Impaired right ventricular systolic function demonstrated by reduced atrioventricular plane displacement in adults with Marfan syndrome

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Aims The right ventricle (RV) ejects the same volume of blood at the same rate as the left ventricle (LV). Mild LV dysfunction has been demonstrated in Marfan syndrome (MFS). However, little attention has been paid to the functioning of the RV. The aim of this study was to assess RV function in unoperated adult MFS patients.

Methods and results In 66 unoperated (15–58 years) MFS patients and 61 controls, rate of pressure rise (dp/dt) in RV, and tricuspid annular motion (TAM) were studied using conventional echocardiography and tissue Doppler imaging (TDI). When compared with controls, MFS patients showed impaired RV systolic function as expressed by a reduced dp/dt, TAM obtained by M-mode echocardiography, and peak TDI systolic velocities at the basal lateral wall (745.36 ± 37.85 vs. 1103.30 ± 27.30 mmHg, P < 0.001; 2.2 ± 0.05 vs. 2.5 ± 0.05 cm, P < 0.001; and 0.13 ± 0.002 vs. 0.16 ± 0.002 m/s, P < 0.001, respectively).

Conclusion This study demonstrated a primary impairment of RV systolic function in MFS. This is the first study to report RV dysfunction in MFS. Such data could prove valuable during the peri-operative and long-term medical management of MFS patients.

KEYWORDS Marfan syndrome; Right ventricular function; Systolic long-axis function; Tissue Doppler imaging

Introduction

Marfan syndrome (MFS) is an inherited disorder of connective tissue characterized by ocular, musculoskeletal, and cardiovascular manifestations and caused by mutations in the fibrillin-1 (FBN1) gene that encodes the protein fibrillin-1.¹ In 1991, the discovery of the FBN1 gene by an international consortium triggered off a sequence of exciting developments in the MFS research field. New insights regarding the protein fibrillin-1 have revealed its role not only as an important component of elastic fibres but also as a regulator of transforming growth factor-β (TGF-β) bioactivity in the extracellular matrix.² Recently conducted experimental studies provide evidence that fibrillin-1 interacts with integrins and affects the cytokine TGF-β, which can influence matrix deposition, cellular proliferation, and cell death within the cardiovascular system.³ Therefore, causative mutations in the FBN1 gene may result in myocardial dysfunction.

Aortic complications have long been recognized as the main cause of premature death from MFS and have been studied extensively. Previous studies by Chatrath et al.⁴ and Meijboom et al.⁵ demonstrated left ventricle (LV) enlargement with normal LV systolic function in 19% and 7% of their MFS study groups, respectively. Moreover, a recent study by De Backer et al.⁶ demonstrated mild abnormalities in LV systolic and diastolic functions in patients with MFS. However, very little attention has been paid to the right ventricle (RV). It is presumed that the RV functions normally, and therefore less time is spent in assessing its performance compared with the aorta and LV.

Precise assessment of RV function is difficult due to the crescent shape of the ventricle and also to its
complex. In clinical practice, a useful way to estimate the RV function is to observe the tricuspid annular motion (TAM). To date, no study has been performed measuring TAM to evaluate RV function in MFS. Since the RV ejects the same volume of blood at the same rate as the LV, we sought to ascertain any abnormalities of RV systolic function in unoperated patients with MFS without significant valvular disease, using two dimensional, two dimensional-targeted M-mode, Doppler and colour tissue Doppler echocardiography.

Methods

Seventy-one consecutive Caucasian patients who conformed to the internationally accepted Ghent criteria for MFS were enrolled in this echocardiographic study conducted at St George's, University of London in collaboration with St George's Hospital NHST. Patients were recruited from the MFS clinics at St George's, Royal Brompton and Harefield Hospitals. In each case, the clinical diagnosis was confirmed by two experienced observers (A.K. and A.H.C.).

The main exclusion criteria were (i) age <15 or >60 years, (ii) aortic dissection or previous cardiac surgery, (iii) valvular disease more than mild in severity, (iv) persistent arrhythmias, (v) systemic and/or pulmonary hypertension, and (vi) other significant clinical disorders known to affect the myocardial function, such as coronary heart disease, diabetes mellitus, renal impairment, anaemia, thyroid, or liver disorders. After the application of these criteria, 5 of the 71 patients had to be excluded, giving a final study population of 66 MFS patients.

At baseline, 22 (33%) of the 66 patients were on treatment with β-blockers specifically prescribed for the management of MFS. Discontinuation of β-blockers for these patients was considered inappropriate for ethical reasons. Following clinical and echocardiographic examination to confirm the diagnosis of MFS, according to the Ghent criteria, the majority of the remaining patients not already on β-blocker therapy were referred to their managing physicians for appropriate treatment. Several patients under our direct supervision despite being fully informed about the risks have chosen to remain untreated for various reasons such as concerns over fatigue, religious issues, and, for male patients, impotence. Twenty-nine out of 66 patients already had a known genotype. T wenty-nine out of 66 patients already had a known genotype.

Assessment of right ventricle systolic function

Tricuspid annular motion was recorded using M-mode and tissue Doppler imaging (TDI) to assess the RV function. Tricuspid and pulmonary regurgitant jets were also recorded using colour Doppler technique.

Assessment of left ventricle systolic function

Left ventricle function was also assessed in the course of this study using conventional echocardiographic techniques. Size and systolic function were both evaluated in accordance with the recommendations for chamber quantification.

Echocardiography

M-mode, two dimensional, colour Doppler, and colour tissue Doppler images were obtained through optimal parasternal, apical, and sub-xiphoid views using the Vivid 7 Vingmed General Electric ultrasound scanner (GE Vingmed Ultrasound, Horten, Norway) equipped with a 4S-MHz probe. Three consecutive cardiac cycles were recorded for each view, with breath held at end expiration. An ECG was recorded simultaneously at a sweep speed of 100 mm/s. Colour Doppler images were acquired at high frame rates of 180 ± 15, using narrow image sectors. All measurements were performed offline using Echopac 6.1, GE workstation.

Assessment of right ventricle thickness, size, and right ventricle/left ventricle ratio

The quantification of RV thickness and size complied with the ASE guidelines. Right ventricle free wall thickness was assessed from the sub-xiphoid view at the end-diastole at the level of the tricuspid valve chordae tendineae using two-dimensional imaging. The assessment of RV size was performed in a true non-foreshortened apical four-chamber view. Right ventricle diameters were measured at the basal and mid-cavity levels at the end-diastole. The RV size was also assessed from the short-axis view at mid-level to avoid false-positive dilatation. To calculate the RV/LV ratio, LV diameters were also measured at the basal level in the apical four-chamber view at the end-diastole. Right ventricle and LV diameters were measured in the transverse plane at their widest points between the inner surface of the free wall and the surface of interventricular septum. The diameter measurements were subsequently indexed for BSA. Pulmonary artery (PA) size, pressures, inferior vena cava (IVC) size, and inspiratory response were calculated in accordance with ASE recommendations for chamber quantification. Pulmonary artery and IVC diameters were also indexed for BSA.

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Reproducibility of tricuspid annular motion measurements

To determine the degree of interobserver and intraobserver variability, TAM measurements were performed by two independent observers in 28 randomly selected patients and normal controls at two different sessions. The inter- and intra-observer reproducibility was calculated using unsigned relative errors \[ 2 \times |A - B| / (A + B) \], where A and B were the repeated measurements of the same method. Statistical analysis of reproducibility of methods was based on comparisons of the absolute values of relative errors using Mann–Whitney test. P-value <0.05 was considered statistically significant.

Statistical analysis

Continuous variables were summarized as means ± SD. Differences in continuous variables between patients with MFS and controls
were investigated using t-test for independent samples, adjusting for unequal variances when appropriate. Categorical variables were expressed as absolute numbers and percentages. The statistical test in these cases was the $\chi^2$ test.

In addition, for each M-mode method (standard M-mode, anatomical M-mode, and colour anatomical M-mode) and TDI technique, the displacement from the free lateral RV wall was tested using multiple regression analysis to detect differences between patients with MFS and controls, adjusting for potential confounders. $dp/dt$ was also tested following the same approach.

$\beta$-Blockers, age, and sex are known confounders and therefore we adjusted for these in all regression analyses. Further investigation was also carried out to assess the existence of other possible confounders. By keeping MFS diagnosis, $\beta$-blockers, age, and sex always within the models, both heart rate (HR) and pulmonary artery systolic pressure (PASP) were revealed as additional confounding variables but only for tricuspid annular displacement. Consequently, the model for the displacement from the free lateral RV wall using TDI and the model for $dp/dt$ included only the MFS diagnosis, $\beta$-blockers, age, and sex. However, the model for the displacement measurements from the free lateral RV wall using the three M-mode methods was additionally adjusted for HR and PASP.

Finally, we performed meta-analyses in order to assess the overall effect of all these confounders on the results obtained from the three M-mode methods. By assuming these methods to be three separate experiments measuring the same underlying parameter, TAM, meta-analysis was considered to be both a valid and an appropriate technique.

The statistical analysis was performed using STATA.

**Results**

**Subjects’ characteristics**

Baseline demographic and clinical characteristics of both groups are presented in Table 1. Heart rate was statistically lower in patients with MFS than in controls. No statistical differences were observed in the other described variables between both groups.

**Right heart and valves**

Values for the right heart size, RV thickness, and systolic blood flow velocities across the right heart valves are shown in Table 2. Right ventricle diameters obtained from the four-chamber view at basal and mid-levels in the end-diastole were significantly larger in MFS patients when compared with controls. Right ventricle end-diastolic size evaluated from the short-axis view at mid-level was also significantly larger in patients with MFS in comparison with controls. All these measurements remained statistically significant after correction for BSA. On the other hand, basal four-chamber LV end-diastolic diameter indexed for BSA showed no differences between the study groups. Consequently, RV/LV ratio was increased in MFS compared with controls. Right ventricle thickness measured from the sub-xiphoid view showed no differences in either group. Right atrial area measured in the four-chamber apical view was found increased in patients with MFS even after being indexed to BSA. Similarly, the PA size was also found to be significantly larger in MFS patients in comparison with controls. After correction for BSA, this difference remained statistically significant. Inferior vena cava size showed no difference in both groups.

With regard to forward blood flow velocities across the pulmonary and tricuspid valves, pulmonary blood flow was decreased in MFS patients, whereas no statistical difference was noted in TR flow between the two groups. None of the study subjects had more than mild tricuspid and/or pulmonary regurgitation.

**Right ventricle function**

Right ventricle function parameters evaluated by two-dimensionally targeted M-mode techniques, Doppler, and TDI are summarized in Table 3. Systolic TAM obtained from the lateral side of the tricuspid annulus using M-mode, anatomical M-mode, and colour anatomical M-mode was significantly reduced in patients with MFS. In all methods,
## Table 1  Baseline characteristics for Marfan syndrome patients and controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>MFS</th>
<th>Controls</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male/female)</td>
<td>37/29</td>
<td>27/34</td>
<td>0.18a</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66 (32 ± 13)</td>
<td>61 (30 ± 7)</td>
<td>0.19</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>66 (75.8 ± 13.5)</td>
<td>61 (78.2 ± 14.6)</td>
<td>0.33</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>66 (185.6 ± 10.1)</td>
<td>61 (183.6 ± 9.5)</td>
<td>0.25</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>66 (56 ± 9)</td>
<td>61 (60 ± 9)</td>
<td>0.01</td>
</tr>
<tr>
<td>β-Blockers (on atenolol/not on atenolol)</td>
<td>22/44</td>
<td>0/61</td>
<td>—</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>66 (2.0 ± 0.2)</td>
<td>61 (2.0 ± 0.2)</td>
<td>0.58</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>66 (115 ± 11)</td>
<td>61 (114 ± 8)</td>
<td>0.73</td>
</tr>
<tr>
<td>PASP (mmHg)</td>
<td>65 (23 ± 3)</td>
<td>61 (23 ± 3)</td>
<td>0.92</td>
</tr>
<tr>
<td>MPADP (mmHg)</td>
<td>65 (9 ± 3)</td>
<td>60 (9 ± 2)</td>
<td>0.73</td>
</tr>
</tbody>
</table>

Results are represented as mean ± SD. 
P-values are obtained from t-tests, adjusted for unequal variances if necessary.

SBP, systolic blood pressure; MPADP, mean pulmonary artery diastolic pressure.

aχ² test.

## Table 2  Echocardiographic parameters in Marfan syndrome patients and controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>MFS</th>
<th>Controls</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal L VEDD (cm)</td>
<td>66 (4.5 ± 0.5)</td>
<td>61 (4.5 ± 0.4)</td>
<td>0.74</td>
</tr>
<tr>
<td>Basal L VEDD/BSA (cm/m²)</td>
<td>66 (2.3 ± 0.3)</td>
<td>61 (2.3 ± 0.3)</td>
<td>0.96</td>
</tr>
<tr>
<td>Basal RVEDD (cm)</td>
<td>66 (3.4 ± 0.5)</td>
<td>61 (2.9 ± 0.4)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Basal RVEDD/BSA (cm/m²)</td>
<td>66 (1.7 ± 0.3)</td>
<td>61 (1.5 ± 0.2)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>RV/LV ratio</td>
<td>66 (0.7 ± 0.1)</td>
<td>61 (0.7 ± 0.1)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Mid-RVEDD (cm)</td>
<td>66 (2.7 ± 0.5)</td>
<td>61 (2.2 ± 0.3)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Mid-RVEDD/BSA (cm/m²)</td>
<td>66 (1.4 ± 0.2)</td>
<td>61 (1.1 ± 0.2)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>RVEDD short axis (cm)</td>
<td>66 (2.5 ± 0.4)</td>
<td>61 (2.0 ± 0.3)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>RVEDD short axis/BSA (cm/m²)</td>
<td>66 (1.3 ± 0.2)</td>
<td>61 (1.0 ± 0.1)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>RV thickness (cm)</td>
<td>66 (0.5 ± 0.1)</td>
<td>61 (0.5 ± 0.0)</td>
<td>0.33</td>
</tr>
<tr>
<td>RA area (cm²)</td>
<td>66 (17.0 ± 3.5)</td>
<td>61 (15.0 ± 2.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>RA area/BSA (cm²/m²)</td>
<td>66 (8.6 ± 1.6)</td>
<td>61 (7.5 ± 1.1)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>PA diameter (cm)</td>
<td>63 (2.4 ± 0.4)</td>
<td>61 (2.1 ± 0.2)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>PA diameter/BSA (cm²/m²)</td>
<td>63 (1.2 ± 0.2)</td>
<td>61 (1.1 ± 0.1)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>IVC size (cm)</td>
<td>66 (2.0 ± 0.4)</td>
<td>60 (2.0 ± 0.3)</td>
<td>0.99</td>
</tr>
<tr>
<td>PA flow velocity (m/s)</td>
<td>66 (0.8 ± 0.1)</td>
<td>60 (0.9 ± 0.1)</td>
<td>0.004</td>
</tr>
<tr>
<td>TR flow velocity (m/s)</td>
<td>65 (2.1 ± 0.2)</td>
<td>61 (2.1 ± 0.2)</td>
<td>0.88</td>
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</tbody>
</table>

Results are represented as mean ± SD. 
P-values are obtained from t-tests, adjusted for unequal variances if necessary.

Basal L VEDD, left ventricular end-diastolic diameter measured in the apical four-chamber view at the base level; Basal RVEDD, right ventricular end-diastolic diameter measured in the apical four-chamber view at the base level; Mid-RVEDD, right ventricular end-diastolic diameter measured in the apical four-chamber view at the level of left ventricular papillary muscles; RA, right atrium; TR, tricuspid regurgitation.

## Table 3  Tricuspid annular motion measurements by M-mode techniques, tissue Doppler imaging, and dp/dt in Marfan syndrome patients and controls

<table>
<thead>
<tr>
<th>Variables</th>
<th>Method</th>
<th>MFS</th>
<th>Controls</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAM (cm)</td>
<td>M-mode</td>
<td>65 (2.22 ± 0.43)</td>
<td>61 (2.48 ± 0.35)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>AM-mode</td>
<td>65 (2.28 ± 0.41)</td>
<td>61 (2.57 ± 0.36)</td>
<td>&lt;0.0005</td>
<td></td>
</tr>
<tr>
<td>CAM-mode</td>
<td>61 (2.35 ± 0.43)</td>
<td>61 (2.53 ± 0.34)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>TDI systolic velocity (m/s)</td>
<td>61 (0.14 ± 0.02)</td>
<td>61 (0.16 ± 0.02)</td>
<td>&lt;0.0005</td>
<td></td>
</tr>
<tr>
<td>RV dp/dt (mmHg/s)</td>
<td>60 (745 ± 308)</td>
<td>61 (1.103 ± 211)</td>
<td>&lt;0.0005</td>
<td></td>
</tr>
</tbody>
</table>

Results are represented as mean ± SD. 
TAM measurements are adjusted for age, sex, HR, and PASP in the control group and additionally for β-blockers in the MFS group. TDI and RV dp/dt measurements are adjusted for age and sex in the control group and additionally for β-blockers in the MFS group.

AM-mode, anatomical M-mode; CAM-mode, colour anatomical M-mode.
Multiple regression analyses demonstrated that the presence of MFS was associated with reduced TAM. Heart rate also showed a statistically significant negative association with TAM. Age was found to be positively correlated with RV long-axis systolic function, whereas PASP was positively correlated only in M-mode technique. Meta-analysis of our results confirmed that MFS patients had reduced TAM when compared with controls (results of meta-analysis are shown in Table 4). The rate of pressure rise in RV (dp/dt) in systole was significantly lower in MFS patients in comparison with controls. Similarly, systolic velocities assessed by TDI were also reduced in MFS patients (Table 3).

Within the group of 29 patients who had known FBN1 mutations, it was not possible to demonstrate correlation between impaired RV long-axis systolic function and the type or location of these mutations.

**Left ventricle function**

With regard to conventional echocardiographic measurements (Table 6), dimensional measurements in diastole and systole were not significantly different between the patients and normal controls. After correcting for age and BSA using Henry’s regression equations, LV end-diastolic diameters expressed as percentage of the predicted value were significantly higher in patients with MFS in comparison with normal controls. However, none of the patients fulfilled the criteria for dilated cardiomyopathy. Ejection fraction evaluated by biplane Simpson’s method was found significantly reduced in MFS, although it was within the normal range. Fractional shortening was comparable between the study groups.

**Discussion**

This study was directed by our clinical observation that the role of RV function is underestimated in patients with MFS. Despite its complex morphology, the function of the RV is comparable with that of the LV. The contribution of the RV to maintaining the cardiac output is equally important to that of the LV. In the literature, there are a few case reports relating to RV function in MFS. To the best of our knowledge, there are no systematic studies on RV systolic function in patients with MFS.

This study is the first to assess RV systolic function and report mild, though statistically significant RV impairment in unoperated patients with MFS. Impaired RV systolic function should be considered primary in our patients, as coexisting diseases which could cause secondary ventricular functional abnormalities have been excluded.

Our data showed a slower increase in the slope of the tricuspid regurgitation velocity curve when compared with controls. Trivial or mild tricuspid regurgitation was present in all our patients and controls, which enabled recordings of systolic regurgitant jet and subsequent dp/dt calculation. dp/dt evaluation by continuous wave Doppler echocardiography represents a validated method which provides non-invasive information concerning biventricular systolic function. In our study, slower increase in systolic tricuspid regurgitant jet velocity was indicative of a slower rise in the systolic pressure within the RV.

In addition, TAM constitutes another well-established, quick but still reliable echocardiographic technique for assessing RV systolic function. Kaul et al. showed that TAM measurements obtained from the four-chamber view...
using two-dimensionally targeted M-mode echocardiography accurately reflected RV systolic function in normal subjects and patients with coronary heart disease. Although TAM does not take account of the total RV function during systole, it is closely correlated with RV EF obtained by nuclear angiography.\(^8,\text{23}\) We therefore decided to include in our investigation this echocardiographic method to assess systolic long-axis function in patients with MFS and healthy volunteers. In this study, the assessment of TAM showed a statistically significant decrease in RV systolic long-axis function in patients with MFS vs. controls. All three M-mode techniques used to measure TAM provided values comparable with each other.

Sanchez-Quintana et al.\(^{24}\) reported that the RV wall in the normal heart is arranged from the base towards the apex in two layers; one superficial layer with fibres running horizontally and another subendocardial layer where fibres run longitudinally. Immunohistochemical data obtained from tissue samples of human and rodent hearts revealed that fibrillin-1 is a major supporting tissue protein in the myocardium.\(^{25,\text{26}}\) Fibrillin-1-positive fibres were oriented in the longitudinal axis of cardiomyocytes; this spatial arrangement is indicative of the important function of the fibrillin-1-rich microfibrils in transmitting the forces of myocardial contraction from myocytes to the extracellular supporting tissue framework.

Meta-analysis of TAM measurements showed that MFS was significantly associated with reduced systolic long-axis function. Heart rate also showed a statistically negative correlation with TAM. Twenty-two out of 66 patients (33%) were on prophylactic treatment with β-blockers. After adjusting for β-blocker therapy, patients with MFS had a slower HR than controls in our series. This could be attributed to intrinsic abnormalities of the conduction system in MFS. More studies are needed to histologically define the structure of conductive tissue and its surrounding extracellular matrix in MFS. According to the Starling effect, bradycardia increases the end-diastolic fibre length, which leads to enhanced length-dependent activation of actin and myosin cross-bridges in the cardiac myocytes and a greater contractility. Despite the slower HR in MFS patients, the RV systolic long-axis function was found impaired.

In our series, age had a significant positive correlation with TAM. Our age group ranged between 15 and 58 years. Fifty-eight healthy subjects out of 61 (95%) and 55 MFS patients out of 66 (83%) were under the age of 45 years. This correlation is similar to that reported by Kukulski et al.\(^{17}\) on RV systolic long-axis function in normal individuals.

Meta-analysis also showed that PASP was positively correlated with TAM. Pulmonary artery systolic pressure measurements were within the normal range in both groups. If we assume that the RV in MFS is fibrillin-1-deficient, even normal values of PASP could impose a significantly increased afterload. In our series, MFS patients had increased RV size, suggesting that the RV attempts to compensate for increased afterload by the Frank–Starling mechanism. In contrast, the positive correlation observed between PASP and TAM in the control group could be explained by increased contractility. Despite the suggested compensatory mechanism in MFS, the RV long-axis systolic function was reduced in patients in comparison with the controls. Follow-up studies are needed to monitor potential changes in afterload with time and to assess the impact on the RV long-axis systolic function in patients with MFS.

### Table 5

<table>
<thead>
<tr>
<th>Variables</th>
<th>M-mode</th>
<th>AM-mode</th>
<th>CAM-mode</th>
<th>TDI systolic velocity (m/s)</th>
<th>RV dp/dt (mmHg/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAM (cm)</td>
<td>MFS patients not on β-blockers</td>
<td>22</td>
<td>2.19 ± 0.43</td>
<td>2.33 ± 0.46</td>
<td>2.36 ± 0.49</td>
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<tr>
<td></td>
<td>MFS patients on β-blockers</td>
<td>22</td>
<td>2.35 ± 0.42</td>
<td>2.42 ± 0.49</td>
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<td></td>
<td>Controls</td>
<td>61</td>
<td>2.48 ± 0.35</td>
<td>2.57 ± 0.36</td>
<td>2.53 ± 0.34</td>
</tr>
</tbody>
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Results are represented as mean ± SD.

Table 5: Tricuspid annular motion measurements by M-mode techniques, tissue Doppler imaging, and dp/dt.

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<td></td>
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<td>22</td>
<td>2.19 ± 0.43</td>
<td>2.33 ± 0.46</td>
<td>2.36 ± 0.49</td>
</tr>
<tr>
<td></td>
<td>MFS patients on β-blockers</td>
<td>22</td>
<td>2.35 ± 0.42</td>
<td>2.42 ± 0.49</td>
<td>2.42 ± 0.49</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>61</td>
<td>2.48 ± 0.35</td>
<td>2.57 ± 0.36</td>
<td>2.53 ± 0.34</td>
</tr>
</tbody>
</table>

Results are represented as mean ± SD.

Table 5: Tricuspid annular motion measurements by M-mode techniques, tissue Doppler imaging, and dp/dt.
Impaired right ventricular systolic function

The RV/LV ratio, which was significantly increased in our MFS patients, is a useful and sensitive measurement to detect and monitor RV dilatation. This calculation is often used to evaluate RV dysfunction and prognosis in various clinical conditions such as pulmonary embolism, congenital heart disease, and/or coronary heart disease.27–29

TDI to assess tricuspid annular velocities represents another reliable echocardiographic technique to assess RV systolic function. In the present study, reduced TDI velocities in systole were indicative of RV systolic dysfunction in MFS.

This study also demonstrated statistically significant LV systolic impairment in MFS patients. In the past 10 years, exciting experimental studies in fibrillin-1-deficient mice have led to the expansion of our knowledge about the structure and assembly of fibrillin-1 microfibrils and its role in the TGF-β regulation and cardiovascular system.5 Dietz et al. report reduced pre-load-recruitable stroke work in the mouse model, which was correlated with increased TGF-β signalling (personal communication). In view of these findings, fibrillin-1 deficiency in the myocardium is likely to be responsible for the observed reduced RV systolic function in our study.

Limitations

Two-dimensionally targeted M-mode imaging is commonly used to assess TAM in everyday clinical practice. However, this technique measures only the overall systolic excursion of the RV free lateral wall towards the apex. Strain and strain rate echocardiography could better quantify changes in regional RV contractility function in MFS.

β-Blocker treatment could affect measurements of TAM, dp/dt, and TDI velocities. Vogel et al.16 demonstrated the impairment of RV contractility with the use of esmolol. However, our analysis showed no differences between patients on and off β-blockers for these values. In contrast, measurements obtained from controls and MFS patients without treatment showed statistically significant differences (Table 5).

In our study, there was a confirmed causative FBN1 mutation in 29 patients. This number of genotyped patients was not sufficient to link RV systolic function with a specific type or location of FBN1 mutation. In a further study, genotypic identification of all patients may provide enough data to correlate FBN1 mutations to RV dysfunction.

In conclusion, our study revealed mild but statistically significant RV systolic dysfunction in patients with MFS. The assessment of RV systolic function should be included in the examination of cardiac function in all patients with MFS. A number of alternative echocardiographic techniques are presently available to allow a clinician to evaluate RV systolic function and monitor the observed abnormalities over time in patients with MFS.

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