Prevalence and Outcomes of Primary Left Ventricular Dysfunction in Marfan Syndrome

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Even in the absence of significant valvular disease, patients with Marfan syndrome (MFS) have evidence of impaired left ventricular (LV) performance, suggestive of a primary cardiomyopathy. However, the true prevalence and long-term outcomes of this disease process remain largely unknown. We performed a retrospective analysis of all adult patients with confirmed MFS followed at Stanford Health Care. Those with significant valvular regurgitation, coronary artery disease, or previous cardiac surgery were excluded. LV systolic dysfunction was defined as a LV ejection fraction (LVEF) <55% on transthoracic echocardiography. A total of 753 patients with confirmed MFS were followed up over a median duration of 8 years (interquartile range 4 to 13). Of those, 241 patients (53% women, 71% White) met inclusion criteria and comprised the study cohort. LV systolic dysfunction was present in 30 patients (12%), with a median age of onset of 25 years (interquartile range 19 to 37), median EF of 52% (interquartile range 48 to 54), and evidence of clinical heart failure (New York Heart Association functional class ≥II) in 10% of patients. LV systolic dysfunction was more common in patients with larger aortic root diameters (≥4.0 cm: Odds ratio = 4.5, 95% confidence interval = 1.2 to 17.1) but was not associated with other cardiovascular manifestations of MFS or traditional atherosclerotic risk factors. In conclusion, apart from significant valvular pathology, LV systolic dysfunction was prevalent in MFS from a young age, suggestive of a primary cardiomyopathy. LV dysfunction was typically mild and subclinical and occurred more commonly in patients with more pronounced aortopathies. **(Am J Cardiol 2022;175:119−126)**

The Marfan syndrome (MFS) is a common inherited disorder of connective tissue caused by pathogenic variants in the gene encoding for the fibrillin-1 protein, which is essential in the maintenance of elastic fiber structural integrity and function.[1,2] As a result, multiple organ systems are affected in MFS,[3] with cardiovascular disease being the leading cause of premature mortality.[4] Regurgitant valvular disease is commonly observed, with resultant ventricular volume loading contributing to the development of a secondary, dilated cardiomyopathy in 30% of patients.[5] Even apart from significant valvular disease, patients with MFS have evidence of ventricular dilation and systolic dysfunction.[6] Murine *FBN1* models similarly demonstrate impaired ventricular contractility and a maladaptive myocardial response to hemodynamic stress.[7] However, the true prevalence and long-term outcomes of a primary cardiomyopathy in MFS remain largely unknown. The aims of this study were therefore to (1) evaluate the prevalence of a primary cardiomyopathy in a large cohort of adults with MFS, (2) elucidate potential risk predictors of disease development and progression, and (3) evaluate long-term cardiovascular outcomes in patients with MFS and a primary cardiomyopathy.

Methods

A single-center, retrospective study was performed in 241 adult patients with a confirmed diagnosis of MFS. Eligible patients were seen for subspeciality cardiology evaluation at Stanford between January 1, 1995 and January 31, 2021 and identified through query of the Stanford Research Repository Database using corresponding International Classification of Diseases, Ninth (759.82) and Tenth (Q87.4) Revision diagnostic codes. Manual chart review of relevant clinical documentation was subsequently performed to confirm the diagnosis of MFS, in accordance with the revised Ghent nosology.[3] Patients were excluded if they had (1) significant valvular regurgitation, defined as more than mild aortic or mitral regurgitation; (2) undergone previous cardiac surgery; or (3) established coronary artery disease, defined as ≥50% luminal stenosis on coronary angiography, requirement for percutaneous coronary intervention, or an Agatston score ≥100 on coronary computerized tomography. This study was approved by the Stanford University Institutional Review Board.

Figure 1 outlines the study cohort selection algorithm. In all patients, a detailed medical history was recorded,

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See page 125 for disclosure information.

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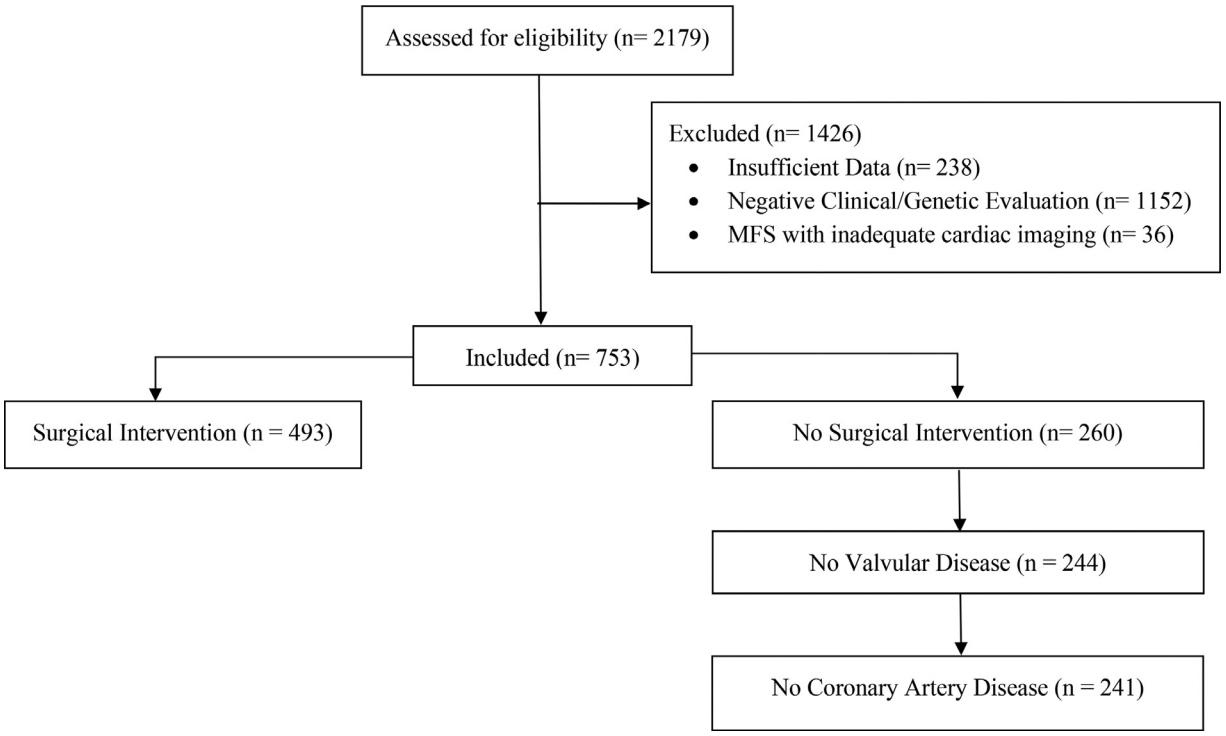

Figure 1. Flow diagram outlining patient selection criteria.

including assessment of standard sociodemographic variables, traditional cardiovascular risk factors, Marfan-associated phenotypic features, and medication use. Long-term cardiovascular outcomes, including the development of clinical heart failure (New York Heart Association [NYHA] functional class ≥II), atrial and ventricular arrhythmias, and requirement for electrophysiologic procedural intervention were additionally documented.

To evaluate for any potential genetic influence on myocardial performance, primary documentation of the *FBN1* variant analysis was obtained for all patients with available genetic testing results. Variants were classified by type, location, and the expected effect on the end gene product, in accordance with the current classification systems for MFS.[8,9]

Standard echocardiographic examination was performed in accordance with the American Society of Echocardiography recommendations.[10] Each echocardiogram was reviewed, measured, and interpreted by a cardiologist who is certified in echocardiography. Measurements performed during the most recent clinical encounter were used for purposes of data analysis. Additionally, in patients with baseline left ventricular (LV) systolic dysfunction, serial measurements were recorded across the duration of follow-up to evaluate for changes in myocardial performance over time.

Mitral valve prolapse was defined as systolic displacement of either mitral leaflet by at least 2 mm above the mitral annular plane in the parasternal long-axis view.[11] Valvular regurgitation was assessed using conventional Doppler interrogation and graded after integration of several semiquantitative parameters, including the vena contracta width, effective regurgitant orifice, and left-sided chamber dimensions.[11] Aortic dimensions were measured in the parasternal long-axis view, with the diameters of the aortic annulus, aortic root, sinotubular junction, and ascending aorta compared with established adult normative values.[12]

Left ventricular dilation was defined as a LV end-diastolic diameter on M-mode assessment of ≥5.8 cm in men (≥3.1 cm/m^2) and ≥5.2 cm in women (≥3.2 cm/m^2) or a LV end-diastolic volume on 2D assessment of ≥150 ml in men (≥75 ml/m^2) and ≥107 ml in women (≥62 ml/m^2).[13] LV diastolic function was assessed using pulsed-wave Doppler interrogation of the mitral valve inflow and tissue Doppler imaging. LV ejection fraction (LVEF) was calculated using Simpson biplane method, with LV systolic dysfunction defined by a LVEF <55%. The severity of LV systolic dysfunction was further subclassified as mild (LVEF = 41 to 54%), moderate (LVEF = 30 to 40%), or severe (LVEF <30%).[13] Quantification of right ventricular (RV) function was performed through measurement of the RV fractional area change and tricuspid annular plane systolic excursion in the apical 4-chamber view.[13]

Statistical analysis was performed using Stata, StataCorp (version 15.1, College Station, Texas). Categoric variables are presented as frequencies with related percentages. Continuous variables are reported as medians with corresponding interquartile ranges (IQR). Comparisons between groups were performed using the Mann-Whitney *U* test and Kruskal-Wallis test for continuous variables and Fisher exact test for categoric variables. Univariate and multivariable logistic regression analyses were then performed to evaluate factors associated with LV systolic dysfunction. A regression model was generated in patients without missing data for the variables with univariate significance. Log transformation and exponentiation were used to normalize skewed variables. Scatterplot matrixes were generated to ensure the assumptions of the model were not violated. The

final multivariable model comprised the following 5 variables: aortic root diameter, mitral valve prolapse, dural ectasia, RV systolic dysfunction, and body mass index (BMI). Statistical significance was defined as a p value <0.05 for all analyses.

Results

Demographic and clinical characteristics of the study population are summarized in Tables 1 and 2. The majority of patients were female (53%), with a median age of 32 years (IQR 24 to 47). Cardiovascular manifestations predominated, with 90% of patients (n = 216) having documented aortic root dilation. Pathogenic *FBN1* variants were documented in 49% of patients (n = 117), encompassing over 100 unique variants. An additional small subset of patients (n = 16) had undergone genetic testing, with detailed *FBN1* variant analyses unavailable for review. At baseline, most patients (78%, n = 188) were maintained on standard medical therapy with β-blockers, angiotensin-converting enzyme inhibitors (ACE-I), and/or angiotensin receptor blockers.

Echocardiographic parameters for LV size and function are summarized in Table 2. LV systolic dysfunction was present in 30 patients (12%), with a median LVEF of 52% (IQR 48, 54). LV systolic dysfunction was predominantly mild (93%), with corresponding LV chamber dimensions at the upper limit of normal. Clinical heart failure (NYHA Class ≥II) was present in 10% of patients (n = 3) with dysfunction, with symptoms predominantly occurring in those with more severe impairment (LVEF <40%, n = 2).

The results of the univariate and multivariable regression analyses for variables associated with LV systolic dysfunction are presented in Table 1 and Figure 2, respectively. There were no differences in the majority of queried sociodemographic and traditional cardiovascular risk variables,

Table 1
Demographic and clinical characteristics of the study population

Variable	Data Points (Number)	All Patients (n = 241)	*Systolic Dysfunction (EF <55%)* Yes (n = 30)	No (n = 211)	p-value
Female	241	127 (53%)	14 (47%)	113 (54%)	0.48
Body Mass Index (kg/m^2)	237	22.1 (19.4, 25.0)	19.5 (17.5, 22.5)	22.3 (19.7, 25.7)	<0.01
Age (years)	241	32 (24, 47)	33 (24, 54)	32 (24, 47)	0.77
Race	241				0.6
White		171 (71%)	24 (80%)	147 (70%)	
Black		6 (2%)	0 (0%)	6 (3%)	
Other		64 (27%)	6 (20%)	58 (27%)	
Marfan Clinical Features					
Arachnodactyly	192	146 (76%)	22 (96%)	124 (73%)	0.02
Pectus	224	122 (54%)	19 (68%)	103 (53%)	0.13
Scoliosis/Kyphosis	229	140 (61%)	20 (71%)	120 (60%)	0.23
Dural Ectasia	134	36 (27%)	8 (44%)	28 (24%)	0.07
Ectopia Lentis	241	87 (36%)	9 (30%)	78 (37%)	0.46
Bullae/Pneumothorax	241	19 (8%)	5 (17%)	14 (7%)	0.06
Cardiac Risk Factors					
Hypertension	241	126 (52%)	17 (57%)	109 (52%)	0.61
Hyperlipidemia	241	34 (14%)	5 (17%)	29 (14%)	0.67
Type II Diabetes	241	6 (3%)	0 (0%)	6 (3%)	0.35
Chronic Kidney Disease	241	5 (2%)	1 (3%)	4 (2%)	0.61
Obstructive Sleep Apnea	241	26 (11%)	3 (10%)	23 (11%)	0.88
Tobacco Use (lifetime)	239	34 (14%)	6 (21%)	28 (13%)	0.29
Alcohol Use (≥2x/week)	238	53 (22%)	5 (18%)	48 (23%)	0.55
Exercise ≥2x/week	234	157 (67%)	18 (62%)	139 (68%)	0.54
Medication Utilization					
ACE-I/ARB	240	75 (31%)	8 (28%)	67 (32%)	0.65
Beta (β)-Blockers	240	158 (66%)	21 (72%)	137 (65%)	0.43
FBN1 Variant Type	117				0.50
Null		41 (35%)	6 (46%)	35 (34%)	0.37
Nonsense		15 (37%)	2 (33%)	13 (37%)	
Frameshift		21 (51%)	4 (67%)	17 (49%)	
Splice-Site		4 (10%)	0 (0%)	4 (11%)	
Exon Deletion		1 (2%)	0 (0%)	1 (3%)	
Missense		68 (58%)	7 (54%)	61 (58%)	0.74
Cysteine Substitution		33 (49%)	4 (57%)	29 (48%)	0.63
Severe *FBN1* Genotype*		88 (75%)	10 (77%)	77 (74%)	0.82
Haploinsufficiency		46 (52%)	6 (46%)	40 (38%)	0.59

FBN1 = fibrillin-1 gene; ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker.
Data are represented as medians with interquartile ranges for continuous variables and n (%) for categorical variables.
* Defined as a null mutation, missense mutation containing a cysteine residue, or involving exons 24-32.

Table 2
Cardiac characteristics of the study population

Variable	Data Points (number)	All Patients (n = 241)	Systolic Dysfunction (EF <55%) Yes (n = 30)	Systolic Dysfunction (EF <55%) No (n = 211)	p-value
Cardiovascular Disease					
Mitral Valve Prolapse	241	129 (54%)	22 (73%)	107 (51%)	0.02
Bicuspid Aortic Valve	241	2 (<1%)	0 (0%)	2 (<1%)	0.59
Aortic Root (cm)	240	4.0 (3.6, 4.4)	4.2 (3.8, 4.6)	4.0 (3.6, 4.3)	0.03
Aortic Dissection	241	10 (4%)	0 (0%)	10 (5%)	0.16
Type A		1 (10%)	0 (0%)	1 (10%)	N/A
Type B		9 (90%)	0 (0%)	9 (90%)	N/A
Cardiac Chamber Dimensions					
LVEDD (cm)	239	4.9 (4.6, 5.3)	5.0 (4.7, 5.3)	4.9 (4.5, 5.3)	0.19
LVEDD/BSA (cm/m^2)		2.5 (2.3, 2.8)	2.6 (2.4, 2.9)	2.5 (2.3, 2.7)	0.051
LVEDV (mL)	203	100.4 (78.9, 128)	104 (74.9, 126)	100 (79.2, 129)	0.97
LVEDV/BSA (mL/m^2)		50.8 (41.2, 64)	50.1 (41.6, 67)	51.8 (41.3, 63.5)	0.53
Cardiac Function					
LV Ejection Fraction (%)	241	61.8 (57.3, 65.0)	51.7 (48.2, 54.1)	62.1 (59.5, 65.6)	N/A
LV Diastolic Dysfunction	241	20 (8%)	3 (10%)	17 (8%)	0.55
RV Systolic Dysfunction	241	9 (4%)	7 (23%)	2 (<1%)	<0.01
NYHA Classification (≥2)	241	9 (4%)	3 (10%)	6 (3%)	0.053
Cardiovascular Outcomes					
Atrial Arrhythmias	241	26 (11%)	6 (20%)	20 (10%)	0.08
Atrial Fibrillation/Flutter		10 (4%)	3 (10%)	7 (3%)	0.09
Sick Sinus Syndrome		3 (1%)	0 (0%)	3 (1%)	0.5
Other*		16 (7%)	3 (10%)	13 (6%)	0.43
Ventricular Arrhythmias	241	11 (5%)	4 (13%)	7 (3%)	0.01
NSVT		11 (5%)	4 (13%)	7 (3%)	0.01
Ventricular Tachycardia		1 (<1%)	0 (0%)	1 (<1%)	0.7
DCCV	241	4 (2%)	2 (7%)	2 (<1%)	0.02
ICD	241	2 (<1%)	2 (7%)	0 (0%)	<0.01
Permanent Pacemaker	241	1 (<1%)	0 (0%)	1 (<1%)	0.7
Cardiac Arrest	241	0 (0%)	0 (0%)	0 (0%)	N/A
Mortality	241	3 (1%)	0 (0%)	3 (1%)	0.5

LVEDD = left ventricular end diastolic diameter; BSA = body surface area; LVEDV = left ventricular end diastolic volume; NYHA = New York Heart Association; NSVT = non-sustained ventricular tachycardia; DCCV = direct current cardioversion; ICD = implantable cardioverter defibrillator.

Data are represented as medians with interquartile ranges for continuous variables and n (%) for categorical variables.

* Other forms of supraventricular tachycardia, including atrioventricular nodal re-entrant tachycardia and atrioventricular re-entrant tachycardia.

including patient age, gender, race, or established coronary artery disease risk equivalents. LV systolic dysfunction was more common in patients with a lower BMI (odds ratio [OR] = 0.87, 95% confidence interval [CI] = 0.75 to 0.99). However, a lower BMI was not independently associated with the severity of dysfunction (LVEF ≤40%: p = 0.1) or clinical heart failure (NYHA Class ≥II: p = 0.4).

Patients with LV systolic dysfunction also had more pronounced aortopathies, with a documented association occurring at aortic root diameters exceeding 4.0 cm (OR = 4.5, 95% CI = 1.2 to 17.1). However, corresponding use of β-blockers and/or ACE-I/angiotensin receptor blockers at the time of data collection was not associated with the presence of LV systolic dysfunction (p = 0.5) nor the severity of systolic impairment (EF 51% [IQR 48 to 54] vs 53% [IQR 51 to 54]; p = 0.7).

Among patients with LV systolic dysfunction, impairment in biventricular performance was frequently noted (OR 27.2, 95% CI = 2.0 to 327.2), with a reduced RVEF documented in 23% of patients (n = 7). RV systolic dysfunction was similarly mild (86%, n = 6) but was not associated with the degree of aortopathy (p = 0.7) or severity of underlying LV systolic impairment (p = 0.7). Dural ectasia was associated with a reduced LVEF (OR 3.9, 95% CI = 1.2 to 12.8), whereas no other typical phenotypic features of MFS were. Although mitral valve prolapse was associated with LV dysfunction on univariate analysis, it was not significant on multivariable analysis (OR = 2.5, 95% CI = 0.6 to 10.4) which was likely due to its predominant association with aortic root dilation.

FBN1 variant analyses were available for 13 patients (43%) with LV dysfunction, with the majority of variants encoding a premature termination codon (46%, n = 6) or affecting a cysteine residue (67%, n = 4) and therefore representing severe *FBN1* genotypes (77%, n = 10). LV systolic dysfunction was not associated with the type of *FBN1* variant (p = 0.5) nor the severity of the *FBN1* genotype (p = 0.8). There was additionally no association between the severity of the *FBN1* genotype and degree of aortic root dilation (4.0 cm [IQR 3.6 to 4.3] vs 3.9 cm [IQR 3.5 to 4.3], p = 0.3).

No patient with LV systolic dysfunction died during the study period. However, cardiovascular morbidity was notably increased in this population. Specifically, despite only

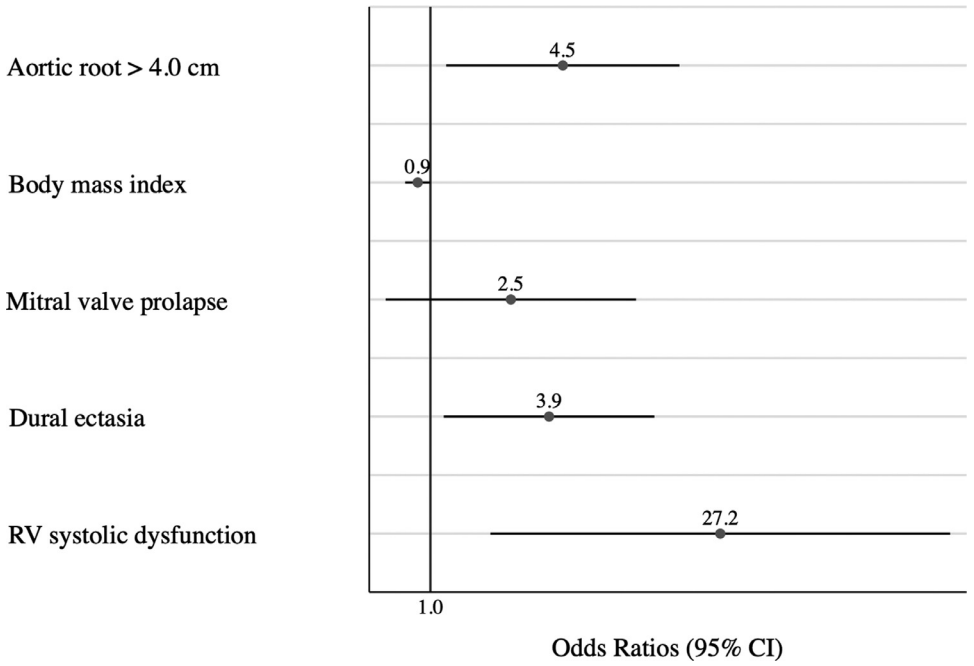

Figure 2. Multivariable model of factors associated with left ventricular systolic dysfunction. Values depicted as odds ratios with 95% CIs. Left ventricular systolic dysfunction was more common in patients with larger aortic root diameters and classic phenotypic features of Marfan syndrome.

mild LV systolic impairment, patients experienced a significant arrhythmic burden, with a cumulative incidence of atrial and ventricular arrhythmias of 20% (n = 6) and 13% (n = 4), respectively. On multivariable analysis, only older age (OR 1.05, 95% CI = 1.02 to 1.09) was associated with an increased risk of tachyarrhythmias.

Approximately 75% of patients with LV systolic dysfunction (22/30) underwent serial echocardiographic evaluation over a median duration of follow-up of 7 years (IQR 1 to 13). Among these patients, myocardial performance was notably impaired from a young age, with a median age at onset of LV systolic dysfunction of 25 years (IQR 19 to 37) and evidence of LV dilation by 26 years (IQR 21 to 42) (Figure 3). LV systolic function also further declined on follow-up, with a median decrease in LVEF by 8.8% (IQR 3.6 to 13.1). On univariate analysis, changes in LV performance occurred independent of the baseline severity of dysfunction (p = 0.5), median change in aortic root diameter (p = 0.3), and related development of atrial (p = 0.9) and/or ventricular (p = 0.2) tachyarrhythmias.

Discussion

To the best of our knowledge, this study presents the largest retrospective analysis of ventricular function in patients with MFS and a primary cardiomyopathy. The principal findings of this study are: first, adults with MFS have evidence of intrinsic myocardial dysfunction from a young age, which is predominantly mild and subclinical in nature. Second, systolic impairment is associated with more pronounced aortic root dilation. Lastly, no definitive genotype-phenotype correlations were found with respect to the development of a primary cardiomyopathy.

We found evidence in support of a primary cardiomyopathy in MFS, with just over 12% of patients having LV systolic dysfunction. Dysfunction was typically mild and asymptomatic, although overt clinical heart failure was present in some. Several previous studies have reported comparable findings, with dysfunction ranging in prevalence from 3% to 68% and being predominantly mild in nature.[5,14–16] However, the ability to draw definitive conclusions from these studies has been limited by small sample sizes, variable study methods, and differing definitions of myocardial impairment.[6] Additionally, uncertainty still persists in known data, with a few previous studies finding no clear evidence of impaired ventricular performance.[17,18] These inconsistencies ultimately prompted a recent meta-analysis encompassing 490 patients with MFS and no risk factors for acquired heart disease.[19] The authors similarly found an increased prevalence of LV dysfunction in patients with MFS compared with age-matched controls. However, a reduced LVEF was documented in only 2 of the 9 included studies, with a mean difference in LVEF of only 2.6%. In the present study, we used a more rigorous methodology by excluding patients with significant valvular disease, previous cardiac surgery, or coronary artery disease. Thus, we have been able to characterize the prevalence of a primary cardiomyopathy in MFS more definitively.

Pathophysiologically, the presence of a primary cardiomyopathy in MFS should be expected. Pathogenic variants in *FBN1* alter the structure and function of the fibrillin-1 protein, which is a vital component of microfibrils within the extracellular matrix.[2] Fibrillin-1 is abundant throughout the normal myocardium and is important in regulating mechanosignaling in response to hemodynamic stress.[20,21] Therefore, as highlighted in murine models, with partial or complete fibrillin-1 deficiency, there is evidence of increased mechanical stress, maladaptive extracellular matrix remodeling, and

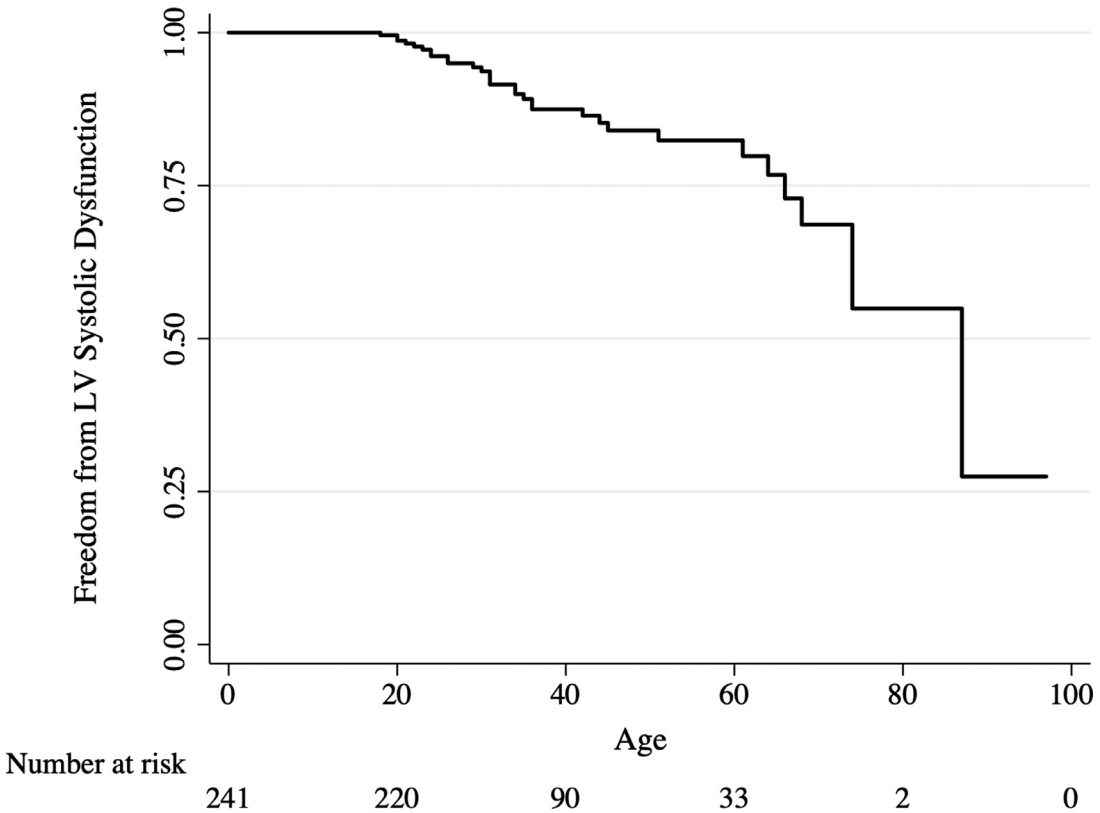

Figure 3. Freedom from the development of left ventricular systolic dysfunction. Among the 241 patients at risk of developing a primary cardiomyopathy, 30 patients (12%) had evidence of left ventricular systolic dysfunction. Ventricular impairment was evident from a young age, with a median age at onset of left ventricular systolic dysfunction of 25 years (IQR 19, 37).

ultimate impaired contractility.[7,21] Further evidence in support of a primary myopathic process can be obtained through simultaneous evaluation of RV performance, with previous studies demonstrating a similar impairment in RV function.[15,22] Our findings mirror these previous studies, with RV dysfunction being 32 times more likely among those with LV dysfunction.

In evaluating potential risk predictors, we found no association between the majority of queried traditional cardiac risk variables and the development of a primary cardiomyopathy. However, LV dysfunction was associated with larger aortic root diameters. It has been well established that aortic elasticity and resultant distensibility are reduced in MFS.[23] Further, as with cardiomyopathy, abnormal mechanosignaling is seen in the presence of aortic pathology.[24] The nature of the association between cardiomyopathy and aortopathy in MFS may therefore reflect abnormal ventriculoarterial coupling.[23,25]

Beyond the effects of abnormal ventriculoarterial coupling, the association between cardiomyopathy and aortopathy may represent a fundamentally more severe MFS phenotype. Patients with neonatal MFS classically have the most severe phenotype, typified by severe aortopathy, valvular disease, and cardiomyopathy.[26] Additionally, certain phenotypic features, including arachnodactyly, low BMI, and distinctive facial features, are more commonly observed among the more severely affected patients.[26] In the present study, dural ectasia and low BMI were similarly associated with a reduced LVEF. These findings, in the presence of a similarly more pronounced aortopathy, suggest that a more severe MFS phenotype may underlie this association.

Despite representing a seemingly more severe MFS phenotype, we did not identify any definitive genotype-phenotype correlations with respect to the development of a primary cardiomyopathy. Specifically, neither the type of *FBN1* variant nor related genotype severity were associated with the development of LV dysfunction. Comparable findings have been shown in relation to other cardiovascular manifestations of MFS.[27] However, in previous studies analyzing patients similarly at risk for developing a primary cardiomyopathy, patients with *FBN1* nonmissense variants were found to have increased LV dilation, diminished LV contractility, and reduced LV strain.[16,28] As genetic testing was performed in only half of our cohort, our study was likely underpowered to detect any definitive genotype-phenotype correlations. However, we hypothesize that with more widespread genetic surveillance, pathogenic *FBN1* variants resulting in haploinsufficiency will lead to more severe cardiovascular phenotypes, as was recently demonstrated in a cohort of 1,500 patients with MFS.[9]

Although our study has several strengths, there are important limitations to be acknowledged. Given the low number of events pertaining to the primary outcome, other variables associated with LV dysfunction may have not reached statistical significance. The small resultant sample size similarly precluded meaningful subgroup analyses, including the evaluation of potential predictors of disease

progression. Additionally, patients diagnosed with MFS before the establishment of the revised Ghent criteria were included in our study and therefore, we cannot exclude the possibility that some patients may have been misclassified on initial evaluation. However, because all patients underwent repeated clinical evaluation by an expert in genetic aortopathies, misclassification was unlikely to be a source of significant bias. Lastly, as the study was conducted at a tertiary referral center, the generalizability of our results to the general adult MFS population may be limited.

In conclusion, apart from significant valvular disease, LV systolic dysfunction is observed in patients with MFS from a young age, suggestive of a primary cardiomyopathy. Systolic impairment was more common among patients with more pronounced aortopathies and therefore may reflect a more severe underlying MFS phenotype. Although dysfunction is often mild and asymptomatic, it can progress over time, with associated long-term cardiovascular morbidity. Further prospective studies are needed to assess the potential benefits of medical therapies on primary myocardial dysfunction in MFS.

Disclosures

The authors have no conflict of interest to declare.

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