Exercise and Physical Activity in Marfan Syndrome and Related Disorders

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Sibley Heart Center and Emory Healthcare, Atlanta, GA
WARNING

Exercise has been known to cause health & happiness 😊
Benefits of Routine Exercise: Health and Well-Being

**Cardiovascular**
- Lower HR, BP
- Lower cholesterol
- Less coronary disease
- Lower risk of heart attack and stroke

**Musculoskeletal**
- less osteoporosis
- less back pain
- balance

**Lower blood sugar**

**Longer life**

**Social aspects**

**Weight loss**

**Lower risk of colon and breast cancer**

**Mental health**
- Less depression
- Less anxiety
- Improved mood
- Improved memory

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**Table 4: Health and Wellness Benefits of Physical Activity and Fitness**

<table>
<thead>
<tr>
<th>Improved Cardiovascular Health</th>
<th>Enhanced Mental Health and Function</th>
<th>Opportunity for Successful Experience and Social Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stronger heart muscle fitness &lt;br&gt;and health</td>
<td>• Relief of depression &lt;br&gt;• Improved sleep habits &lt;br&gt;• Fewer stress symptoms &lt;br&gt;• Ability to enjoy leisure and work &lt;br&gt;• Improved brain function</td>
<td>• Improved self-concept &lt;br&gt;• Opportunity to recognize and accept personal limitations &lt;br&gt;• Improved sense of well-being &lt;br&gt;• Enjoyment of life and fun &lt;br&gt;• Improved quality of life</td>
</tr>
<tr>
<td>• Lower heart rate &lt;br&gt;• Better electric stability of heart &lt;br&gt;• Decreased sympathetic control of heart &lt;br&gt;• Increased O₂ to brain &lt;br&gt;• Reduced blood fat, including low-density lipoproteins (LDLs) &lt;br&gt;• Increased protective high-density lipoproteins (HDLs) &lt;br&gt;• Delayed development of atherosclerosis &lt;br&gt;• Increased work capacity &lt;br&gt;• Improved peripheral circulation &lt;br&gt;• Improved coronary circulation &lt;br&gt;• Resistance to “emotional storm” &lt;br&gt;• Reduced risk for heart attack &lt;br&gt;• Reduced risk for stroke &lt;br&gt;• Reduced risk for hypertension &lt;br&gt;• Greater chance of surviving a heart attack &lt;br&gt;• Increased oxygen-carrying capacity of the blood</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Improved Appearance</th>
<th>Improved Flexibility</th>
<th>Greater Lean Body Mass and Less Body Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Better figure/physique &lt;br&gt;• Better posture &lt;br&gt;• Fat control</td>
<td>• Greater work efficiency &lt;br&gt;• Less susceptibility to disease &lt;br&gt;• Improved appearance &lt;br&gt;• Less incidence of self-concept problems related to obesity</td>
<td>• Greater work efficiency &lt;br&gt;• Less chance of muscle injury &lt;br&gt;• Less chance of joint injury &lt;br&gt;• Decreased chance of developing low back problems &lt;br&gt;• Improved sports performance</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bone Development</th>
<th>Reduced Cancer Risk</th>
<th>Reduced Effect of Acquired Aging</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Greater peak bone density &lt;br&gt;• Less chance of developing osteoporosis</td>
<td>• Reduced risk for colon and breast cancer &lt;br&gt;• Possible reduced risk for rectal and prostate cancers</td>
<td>• Improved ability to function in daily life &lt;br&gt;• Better short-term memory &lt;br&gt;• Fewer illnesses &lt;br&gt;• Greater mobility &lt;br&gt;• Greater independence &lt;br&gt;• Greater ability to operate an automobile &lt;br&gt;• Lower risk for dementia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Health Benefits</th>
<th>Improved Wellness</th>
<th>Improved quality of life &lt;br&gt;Leisure-time enjoyment &lt;br&gt;Improved work capacity &lt;br&gt;Ability to meet emergencies &lt;br&gt;Improved creative capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Decreased diabetes risk &lt;br&gt;• Quality of life for diabetics &lt;br&gt;• Improved metabolic fitness &lt;br&gt;• Extended life &lt;br&gt;• Decrease in dysfunctional years &lt;br&gt;• Aids for some people who have arthritis, PMS, asthma, chronic pain, fibromyalgia, or impotence &lt;br&gt;• Improved immune system</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

www.cwcboe.org
How do we counsel individuals with hereditary aortic disease (Marfan, Loeys-Dietz, FTAA, vEDS) regarding exercise, both for the athlete and non-athlete?

What type of exercise is safe?

How much exercise is safe?

Do we always have the right answer?

We typically err on the side of safety…

We do not have any outcomes data in this area to guide us.
Physical Activity Concerns in Marfan Syndrome and Related Disorders

Ocular
  retinal detachment, lens dislocation

Musculoskeletal
  back, feet, hips

Pulmonary
  pneumothorax, restrictive lung disease

Cardiovascular
  cardiomyopathy
  valvular disease
  arrhythmias
  mechanical valve/anticoagulation
Physical Activity Concerns in Marfan Syndrome and Related Disorders

aorta
The demands on the cardiovascular system differ among various types of exercise and physical activity.

**Dynamic (isotonic) exercise**

- refers to shortening or lengthening of muscle fibers during contraction
- results in muscle movement
- blood vessels dilate
- modest increase in mean BP
Physiologic response to exercise: Not all types of physical activity are the same

Dynamic (isotonic) exercise

- refers to shortening or lengthening of muscle fibers during contraction
- results in muscle movement
- blood vessels dilate
- modest increase in mean BP

Static (isometric) exercise

- refers to muscle contraction without movement
- vasoconstriction to non-contracting muscles
- ↑ flow to contracting muscles
- associated with increases in BP
**Competitive Athletics**

- Systematic training
- Primary pursuit is athletic excellence and achievement
- Typically push to highest natural physical limits

**Recreational Athletics**

- Non-competitive
- Light-to-moderate exercise
- Fitness and fun
**Competitive Athletics**

- Systematic training
- Primary pursuit is athletic excellence and achievement
- Typically push to highest natural physical limits

**Recreational Athletics**

- Non-competitive
- Light-to-moderate exercise
- Fitness and fun
Blood pressure and heart rate response to exercise depends upon the type of activity, the level of intensity, and the conditioning of the individual.

The **Metabolic Equivalent of Task (MET)**, or simply metabolic equivalent, is a physiological measure expressing the energy cost (or calories) of physical activities.

One MET is the energy equivalent expended by an individual while seated at rest.

While exercising, the MET equivalent is the energy expended compared to rest, so MET values indicate the intensity.

An activity with a MET value of 5 means you are expending 5 times the energy (number of calories) than you would at rest.
Can One Predict BP Response to Various Levels of Physical Activity?

Systolic blood pressure may increase by 8 to 12 mm Hg per MET of aerobic activity with only minimal effect on diastolic BP.

Because higher blood pressure leads to greater aortic wall stress, it is recommended to limit activities which require extreme or maximal exertion, especially those requiring straining.
<table>
<thead>
<tr>
<th>Light &lt;3.0 METs</th>
<th>Moderate 3.0–6.0 METs</th>
<th>Vigorous &gt;6.0 METS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Walking—slowly</td>
<td>• Walking—very brisk (4 mph)</td>
<td>• Walking/hiking</td>
</tr>
<tr>
<td>• Sitting—using computer</td>
<td>• Cleaning—heavy (washing windows, vacuuming, mopping)</td>
<td>• Jogging at 6 mph</td>
</tr>
<tr>
<td>• Standing—light work</td>
<td>• Mowing lawn (power mower)</td>
<td>• Shoveling</td>
</tr>
<tr>
<td>(cooking, washing dishes)</td>
<td>• Bicycling—light effort (10–12 mph)</td>
<td>• Carrying heavy loads</td>
</tr>
<tr>
<td>• Fishing—sitting</td>
<td>• Badminton—recreational</td>
<td>• Bicycling fast (14–16 mph)</td>
</tr>
<tr>
<td>• Playing most musical</td>
<td>• Tennis—doubles</td>
<td>• Basketball game</td>
</tr>
<tr>
<td>instruments</td>
<td>• Leisurely swimming</td>
<td>• Soccer game</td>
</tr>
<tr>
<td></td>
<td>• Table tennis</td>
<td>• Tennis—singles</td>
</tr>
<tr>
<td></td>
<td>• Yoga</td>
<td>• Heavy farming (bailing hay)</td>
</tr>
<tr>
<td></td>
<td>• Pilates</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Water aerobics</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Golf (walking, pulling cart)</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from: http://www.health.harvard.edu/heart-health/the-case-for-measuring-fitness
• The AHA/ACC Scientific Statement on Eligibility and Disqualification Recommendations for Competitive Athletes with Cardiovascular Abnormalities has divided sports into a classification scheme based upon peak static and dynamic components achieved during training and competition and potential for bodily contact.
Classification of Sports


Weight lifting, rock climbing...

Cycling, rowing

Golf, bowling, yoga...

Soccer, field hockey
## Competitive Sports according to impact and age/education level

From: Levine et al. JACC 2015;66:230-3

<table>
<thead>
<tr>
<th>Impact</th>
<th>Junior High School</th>
<th>High School/College</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expected</td>
<td>American football, Ice hockey, Lacrosse, Wrestling, Karate/Judo, Fencing, Boxing</td>
<td>American football, Soccer, Ice hockey, Lacrosse, Basketball, Wrestling, Karate/Judo, Downhill skiing, Squash, Fencing, Boxing</td>
</tr>
<tr>
<td>May Occur</td>
<td>Soccer, Basketball, Downhill skiing, Equestrian, Squash, Cycling</td>
<td>Field hockey, Equestrian, Cycling, Baseball/softball, Gymnastics, Figure skating</td>
</tr>
<tr>
<td>Not Expected</td>
<td>Baseball/softball, Cricket, Golf, Riflery, Gymnastics, Volleyball, Swimming, Track and Field, Tennis, Figure skating, Cross-country skiing, Rowing, Sailing, Archery, Weightlifting, Badminton</td>
<td>Cricket, Golf, Riflery, Volleyball, Swimming, Track and Field, Tennis, Cross-country skiing, Rowing, Sailing, Archery, Weightlifting, Badminton</td>
</tr>
</tbody>
</table>
### Competitive Sports according to impact and age/educational level

From: Levine et al. JACC 2015;66:230-3
Exercise and the Aorta

Does exercise cause aortic dissection?

Does exercise lead to progression dilatation (enlargement) of the aorta?
Studies of bodybuilders have demonstrated systolic BP >300 mm Hg during maximal weightlifting.

Increase in BP occurs during Valsalva maneuver (bearing down).

Surges in BP can occur during intense isometric activity which may place significant transient stress on the aorta.

There are reports of acute aortic dissection related to intense physical activity such as weight lifting.
Exercise and the Aorta

Does exercise cause aortic remodeling and enlargement?
Exercise and the Aorta

Does exercise cause aortic remodeling and enlargement?

Aortic root size in >5000 elite athletes as compared to controls.

Mean aortic root size 3.2 mm larger in elite athletes

Aortic dimensions in endurance trained athletes tended to be larger than in strength-trained athletes.

Not controlled for BSA in many of the studies.

100 Male Professional strength-trained athletes (weight lifting, power lifting, body building) (mean age 22.1 ± 3.6 years) referred to the Institute of Sports Science in Iran, 2001-2005.

Individuals with Marfan syndrome, Ehlers-Danlos syndrome and bicuspid aortic valve were excluded.

128 healthy age- and height-matched men were controls.

BP significantly higher in weight lifters 137/86 vs. 112/72
## Aortic Root Size in Elite Strength-Trained Athletes

Babaee Bigi et al. *Am J Cardiol* 2007;100:528-530

<table>
<thead>
<tr>
<th></th>
<th>Strength-Trained Athletes</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Sinus of Valsalva (cm)</td>
<td>3.82</td>
<td>0.41</td>
</tr>
<tr>
<td>Sinotubular junction (cm)</td>
<td>3.41</td>
<td>0.28</td>
</tr>
<tr>
<td>Ascending aorta (cm)</td>
<td>3.61</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Height, BP and duration of High Intensity Training all correlated with aortic root size.
Aortic root size was largest in the elite strength-trained athletes who trained the longest.

(<18 months to >54 months)
Sudden Death in Athletes is Uncommon


Incidence of Sudden Cardiac Death in Athletes

~1 in 200,000 young people of high school age per year
~1 in 123,000 male high school and college athletes per year
~1 in 769,000 female high school and college athletes per year
800 sudden deaths related to sports in competitive athletes over a 27 year period.

- 19 (2%) aortic rupture
What is known about the risk of aortic dissection during exercise in Marfan Syndrome?

Very little data

Anecdotal information; high-profile cases…
What is known about the risk of aortic dissection during exercise in Marfan Syndrome?

Very little data

Anecdotal information; high-profile cases...

Chris Patton 1976

Flo Hyman 1986
Sudden Death due to Aortic Dissection or Rupture in Competitive Athletes


US National Registry of Sudden Death in Athletes <40 years old
2588 deaths in registry
25 (1%) due to aortic dissection or rupture

Marfan syndrome either diagnosed (or suspected) in 12 cases

10:1 male to female

17.6 ± 5 years old (range 11-36 years)

Basketball/football/baseball most common sports associated with SD.

2/3 of cases of aortic dissection occurred during physical exertion
What is known about the effect of intense exercise on the aorta in one with Marfan Syndrome?
The AHA/ACC has published Guidelines regarding a safe approach to competitive sports in people with Marfan syndrome and related disorders.

AHA/ACC SCIENTIFIC STATEMENT

Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Task Force 7: Aortic Diseases, Including Marfan Syndrome

A Scientific Statement From the American Heart Association and American College of Cardiology
Journal of the American College of Cardiology 2015;66:2398-2405

Alan C. Braverman, MD, FACC, Chair*
Kevin M. Harris, MD, FACC*
Richard J. Kovacs, MD, FAHA, FACC*
Barry J. Maron, MD, FACC*
<table>
<thead>
<tr>
<th>Society</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COMPETITIVE ATHLETES</strong></td>
<td>It is reasonable for athletes with Marfan syndrome to participate in <em>low and moderate static/low dynamic competitive sports (classes IA and IIA)</em> if they do not have ≥1 of the following:</td>
</tr>
<tr>
<td></td>
<td>a. Aortic root dilatation</td>
</tr>
<tr>
<td></td>
<td>b. Moderate to severe mitral regurgitation</td>
</tr>
<tr>
<td></td>
<td>c. Left ventricular systolic dysfunction (ejection fraction &lt;40%)</td>
</tr>
<tr>
<td></td>
<td>d. Family history of aortic dissection at an aortic diameter &lt;50 mm</td>
</tr>
</tbody>
</table>

**IA**: Golf, billiards, bowling, cricket, curling, riflery

**IIA**: Archery

*Braverman AC et al. J Am Coll Cardiol 2015;66:2398-2405*
<table>
<thead>
<tr>
<th>Society</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACC/AHA Guidelines* (2015)</td>
<td>It is reasonable for athletes with Loeys-Dietz syndrome, FTAA syndrome or vascular Ehlers-Danlos syndrome to participate in <strong>low static, low dynamic sports (class IA)</strong> if they do not have any of the following:</td>
</tr>
</tbody>
</table>
|                               | a. Aortic enlargement or dissection, or branch vessel enlargement  
|                               | b. Moderate to severe mitral regurgitation  
|                               | c. Extracardiac organ system involvement that makes participation hazardous                                                                                                                                 |

**IA:** Golf, billiards, bowling, cricket, curling, riflery

*Braverman AC et al. J Am Coll Cardiol 2015;66:2398-2405*
<table>
<thead>
<tr>
<th>Society</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMPETITIVE ATHLETES</td>
<td>Athletes with Marfan syndrome, familial TAA syndrome, Loeys-Dietz syndrome, unexplained aortic aneurysm, vascular Ehlers-Danlos syndrome, or a related aortic aneurysm disorder <strong>should not participate in any competitive sports</strong> that involve <strong>intense physical exertion</strong> or the potential for <strong>bodily collision</strong></td>
</tr>
</tbody>
</table>

*Braverman AC et al. J Am Coll Cardiol 2015;66:2398-2405*
Beta-blockers: reduce heart rate and lessen the force generated by the heart during contraction

- Will limit heart rate response during physical activities
- Do not allow the person with Marfan syndrome or a related disorder to perform strenuous exercise or contact sports

Losartan: does not have any effect on heart rate at rest or with exertion

Warfarin (Coumadin): anticoagulant which increases risk of bleeding related to trauma, falls, etc.

- Avoid contact sports, activities at risk for bleeding during fall (skiing, etc.)
Mild aerobic exercise protects aortic structure and function in a mouse model of Marfan syndrome.


4-week old Marfan and wild-type mice were subjected to voluntary and forced exercise regimens, or a sedentary lifestyle for 5 months.
Marfan mice that exercised had improved aortic wall structure and function, with beneficial effect optimum at low intensity exercise (~60% of $V_0_2$ max) and tapering off at higher intensity of exercise (85% of $V_0_2$ max).

Enzymes which lead to the breakdown of matrix proteins (MMP-2 and MMP-9) demonstrated less expression within the aortic wall of Marfan mice that exercised.
Survivors of Aortic Dissection: Activity, Mental Health, and Sexual Function


314 survivors of acute aortic dissection surveyed regarding lifestyle modifications, exercise practice and emotional state. Response rate was 42%.

- 32% with new-onset depression
- 32% with new onset anxiety
- 24% no longer engaged in any exercise
- Majority of patients no longer sexually active after aortic dissection

Those who exercised routinely had less depression and lower BP.
What advice is recommended regarding *recreational (non-competitive)* exercise and physical activity in individuals with Marfan syndrome and related disorders?
## Guidelines for Recreational (Non-Competitive) Sports and Exercise

<table>
<thead>
<tr>
<th>Society/Organization</th>
<th>Recommendations for those with Marfan syndrome and Related Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recreational (Non-Competitive) Exercise</strong></td>
<td></td>
</tr>
</tbody>
</table>
| ACC/AHA, ESC                          | • Avoid collision sports and strenuous activities involving lifting, pushing or straining that require Valsalva  
• Avoid intense isometric activities                                           |
| Marfan Foundation                     | • Favor non-competitive, dynamic exercises such as walking, jogging, leisurely bicycling or slow-paced tennis  
• Avoid isometric activities (push-ups, sit-ups, weightlifting)  
• Avoid intense contact sports                                                   |
| Loeys-Dietz Foundation                | • Remain active with aerobic activities performed in moderation (hiking, biking, jogging, swimming)  
• Avoid competitive sports, esp. contact sports, or muscle straining activities performed to the level of exhaustion  
• Avoid straining activities (push-ups, chin-ups, sit-ups)                     |

Recreational (non-competitive) Sports and Exercise Recommendations in Marfan syndrome and Related disorders (in the absence of significant aortic dilatation)

<table>
<thead>
<tr>
<th>Permitted</th>
<th>Intermediate*</th>
<th>Strongly Discouraged</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowling</td>
<td>Singles tennis</td>
<td>Body building</td>
</tr>
<tr>
<td>Golf</td>
<td>Baseball/Softball</td>
<td>Ice hockey</td>
</tr>
<tr>
<td>Brisk walking</td>
<td>Hiking</td>
<td>Rock climbing</td>
</tr>
<tr>
<td>Modest hiking</td>
<td>Swimming (lap)</td>
<td>Windsurfing</td>
</tr>
<tr>
<td>Doubles tennis</td>
<td>Horseback riding</td>
<td>Surfing</td>
</tr>
<tr>
<td>Treadmill</td>
<td>Biking</td>
<td>Scuba Diving</td>
</tr>
<tr>
<td>Stationery bike</td>
<td>Ice skating</td>
<td>Weightlifting</td>
</tr>
<tr>
<td>Archery</td>
<td>Racquetball</td>
<td>Football</td>
</tr>
<tr>
<td>Table tennis</td>
<td>Dancing</td>
<td></td>
</tr>
<tr>
<td>Light weightlifting</td>
<td>Jogging</td>
<td></td>
</tr>
<tr>
<td>with repetitions</td>
<td>Badminton</td>
<td></td>
</tr>
<tr>
<td>Yoga, Pilates</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*intermediate activities should be assessed clinically with recommendations based on individual circumstances

Recommendations for Physical Activity and Exercise in Marfan Syndrome and Related Disorders

Stay at an aerobic level of exercise wherein one can talk in a conversational voice during the activity, or using a perceived activity scale:

<table>
<thead>
<tr>
<th>RPE Scale</th>
<th>Rate of Perceived Exertion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>10</strong></td>
<td><strong>Max Effort Activity</strong></td>
</tr>
<tr>
<td></td>
<td>Feels almost impossible to keep going. Completely out of breath, unable to talk. Cannot maintain for more than a very short time.</td>
</tr>
<tr>
<td><strong>9</strong></td>
<td><strong>Very Hard Activity</strong></td>
</tr>
<tr>
<td></td>
<td>Very difficult to maintain exercise intensity. Can barely breath and speak only a few words</td>
</tr>
<tr>
<td><strong>7-8</strong></td>
<td><strong>Vigorous Activity</strong></td>
</tr>
<tr>
<td></td>
<td>Borderline uncomfortable. Short of breath, can speak a sentence.</td>
</tr>
<tr>
<td><strong>4-6</strong></td>
<td><strong>Moderate Activity</strong></td>
</tr>
<tr>
<td></td>
<td>Breathing heavily, can hold short conversation. Still somewhat comfortable, but becoming noticeably more challenging.</td>
</tr>
<tr>
<td><strong>2-3</strong></td>
<td><strong>Light Activity</strong></td>
</tr>
<tr>
<td></td>
<td>Feels like you can maintain for hours. Easy to breathe and carry a conversation</td>
</tr>
<tr>
<td><strong>1</strong></td>
<td><strong>Very Light Activity</strong></td>
</tr>
<tr>
<td></td>
<td>Hardly any exertion, but more than sleeping, watching TV, etc.</td>
</tr>
</tbody>
</table>

www.thefittutor.com
Physical activity is important for one’s health and well-being.
Thank You and “Protect the Tube of Life!”