the mitral annulus. Morphologically, fibroelastic deficiency was suspected, and the patient was scheduled for surgery.

DISCUSSION

We have presented 3 comparative cases of MVP with different phenotypes, in patients for whom detailed 3-dimensional analysis was performed with cardiac CT (**Central Illustration**). Echocardiographic evaluation of disjunction is generally challenging because of limited spatial resolution and field of view (4). If cardiac CT is performed to substitute for preoperative invasive coronary angiography, as in the present cases, comprehensive 3-dimensional evaluation of disjunction becomes feasible. Varied 3-dimensional extent of disjunction in these cases supports that correlating two-dimensionally assessed disjunctions without focusing on underlying phenotypes of MVP is insufficient (4).

EXTENT OF DISJUNCTION. When assessed 3-dimensionally during systole, disjunction was observed in 96.0% of structurally normal hearts, showing a characteristic bimodal distribution pattern in continuity with bilateral commissures (4). The median value of its height was 3.0 mm (range, 1.5 to 7.0 mm), and its mean circumferential extent was 105.1° ± 49.2° (39.0% ± 18.2% of the entire attachment of the posterior mitral leaflet) (4). In comparison with these values, the distribution pattern of disjunction was extensive only in patient 1 (height, 8.2 mm circumferential extent, 235°; 88.7%) but was similar or less extensive in patient 2 (height, 4.0 mm; circumferential extent, 85°; 30.4%) and patient 3 (height, 1.5 mm; circumferential extent, 91°; 31.8%) (**Figure 3**).

The functional impact of this extensive disjunction remains unknown. In Barlow disease, extensive disjunction may be associated with paradoxical systolic dilatation of the mitral annulus (patient 1), combined with a loss of the physiological saddle shape (5). Conversely, extensive pathologic disjunction may be a simple byproduct of excessive connective tissue. This is an important clinical question because the necessity of disjunction correction during mitral valve surgery is controversial (8).

In contrast to patient 1, the extent of disjunction in patients 2 and 3 remained less extensive, and dilatation of the left ventricle, left atrium, and mitral annulus were less marked. Inasmuch as fibroelastic deficiency is characterized by deficiency of connective tissue (2), the lack of pathologic expansion of disjunction seems reasonable.

FUTURE DIRECTION. The present observations raise the following important questions: 1) Is a pathologic disjunction related to Barlow disease exclusively? 2) What are the functional contributions of pathologic disjunction? 3) How does pathologic disjunction progress along with the clinical course? 4) What are the optimal cutoff values to define pathologic disjunction when evaluating it in a 3-dimensional fashion? 5) Should this pathologic disjunction be corrected during surgery? Further investigations are necessary to answer these questions.

CONCLUSIONS

We found a significant difference in the 3-dimensional extent of disjunction in cases with different phenotypes of MVP. Barlow disease is likely to be a major subset of MVP accompanied by pathologically extensive disjunction, whereas fibroelastic deficiency seems to be less associated with it. Considering the current controversies surrounding disjunction, these observations are critical, calling for detailed research in the future.

ACKNOWLEDGMENTS The authors thank Takuro Nishio, Akiyo Fukutomi, Tomoki Maebayashi, Kiyosumi Kagawa, and Noriyuki Negi for their support in the image acquisition and processing.

FUNDING SUPPORT AND AUTHOR DISCLSOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS **anatomy, Barlow disease, computed tomography, fibroelastic deficiency, mitral annular disjunction, mitral valve prolapse**