Echocardiographic Features and Clinical Outcomes of Flail Mitral Leaflet without Severe Mitral Regurgitation

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Background: Flail mitral leaflet is a common complication of degenerative mitral regurgitation (MR) and is generally equated with severe MR. However, a flail mitral leaflet is not always associated with severe MR. The hemodynamic and clinical significance of a flail leaflet in the absence of severe MR has not been characterized. The authors identified cases of flail mitral leaflet associated with only mild or moderate MR and evaluated their echocardiographic features and clinical outcomes.

Methods: The echocardiography database at Cedars-Sinai Medical Center was queried for reports of flail mitral valve leaflet. Cases of possible flail and ≤3+ MR were identified and adjudicated for the presence of definite flail and ≤2+ MR. These patients were retrospectively evaluated by chart review to determine clinical outcomes.

Results: Seven hundred six cases of possible flail were identified, of which 143 were identified as having ≤3+ MR. Of these, 14 cases were identified with definitive echocardiographic evidence of a flail mitral leaflet and ≤2+ MR. Over a median of 361 days of follow-up, MR progressed in severity in only one patient, in association with endocarditis and death. All other patients were free of progression of MR, heart failure, or mortality during follow-up.

Conclusions: A flail mitral leaflet is not synonymous with severe MR and can be associated with only mild or moderate MR. Furthermore, patients with flail mitral leaflet and only mild to moderate MR were clinically stable. Thus, an integrated, multiparametric approach should be used to assess MR severity, even in the presence of a flail mitral leaflet. (J Am Soc Echocardiogr 2017;30:1162-8.)

Key Words: Flail, Mitral regurgitation, Moderate

Degenerative mitral regurgitation (MR) is one of the most common forms of valvular heart disease in the United States, occurring in approximately 2% of the population.[1] It is usually associated with myxomatous changes to the mitral valve leaflets. A flail mitral valve leaflet, in which there is failure of leaflet coaptation and atrial displacement of a leaflet tip, has been shown to develop in 16% of patients with mitral valve prolapse over 2 years.[2]

Flail mitral leaflets are generally thought to be associated with hemodynamically significant MR.[3] As such, guideline recommendations classify flail mitral leaflet as a specific criterion for severe MR and state that it almost always denotes severe MR, even in the absence of other Doppler parameters, which can be difficult to obtain reliably in the presence of an eccentric jet.[4,5] Furthermore, the multinational Mitral Regurgitation International Database registry used a flail mitral leaflet as a surrogate to define severe MR.[6] However, a flail mitral leaflet can be associated with mild or moderate MR.[7] The hemodynamic and clinical significance of a flail leaflet in the absence of severe MR has not been specifically characterized. In this study, we sought to confirm the existence of patients with flail mitral valve leaflet pathology but moderate or less MR and to identify their echocardiographic features and clinical outcomes.

METHODS

The echocardiography database at Cedars-Sinai Medical Center (Los Angeles, CA) was queried from January 2010 to March 2016 for transthoracic echocardiography (TTE) or transesophageal echocardiography (TEE) reports containing the search term *flail* in the description of the mitral valve but in which the severity of the MR was graded as moderate to severe (3+), moderate (2+), or mild (1+). Each case was reviewed by two cardiologists who were blinded to all clinical data to confirm the presence of a flail leaflet on either TTE or TEE and to grade the severity of MR according to guideline recommendations, with special emphasis on the use of a multimodality approach to grade severity.[4,5,8] Cases were excluded if either reviewer classified MR as moderate to severe (3+) or severe (4+), if MR was felt to be 3+ or 4+ on subsequent echocardiography within 30 days or any preceding echocardiographic examination, or if the absence of severe MR was not definite by a multimodality approach. Cases in which only TEE was available to confirm the severity of MR (without TTE within 48 hours) were excluded because of the possibility of underestimating MR severity in the setting of sedation given for TEE. Flail was defined according to

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Abbreviations

EROA = Effective regurgitant orifice area

MR = Mitral regurgitation

PISA = Proximal isovelocity surface area

TEE = Transesophageal echocardiography

TTE = Transthoracic echocardiography

standard criteria used in prior studies as failure of coaptation of a portion of the mitral valve with rapid systolic motion of a leaflet tip into the left atrium.[7,9,10] Cases were excluded if a flail leaflet portion, as defined by these criteria, could not be unequivocally identified on TTE or TEE.

The proximal isovelocity surface area (PISA) method was used to calculate the effective regurgitant orifice area (EROA).[5,11] The regurgitant volume was calculated as the product of the EROA and the mitral regurgitant velocity-time integral. The regurgitant fraction was calculated as the regurgitant volume divided by sum of the regurgitant volume and the left ventricular outflow tract stroke volume. Left ventricular enlargement was defined as left ventricular end-systolic diameter $\geq$ 4.0 cm.[4] Left atrial enlargement was defined as left atrial volume index > 34 mL/m^2 or as left atrial area > 20 cm^2 if volumetric data were not available.

Clinical details and outcomes, including hospital admission, progression to severe MR, mitral valve surgery, and mortality, were obtained by retrospective chart review. Follow-up duration was determined from the time of index echocardiography to the most recent clinical encounter documented in the medical record.

RESULTS

In total, 1,161 echocardiography reports from 706 patients were identified containing the search term *flail* in the description of the mitral valve. Of these, 38 patients were identified with suspected ≤2+ MR, and 105 patients were identified with suspected 3+ MR. Following adjudication, a total of 28 patients were excluded because of the absence of clear echocardiographic evidence of flail leaflet, and 101 patients were excluded because of the presence of ≥3+ MR (Figure 1). Fourteen remaining patients were identified with clear evidence of a flail mitral leaflet but with ≤2+ MR (Table 1). A flail mitral leaflet was clearly visualized on TTE in 10 of these patients. In the other four patients, it was not clearly seen on TTE but was seen on TEE performed within 48 hours of the original TTE, without interval change in the severity of the MR or clinical status of the patient.

Baseline transthoracic echocardiographic data from these patients are summarized in Table 1 and depicted in Figures 2 and 3, and Video 1 (available at www.onlinejase.com). MR was graded by TTE as 1+ in three patients and 2+ in 11 patients. None of the patients were hypotensive at the time of TTE. The anterior leaflet was flail in two patients and the posterior leaflet was flail in 12 patients. The vena contracta was <7 mm in all patients, and calculated EROA by the PISA method was <40 mm^2 in all patients. Regurgitant fraction was also <50%, and jet area by color Doppler was less than 40% of left atrial area in all patients. An E-dominant mitral inflow pattern was noted in only three of 14 patients. Pulmonary vein flow was systolic predominant in seven patients, was diastolic predominant in three patients, was codominant in one patient, was not well seen in one patient, and showed systolic flow reversal in two patients. Holosystolic regurgitant flow on continuous-wave transmitral Doppler was seen in six of 13 patients (data not available for one patient). The left ventricle was dilated in only one patient, and this finding predated the first documented occurrence of a flail leaflet.

Clinical data, outcomes, and follow-up duration are displayed in Table 2. Thirteen of 14 patients were male. Age ranged from 54 to 99 years, with a mean of 76 years. None of the patients had symptoms attributable to MR or unexplained dyspnea at the time of echocardiography. Four patients were prescribed loop diuretics, but in one of these patients, the diuretic was prescribed for management of cirrhosis, and in the other three patients, the loop diuretics were prescribed for long-term management of stable preexisting heart failure. Follow-up time ranged from 7 days to >10 years, with a median of 361 days. One patient underwent mitral valve surgery for moderate MR at the time of coronary artery bypass graft surgery. Another patient was hospitalized for mitral valve endocarditis with symptomatic

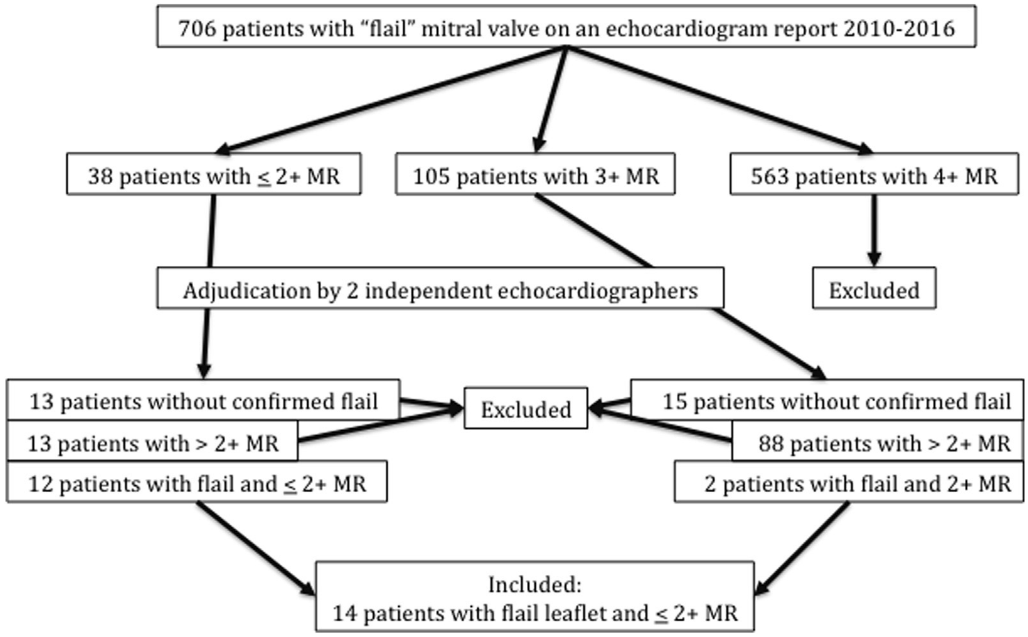

Figure 1 Flowchart outlining patient identification and adjudication for inclusion in the study.

Table 1 Echocardiographic data from patients with flail mitral valve leaflet without severe MR

ID	MR severity	Blood pressure (mm Hg)	Flail on TTE	TEE done	Flail portion	VC (mm)	EROA (mm^2)	RV (mL)	RF (%)	E (cm/sec)	E < A	PV flow	Holosystolic	Jet area > 40% left atrium	LV dilation	LA dilation	PASP > 50 mm Hg	EF (%)
1	1+	124/49	0	+	A	0	0	0	0	76	+	S	0	0	0	0	0	63
2	1+	132/60	0	+	A	1.0	5	2	2	56	+	S	0	0	0	0	0	55
3	1+	138/64	0	+	P	4.0	15	12	13	62	+	C	0	0	0	+	+	45
4	2+	122/87	0	+	P	—	—	—	—	—	0	D	—	—	0	+	0	65
5	2+	143/84	+	0	P	2.4	29	44	44	112	+	S	+	0	0	+	0	45
6	2+	120/80	+	0	P	2.8	10	17	20	102	0	S	+	0	0	0	0	63
7	2+	161/91	+	+	P	3.8	18	22	27	68	+	D	0	0	0	+	0	68
8	2+	131/77	+	+	P	4.2	22	18	30	41	+	S	0	0	+	0	0	43
9	2+	130/81	+	0	P	4.4	20	26	23	55	+	S	+	0	0	0	0	55
10	2+	131/81	+	0	P	4.5	29	62	48	64	+	R	+	0	0	0	0	65
11	2+	—	+	+	P	5.7	30	45	40	83	+	S	+	0	0	+	0	62
12	2+	125/76	+	0	P	6.2	17	21	29	84	0	R	+	0	0	0	0	68
13	2+	160/81	+	0	P	6.3	35	31	33	80	+	D	0	0	0	+	+	56
14	2+	122/73	+	+	P	6.5	29	37	41	87	+	—	+	0	0	+	0	73

A, Anterior mitral leaflet; *C*, codominance; *D*, diastolic flow predominance; *E*, early mitral inflow peak velocity; *EF*, ejection fraction; *LA*, left atrial; *LV*, left ventricular; *P*, posterior mitral leaflet; *PASP*, pulmonary artery systolic pressure; *PV*, pulmonary vein; *R*, systolic flow reversal; *RF*, regurgitant fraction; *RV*, regurgitant volume; *S*, systolic flow predominance; *VC*, vena contracta; +, present; *0*, not present; —, data not available.

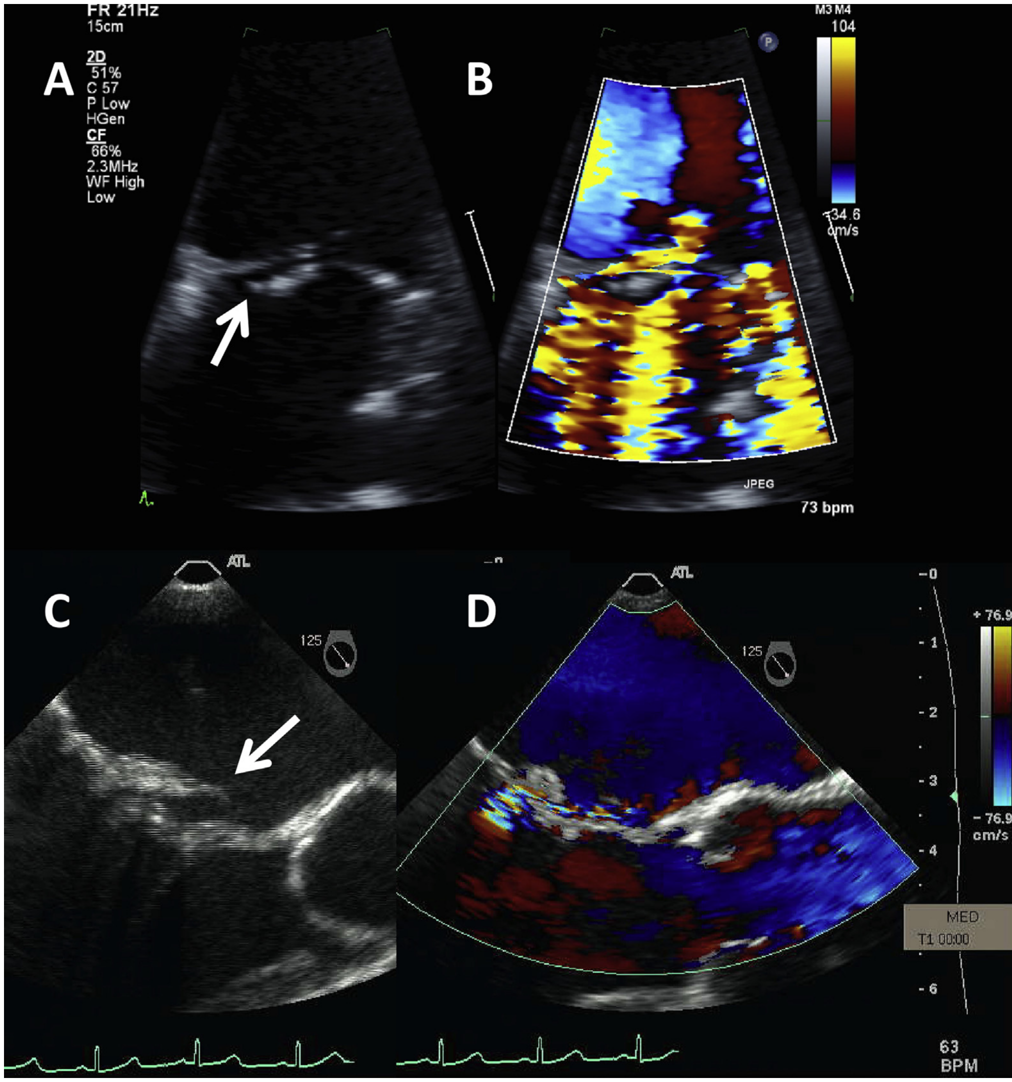

Figure 2 Representative case (case 11, Tables 1–3) of a flail mitral leaflet with moderate MR. **(A)** Apical four-chamber view on TTE displays a flail posterior leaflet (*white arrow*). **(B)** Color Doppler reveals an eccentric MR jet with a PISA radius consistent with moderate MR. **(C)** TEE performed on the same patient confirmed a flail posterior mitral leaflet (*white arrow*) with color Doppler features **(D)** consistent with moderate MR.

heart failure and severe MR after approximately 11 months of follow-up and ultimately died after he was deemed a poor candidate for surgery. All other patients were alive and free of symptomatic heart failure or mitral valve surgery at last follow-up.

Repeat echocardiography was performed in nine of 14 patients during the follow-up period (Table 3). All but one of these patients showed no significant progression in MR severity, with the exception of the one patient who developed endocarditis. The vena contracta was <7 mm, and calculated EROA by the PISA method was <40 mm^2 in all eight patients without progression. An E-dominant mitral inflow pattern was noted in only one of eight patients.

DISCUSSION

In this report, we present 14 cases of flail mitral leaflet without associated severe MR. Although our series is not the first report of this phenomenon, to our knowledge this is the first description of the echocardiographic features and clinical outcomes of this group of patients. Although early studies reported nearly universally severe MR in the presence of a flail leaflet,[12,13] more contemporary studies have found that 3% to 13% of patients with flail mitral valve may have <3 to 4+ MR.[7,14,15] Specifically, Ling *et al.*[7] reported less than grade 3 MR in 25 of 193 patients by Doppler echocardiography and four of 75 patients with left ventriculography, and recent data from the Mitral Regurgitation International Database registry suggest that 8% of 1,875 patients with flail mitral pathology had <3+ MR.[15]

In this study, some echocardiographic parameters in individual patients, when viewed in isolation, were consistent with severe MR. For example, in patient 10, systolic flow reversal was noted in the pulmonary veins, and the regurgitant volume was calculated to be >60 mL (Table 1). However, the vena contracta width, EROA, A-dominant mitral inflow pattern, and lack of left ventricular dilation in this patient were consistent with moderate MR. Therefore, in this case example and all others, moderate MR severity was confirmed by using an integrated assessment as recommended by guidelines and expert consensus.[4,8]

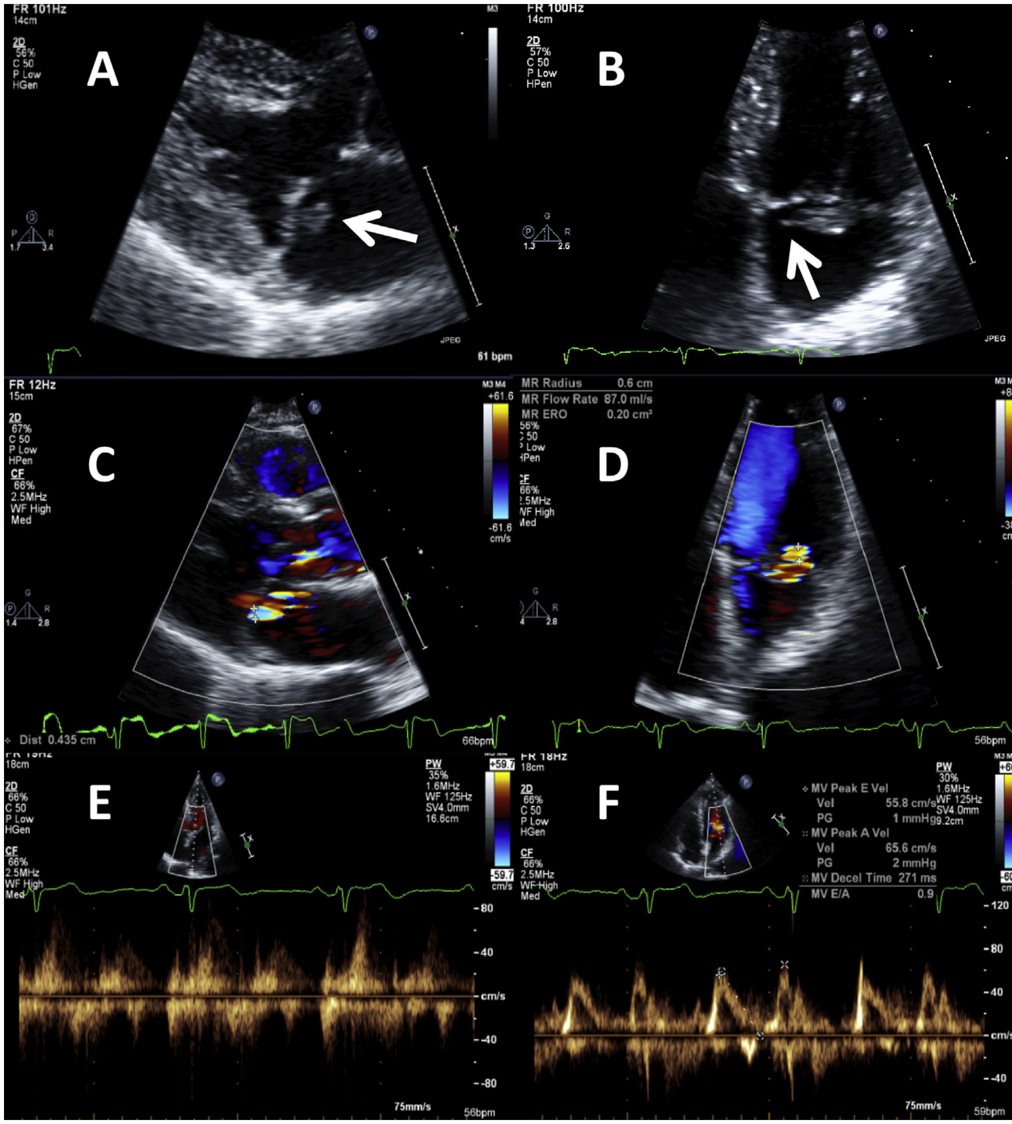

Figure 3 Representative case (case 9, Tables 1–3) of a flail mitral leaflet with moderate MR. Parasternal long-axis view **(A)** and apical four-chamber view **(B)** on TTE display a flail posterior mitral leaflet (*white arrows*). **(C)** Color Doppler imaging from a parasternal long-axis view on TTE shows an eccentric MR jet with a vena contracta diameter of 4.4 mm, consistent with moderate MR. **(D)** Color Doppler imaging from an apical four-chamber view on TTE shows a PISA radius of 6 mm, consistent with moderate MR. **(E)** Pulsed-wave Doppler signal of the pulmonary vein inflow obtained from the apical four-chamber view on TTE reveals systolic predominant flow, consistent with normal left atrial filling pressure. **(F)** Pulsed-wave Doppler signal from the mitral inflow obtained from the apical four-chamber view on TTE reveals normal E velocity and A-wave predominance, consistent with normal left atrial filling pressure.

The most recent guidelines on management of valvular heart disease, published in 2014, describe flail mitral pathology as an anatomic criterion for severe MR,[4] and registry data on which these guidelines are based have equated flail mitral pathology with severe MR.[6,14-17] Our series of patients serves to confirm that flail mitral pathology is not necessarily synonymous with severe MR. Therefore, use of this entry criterion in these registry studies may dilute their data, which were intended to reflect the presence of severe MR.

Previously it was shown in some[2] but not all[18] series that development of a flail leaflet represents a significant independent predictor of MR progression. However, the clinical outcomes in our study of patients with flail mitral leaflet but only mild to moderate MR were favorable, despite the relatively advanced age of the cohort, supporting the absence of hemodynamically significant MR. Therefore, it is possible for flail to be associated with chronic, stable, nonsevere MR, with good clinical outcomes. However, the findings of this study should not be interpreted to imply that a flail mitral leaflet is without clinical significance when associated only mild or moderate MR. It is certainly possible that the initial structural damage to the mitral apparatus could portend future progression of valvular damage and dysfunction. Larger studies with long-term follow-up would be needed to reach definitive conclusions about the clinical stability of this cohort of patients. Although the relative absence of adverse events in this small study is reassuring, close clinical monitoring remains critical to monitor for progression of MR or occurrence of symptoms.

There were several limitations to this study. First, patients were only identified and followed retrospectively, and follow-up time was not standardized and in some cases (as in the case with only 7 days of

Table 2 Clinical data and follow-up of patients with flail mitral valve leaflet without severe MR

			Baseline			Follow-up				
ID	Age (y)	Gender	Unexplained dyspnea	Loop diuretic	Afterload reducer	Duration (d)	Progression to severe MR	Mitral valve surgery	Heart failure admission	Mortality
1	77	M	0	0	+	152	0	0	0	0
2	82	F	0	0	+	106	0	0	0	0
3	72	M	0	0	+	688	0	+*	+*	0
4	69	M	0	0	+	352	0	0	0	0
5	91	M	0	+	0	215	—	0	0	0
6	54	M	0	0	0	185	—	0	0	0
7	77	M	0	+	+	777	0	0	0	0
8	78	M	0	0	+	369	+†	0	+†	+†
9	68	M	0	0	+	1,640	0	0	0	0
10	69	M	0	0	+	1,460	0	0	0	0
11	77	M	0	0	+	10 y, 7 mo	0	0	0	0
12	67	M	0	+‡	0	47	—	0	0	0
13	99	M	0	+	+	695	—	0	0	0
14	80	M	0	0	0	7	—	0	0	0

F, Female; *M*, male; +, present; *0*, not present; —, data not available.
*Coronary artery bypass grafting with concomitant mitral valve repair on day 29; postoperative heart failure on admission day 115.
†Mitral valve endocarditis with severe MR and heart failure on day 323; nonoperative candidate.
‡Diuretic prescribed for cirrhosis.

Table 3 Follow-up echocardiographic data from patients with flail mitral valve leaflet

ID	MR severity	Blood pressure (mm Hg)	Follow-up (d)	VC (mm)	EROA (mm^2)	RV (mL)	RF (%)	E (cm/s)	E < A	PV flow	Holosystolic	Jet area > 40% left atrium	LV dilation	LA dilation	PASP > 50 mm Hg	EF (%)
1	1+	131/45	152	1.7	0	0	0	118	+	S	0	0	0	0	0	50
2	1+	120/65	106	1.0	0	0	0	75	+	S	0	0	0	0	0	60
3	2+*	—	29	4.1	20	35	33	66	0	S	0	0	0	+	+	45
4	2+	124/78	352	3.8	24	11	16	196	0	D	0	0	0	+	0	60
7	2+	165/66	691	5.5	14	5	13	84	+	S	0	0	0	+	0	63
8	4+	124/69	323	4.5	55	67	52	160	0	D	+	+	+	+	0	35
9	2+	130/81	1,640	6.0	20	30	33	56	+	S	+	0	0	0	0	55
10	2+	131/81	1,460	3.8	23	38	43	55	+	R	+	0	0	0	0	68
11	2+	126/69	10 y, 7 mo	5.2	29	43	45	67	+	S	+	0	0	+	0	56

D, Diastolic flow predominance; *E*, early mitral inflow peak velocity; *EF*, ejection fraction; *LA*, left atrial; *LV*, left ventricular; *PASP*, pulmonary artery systolic pressure; *PV*, pulmonary vein; *R*, systolic flow reversal; *RF*, regurgitant fraction; *RV*, regurgitant volume; *S*, systolic flow predominance; *VC*, vena contracta; +, present; *0*, not present; —, data not available.
*Data from intraoperative TEE.

follow-up) was too short to reach conclusions about clinical stability. Second, although our data did not suggest that the absence of severe MR was related to low blood pressure, the limited number of subjects in this series precluded statistical confirmation. Furthermore, there may have been additional cases of flail mitral valve pathology without severe MR that were not included, if the original interpreting echocardiographer graded the MR as 4+ solely because of the presence of a flail mitral leaflet. Because recognition of a flail leaflet may be more difficult in the presence of mild or moderate MR, there may have been additional cases that were never identified in our database. We also excluded cases in which flail may have been present but could not be demonstrated unequivocally. Given these limitations, the true prevalence of flail mitral leaflet with less than severe MR may be greater than one would estimate from our study. In addition, it is possible that MR was underestimated in some of our patients. Importantly, a flail mitral leaflet commonly results in an eccentric jet, which can lead to difficulty aligning the ultrasound beam with the jet direction and consequently to underestimation of MR severity by the PISA method or vena contracta width. To characterize MR severity in the setting of an eccentric jet, a proper multimodality approach, as was used during our adjudication process, should place added emphasis on mitral inflow velocity and pattern, duration of regurgitation, pulmonary vein flow pattern, and chamber sizes. Finally, we were unable to define the mechanism of nonsevere MR in the setting of flail. However, it is possible that this phenomenon may be the result of a shorter interchordal span of unsupported leaflet tissue separating the points of primary chord attachment.

CONCLUSIONS

We have shown that a flail mitral leaflet can be associated with mild or moderate MR as assessed by echocardiographic guideline criteria. Our data show that a flail mitral leaflet does not always equate to severe MR and that it should not be used as a surrogate for severe MR when studying the clinical course of patients with chronic severe MR. Future guideline recommendations and clinical investigation of chronic severe MR should not use a flail mitral leaflet as a single defining criterion for severity. Rather, an integrated assessment of multiple parameters of Doppler hemodynamics must still be used to assess MR severity even in the presence of this anatomic abnormality.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.echo.2017.06.019.

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