HEART AND BLOOD VESSELS IN MARFAN SYNDROME

People with Marfan syndrome frequently have problems with their heart and blood vessels. Sometimes, these problems are very serious. The most common complication affects the aorta (the main blood vessel carrying blood from the heart to the rest of the body). Heart valves may be affected as well. Less often, blood vessels other than the aorta are affected. Early and accurate diagnosis is important so that medical issues with the heart and blood vessels can be identified and managed before they become potentially life-threatening emergencies.

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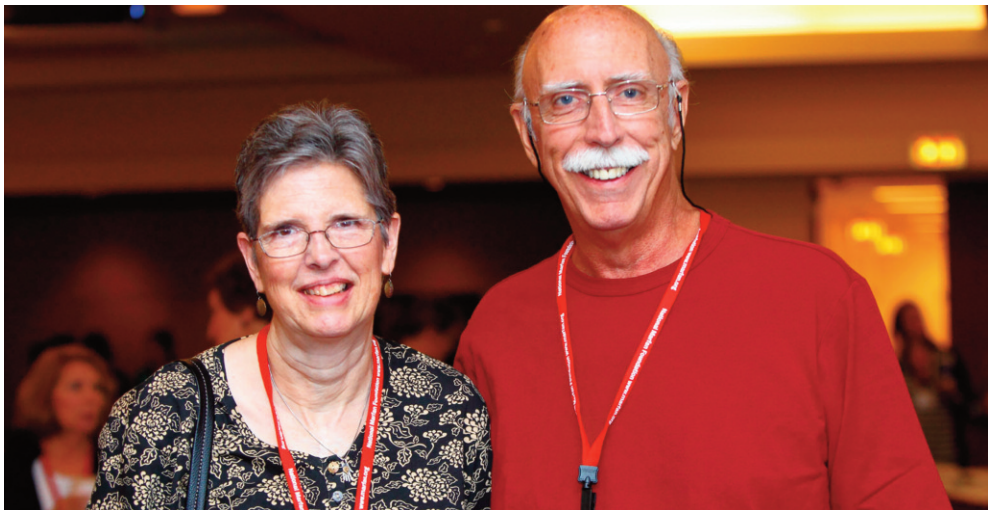

Medical issues related to the heart and blood vessels affect about 9 out of every 10 people diagnosed with Marfan syndrome. The good news is that there are many treatment options, including medication and surgery, as well as adjustments you can make on your own to your physical activity routines. Proper management can help relieve or prevent many of the complications that can interfere with daily life. Medical treatment and ongoing follow-up can usually prevent life-threatening complications.

What are the common types of heart and blood vessel problems in people with Marfan syndrome?

The most common heart and blood vessel problems in people with Marfan syndrome are:

Aortic Dilation and Aortic Aneurysm

In Marfan syndrome and some related disorders, the aorta may become enlarged (aortic dilation) and the walls of the aorta may bulge (aortic aneurysm).

These are very serious problems because a significantly enlarged aorta is at risk for tearing or rupturing (aortic dissection). For most people with Marfan syndrome, the problem starts in the segment of the aorta closest to the heart (the aortic root). Doctors use a person's age, height, and weight to determine whether or not the aorta is enlarged.

Doctors use the term "Z-score" to describe the size of an aorta. The Z-score is a number that determines how far the aorta's size is from normal. Z-scores are used because the size of the aorta changes dramatically from childhood to adulthood, so the size measurement alone is not informative unless placed in relation to your age, as well as height, weight, and gender. Both aortic size measurement and Z-score are important; however, the Z-score is used more often for children because the aorta is still growing and it provides an indication of how large the aneurysm is compared to the body size and this is more valuable information than the actual aortic size, especially when deciding about the timing of preventative aortic aneurysm surgery. Talk with your doctors about what size aorta is within normal limits for you.

Aortic Dissection

Aortic dissection is a tear between layers of the aorta. When this happens, blood begins to flow between the layers and can lead to an aneurysm or rupture. Most people know when this happens because of abrupt onset of severe pain in the center of their chest, stomach (abdomen), or back. The pain may be described as "sharp," "tearing," or "ripping." The location of the pain may change, travelling from the chest to the back and/or abdomen. Sometimes, the pain is less severe, but people still have the feeling that "something is very wrong." If a dissection is suspected, you need immediate medical attention and should go to a hospital emergency department right away.

There are two types of aortic dissection:

- Dissection of the ascending aorta. The ascending aorta is the part of the blood vessel that begins closest to the heart; it is usually about the first two inches of the vessel. A dissection of the ascending aorta is the most common in Marfan syndrome and it is life-threatening. When this happens, a person needs immediate surgery. Most ascending dissections in Marfan syndrome continue into the descending and abdominal aorta.
- Dissection of the descending aorta. The descending aorta comes down after the aortic arch and goes downward into the chest cavity and below the waist. A dissection in this part of the blood vessel can often be managed with medication and monitoring. Surgery is needed only if there are serious complications, such as loss of blood flow to vital organs, aortic rupture, or an extremely enlarged aorta.

Mitral Valve Prolapse

Mitral valve prolapse is present in 5 percent of the general population and about 60% of people with Marfan syndrome. Mitral valve prolapse is a condition in which the flaps (leaflets) of one of the heart's valves (the mitral valve, which regulates blood flow on the left side of the heart) are "floppy" and don't close tightly. Symptoms can include irregular or rapid heartbeats and shortness of breath. Sometimes, mitral valve prolapse can cause a heart murmur, an abnormal sound that a doctor can hear through a stethoscope. The murmur is related to "leaking" of the valve or regurgitation of blood backwards into the upper heart chamber when the heart beats. A small amount of leaking is common and usually not a problem, but surgery may be needed if the mitral valve leaks severely and causes breathlessness or abnormal heart function. Mitral valve prolapse with leakage

is a leading cause of surgery in the pediatric population and meant to help prevent progressive heart enlargement and irreversible heart dysfunction (cardiomyopathy). Mitral valve leakage is often under recognized and under estimated and can masquerade as asthma or pneumonia. The degree of leaking or regurgitation of the mitral valve can be difficult to determine by transthoracic echocardiogram alone, and in some cases, a transesophageal echocardiogram or other tests may be necessary.

Aortic Valve Regurgitation

Aortic valve regurgitation is caused when the aortic valve does not fully close and blood leaks back into the heart. This often happens when the aorta is significantly enlarged and the leaflets of the valve cannot fully come together. Symptoms a person may have include forceful heartbeats and shortness of breath during light activity. Aortic regurgitation can also cause a heart murmur and can accompany an acute aortic dissection.

Heart Failure

Heart failure is an uncommon complication that can occur in Marfan syndrome at any age. Heart failure means that the heart muscle has lost the ability to keep up with the demands of the tissues for the delivery of oxygen and other nutrients. This can occur when the heart has been asked to do an excessive amount of work over a long period of time, such as keeping up with a severe amount of leakage through a heart valve. Occasionally the cause cannot be identified.

Early signs of heart dysfunction include heart enlargement and a reduced capacity to squeeze (often called ejection fraction or fractional shortening). If caught early, heart dysfunction can return to normal if the underlying problem is identified and fixed. Medications such as the beta blockers, carvedilol or metoprolol XL, and angiotensin converting enzyme inhibitors (ACE-inhibitors) or, angiotensin receptor blockers (ARBs) are used to help this process. Your doctor may see you more frequently and ask for more frequent echocardiograms if there is any concern about progressive valve leakage, heart size and heart function. Sometimes a specialized imaging study called a cardiac MRI is used to obtain very detailed information about the heart size and function. Later signs of heart failure include a buildup of fluid in the lungs, often associated with shortness of breath, reduced exercise capacity and/or difficulty lying flat comfortably. Severe heart failure can be irreversible, even after correction of the initiating problem. For this reason, your doctors might consider repairing or replacing a heart valve early in the progression of heart dysfunction. On rare occasions, people with Marfan syndrome and heart failure have received a heart transplant, with the potential for an improved long-term outcome.

How are the common types of heart and blood vessel problems treated in people with Marfan syndrome?

Treatment for heart and blood vessel problems may involve medications (drugs), regular testing to monitor the heart and blood vessels, surgery, or a combination of these depending on your individual circumstances. In addition, there are steps you can take to prevent or manage some of the problems that may develop.

Medications

Medications can help treat many types of problems with the heart and blood vessels. It is recommended that either a beta blocker or angiotensin receptor blocker (ARB) be started at the time of diagnosis

of Marfan syndrome with the goal of reducing the rate aortic root enlargement. Doses suggested are those given in the 2014 Atenolol vs. Losartan randomized trial.

- Atenolol should be increased to a maximum dose of 4 mg/kg/day (not to exceed 250 mg/day) with a goal of a 20% or greater decrease in average heart rate measured on a 24-hr recording. This high dose of atenolol is generally well tolerated.
- Alternatively, in patients who cannot tolerate beta blockers, angiotension receptor blockers (ARBs) such as losartan, provide a similar amount of protection against aortic enlargement. Losartan should be started at an initial dose of 0.4 mg/kg/day and increased based on weight to a maximum dose up to 1.4 mg/kg/day, not to exceed 100 mg.
- Since the trial data provides evidence that in younger patients both drugs are associated with a greater decrease in aortic-root z-score over time, beta blockers or angiotension receptor blockers should be prescribed at the time of diagnosis even in the youngest children. Therefore, it is recommended that once a diagnosis is made, with or without aortic dilation, medical therapy should be started, maintained and continued after surgery indefinitely.
- Based on the patient's history, individualized treatment plans must be developed when deciding on which medical therapy to use (beta blocker [atenolol] or ARB [losartan]). However, since the trial only investigated use of either atenolol or losartan, that is the only hard evidence-based recommendation that can made at this time. There are other ongoing trials which may provide additional information about combination therapy with both ARB drug and beta blocker.
- There has been a small study of ACE-inhibitor therapy in Marfan syndrome; more information is needed before recommending the use of this class of agents for the prevention of aortic disease in Marfan syndrome.
- In patients with weakness of the heart muscle (cardiomyopathy or left ventricular dysfunction), medications including beta blockers and either ACE-inhibitors or ARB drugs are used. However, instead of atenolol, beta blockers approved for use in heart failure include carvedilol and meto-prolol-XL. Other medications which may be used in this condition include hydralazine, long-acting nitrates, and diuretics, including spironolactone.

Tests to Monitor Cardiovascular (Heart and Blood Vessel) Problems

People with Marfan syndrome must have regular tests to monitor for (watch for) problems with their heart and blood vessels, especially their aorta, before there is an emergency. The most effective tests that doctors use in Marfan syndrome are:

- Transthoracic Echocardiogram (TTE). This is a heart ultrasound done from the chest wall which shows all the heart structures including blood valves and the part of the aorta closest to the heart.
- MRA (magnetic resonance angiogram) or CT (computed tomography) scans. These show all segments of the aorta.
- Cardiac MRI (magnetic resonance imaging) is a specialized test that is used to get detailed information regarding heart and valve structure and function. This test can be very useful in deciding if and when to perform surgery for repair of a heart valve that is leaking.

- Transesophageal echocardiogram (TEE). This is a special type of echocardiography that shows the ascending and descending thoracic aorta in addition to the heart valves. The test is done by placing a small camera in the esophagus (swallowing tube) and therefore requires sedation, which is a combination of medicines to help you relax and block pain (an anesthetic) during a medical procedure. The TEE is especially helpful in determining the cause and severity of a leaking mitral valve, especially when not adequately visualized during a transthoracic echocardiogram.

Plain X-rays and EKGs are not useful in evaluating the aortic problems in Marfan syndrome.

What can you do on a day-to-day basis?

There are many things that you can do on a day-to-day basis to care for your heart and blood vessels when you have Marfan syndrome or a related disorder. Although you might not want to think about the emergencies that can occur, understanding your condition and preparing in advance to handle emergencies can put you and your family more at ease in case something serious happens.

Here are the steps we recommend.

- Take medications as prescribed by your doctor to reduce stress on your aorta.
- Have an echocardiogram (echo/TEE) or other heart study at least once a year. Your doctor may want you to have more frequent echos (every three to six months) to make sure your aorta is growing very little or not at all.
- Do not put extra stress on your aorta. You should do regular exercise, but focus on walking rather than jogging or riding your bicycle slowly rather than racing. Do not play competitive sports such as basketball, football, or soccer. Make sure that your job does not require any heavy lifting. In addition, read our Physical Activity Guidelines, which you can find on our website at marfan.org.
- Talk to your healthcare team if your child has Marfan syndrome. It is recommended to start medications as soon as a Marfan diagnosis is made.
- Let your doctor know if you are, or plan to become, pregnant. There are special risks and treatments for pregnant women who have Marfan syndrome. More information can be found on our website.
- Notify your doctor if you or your family member experiences shortness of breath, a decreasing ability to perform exercise, trouble lying flat, or any other indication of a worsening breathing problem.

How do you handle cardiac emergencies, such as aortic dissection?

People with Marfan syndrome have a risk of aortic dissection—a potentially life-threatening emergency—that is up to 250 times greater than the risk in the general population.

If you have unexplained chest, back, or abdominal pain, it is critical for you to inform emergency medical personnel that you have Marfan syndrome.

Emergency personnel often won't think about aortic dissection as a possibility unless they know you have Marfan syndrome or a related disorder or if you have very obvious outward physical characteristics that would suggest these conditions.

- Advocate for yourself by telling emergency personnel that you have Marfan syndrome or a related condition and may be experiencing an aortic dissection.
- Communicate effectively with doctors and nurses in the emergency department.

Here are some important tips to help you communicate effectively with emergency department staff to assure you receive appropriate care.

- **Complete our Emergency Preparedness Kit**
  Before any emergency happens, complete our Emergency Preparedness Kit, available on our website at marfan.org, and bring it with you to the emergency department should the need arise. It includes an Emergency Alert Card, which identifies you as a person with Marfan syndrome or a related disorder who is at increased risk for aortic dissection. This card also identifies the proper tests to confirm or rule out an aortic dissection.
- **Describe the pain completely**
  Be prepared to answer the following questions. If your doctor does not ask, speak up and tell him or her anyway.
  - Where is the pain located?
  - How severe is the pain?
  - When did it start?
  - What does the pain feel like?
  - Does the pain radiate (move) to other areas of the body (for example, the back, neck, or arms)?
  - Is this kind of pain like anything you have ever felt before?
- **Express a sense of urgency**
  Emphasize to the nurse or doctor that you:
  - Have Marfan syndrome or a related disorder
  - Are at high risk for aortic dissection
  - Are concerned about this pain being from a dissection
- **Contact your primary care doctor**
  Provide your doctor's name and phone number to emergency department staff and ask them to call at once for any additional information that may be needed for your treatment.
- **Wear a medical alert bracelet**
  Medical alert bracelets are helpful, especially if you are unable to provide your medical history. The bracelet can relate a few key words or phrases that may be helpful to emergency department personnel. People with Marfan syndrome might want to include on their bracelet: Marfan syndrome, aortic aneurysm, risk for aortic dissection, heart valve, Coumadin. Talk to your doctor about what is most appropriate for you to put on your bracelet.

- **Communicate what you know about the tests that confirm or rule out a diagnosis of aortic dissection**
  The most effective tests to confirm or rule out an aortic dissection are a CT scan of the chest with IV contrast or a transesophageal echocardiogram (TEE). An MRA is occasionally used as a first test. The diagnostic test used by the hospital depends on what they have available and their expertise. If you have an allergy to IV dye, shellfish, or iodine, tell the emergency department staff. It is important to remember that a chest x-ray is not diagnostic for aortic dissection and, if dissection is suspected, a normal chest x-ray should not deter further evaluation.
- **Check the capabilities of your local hospitals**
  Before an emergency arises, you might want to check with hospitals in your area to find out if they are able to offer the appropriate tests easily in the emergency department, and if they are equipped to perform emergency cardiac surgery should it be necessary.
- **Prepare family members to be your advocate before an emergency arises.**
  Family members can be helpful. They can tell emergency department personnel about your health condition, especially your experience with Marfan syndrome, aortic aneurysm, prior dissection or heart surgery, medications, and anything they know about your current symptoms. They can also provide the name and number of your doctor. Make sure your family has this information should you be unable to communicate in an emergency situation.
- **Express your concerns to emergency department staff; be persistent.**
  You may be intimidated in an emergency department, but it is critical that you:
  - Tell the doctor all you can about your symptoms.
  - Repeat your concerns if you feel that you are not being taken seriously.
  - Ask for another doctor to see you for another opinion if you are in a large emergency department and do not agree with the opinion of the first doctor who examines you.

Do you have questions? Would you like more information?

- Call our help center, 800-862-7326, ext. 126 to speak with a nurse who can answer your questions and send you additional information.
- Visit our website at marfan.org. You can print information that interests you and ask questions online.