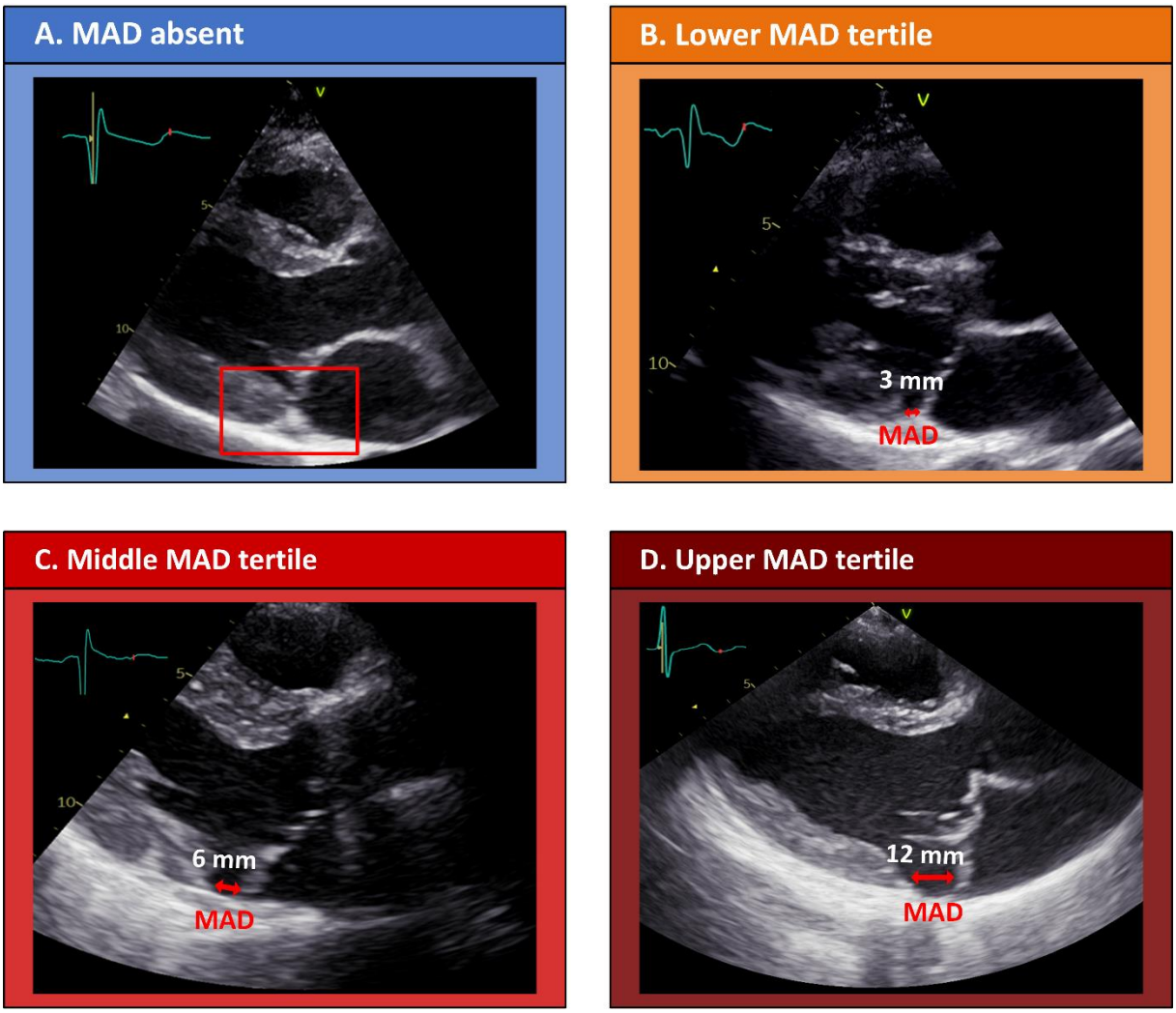
Supplementary Online Content

Demolder A, Timmermans F, Duytschaever M, Muiño-Mosquera L, De Backer J. Association of mitral annular disjunction with cardiovascular outcomes among patients with Marfan syndrome. *JAMA Cardiol.* Published online July 7, 2021. doi:10.1001/jamacardio.2021.2312

eFigure. Echocardiographic Examples of Mitral Annular Disjunction
eTable 1. Interobserver and Intraobserver Statistics
eTable 2. ECG Characteristics
eTable 3. Genotype Comparison
eTable 4. Clinical Characteristics of Patients With Sustained VT/SCD, Prior to the Arrhythmic Event

This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure. Echocardiographic Examples of Mitral Annular Disjunction



Abbreviation: MAD, mitral annular disjunction.

Figure legend: A, Echocardiographic example of a patient without MAD (red box). B, C and D, Echocardiographic images of patients with different severities of MAD indicated by the red arrows (lower, middle and upper tertiles of MAD distance).

eTable 1. Interobserver and Intraobserver Statistics

	Inter-observer statistics					
	MAD(-) vs. MAD(+)	95% CI	*P* value	MAD(+)≤10mm vs. MAD(+)>10mm	95% CI	*P* value
Cohen's Kappa	0.84	0.63 – 1	**<0.001**	0.90	0.71 – 1	**<0.001**
ICC for MAD distance	0.89, 95% CI (0.75-0.96)					

	Intra-observer statistics					
	MAD(-) vs. MAD(+)	95% CI	*P* value	MAD(+)≤10mm vs. MAD(+)>10mm	95% CI	*P* value
Cohen's Kappa	0.92	0.78 – 1	**<0.001**	0.90	0.71 – 1	**<0.001**
ICC for MAD distance	0.93, 95% CI (0.84-0.97)					

Abbreviations: ICC, intraclass correlation coefficient; MAD, mitral annular disjunction.

eTable 2. ECG Characteristics

Characteristic	Median (IQR)			*P* value
	Total (n=142)	MAD - (n=94)	MAD + (n=48)	
PR-interval, ms	154 (142-172)	155 (142-173)	153 (140-170)	0.432
QRS-duration, ms	94 (88-102)	94 (86-101)	96 (90-102)	0.284
QT duration, ms	407 (382-429)	409 (384-430)	400 (382-428)	0.338
QTc duration, ms	420 (401-437)	419 (401-437)	423 (402-437)	0.449

Abbreviation: MAD, mitral annular disjunction.

eTable 3. Genotype Comparison

	Total (n=142)	MAD(-) (n=94)	MAD(+) (n=48)	*P* value
Type of *FBN1* variant, No. (%)				
Missense	73 (51)	49 (52)	24 (50)	0.810
Nonsense	29 (20)	20 (21)	9 (19)	0.724
Frameshift	26 (18)	15 (16)	11 (23)	0.310
Splice-site	11 (8)	7 (7)	4 (8)	1.000
In-frame	3 (2)	3 (3)	0 (0)	0.551
Localization: exon 24-32, No. (%)	16 (11)	10 (11)	6 (13)	0.740
Variant affecting cysteine, No. (%)	42 (30)	26 (28)	16 (33)	0.483
Effect on the protein, No. (%)				
Haploinsufficiency	54 (38)	34 (36)	20 (42)	0.523

Abbreviation: MAD, mitral annular disjunction.

eTable 4. Clinical Characteristics of Patients With Sustained VT/SCD, Prior to the Arrhythmic Event

Patient	Age	SCD/ VT	EF, %	MR	AR	Aortic sinus, mm	Aortic root Z-score	Aortic surgery	Mitral surgery	QTc, ms	MVP	MAD length, mm
001	28	SCD	65	None	Trivial	38	2.75	None	None	436	No	11
002	11	SCD	68	Trivial	1/4	-	-	Yes	None	437	Yes	11
003	52	VT	52	1/4	None	-	-	Yes	None	462	No	13
004	30	VT	47	1/4	None	-	-	Yes	Yes	467	Yes	12
005[a]	15	VT	63	1/4	1/4	-	-	Yes	None	487	Yes	12

[a]Received a heart transplantation later on due to development of progressive heart failure

Abbreviations: AR, aortic regurgitation; EF, ejection fraction; LVEDD, left ventricular end-diastolic diameter; MAD, mitral annular disjunction; MR, mitral regurgitation; MVP, mitral valve prolapse; SCD, sudden cardiac death; VT, sustained ventricular tachycardia.