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ORIGINAL ARTICLE

Can 10 000 Healthy Steps a Day Slow Aortic Root Dilation in Pediatric Patients With Marfan Syndrome?

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BACKGROUND: Stiffer aortas are associated with a faster rate of aortic root (AoR) dilation and higher risk of aortic dissection in patients with Marfan syndrome. We have previously shown that mild aerobic exercise reduces aortic stiffness and rate of AoR dilation in a Marfan mouse model. In this study, we investigated if these results could be translated to pediatric patients with Marfan syndrome.

METHODS AND RESULTS: We enrolled 24 patients with Marfan syndrome aged 8 to 19 years to participate in a 6-month physical activity intervention, excluding those with ventricular dysfunction or prior history of aortic surgery. We instructed patients to take 10 000 steps per day, tracked by an activity tracker. At baseline and 6 months, we measured AoR dimension, arterial stiffness, endothelial function, physical activity indices, inflammatory biomarkers, and coping scores. Controls consisted of 15 age-matched patients with Marfan syndrome. Twenty-four patients with Marfan syndrome (median age, 14.4 years [interquartile range {IQR}, 12.2–16.8], 14 male patients) were enrolled. Baseline assessment demonstrated that the majority of these patients were sedentary and had abnormal arterial health. Twenty-two patients completed the intervention and took an average of 7709±2177 steps per day (median, 7627 [IQR, 6344–9671]). Patients wore their Garmin trackers at a median of 92.8% (IQR, 84%–97%) of their intervention days. AoR *Z* score in the intervention group had a significantly lower rate of change per year compared with the controls (rate of change, −0.24 versus +0.008; *P*=0.01).

CONCLUSIONS: In this clinical intervention in pediatric patients with Marfan syndrome, we demonstrated that a simple physical activity intervention was feasible in this population and has the potential to decrease the AoR dilation rate.

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Key Words: aortic root ■ children ■ dilation ■ exercise ■ Marfan syndrome

Aortic root (AoR) dissection remains the most life-threatening complication of Marfan syndrome (MFS), characterized by weakening of the aortic wall because of fragmentation of elastin fibers that is reportedly associated with a significant increase in the expression levels of TGF-β1 (transforming growth factor β1) in the blood and aortic tissue.[1] Increase in circulating TGF-β1 along with unrestrained production and activation of matrix metalloproteinases (MMPs), particularly MMP-2 and MMP-9, results in augmented degradation of aortic elastin fibers and subsequent weakening of the aortic wall, leaving it more prone to dissection and rupture. To date, because of the risk of aortic dissection, clinical emphasis has focused on educating patients with MFS on what types of exercise to avoid, rather than promoting safe and effective ways to incorporate regular exercise into their lifestyles. Patients with MFS also often have sedentary lifestyles because of self-imposed

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CLINICAL PERSPECTIVE

What Is New?

- Pediatric patients with Marfan syndrome lead sedentary lives.
- A simple physical activity intervention, defined as 10 000 steps per day, is feasible in this population.
- This simple physical activity intervention has the potential to decrease the aortic root dilation rate.

What Are the Clinical Implications?

- These results might help shift the focus from exercise restrictions in pediatric patients with Marfan syndrome to promotion of exercise.
- Our findings warrant further clinical studies to carefully evaluate the impact of exercise, possibly different types of exercise, on aortic root dilation in this patient population, probably best achieved by a multicenter randomized exercise intervention.

Nonstandard Abbreviations and Acronyms

AoR	aortic root
MFS	Marfan syndrome
MMP	matrix metalloproteinase
TGF-β1	transforming growth factor β1

limitations and difficulty coping with their diagnosis.[2] In our recent published report using a well-established mouse model of MFS that carries a missense mutation in the gene encoding for fibrillin-1 protein (*FBN1 C1041G*$^{+/-}$), we showed that daily mild aerobic exercise (55%–65% maximal oxygen consumption) can block progression of AoR aneurysm in mice, while significantly improving aortic wall elasticity and elastin fiber structural integrity.[3] In addition, beneficial effects of exercise on AoR growth and wall elasticity were associated with a significant decrease in the expression levels of MMP-2 and MMP-9 within the aortic wall tissue.[3] In this study, we investigated if these results could be translated to pediatric patients with MFS. Here, we report the impact of a simple physical activity intervention, taking 10 000 steps per day for 6 months, on the AoR dilation rate and stiffness as well as coping mechanisms in pediatric patients with MFS.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Participants and Recruitment

Participants were identified from the clinic roster at Lucile Packard Children's Hospital. Subjects were eligible if they met all the inclusion criteria as follows: (1) MFS by revised Ghent criteria[4]; (2) aged 8 to 19 years; and (3) cardiac clearance to exercise by cardiologist. Subjects who had ventricular dysfunction or prior history of AoR surgery were excluded.

All study materials and procedures were approved by the Stanford University Institutional Review Board (IRB-37176). Approval of the protocol and any changes were maintained throughout the study. Participants and parents signed assent and consent forms. Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of our research.

Fifteen age-matched controls with 2 echocardiograms at least 6 months apart were randomly chosen from the list of eligible patients with MFS. Two of these patients were initially approached for participation in the intervention and declined to participate, citing lack of time or personal reasons.

Study Visit Testing

Participants visited our center for study testing at baseline and at 6 months. Height, weight, and blood pressure (BP) were obtained. Other study testing included (1) endothelial function testing, (2) arterial stiffness testing, (3) echocardiogram, (4) bloodwork (lipid profile), (5) questionnaires, and (6) physical activity monitoring by accelerometry.

Endothelial function and arterial stiffness were evaluated following the previously described protocols for endothelial pulse amplitude testing (Itamar Medical, Caesarea, Israel)[5] and noninvasive applanation tonometry (SphygmoCor; ATCOR-Medical, Sydney, Australia).[6] The applanation tonometry was used to obtain augmentation index and pulse wave velocity.

The echocardiogram was performed by a pediatric sonographer to acquire the 2-dimensional AoR video clips over 10 consecutive beats. The AoR was measured by a blinded observer in triplicate in both systole and diastole following the pediatric American Society of Echocardiography guidelines.[7] To measure intraobserver variability, 10 studies were randomly chosen and remeasured by a second blinded observer.[8] *Z* scores for all AoR measurements were calculated using Boston Children's Hospital's *Z* score website (http://zscore.chboston.org). Elastic modulus and β-stiffness index were calculated using the following formulae:

$$\text{Elastic Modulus} = (\text{Systolic BP} - \text{Diastolic BP} \left[(\text{AoR\_Systole} - \text{AoR\_Diastole})/\text{AoR\_Diastole.}\right])$$

$$\beta - \text{Stiffness index} = \left[\ln(\text{Systolic BP}/\text{Diastolic BP})\right] / \left[(\text{AoR\_Systole} - \text{AoR\_Diastole})/\text{AoR\_Diastole.}\right]$$

Participants were given a Garmin Vivofit 3 (Olathe, KS), which synched their step count to a dashboard accessible by the study coordinator. Accelerometry via Geneactiv (Activinsights, Kimbolton, United Kingdom) was used to measure participant activity levels over 7 days at baseline.[9]

Participants and their parents also completed a questionnaire at each visit, including the brief coping orientation to problems experienced survey, a validated multidimensional coping inventory to assess a broad range of coping styles.[8]

Intervention

Study participants were instructed to aim for 10 000 steps per day for the duration of the 6-month intervention. The study coordinator checked in with the participants weekly either by text, phone call, or email based on participant preference to remind participants to wear the Garmin device daily, provide encouragement and ideas on how to incorporate more steps, and noted any changes or issues that occurred during the week.

Adherence to wearing the Garmin was defined as any days with ≥1000 steps.[10] Average daily steps per month were determined by total steps during the month divided by the number of days the device was worn that month.

Measurements of Plasma Biomarkers

Blood samples were collected from study participants at baseline and 6 months after the intervention start time using a BD Vacutainer tube containing K2 EDTA 10.8 mg as an anticoagulant (catalog number 367863; Franklin Lakes, NJ). Collected blood (5 mL) was centrifuged for 30 minutes at 1000*g* in a refrigerated centrifuge, followed by centrifugation at 10 000*g* for 10 minutes to ensure the removal of platelets and avoid potential platelet degranulation. Plasma samples were immediately collected and aliquoted (300 μL) into small CryoTubes (Thermo Scientific Nalgene System, Rochester, NY) and stored at −80 °C for future assays. Later, the standard ELISA was used to measure total circulating TGF-β1 (human TGF-β1 ELISA kit, Abcam number 100647), MMP-2 (human MMP2 ELISA Kit, Abcam number 267813), and MMP-9 (human MMP9 LISA Kit, Abcam number 246539) in plasma samples using commercially available kits (Abcam, Waltham, MA) and according to the manufacturer's protocol as described previously.[11] The plasma levels of the blood biomarkers were compared between samples collected at baseline and after intervention.

Statistical Analysis

We used a Wilcoxon signed rank test for paired comparisons between baseline and postintervention values for each patient. The median and interquartile ranges were calculated. We also reported the standardized mean difference, which showed the standardized magnitude of between-group differences and allowed us to compare differences across variables with different scales. The interobserver variability for AoR measurements by echocardiography was reported as percent difference calculated as difference between the average of triplicate measurements divided by the average ×100. Statistical analysis was performed using Stata 16.0 (StataCorp, College Station, TX). Statistical significance was defined at $P<0.05$. Data were collected in research electronic data capture (Stanford University).

RESULTS

Study Cohort

Twenty-four patients enrolled and completed the baseline study visit (14 male patients, 10 female patients; median age at baseline, 14.4 years) (Table 1). Twenty-two out of 24 participants were on atenolol and/or losartan, and 2 reported taking no prescription medications. Two participants did not return for postintervention testing and were lost to follow-up. Two participants were injured because of non–study-related causes that temporarily affected their ability to

Table 1. Clinical Characteristics of Intervention Patients Versus Controls at Baseline

Clinical characteristics at baseline	Intervention median (IQR), N=24	Control median (IQR), N=15	SMD	*P* value
Age, y	14.4 (12.2–16.8)	12.5 (11.2–15.2)	−0.49	0.11
Body surface area, m^2	1.7 (1.4–1.9)	1.6 (1.4–1.7)	−0.30	0.26
Systolic blood pressure, mm Hg	109 (99–117)	111 (103–118)	0.35	0.50
Diastolic blood pressure, mm Hg	70 (63–75)	68 (63–79)	0.37	0.48
Aortic root dimension, systole, cm	3.4 (3.1–4.0)	3.3 (3.2–3.8)	−0.06	0.91
Aortic root *Z* score	2.3 (1.7–4.3)	2.9 (2.4–4.5)	0.16	0.29
Aortic root β-stiffness index	6.8 (4.7–11.0)	4.8 (4.0–9.3)	−0.37	0.24
Aortic root elastic modulus, mm Hg	603 (411–923)	465.2 (367–779)	−0.24	0.42

IQR indicates interquartile range; and SMD, standardized mean difference.

adhere to the intervention. Nonetheless, both participants completed the 6-month intervention and came in for their follow-up study visit at the end of 6 months.

Baseline Measurements in Intervention Patients

Our baseline assessment by an accelerometer showed that participants spent the majority of their time in sedentary or light activity, with a median of 73.1% (interquartile range [IQR], 69.6%–79.2%) and a median of 10.6% (IQR, 8.7%–11.5%), respectively (Table 2).

AoR *Z* scores at baseline were at a median of 2.26 (IQR, 1.71–4.13). Eight out of 24 patients had AoR *Z* scores between 0 and 2, 6 patients had AoR *Z* scores between 2 and 3, 3 patients had AoR *Z* scores between 3 and 4, and 7 patients had *Z* scores above 4.

Median augmentation index (at 75 bpm) was 6.3 (IQR, 2.5–12.8), with 23 out of 24 participants having abnormal values above −2 at baseline. Median pulse wave velocity was 5.5 (IQR, 4.8–5.9) m/s, with 14 out of 24 participants having abnormal values at baseline (>4.5 m/s for age <14 years) and >5.5 m/s for age ≥14 years. All of the 15 patients who had endothelial function testing had abnormal endothelial function defined as <1.9 reactive hyperemia index at baseline. The median value for the cohort was 1.3 (IQR, 0.9–1.5).

Adherence and Step Count in Intervention Patients

The participants wore the Garmin device at a median of 92.8% (IQR, 84%–97%) of days during the intervention. In their first month of the intervention, participants took a monthly average of 8016±2388 steps per day. During their first month, 11 participants took an average of 5000 to 7499 steps per day, 6 participants took an average of 7500 to 10 000 steps per day, and 5 participants took an average of >10 000 steps per day.

Five participants took an average of at least 10 000 daily steps throughout the 6-month intervention. In their last month of intervention, participants took an average of 7415±2753 steps per day. Four participants took an average of <5000 steps, 6 participants took an average between 5000 and 7499 steps per day, 8 participants took an average of 7500 to 10 000 steps per day, and 4 participants took an average of >10 000 steps per day in the last month of the intervention.

Baseline Versus Postintervention Measurements in Study Participants

After intervention, there were no significant changes in any of the study testing indices from baseline (Table 2).

Baseline Versus Follow-Up Measurements in Controls

The median age of 15 control patients was 12.5 years (IQR, 11.2–14.7 years), similar to intervention patients. Thirteen of these patients were on atenolol and/or losartan. At their first echocardiogram, the median AoR *Z* score was 2.9 (IQR, 2.4–3.9). At the follow-up echocardiogram, the median AoR *Z* score was 3.3 (IQR, 2.4–4.2).

Aortic Measurements in Intervention Patients Versus Controls

At baseline, there were no differences in AoR *Z* scores or AoR stiffness indices between the intervention and age-matched control patients (Table 1). As shown in Figure 1, AoR dimension rate of change per year was 0.13 cm/y in controls versus −0.01 cm/y in the intervention group (P=0.17). AoR *Z* score rate of change per year was 0.008 in controls versus −0.24 in the intervention group (P=0.01). Lastly, AoR stiffness (β-stiffness) rate of change per year was 3.83 in controls versus 0.37 in the intervention group (P=0.25) (Figure 1).

Coping Orientation to Problems Experienced Survey Results in Intervention Patients

At baseline, coping mechanisms that were reported as having the highest scores were acceptance, self-distraction, and positive reframing (Table 2). After intervention, the 3 most used coping mechanisms remained unchanged. Use of dysfunctional coping mechanisms remained low, with substance use, behavioral disengagement, and venting receiving the lowest possible median scores at both baseline and after intervention.

Biomarker Analysis in Intervention Patients

There was no significant difference in the plasma levels of MMP-2, MMP-9, and total TGF-β1 in study participants from baseline to after intervention (Figure 2).

Interobserver Variability for Aortic Measurements

There was excellent agreement on AoR measurements by echocardiography between the 2 observers, with a median difference of 1.5% (range, 0.29%–5.6%).

DISCUSSION

In this clinical intervention in pediatric patients with MFS, we demonstrated that a simple physical activity

Table 2. Clinical Characteristics in the Intervention Patients at Baseline and After Intervention

Characteristic	Baseline median (IQR), N=24	After intervention median (IQR)*		
Anthropometrics		N=23	SMD	*P* value
Height, cm	175 (166–184)	177 (169–185)	−0.11	0.72
Weight, kg	59 (42–74)	62 (42–72)	−0.02	0.97
Body mass index, kg/m^2	18 (15–23)	18.4 (15–22)	0.17	0.88
Blood pressure	N=24	N=23		
Average systolic blood pressure, mm Hg	109 (99–117)	110 (103–117)	−0.14	0.59
Average diastolic blood pressure, mm Hg	70 (63–75)	69.3 (67–75)	−0.30	0.59
Vascular testing	N=24	N=22		
Endothelial function, RHI, n=15 pre, 15 post*	1.3 (0.9–1.5)	1.6 (1.2–1.7)	−0.71	0.074
Average pulse wave velocity, m/s	5.5 (4.8–5.9)	5.7 (5.3–6.1)	−0.37	0.23
Average augmentation index at 75 bpm, %	6.3 (2.5–12.8)	3.8 (1.0–12.3)	0.04	0.52
Echocardiographic data	N=24	N=22		
Aortic root dimension, systole, average, cm	3.4 (3.1–4)	3.3 (3.1–3.8)	0.08	0.81
Aortic root *Z* score	2.3 (1.7–4.3)	2.1 (1.4–3.8)	0.12	0.54
Aortic root β-stiffness index, n=22 post	6.8 (4.7–11)	6.8 (5.1–8.4)	0.07	0.81
Aortic root elastic modulus, n=22 post	603 (411–923)	592 (457–726)	0.013	0.93
Bloodwork	N=23	N=18		
Cholesterol, mg/dL	138 (127–158)	141 (122–147)	0.14	0.81
Triglyceride, mg/dL	63 (40–104)	87 (58–102)	−0.19	0.41
High-density lipoprotein, mg/dL	46 (42–59)	45 (36–56)	0.13	0.58
Low-density lipoprotein, mg/dL	80 (69–89)	72 (62–86)	0.21	0.49
COPE survey scores	N=22	N=21		
Self-distraction	5 (3–7)	6 (4–7)	−0.21	0.53
Active coping	4 (4–6)	5 (4–6)	−0.07	0.67
Denial	2 (2–2)	2 (2–2)	−0.29	0.57
Substance use, n=15 pre, 14 post	2 (2–2)	2 (2–2)	−0.33	0.48
Use emotional support	4 (3–6)	4 (3–6)	0.12	0.56
Behavioral disengagement	2 (2–3)	2 (2–3)	0.04	0.92
Venting	2 (2–4)	3 (2–4)	−0.17	0.63
Positive reframing	5 (4–7)	5 (4–6)	0.19	0.61
Planning	4 (2–5)	4 (2–5)	−0.17	0.47
Humor	5 (2–7)	4 (2–6)	0.31	0.31
Acceptance	7 (6–8)	8 (5–8)	−0.12	0.52
Religion	5 (3–6)	4 (3–6)	0.04	0.92
Self-blame	3 (2–3)	3 (2–3)	0.10	0.89

COPE indicates coping orientation to problems experienced; IQR, interquartile range; RHI, reactive hyperemia testing; and SMD, standardized mean difference.

*We started performing endothelial function testing later in the study and only tested 15 patients.

intervention of 10 000 steps per day for 6 months was feasible in this population and has the potential to decrease the AoR dilation rate. Because the focus has been more on exercise restrictions for patients with MFS rather than promotion of exercise, these results might help shift the paradigm in this patient population.[12]

Average daily steps for healthy children have been reported as 10 000 to 13 000 steps per day for girls and 12 000 to 16 000 steps per day for boys aged 5 to 19 years, with steps decreasing throughout adolescence, with average steps for 18-year-olds at 8000 to 9000 per day. In children with illnesses, increasing physical activity remains a challenge.[13]

A 2003 to 2004 study that examined sedentary behaviors in 6329 participants aged ≥6 years, who wore an activity monitor for at least 7 days, found that participants spent 54.9% of monitored time, or 7.7 hours, in sedentary activity.[14] In our participants, at baseline, a median of 73.1% (IQR, 69.6%–79.2%) of a 7-day period was spent

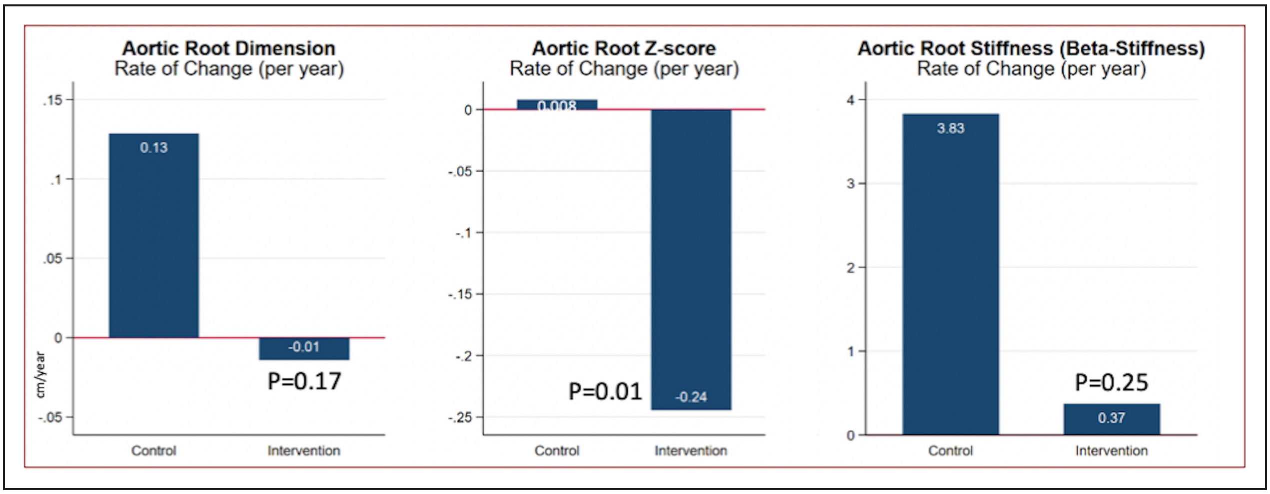

Figure 1. Aortic root *Z* score and stiffness in patients with Marfan syndrome in controls versus intervention group.
Aortic root *Z* score in the intervention group has a significantly lower rate of change per year compared with the controls.

in sedentary activity as tracked by the accelerometer, which is much higher than in healthy populations.

Several factors play into the adherence to any exercise intervention, such as wearing the physical activity monitor, follow-up with the intervention team, and peer support. During the period of our intervention, our participants wore their physical activity monitor most of the time. A study by Evans et al investigated the adherence of wearing of physical activity monitors in fifth-grade students and found that average adherence of wearing the device was 64.1%. After this feasibility testing, these investigators assigned the children to different groups, including physical activity monitor only, physical activity monitor plus goal and incentive-based intervention, and controls. Average adherence was 73.4% and 80.2% for monitor + intervention versus monitor-only groups, respectively, and no significant differences in changes in steps in any group was observed.[15] Our participants wore the device 92.8% of their intervention days, which could potentially be attributed to our weekly reminder texts. Although we should point out that 1 of our participants mentioned that they thought it was uncool to wear the device.

In our study, all our participants had stiff aortas and most had abnormal endothelial function. Previous exercise intervention studies have shown improvements in arterial stiffness and endothelial function in pediatric patients, even over an intervention duration of 3 months.[16,17] These studies, however, were combined with dietary intervention or monitoring. Although we did not see any statistically significant changes in any of the indices in the current study, endothelial function improved in 12 patients, and pulse wave velocity and augmentation index (augmentation index adjusted for a heart rate of 75) decreased in 7 and 13 patients, respectively, suggesting that vascular health is trending in the right direction and improving for some of these patients.

In the MFS mouse model, we and others have shown that a mild treadmill exercise regimen over a 5-month period can significantly lower AoR dilation.[3,18] Although the previous study by our group showed improvement in aortic wall rupture point and reversibility of elasticity in the aortic segments isolated from exercised MFS mice,[3] another study by Mas-Stackurska et al did not report any difference in AoR stiffness between the exercise and sedentary groups.[18] In the current report, our results support the translation of previous findings using the MFS animal model, because the AoR *Z* score in the intervention group had a significantly lower rate of change per year compared with the controls (rate of change, −0.24 versus +0.008; *P*=0.01). However, we did not detect any significant difference in AoR stiffness (rate of change, 0.37 versus 3.82; *P*=0.25) in our study cohort.

It is well established that MMP-2 and MMP-9 contribute to the progression of aortic wall destruction mainly by degrading medial elastin fibers, and that MMP inhibition can block the progression of aortic aneurysm in the mouse model.[19–21] In addition, because of mutations in the fibrillin-1 gene in MFS, the abnormal fibrillin-1 protein is not capable of sequestering TGF-β1 within the extracellular matrix space, therefore leading to an increase in TGF-β1expression and bioavailability in the blood circulation and aortic tissue.[22,23] Other groups have reported an increase in circulating levels of TGF- β1 in patients with MFS blood.[22,24] However, in our previously published study, we were not able to detect any significant differences in total and free TGF-β1 levels in the blood samples collected from a MFS cohort as compared with healthy controls.[11] We also reported an increase in MMP-2 expression, with no detectable difference observed in MMP-9 expression

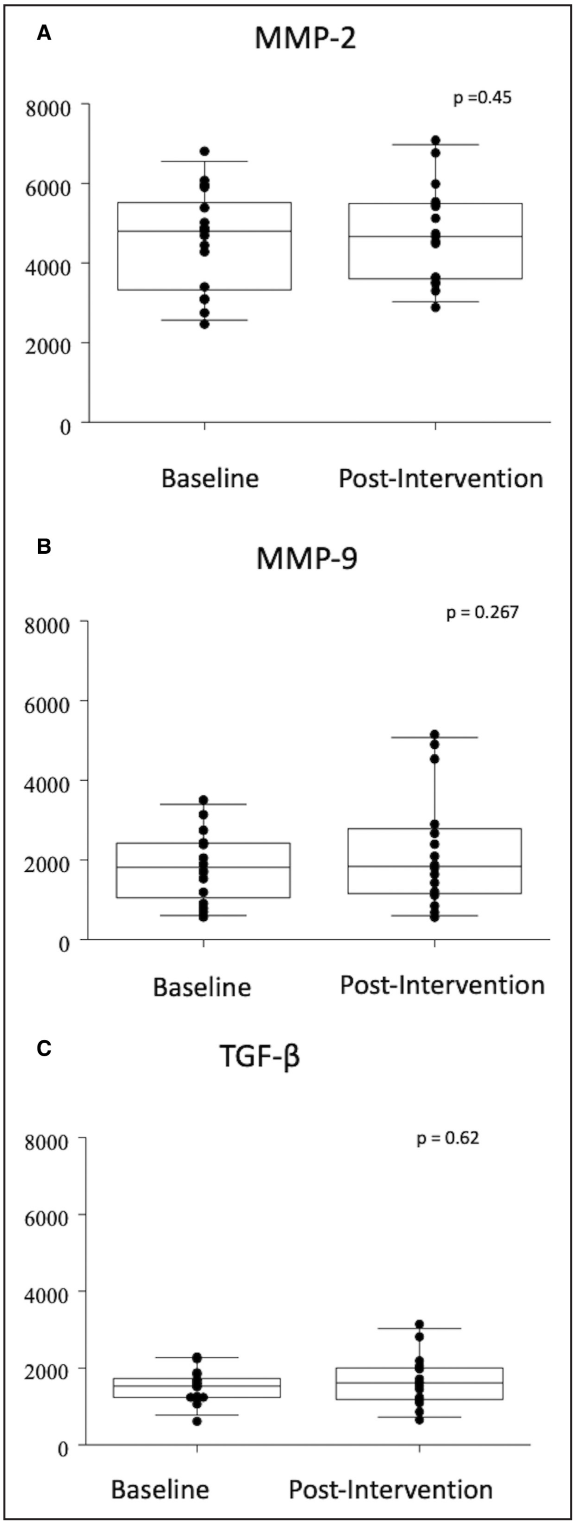

Figure 2. Biomarker analysis from baseline to after intervention in study participants.
There was no significant difference in the plasma levels of MMP-2 (**A**), MMP-9 (**B**), and TGF-β1 (**C**) in study participants from baseline to after intervention. MMP indicates matrix metalloproteinase; and TGF-β, transforming growth factor β.

levels between MFS and control subjects.[11] In the present study, we measured the levels of total TGF-β1, MMP-2, and MMP-9 in our cohort at baseline and after intervention, and did not detect any significant differences. Although, the lack of impact of our intervention on the expression levels of these important disease markers could be because of various factors, such as the nature or design of this specific intervention or the age of the participants, the observation warrants further investigations on whether these markers can be considered as reliable blood biomarkers for diagnostic or prognostic purposes in patients with MFS. It is also noteworthy to add that recent studies have questioned the importance of TGF-β as the main pathologic factor through all stages of aneurysm formation and development in MFS,[25,26] therefore reintroducing TGF-β as a marker of impaired aortic tissue repair machinery rather than the main primary culprit responsible for initiating aortic wall aneurysm formation.[26,27] It is also important to look at the effects of a long-term exercise intervention on blood biomarkers in this patient population.

To date, only a few prior studies have reported on coping mechanisms in patients with genetic aortic disorders.[28,29] In 1 of these studies, 21 adults showed that dysfunctional coping mechanisms were infrequent; however, 22% participants reported little or no acceptance, and 43% avoided life planning in response to a diagnosis of genetic aortic disorder.[29] These reports agree with our findings. Another study by Thiejssen et al showed differences in coping styles between men and women, where men scored significantly higher on the denial coping style than women.[28] There is a report on the impact of exercise in children with chronic illness such as cancer, where physical exercise is related to higher quality of life.[30]

LIMITATIONS

This intervention was not a controlled or randomized intervention because the control group was a clinical cohort; thus, selection bias could have influenced our results. It is conceivable that those who were willing to participate in the study were already engaging in regular exercise or had better adherence to their prescribed medications, thus contributing to more positive health outcomes (slower AoR dilation rates) compared with controls. Because there are no clear pediatric guidelines on exercise participation in children with MFS, patient selection might also be biased by the cardiologist. It is also a relatively small cohort, which limits further subanalyses. We are also limited in our observation of patients' adherence of relying on wearing their activity tracker. Reports on activity tracker usage acknowledge that tracker data are typically incomplete, because individuals tend to not wear their devices all day.[31] The data may be underreporting the actual daily step counts, because the tracker does not state how many hours a day the participants wore the devices, which could range from all waking hours to just a subset of hours in a day. When no steps were counted on a certain day, we were not sure if the participants were truly sedentary or active on that specific day.

CONCLUSIONS

In this clinical intervention in pediatric patients with MFS, we demonstrated that a simple physical activity intervention of 10 000 steps per day for 6 months was feasible in this population and has the potential to decrease the AoR dilation rate. Because the focus has been more on exercise restrictions for patients with MFS rather than promotion of exercise, these results might help shift the paradigm in this patient population. Our preliminary findings warrant further clinical studies to carefully evaluate the impact of exercise, possibly different types of exercise, on AoR dilation in this patient population, probably best achieved by a multicenter randomized exercise intervention.

ARTICLE INFORMATION

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Disclosures

None.

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