

# Aortic root dilation in adult patients with Marfan syndrome: Does aortic root stiffness matter?



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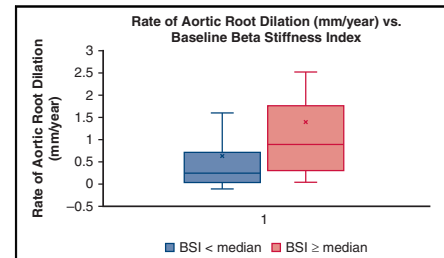
## ABSTRACT

**Objective:** Aortic root (AoR) size remains an imperfect predictor of rate of aortic dilation in Marfan syndrome (MFS). Indicators of vascular phenotype such as aortic stiffness have been proposed as additional predictors. In this study we assessed the rate of AoR dilation and stiffness in adult patients with MFS.

**Methods:** We performed a retrospective chart review. We included adult patients with MFS (aged 20-40 years) with at least 2 local echocardiograms 6 months apart (no aortic surgery in-between). A blinded observer analyzed the echocardiograms. AoR dilation rate and stiffness were calculated.

**Results:** Thirty-two patients (53% women; median age, 21.1; interquartile range [IQR], 19-24 years at first echocardiogram) were included. AoR dilation rate in the entire cohort was 0 to 8 mm/year (median, 0.465; IQR, 0.23-1.45 mm/year). Multiple linear regression analysis showed that baseline AoR stiffness was associated with AoR dilation rate ( $\beta = 0.0004$ ;  $P < .001$  for elastic modulus), whereas baseline age and baseline AoR dimension were not. Eighteen of these 32 patients (56%) eventually had AoR surgery (Sx) and 14 did not have surgery (NSx). At baseline, Sx and NSx patients were similar in age. AoR dimension was larger (Sx, 4.27 cm; IQR, 4.05-4.49 cm vs NSx, 3.73 cm; IQR, 3.37-4.09 cm;  $P = .011$ ) and AoR stiffness was higher in Sx patients (beta stiffness index: median, 23.2; IQR, 17.8-28.6 vs median, 15.6; IQR, 11.6-19.7;  $P = .024$ ). AoR dilation rate was greater in Sx patients, independent of baseline AoR dimension ( $1.63 \pm 0.41$  mm/year vs  $0.38 \pm 0.08$  mm/year;  $P = .01$ ).

**Conclusions:** Our results showed that AoR dilation rate varies among adult patients with MFS and is associated with baseline AoR stiffness, measured by echocardiography. Further studies are warranted to determine how aortic stiffness can be implemented clinically to refine management in patients with MFS. (JTCVS Open 2022;10:113-20)



Patients with Marfan syndrome with stiffer aorta have faster aortic root dilation.

## CENTRAL MESSAGE

Aortic root stiffness is associated with the rate of aortic root dilation in patients with Marfan syndrome and can potentially be used to refine management by identifying patients at risk for faster aortic root dilation.

## PERSPECTIVE

Aortic root size remains an imperfect predictor of rate of aortic dilation or dissection in Marfan syndrome. We demonstrated that aortic root dilation rate varies among adult patients with Marfan syndrome and is associated with baseline aortic root stiffness. Aortic stiffness can potentially refine management in patients with Marfan syndrome by identifying those at risk for faster aortic root dilation.

Marfan syndrome (MFS) is an inherited, multisystem connective tissue disorder, with hallmark features noted in the cardiovascular, ocular, and skeletal systems.<sup>1</sup>

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Clinical diagnosis depends on a combination of major and minor signs defined in the revised 2010 Ghent criteria.<sup>2</sup> MFS patients have progressive aortic root (AoR) dilation, which can precipitate aortic dissection and/or rupture leading to sudden death.<sup>3-5</sup> In individuals with MFS, more than 90% of known causes of death are due to cardiovascular complications.<sup>6</sup> Life expectancy for this patient population has increased significantly due to earlier diagnosis and close monitoring by noninvasive imaging leading to timely referral for prophylactic surgery on the AoR.<sup>5</sup>

Current guidelines recommend prophylactic surgery in adults when the AoR dimension exceeds a cutoff of 5 cm or if the rate of AoR dilation exceeds 5 mm/year based on serial echocardiography.<sup>7</sup> Additional factors that prompt

### Abbreviations and Acronyms

AoR	= aortic root
EM	= elastic modulus
MFS	= Marfan syndrome
NSx	= no surgery
SI	= stiffness index
Sx	= Surgery

surgical intervention in patients with AoR dimensions as low as 4.5 cm, include a family history of premature aortic dissection and the presence of significant aortic regurgitation.<sup>8</sup> However, despite AoR dimension being the strongest predictor of adverse clinical outcomes and the main indication for surgery,<sup>7</sup> AoR dilation and its progression vary widely, with some patients having slow progression and others having rapid progression in early adolescence.<sup>8</sup> Perhaps even more concerning than the high variability in progression rates are the studies demonstrating dissection rates as high as 15% in patients with AoR dimensions below the 5 cm cutoff.<sup>3,7,9,10</sup> AoR size therefore remains an imperfect predictor of risk of AoR dissection.<sup>11</sup> Thus, there is a critical need to validate additional prognostic criteria by noninvasive imaging techniques to improve treatment planning in patients with MFS.

Aortic wall properties in MFS are abnormal. Patients with MFS have stiffer aortas compared with unaffected controls, even when the AoR measures within normal limits.<sup>12,13</sup> To refine medical and surgical management guidelines of patients with MFS, in addition to genetic mutation status, indicators of vascular phenotype severity such as aortic stiffness and tortuosity have also been proposed.<sup>12,14-18</sup>

However, there have been only a few studies examining the relationship between aortic stiffness and AoR dilation and/or the risk of adverse clinical outcomes. Results have been somewhat contradictory, but there is evidence that noninvasive aortic stiffness measures may identify patients at higher risk of progressive AoR enlargement and adverse clinical outcomes.<sup>12,14-16,19-21</sup> The goal of the current study was to evaluate the rate of AoR dilation in adult patients with MFS and to assess if the dilation rate is influenced by AoR stiffness.

## METHODS

We performed a retrospective review of medical records and echocardiograms of adult patients with MFS followed in our institution. The protocol was approved by the Internal Review Board for Stanford University Medical School (No.: 35840, approval date: November 10, 2015)

### Patient Population

The inclusion criteria were diagnosis of MFS (defined by most recently revised Ghent criteria),<sup>2</sup> age 20 to 40 years at time of data collection, and at least 2 echocardiograms available performed 6 months apart at our

institution. Patients were excluded in the case that they underwent AoR surgery without having had 2 echocardiograms that were 6 months apart.

### Analysis of Echocardiograms

All echocardiograms were reviewed by 1 blinded observer. A second observer reviewed 10% of the studies for assessment of interobserver variability. For the nonsurgery (NSx) group, the most recent echocardiogram was used for the second echocardiogram. For the surgery (Sx) group, the last echocardiogram before Sx was used. In the parasternal long-axis plane, AoR dimension at the sinuses of Valsalva was measured inner-edge-to-inner-edge at the maximum and minimum dimensions in systole and diastole in triplicate (Figure 1).

AoR dilation rate was calculated using the following formula:

$$\bullet \text{ Dilation rate} = (SD_2 - SD_1) / \text{Time}$$

Where  $SD_1$  = maximum AoR dimension in systole measured in millimeters at the time of the first echocardiogram,  $SD_2$  = maximum AoR dimension in systole measured in millimeters at the time of the last echocardiogram, and time = elapsed time in years between echocardiograms.

Arterial stiffness of the AoR was calculated using the following formulas for the arterial pressure-strain elastic modulus (EM) in millimeters mercury and the beta stiffness index (SI):

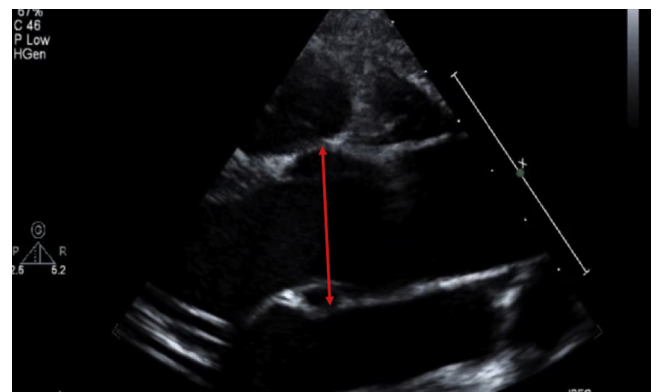
- $EM^{21} = (SBP - DBP) / [(SD - DD) / DD]$
- $Beta\ SI^{20} = [\ln(SBP / DBP)] / [(SD - DD) / DD]$

Where SBP = systolic blood pressure in millimeters mercury, DBP = diastolic blood pressure in millimeters mercury, SD = maximum AoR dimension in systole measured in millimeters, and DD = minimum AoR dimensions in diastole measured in millimeters.

The EM is a quantity that measures an object or substance's resistance to being deformed elastically when stress is applied to it.<sup>21</sup> The EM of an object is defined as the slope of its stress-strain curve in the elastic deformation region: A stiffer material will have a higher elastic modulus. Presence and degree of mitral and aortic valve regurgitation were documented. If available on the echocardiogram report, the height, weight, and systolic and diastolic blood pressure were recorded.

### Medical Record Analysis

An electronic medical record review was conducted to collect the following information: Ghent criteria that fulfilled the MFS diagnosis, age at diagnosis, phenotype as documented in clinic letters, genetic mutations, family history of MFS, family history of aortic dissection, documented indication for AoR surgery, pharmacologic regimen, other



**FIGURE 1.** Two-dimensional echocardiographic image demonstrating inner-edge-to-inner-edge measurement of aortic root dimension in systole.

comorbidities, and surgical history. If not available on the echocardiogram report, the height, weight, and systolic and diastolic blood pressure reported on the associated clinical visit on the same day of the echocardiogram were recorded.

### Statistical Methods

Descriptive statistics were presented as mean with lower and upper bounds of the 95% CIs in parentheses or median with interquartile range in parentheses as indicated. Parametric continuous data were analyzed with the Student *t* test. For nonparametric data, the Mann-Whitney *U* test was used for assessment. Linear and multiple linear regression analyses were used to assess for significant association between the age at first echocardiogram, baseline stiffness measures, and AoR dilation rate. We further assessed the behavior of AoR dilation at above and below the median baseline stiffness values because there are no normative data for aortic stiffness in Marfan syndrome populations. As a subanalysis, we explored differences between patients who eventually underwent AoR surgery versus not.

## RESULTS

### Baseline Characteristics

There were 32 patients who met inclusion criteria. Baseline subject characteristics are illustrated in Table 1. For the entire cohort, median age at the time of the first echocardiogram was 21.1 years (range, 19-24 years). Seventeen (53%) of the patients in the full cohort were women and the majority (81%) of the patients were White/Caucasian. Thirteen (52%) patients in the full cohort had a confirmed *FBNI* mutation. Thirteen (41%) patients out of the total cohort had documented ectopia lentis. Only 25 patients had undergone genetic testing.

At the first echocardiogram, the median AoR measured at 4.27 cm (interquartile range [IQR], 4.05-4.49 cm). Four patients (13%) had moderate or more aortic valve regurgitation at the time of the baseline echocardiogram. Six (19%) patients in the cohort had moderate or more valve regurgitation at baseline echocardiogram. The median systolic and diastolic blood pressures of patients were within normal limits at the time of the first echocardiogram.

Twenty-eight (88%) patients were taking a beta blocker, 3 patients (9%) were taking both beta blockers and angiotensin receptor blockers, 2 patients (6%) were taking an angiotensin receptor blocker, 1 patient (3%) was taking a calcium channel blocker, and 1 patient (3%) was taking an angiotensin converting enzyme inhibitor.

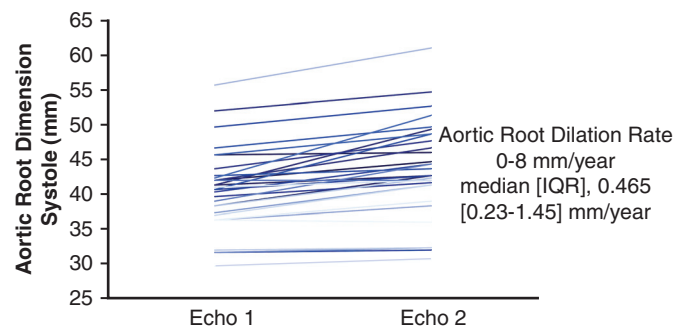
### Rate of AoR Dilation and Baseline AoR Stiffness

The rate of AoR dilation in the entire group ranged from 0 to 8 mm/year (median, 0.465; IQR, 0.23-1.45 mm/year) (Figure 2) and correlated with baseline AoR stiffness (EM:  $r = 0.57$ ;  $P < .001$  and BSI:  $r = 0.534$ ;  $P = .002$ ). Multiple linear regression analysis using baseline age, baseline AoR dimension, and baseline AoR stiffness (EM and beta stiffness) in the model as independent variables showed that baseline AoR stiffness is associated with AoR dilation rate ( $\beta = 0.04$ ;  $P = .001$  for beta stiffness and  $\beta = 0.0004$ ;  $P < .001$  for EM), whereas baseline age and baseline AoR dimension were not (Table 2).

TABLE 1. Baseline characteristics

Characteristic	Entire cohort (N = 32)	Surgery (n = 18)	No surgery (n = 14)
Patients with Marfan syndrome			
Age at first echocardiogram (y)	21.1 (19-24)	21.6 (20-29)	20.6 (19-24)
Age at surgery (y)	25.1 (22-30)	25.1 (22-30)	N/A
Male	15 (47)	11 (61)	4 (29)
Race			
White/Caucasian	26 (81)	15 (83)	11 (79)
Asian	4 (13)	1 (6)	3 (21)
Unknown	2 (6)	0	2 (14)
Ectopia lentis			
Yes	13 (41)	6 (33)	7 (50)
No	12 (38)	7 (39)	5 (36)
Unknown	7 (22)	5 (28)	2 (14)
Family history			
Yes	15 (47)	6 (33)	9 (64)
No	10 (31)	6 (33)	4 (28)
Unknown	7 (22)	6 (33)	1 (7)
Medications			
Beta blocker*	28 (88)	16 (89)	12 (86)
Angiotensin receptor blocker*	5 (16)	2 (11)	3 (21)
Calcium channel blocker	1 (3)	1 (6)	0
Angiotensin converting enzyme inhibitor	1 (3)	0	1 (7)

Values are presented as median (interquartile range) or n (%). \*Three patients were taking both beta blocker and angiotensin receptor blockers.



**FIGURE 2.** Rates of aortic root dilation of the participants. *Line* slopes reflect the rate of change of aortic root dimension (millimeters/year) over a 1-year period for each patient. *Echo*, Echocardiogram; *IQR*, interquartile range.

When using the median beta stiffness and EM values at baseline as cutoff values, there was a significant difference ( $P = .013$ ) in the rate of AoR dilation for patients with a baseline EM lower than the median (1233 mm Hg) and for those with a baseline EM higher than the median in this cohort (Figure 3, A). There was also a significant difference ( $P = .032$ ) in rate of AoR dilation for patients with a baseline beta SI lower than the median (13.48) and for those with a baseline beta SI higher than the median in this cohort (Figure 3, B). The interobserver variability for AoR measurements by echocardiography was excellent with a mean percent difference of 0.8%. The methods and results of our study are summarized in Figure 4.

**Subanalysis**

Eighteen (56%) of the 32 patients underwent AoR surgery. The documented indication for AoR surgery was AoR dimension and/or AoR dilation in all patients. No patient had aortic dissection. There was no significant difference between the Sx and NSx patients at the time of the baseline echocardiogram in age, gender, race, or blood pressure (Table 3).

Thirteen (52%) patients in the full cohort had a confirmed *FBNI* mutation, with 2 (11%) patients in the Sx group and 11 (79%) in the NSx group. Sixteen (89%) patients in the

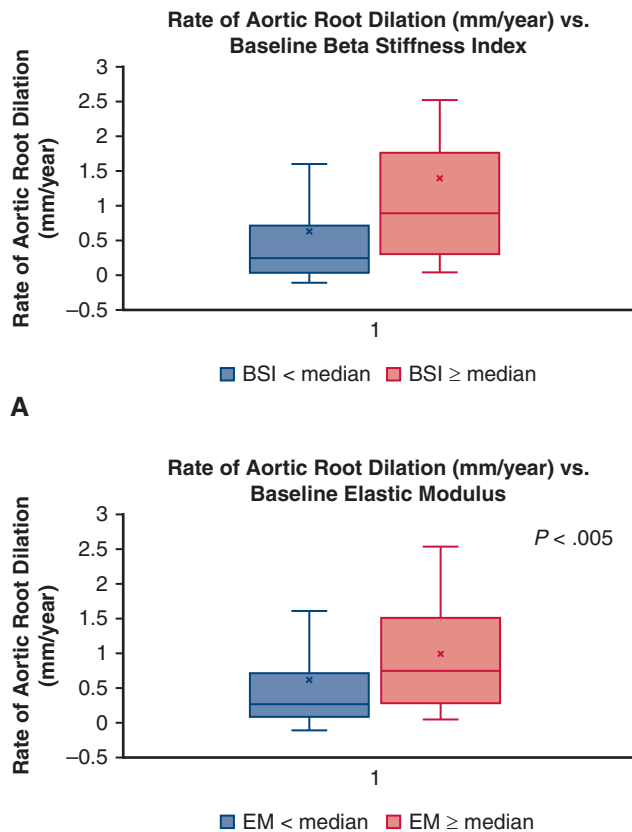
Sx group and 12 (86%) patients in the NSx group were taking a beta blocker. Additionally, in the Sx group, 2 patients (11%) were taking an angiotensin receptor blocker and 1 patient (6%) was taking a calcium channel blocker. In the NSx group, 3 patients (21%) were taking an angiotensin receptor blocker, and 1 patient (7%) was taking an angiotensin converting enzyme inhibitor.

Sx patients had larger initial AoR dimensions both in systole (Sx: median, 4.27 cm; IQR, 4.05-4.49 cm vs NSx: median, 3.73 cm; IQR, 3.37-4.09 cm;  $P = .011$ ) and diastole (Sx: median, 4.13 cm; IQR, 3.92-4.33 cm vs NSx: median, 3.59; IQR, 3.25-3.94 cm;  $P = .010$ ). Sx patients also had significantly higher beta SI (Sx: median, 23.2; IQR, 17.8-28.6 vs NSx: 15.6 median, IQR, 11.6-19.7;  $P = .024$ ) and EM (Sx: median, 1967 mm Hg; IQR, 1549-2385 mm Hg vs NSx: median, 1353 mm Hg; IQR, 1017-1689 mm Hg;  $P = .021$ ) than the NSx patients at the time of the first echocardiogram. Sx patients had larger follow-up AoR dimensions both in systole (Sx: median, 4.62 cm; IQR, 4.37-4.88 cm vs NSx: median, 4.01 cm; IQR, 3.57-4.45 cm;  $P = .018$ ) and diastole (Sx: median, 4.46 cm; IQR, 4.22-4.70 cm vs NSx: median, 3.83 cm; IQR, 3.40-4.26 cm;  $P = .012$ ) when compared with the NSx group (Figure 3). The rate of AoR dilation was significantly greater for the Sx group (Sx:  $1.63 \pm 0.41$  mm/year; NSx:

**TABLE 2. Multiple regression analysis**

Predictor variable	Coefficient	SE	P value
Aortic root dilation rate			
Age at first echocardiogram	-0.0888	0.0603	.1523
Aortic root dimension at first echocardiogram	0.0811	0.0399	.0524
Aortic root beta stiffness at first echocardiogram	0.0397	0.0114	<b>.0017</b>
Age at first echocardiogram	-0.0929	0.0585	.1237
Aortic root dimension at first echocardiogram	0.0791	0.0387	.0518
Aortic root elastic modulus at first echocardiogram	0.0004	0.0001	<b>.0007</b>

Bold values refer to statistical significance. *SE*, Standard error.



**FIGURE 3.** A, Rate of aortic root dilation for patients with beta stiffness indices (*BSIs*) above and below the median at baseline ( $>$ median is stiffer). B, Rate of aortic root dilation for patients with an elastic modulus (*EM*) above and below the median at baseline ( $>$ median is stiffer). The *upper and lower borders* of the box represent the upper and lower quartiles. The *middle horizontal line* represents the median. The *upper and lower whiskers* represent the maximum and minimum values of nonoutliers. *Extra dots* represent outliers.

$0.38 \pm 0.08$  mm/year;  $P = .01$ ) compared with the NSx group.

The follow-up time from first to last echocardiogram was  $43.4 \pm 7.7$  months in the Sx group and  $85.9 \pm 10.8$  months in the NSx group. At the time of the follow-up echocardiogram, the incidence of greater than trivial mitral valve regurgitation remained the same for the Sx group and increased to 11 (79%) in the NSx group. Additionally, at follow-up echocardiogram, 13 (72%) patients in the Sx group had greater than trivial aortic valve regurgitation and the number remained at 4 (28%), unchanged, in the NSx group.

## DISCUSSION

AoR dilation rate and dimension are the main clinical tools to determine the timing of AoR surgery in patients with MFS.<sup>7</sup> In this cohort, we demonstrated that AoR dilation rate varies among adult MFS patients and is associated

with baseline AoR stiffness, measured by echocardiography. In addition, we demonstrated that Sx group had higher AoR stiffness at baseline and faster AoR dilation compared with the NSx group.

Altered extracellular matrix composition in aortic media manifesting as elevated aortic stiffness, along with altered hemodynamic shear forces contribute to progressive aortic dilation in patients with MS.<sup>13,15</sup> Aortic stiffness assessed by echocardiography, cardiac magnetic resonance imaging, and arterial tonometry has more recently been proposed as supplementary prognostic information to AoR dimension although studies have been few.<sup>12,14,16</sup> The largest study to date assessing pediatric and young adult patients (aged 6 months to 25 years) with MFS by the Pediatric Heart Network (funded by the National Institutes of Health/National Heart, Lung, and Blood Institute), reported a higher baseline AoR stiffness, measured by echocardiogram, is associated with faster rate of AoR dilation.<sup>12</sup> Similarly, Prakash and colleagues<sup>16</sup> reported higher aortic stiffness measured by cardiac magnetic resonance imaging to be associated with higher rates of AoR dilation in children and young adults (median age, 20 years) with connective tissue disorders, in addition to segmental stiffness variation across the aorta with the AoR being significantly stiffer than the ascending or descending aorta. Our findings confirmed that these findings translate into the adult MFS population because baseline EM and beta SI values measured by echocardiography are associated with significantly higher rates of aortic dilation. By validation of these prior findings in the adult MFS population, we hope to introduce a simple tool that could be incorporated to the surveillance of adult MFS patients. A simple measurement of maximum and minimum measurements of the AoR at the level of sinuses of Valsalva by echocardiography allows calculation of stiffness and has the potential to predict AoR dilation.

The study by the Pediatric Heart Network also reported that baseline AoR EM independently predicted the composite clinical outcome of aortic-root surgery, dissection, or death, even after adjusting for baseline age and AoR  $z$  score,<sup>12</sup> similarly to Prakash and colleagues<sup>16</sup> who reported higher aortic stiffness measures to be associated with higher rates of surgery. Our data in adult MFS patients suggest the same with a significant association between baseline EM and beta SI and AoR surgery.

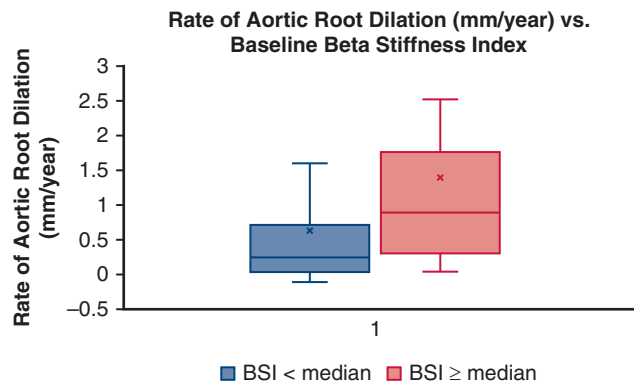
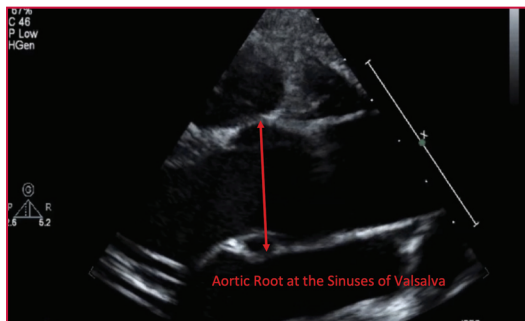
Some studies have suggested a differential effect on rate of AoR dilation between different pharmacotherapies, such as atenolol reducing stiffness in their cohort, whereas losartan did not demonstrate a significant difference.<sup>12</sup> Other groups, such as Bhatt and colleagues<sup>19</sup> reported potential benefits of both medications via distinct mechanisms of action. Although data remain somewhat contradictory at this time, perhaps baseline measures of stiffness will not only identify high risk patients who should be treated more aggressively with pharmacotherapy, but also help to choose



**Aortic Root Dilation in Adult Marfan Patients: Does Aortic Stiffness Matter?**

- 32 adult Marfan patients
- Aortic root dilation rate and stiffness were calculated by 2D echocardiography.

$$\text{Beta stiffness index} = [\ln(\text{Systolic BP}/\text{Diastolic BP})] / [(\text{Aortic Root in Systole} - \text{Aortic Root in Diastole}) / \text{Aortic Root in Diastole}] \text{ BP} = \text{blood pressure}$$



**Aortic root dilates faster in Marfan patients with stiffer aortas!**

- Aortic root dilation rate in the entire cohort was 0-8 mm/year and correlated with baseline aortic root stiffness (beta stiffness index,  $r = 0.534$ ,  $P = .002$ ) but not with baseline age or aortic root dimension.

• Aortic root stiffness, easily obtained by 2D echocardiography, could potentially identify patients that could benefit from more aggressive pharmacotherapy and personalize surveillance protocols in Marfan patients.

**FIGURE 4.** Aortic root dilates faster in patients with Marfan syndrome with stiffer aortas. The upper and lower borders of the box represent the upper and lower quartiles. The middle horizontal line represents the median. The upper and lower whiskers represent the maximum and minimum values of nonoutliers. Extra dots represent outliers. EM, Baseline elastic modulus; BSI, baseline beta stiffness index.

the more effective agent. Of note, most of our patients were treated with a beta blocker and very few with an angiotensin receptor blocker, limiting assessment of differential effects of these drugs on stiffness in our cohort.

Also of interest, recent studies have shown an increase in AoR stiffness despite normal AoR dimensions<sup>13</sup> and an increase in aortic stiffness in the normal-sized aorta distal to the AoR.<sup>22</sup> In adult patients with MFS, per the 2010 American College of Cardiology/American Heart Association/American Association for Thoracic Surgery thoracic aorta guidelines, pharmacotherapy is recommended regardless of AoR dimension<sup>7</sup>; however, risk stratification remains an important issue to address.

The findings that stiffness measurements are abnormal even in the setting of normal AoR size, in addition to our data that AoR dilation is associated with baseline stiffness measures in adult patients with MFS, suggests potential utility of stiffness measurements in identifying high-risk MFS, who could potentially benefit from additional pharmacologic therapy or closer monitoring. Because there are no normative data in aortic stiffness in patients with Marfan syndrome, the median cutoff values we reported might provide some threshold for clinicians. Baseline aortic stiffness measurement not only has the potential to identify patients at higher risk, but it could also potentially guide individualized echocardiogram surveillance. Individualized

echocardiogram surveillance would allow for more frequent assessment in high-risk patients, while lessening the burden of unnecessary appointments on lower risk patients. The potential effect this could have on resource utilization should be assessed in future studies.

**Limitations**

There are several limitations to our study, including the small size of the patient cohort and the retrospective nature of the data collection, which did not allow for assessment of potential effects of pharmacologic therapy and genotype or granular data on indications for AoR surgery. Additionally, there were some limitations in obtaining full clinical data, including indication for AoR surgery for each patient given the inconsistencies in electronic medical review charting. It is also important to recognize that the blood pressure measurements were obtained during the clinic visit within a few hours of the echocardiogram, but not necessarily at the same time the AoR images were acquired or several times allowing an average that is suboptimal; however, it does reflect clinical practice. Finally, many patients had echocardiograms performed before their transfer of care to our institution and we did not have access to that information. Because some patients are referred to our center later during their MFS follow-up for close monitoring before aortic surgery, our study might inherently have ascertainment bias.

TABLE 3. Measurements at the time of the first and at follow-up echocardiogram

Measurement	Surgery	No surgery	P value
At first echocardiogram			
Systolic blood pressure (mm Hg)	113.4 (105.8-121.2)	110.4 (104.1-116.8)	.529
Diastolic blood pressure (mm Hg)	65.1 (59.4-70.7)	68.4 (63.1-73.6)	.368
Aortic root dimension, systole (cm)	4.27 (4.05-4.49)	3.73 (3.37-4.09)	.011
Aortic root dimension, diastole (cm)	4.13 (3.92-4.33)	3.59 (3.25-3.94)	.010
Elastic modulus (mm Hg)	1967 (1549-2385)	1353 (1017-1689)	.021
Beta stiffness index	23.2 (17.8-28.6)	15.6 (11.6-19.7)	.024
At follow-up echocardiogram			
Systolic blood pressure (mm Hg)	123.1 (113.8-132.5)	116.4 (110-123)	.233
Diastolic blood pressure (mm Hg)	70.8 (66.3-75.3)	70.1 (62.8-77.4)	.851
Aortic root dimension, systole (cm)	4.62 (4.37-4.88)	4.01 (3.57-4.45)	.018
Aortic root dimension, diastole (cm)	4.46 (4.22-4.70)	3.83 (3.40-4.26)	.012
Elastic modulus (mm Hg)	1669 (1258-2079)	1842 (596-4330)	.639
Beta stiffness index	19.5 (6.5-54.2)	18.7 (4.1-56)	.902

Values are presented as median (interquartile range).

## CONCLUSIONS

In this cohort, we demonstrated that AoR dilation rate varies among adult patients with MFS and is associated with baseline AoR stiffness, measured by echocardiography. Patients who underwent AoR surgery had higher AoR stiffness at baseline as well as faster AoR dilation compared with patients who did not undergo AoR surgery during the follow-up period, independent of the baseline AoR dimension. Our data suggest that baseline measures of stiffness could potentially allow for more precise prognostication in adult patients with MFS. This measure, easily obtained by 2-dimensional echocardiography, could potentially identify patients who could benefit from more aggressive pharmacotherapy and personalize surveillance protocols in this patient population. Further studies are warranted to determine how aortic stiffness can be implemented clinically to refine management in patients with MFS.

## Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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