Exercise, Sports Participation, and Quality of Life in Young Patients with Heritable Thoracic Aortic Disease

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ABSTRACT

MILLETTE, T. J., R. K. RAMCHARITAR, O. J. MONFREDI, M. J. THOMAS, M. R. CONAWAY, and P. N. DEAN. Exercise, Sports Participation, and Quality of Life in Young Patients with Heritable Thoracic Aortic Disease. *Med. Sci. Sports Exerc.*, Vol. 57, No. 2, pp. 260–266, 2025. **Introduction:** Patients with heritable thoracic aortic disease (HTAD) are often restricted from sports and certain types of exercise. This study was designed to investigate the effect of lifetime exercise exposure and competitive sports participation on quality of life (QOL) in patients 15–35 yr old with syndromic (Marfan syndrome, Loeys–Dietz syndrome, and vascular Ehlers–Danlos syndrome) and nonsyndromic HTAD (nsHTAD). **Methods:** This cross-sectional study used questionnaires to assess lifetime exercise exposure and utilized the PedsQL QOL Inventory. We developed an exercise exposure score (EES) to quantify lifetime exercise exposure. Questionnaires were completed via telephone with complimentary medical record review. **Results:** Forty patients were enrolled. Mean age was 26 yr. The diagnosis was Marfan syndrome in 83%. Despite 88% of patients being restricted by their provider, 65% reported competitive sports participation and 93% reported recreational exercise. Participants with an EES greater than the median had significantly better total QOL scores compared with those below the median (78 vs 65, $P = 0.03$). There were significant positive correlations between current frequency of exercise and psychosocial QOL (slope = 3.9, 95% CI = 1.2–6.6, $P = 0.005$), physical QOL (slope = 8.1, 95% CI = 4.1–12, $P < 0.001$), and total QOL score (slope = 6.0, 95% CI = 3.1–9.0, $P < 0.001$). We found no difference in aortic size or need for surgical intervention between those above and below the median EES, or between those who did and did not participate in competitive sports. **Conclusions:** Despite exercise restrictions, young HTAD patients are physically active. Increased lifetime exercise and current physical activity levels were associated with improved QOL in HTAD patients.

Key Words: AORTIC DISSECTION, MARFAN SYNDROME, PHYSICAL ACTIVITY

Although current guidelines encourage regular low-intensity physical activity for individuals with heritable thoracic aortic disease (HTAD), most competitive sports and activities are discouraged (1). The increase in blood pressure, cardiac output, and aortic wall stress that occur with more intense physical activity potentially translates into a higher risk of acute aortic dissection and/or acceleration of aortic dilation (1–3). Despite these concerns, current exercise restrictions are not supported by outcomes-based data linking exercise to adverse outcomes. Moreover, murine models suggest that dynamic exercise may actually mitigate progression of aortopathy in Marfan syndrome (MFS) (4,5).

The benefits of exercise and sports participation on physical and psychological health in the general population are well established (6–9). Those with HTAD already demonstrate poorer quality of life (QOL) and are overall less physically active compared with the general population (10–13). Restricting these same individuals from sports participation may have additive unintended detrimental consequences in this already vulnerable population. Although the most recent AHA recommendations still favor strict restriction for the majority of patients with HTAD, there is a paradigm shift toward a model of shared decision-making surrounding exercise and sports (14,15).

The first aim of this study was to evaluate sports participation and lifetime exercise exposure in patients with HTAD. Second, we sought to determine if greater exercise exposure or participation in competitive sports was associated with improved QOL. The last aim was to determine if greater exercise exposure or participation in competitive sports was associated with adverse cardiovascular events like aortic dilation or dissection.

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Submitted for publication May 2024.
Accepted for publication September 2024.
Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.acsm-msse.org).

0195-9131/25/5702-0260/0
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DOI: 10.1249/MSS.0000000000003570

METHODS

Study design. We performed a single-center, cross-sectional study of patients 15–35 yr old with HTAD. Using ICD-10 codes for the diagnoses of MFS, Loeys–Dietz syndrome (LDS), vascular Ehlers–Danlos syndrome (vEDS), and nonsyndromic HTAD (nsHTAD) (collectively referred to as HTAD hereafter), we queried our electronic medical records system for patient encounters occurring in the 5-yr span from September 1, 2017, to September 1, 2022. Inclusion criteria were current age between 15 and 35 yr, diagnosis of HTAD, ability to provide assent/consent, and ability to complete a questionnaire over the phone. The only exclusion criteria were inability to obtain consent, assent, or contact over the phone. For those below the age of 18 yr (n = 4), verbal assent was obtained from the participant and verbal consent was obtained from their parent. Participants 18 yr and older provided only verbal consent. All interviews were performed via telephone by a single author. The University of Virginia Institutional Review Board for Health Sciences Research approved the study.

Exercise history analysis. We devised an exercise questionnaire to allow us to quantify lifetime exercise exposure. Information collected included the following:

1) Days per week of at least 30 min of moderate to vigorous exercise for ≤14, 15–18, >19 yr of age, and currently. We defined moderate to vigorous exercise as "exercise that causes large increases in heart rate or respiratory rate such that one would not be able to carry on a normal conversation." This definition was extrapolated from that found in the National Health and Nutrition Examination Survey Physical Activity and Physical Fitness questionnaire (14).
2) Competitive sports participation, defined as "an organized team or individual sport that requires systematic training and regular competition against others and places a high premium on athletic excellence and achievement" (15,16).
3) Recreational sports/exercise participation, defined as "activities involving a range of exercise levels from modest to vigorous, that can be practiced on a regular or more inconsistent basis, and that do not require systematic ongoing training or the pursuit of excellence. These sports do not necessarily include a high level of pressure to excel against others." Employment requiring moderate to vigorous physical exertion or exertion beyond the recommended activity restrictions was considered equivalent to participation in a recreational sport.
4) History of physical activity restriction by their provider.

To determine lifetime exercise exposure, before patient enrollment the study team designed an exercise exposure score (EES). This score was created by assigning three points for each competitive sports season and one point for each recreational sports season (or for each year of participation if there was no defined "season"). The EES was calculated from the sum of lifetime competitive and recreational sports participation. For example, if a patient played four seasons of competitive basketball and four seasons of competitive volleyball, they were given a score of 24 (4 seasons × 3 + 4 seasons × 3). If a patient did 3 yr of recreational swimming and two seasons of competitive soccer, they were given a score of 9 (3 yr × 1 + 2 seasons × 3). With the exception of varsity-level competitive sports, sports and exercise before age 14 yr was not included in the EES, as youth sports below this age tend to involve less strenuous training and competition.

QOL analysis. PedsQL Young Adult Quality of Life Inventory and PedsQL Adult Quality of Life Inventory were used for QOL assessment (17). PedsQL scores range from 0 to 100 with a higher score indicative of a higher QOL.

Medical record review. After completion of a participant's phone interview, we accessed the medical record to obtain aortic root and ascending aorta diameters from the most recent echocardiogram, CT, and/or MRI. Measurements were taken from the official imaging report or, in the few echocardiograms in which complete measurements were not listed in the official report, measured according to American Society of Echocardiography recommendations (18). Reviews of additional medical history, including aortic surgery, past and current medications, and available genetic testing, were collected. In patients with histories of prior aortic surgery, only preoperative aortic measurements were collected.

Statistical analysis. The nonparametric Kruskal–Wallis test was used to compare continuous variables like QOL scores between groups, defined by thresholds for EES or participation in competitive sports. The Spearman rank correlation and the linear regression analysis were used to estimate the association between exercise scores, frequency of exercise, and QOL measures. The chi-squared test was used to test for associations between categorical variables such as aortic dilation above or below the median and the need for surgery.

RESULTS

Chart review identified 132 patients with HTAD. Of these, 87 were unable to be contacted, 2 were unwilling to participate, 1 was deceased, and 2 were unable to participate due to significant developmental delay and inability to complete the questionnaires independently. The deceased patient died at 23 yr old from MFS-associated acute aortic dissection. In the 7 months before death, his aortic root and ascending aorta demonstrated rapid dilation—from 4.4 to 4.8 cm and from 4.8 to 5.3 cm, respectively. He reportedly participated in no regular competitive or recreational exercise and was taking losartan and atenolol at the time of his death. The remaining 40 subjects were included.

In this cohort of 40 participants, the mean age was 26 yr, 55% were male, and 83% were White. The most common HTAD diagnosis was MFS (83%, n = 33), followed by vEDS (10%, n = 4), LDS (5%, n = 2), and nsHTAD (2.5%, n = 1) (Table 1).

Of the 33 participants with MFS, 23 had confirmed pathogenic FBN1 variants. Six were diagnosed clinically via the revised Ghent nosology and had inconclusive or no/unavailable genetic testing, although three of those who were not tested had

TABLE 1. Baseline characteristics.

Demographics	Value
Sample size (*n*)	40
Mean age	26
Male, *n* (%)	22 (55)
Race, *n* (%)	33 (83)
Diagnosis, *n* (%)	
MFS	33 (83)
vEDS	4 (10)
LDS	2 (5)
nsHTAD	1 (2.5)
Lifetime recreational/occupational exercise, *n* (%)	37 (93)
Lifetime competitive sports, *n* (%)	26 (65)
Median EES	20 (range 0–60)
Exercise restriction, *n* (%)	35 (88)
Medically managed, *n* (%)	32 (80)
Beta-blocker	19 (48)
ARB	13 (33)

first-degree relatives with confirmed pathogenic FBN1 variants. The specific mode of diagnosis was not able to be definitively confirmed in the remaining four participants with MFS. Each of these patients reported their diagnosis was made by some combination of aortic root dilation, systemic score, and/or genetic testing by their cardiologist, vascular medicine specialist, or geneticist. Of the other seven participants without MFS, five had confirmed pathogenic or likely pathogenic genetic variants. Of the remaining two participants, one had a clinical diagnosis of nsHTAD and the other had LDS with genetic test results that were unavailable (Supplemental Table 1, Supplemental Digital Content, http://links.lww.com/MSS/D97)

There were 18 different adult cardiologists, pediatric cardiologists, and/or vascular medicine physicians caring for these patients, although a core group of three providers cared for the majority of the patients (22 of 40).

Six individuals (15%) had undergone surgery for aortic aneurysm or dissection before interview. One of these was a collegiate basketball player with MFS who had a history of acute aortic dissection that occurred at 22 yr of age while asleep. Before this, he had continued to compete under a shared decision-making agreement with his cardiologist. However, he missed his last cardiology follow-up visit 8 months before dissection. Aortic root diameter at that time was 4.1 cm, which was stable from his previous echocardiogram 6 months prior.

Most of our participants (35 of 40, 88%) reported receiving activity restriction advice from their provider. The five subjects who were not restricted included one with LDS and three with MFS who had normal aortic dimensions. The fifth was the collegiate basketball player mentioned previously. Seven participants reported a history of activity restrictions that were relaxed after years of no significant progression of aortic dilation. Eighty percent (*n* = 32) reported current medical therapy targeting afterload reduction, most commonly beta-blockers (*n* = 19), angiotensin receptor blockers (ARB) (*n* = 13), or both (*n* = 9) (Table 1).

Current frequency of moderate to vigorous exercise ranged from 0 to 7 $d \cdot wk^{-1}$ with mean of 2.2 $d \cdot wk^{-1}$ (Fig. 1).

The large majority (93%) reported some degree of recreational sports participation, with 65% (*n* = 26) reporting competitive sports participation (Table 1). Of those who engaged in competitive sports, only three participated in sports considered safe by current AHA/ACC guidelines (golf, equestrian sports) (Supplemental Table 1, Supplemental Digital Content, http://links.lww.com/MSS/D97) (1,19,20). Four participants' occupations involved demanding physical labor with moderate to vigorous exertion, each year of which was included in their EES as a recreational sports season. These occupations included logging/diesel mechanic, chicken processing plant worker, farmhand, and "field work" for the information and technology industry (details in Supplemental Table 1, Supplemental Digital Content, http://links.lww.com/MSS/D97).

Exercise participation varied widely within our cohort, with EES ranging from 0 to 60 and a median EES of 20—equivalent to 6.5 competitive sports seasons or 20 yr or seasons of recreational sports (Fig. 2). Nearly all participants (90%) with EES greater than the median reported competitive sports participation.

PedsQL physical, psychosocial, and total QOL scores were similar to those previously reported for patients with chronic illnesses, including MFS (12,17).

Participants with EES > median demonstrated higher total QOL scores when compared with those with EES ≤ median

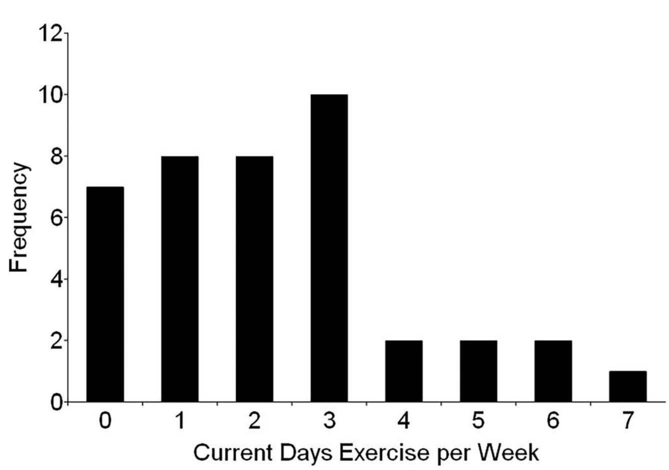

FIGURE 1—Distribution of current days per week of exercise. The mean number of days of exercise per week was 2.2.

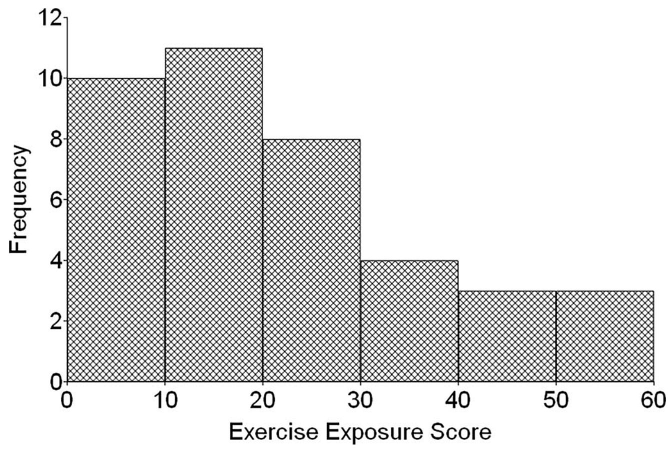

FIGURE 2—Distribution of EES. There was a wide range of EES (0–60). Median EES was 20.

(P = 0.03) (Table 2). Patients who reported participation in competitive sports (n = 26) had higher mean physical, psychosocial, and total PedsQL scores, although this did not reach statistical significance (Table 3).

Linear regression of PedsQL scores on current exercise showed positive relationships between psychosocial (r = 0.56), physical (r = 0.55), and total PedsQL scores (r = 0.43). Each additional day of exercise per week was associated with a 3.9 point (95% confidence interval [CI] = 1.2–6.6, P = 0.005) increase in psychosocial QOL score (Fig. 3A), an 8.1 point (95% CI = 4.1–12.1, P < 0.001) increase in physical QOL score (Fig. 3B), and a 6.0 point (95% CI = 3.1–9.0, P < 0.001) increase in total QOL score (Fig. 3C). Nearly identical results were observed when the same statistical analyses were repeated using only participants with the diagnosis of MFS. A modest but nonstatistically significant relationship was observed with a linear regression model of QOL scores on EES. Each 10-point increase in EES was associated with a 1.9 point increase in the psychosocial QOL score (r = 0.24, 95% CI = −1.3 to 5.2, P = 0.24), a 4.1 point increase in the physical QOL score (r = 0.22, 95% CI = −1.0 to 9.3, P = 0.11), and a 3.0 point increase in total QOL score (r = 0.30, 95% CI = −0.7 to 6.8, P = 0.12).

Beta-blockers were the most commonly prescribed medication, currently taken by 48% of participants (n = 19). Ten of these 19 reported concomitant use of either ARB (n = 9) or angiotensin converting enzyme (ACE) inhibitor (n = 1). There were no significant differences in psychosocial QOL (P = 0.89), physical QOL (P = 0.33), or total QOL (P = 0.55) scores between those currently on beta-blocker therapy and those who were either on no cardiac medications (n = 17) or ARB monotherapy (n = 4).

There were no differences in the prevalence of aortic root or ascending aorta dilation (≥4 cm) or history of surgical intervention after stratifying by EES greater than or less than the median (Table 4). Similar results were found after stratifying by history of competitive sports participation and by history of moderate to vigorous exercise participation of at least 2 d·wk^{-1}.

DISCUSSION

This is the first study demonstrating that, despite activity restriction recommendations, individuals with HTAD participate in a range of types and intensities of competitive sports and exercise throughout adolescence and young adulthood. This study is also the first to demonstrate that participation is associated with improved QOL in patients with HTAD.

Awareness of current and past exercise exposure in the HTAD population is important for providers as they care for these patients. Overall, our cohort reported a considerable amount of lifetime physical activity, with 65% reporting lifetime competitive sports participation and 93% reporting involvement in recreational sports. Among the competitive athletes, all but three participated in sports considered to be high risk.

AHA/ACC guidelines limit sports participation to low to moderate static/low dynamic sports (class IA and class IIA; e.g., yoga, golf, archery) (1). Similarly, European Society of Cardiology guidelines suggest avoidance of high-intensity exercise, contact, and power sports for patients with HTAD, even in the absence of aortic dilation (21). Both sets of guidelines become increasingly more restrictive in the presence of aortic dilation >4 cm or other risk factors. The caution advised regarding sports participation is supported by expert opinion based on animal models, engineering models, case series, and physiologic extrapolations rather than outcomes-based data (2,3,22,23). This paucity of data limits the ability of

TABLE 2. PedsQL stratified by EES.

	EES > Median (n = 20)	EES ≤ Median (n = 20)	P Value
PedsQL physical	79 (14)	69 (17)	0.074
PedsQL psychosocial	77 (21)	60 (29)	0.079
PedsQL total	78 (16)	65 (21)	0.030

Standard deviation in parentheses.

TABLE 3. PedsQL stratified by competitive sports participation.

	Competitive Sports (n = 26)	No Competitive Sports (n = 14)	P Value
PedsQL physical	77 (17)	69 (13)	0.12
PedsQL psychosocial	72 (27)	62 (24)	0.13
PedsQL total	75 (21)	65 (15)	0.07

Standard deviation in parentheses.

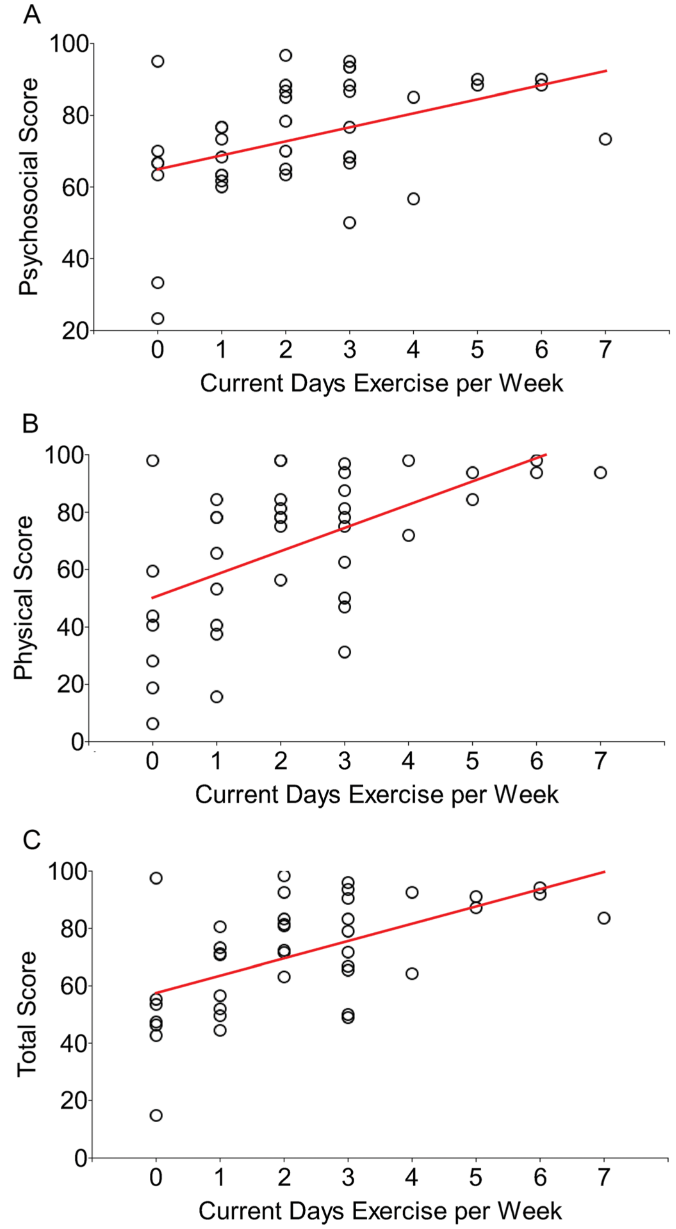

FIGURE 3—Correlation of (A) psychosocial, (B) physical, and (C) total PedsQL scores with current exercise days per week. Each additional day of exercise per week is associated with a 3.9-point increase in psychosocial QOL score, an 8.1-point increase in physical QOL score, and a 6.0 point increase in total QOL score. A. Psychosocial subscale, slope = 3.9, 95% CI = 1.2–6.6, P = 0.005. B. Physical subscale, slope = 8.1, 95% CI = 4.1–12.0, P < 0.001. C. Total score, slope = 6.0, 95% CI = 3.1–9.0, P < 0.001.

providers to confidently determine which HTAD patients should participate and which types of exercise are appropriate.

The second significant finding of our study was that exercise exposure and current exercise participation are associated with improved QOL. Those with HTAD are known to have lower QOL scores and are less physically active compared with the general population (10–13). Our findings suggest that exercise may be a modifiable risk factor, such that improved physical activity and exercise may bolster QOL in the HTAD population. Specifically, we found that higher EES, a surrogate for lifetime exercise exposure, and current exercise frequency were both positively associated with QOL scores. We identified measurable improvements in psychosocial, physical, and total PedsQL scores (3.9, 8.1, and 6.0 points, respectively) with each additional day of current exercise per week. For context, Handisides et al. (12) reported differences in PedsQL scores of 4 to 11 points between those with and

TABLE 4. Prevalence of aortic dilation and need for aortic surgery stratified by EES.

	EES > Median	EES ≤ Median	*P* Value
Aortic root ≥4 cm	5/17 (29%)	4/19 (21%)	0.56
Ascending aorta ≥4 cm	1/20 (5%)	1/20 (5%)	1.0
Surgical intervention	3/20 (15%)	3/20 (15%)	1.0
Aortic root diameter (cm)	Mean = 3.7, median = 3.7	Mean = 3.6, median = 3.6	0.70
Ascending aorta diameter (cm)	Mean = 3.0, median = 2.9	Mean = 2.8, median = 2.8	0.39

without MFS. Although there was a significant improvement in total QOL score when stratifying by EES >/≤ the median, the linear relationship was not as strong as that observed between current exercise frequency and QOL, which suggests that current exercise more strongly influences current QOL than does overall lifetime exercise exposure.

In addition to clear cognitive, social, and psychological benefits, sports participation in childhood can translate into a more physically active adulthood (6–8,24,25). The benefits of physical activity in reducing cardiovascular risk in the general population are widely accepted, with well-supported evidence of improved mortality in multiple cardiovascular disease processes (9,26,27). Permitting a wider range of exercise for HTAD patients could help mitigate the risk of developing superimposed acquired cardiovascular disease later in life.

Although this study was not powered to evaluate the safety of exercise in patients with HTAD, it was encouraging that there was no difference in aortic size or need for surgical intervention between those above and below the median EES, or between those who did and did not participate in competitive sports. This is in keeping with recent murine models that evaluated the effect of exercise on aortic size. In 2017, findings from two separate murine models were published, suggesting that exercise may actually confer significant benefits on MFS-associated aortopathy (4,5). Mas-Stachurska et al. found that, in comparison to sedentary littermates, mice with MFS who engaged in moderate-intensity aerobic exercise demonstrated a significantly reduced rate of aortic root dilation, left ventricular hypertrophy, and demonstrated no additional structural damage to the aortic tunica media. Similarly, Gibson et al. (4) demonstrated improved aortic structure and function in MFS mice subjected to exercise compared with their sedentary counterparts, although this effect was attenuated with the highest intensity exercise group (85% $\dot{V}O_{2max}$). Counterintuitively, this implies that the hemodynamic changes that occur with exercise, such as increased cardiac output, blood pressure, and shear stress on the aortic wall, do not have a significantly detrimental effect on aortopathy in MFS and aortic dilation may instead be driven by other factors.

As has occurred in the management of athletes with hypertrophic cardiomyopathy and long QT syndrome, some cardiologists are moving toward a shared decision-making model with individualized risk stratification and counseling for those with HTAD (19,28–32). Weyland et al. (28) recently surveyed a group of pediatric HTAD providers and identified a trend toward more lenient exercise restrictions compared with current guidelines, but notable variation in practice still exists.

Shared decision-making in cardiology and sports medicine should always consider the balance between the risks and the benefits of the decision at hand. This study certainly does not conclude that competitive sports will be safe in all HTAD patients, but it helps define the benefit side of this balance because exercise exposure was associated with a significant benefit in QOL. Our hope is that now that we have demonstrated that patients with HTAD are participating in sports and exercise and this participation is associated with improved QOL, other studies can be designed and performed to quantitatively evaluate the risk of participation (similar to studies in hypertrophic cardiomyopathy and long QT syndrome).

Limitations. These results should be interpreted with consideration of several limitations. The small sample size of 40 participants limits statistical power, particularly in regard to the association between exercise and adverse outcomes. Multicenter studies will be important to increase the number of patients from whom observations can be drawn. We devised the EES during the study design process, before conducting interviews as a method to quantify lifetime exercise exposure. Although this is not a validated method of quantifying exercise exposure, the definitions and questions used in the exercise questionnaire were adapted primarily from the National Health and Nutrition Examination Survey on physical activity (14). Calculation of EES required participants, whose mean age was 26 yr, to report their history of sports and exercise participation beginning at age 14 yr. This inherently introduces the possibility of significant recall bias, which is another limitation of this work.

CONCLUSIONS

This single-center, cross-sectional study suggests that lifetime exercise exposure and frequency of current exercise are associated with improved QOL in young patients with HTAD. We found no increased risk of adverse outcomes in HTAD patients who participated in either competitive sports or higher levels of exercise through their lifetime, although the small sample size limits statistical power and the ability to draw definitive conclusions. Although encouraging, further study is required to more fully assess the effects of exercise on aortopathy in patients with HTAD.

This study received no funding. The authors have no conflicts of interest to disclose. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The results of the present study do not constitute endorsement by the American College of Sports Medicine. Abstract presented at American Heart Association Scientific Sessions on November 13, 2023. All authors made substantial contributions to the conception and/or analysis of the work, reviewed it critically for important intellectual content, gave approval of the final draft, and agreed to be accountable for all aspects of the work. The data generated during and/or analyzed during the current study are stored in a private database and are not publicly available due to possible presence of protected health information. Data will be shared on reasonable request to the corresponding author.

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