Genetic Insights: quick reference guide for healthcare providers

This guide is intended to facilitate discussion between a provider and their patient.

Genetic Insights test results: **Marfan syndrome**

Key results

A pathogenic or likely pathogenic variant associated with Marfan syndrome was found in the *FBN1* gene.

People with Marfan syndrome have a significantly increased risk of developing an aortic aneurysm and/or dissection and may have other health concerns.

Next steps

Clinical recommendations	Resources
Genetic Insights is a screening test and not intended for diagnosis. A follow-up genetic test should be performed in a clinical setting before any other action is taken.	**Ready to order?** Check with your institution and/or patient's insurance about the preferred testing laboratory. Blueprint Genetics® offers Marfan syndrome testing. To confirm this test result, **targeted variant testing** for the variant identified is available. You can order a confirmation test here: Blueprint Genetics/TVT **Have questions?** Call **1.866.GENE.INFO** (1.866.436.3463) to speak to a specialized Quest genetic counselor or geneticist available to healthcare providers to discuss test selection and results.
Refer your patient to a genetic counselor. *Genetic counselors can provide counseling on the implications of this test result and next steps for your patient.*	Your patient can schedule a 1-on-1 remote genetic counseling session through their online Genetic Insights Connective Tissue Disorder report at no additional cost. To find a genetic counselor with expertise in connective tissue disorder genetics practicing in your patient's area for an in-person session, please visit FindAGeneticCounselor.NSGC.org

Patient conversation starters:

Patient conversation starters summarize the preceding information in plain language to support meaningful conversations between you and your patient.

FindAGeneticCounselor.NSGC.org

Your Genetic Insights test is a screening test. The next step is to have your result confirmed with a second genetic test.

It's also important that you talk with a genetic counselor. Genetic counselors are experts in genetics and can help you understand this result and potential next steps.

You can access a genetic counselor through your online Genetic Insights dashboard at no additional cost to you, and we can discuss a referral to a local genetic counselor.

Visit QuestDiagnostics.com/Genetic-Health-Screening for more information about this test.

What is Marfan syndrome?

Marfan syndrome is a hereditary connective tissue disorder characterized by cardiovascular, ocular, and skeletal findings.[1] It is the result of a pathogenic or likely pathogenic variant in the *FBN1* gene.

People with Marfan syndrome are at a significantly increased risk of developing an aneurysm, dissection, and/or rupture of the aorta.[1,2]

Aortic aneurysms are often asymptomatic, and individuals may first present with an acute aortic dissection with high morbidity and mortality.[1,2]

There is clinical variability between individuals with Marfan syndrome.[1] Features outside of vascular involvement may include mitral valve prolapse, myopia, lens dislocation, joint laxity, and bone overgrowth.[1]

Clinical diagnosis is typically made by a specialist, such as a medical geneticist, based on standardized clinical criteria, and management is best coordinated by a multidisciplinary care team.[1]

See the Management options section for more detail.

Patient conversation starters:

Marfan syndrome is a connective tissue disorder; that means the tissues that help connect our bodies together—like the blood vessels and bones—can be affected. It is caused by having a DNA variant in a certain gene.

People with Marfan syndrome have a higher than typical chance of having a tear in a major blood vessel like the aorta. But not everyone with Marfan syndrome will have a tear in a blood vessel.

People with Marfan syndrome should see a specialist, including a geneticist, to help monitor for and prevent health issues.

What this result means for family members

There are 2 primary ways someone can have a DNA variant associated with Marfan syndrome:

The DNA variant can be inherited from a biological parent. In this case, at least 1 parent has the same DNA variant. Each full sibling and each child of someone with the variant has a 50% chance of having it.

The DNA variant can arise in someone for the first time (called a de novo variant). In this case, their children have a 50% chance of having the variant. Neither biological parent nor any siblings are likely to have the variant.

In people with a confirmed DNA variant associated with Marfan syndrome, genetic testing for family members may help inform their risks and screening protocols.[3] Therefore, it is strongly recommended that individuals share these results with their biological relatives.

Patient conversation starters:

There are 2 ways someone can end up having a DNA variant linked to Marfan syndrome.

- First, it can be passed down from a parent. In this case, 1 parent would have that same DNA variant. Full siblings would have a 50% chance (1 in 2 chance) of having the DNA variant
- Second, it is possible that the DNA variant arises in someone in a family for the first time. In this case, parents and siblings are not likely to have the DNA variant

However, in either case, each child of someone with a DNA variant linked to Marfan syndrome has a 50% chance of having the same DNA variant.

Sharing this result with your family members is important so that they can talk to a healthcare provider about genetic testing for Marfan syndrome.

Management options

There are management and treatment options for people with Marfan syndrome. Select clinical guidelines from the American College of Cardiology Foundation/American Heart Association[2] include:

Scenario	Option(s)
Screening	An echocardiogram is recommended at the time of diagnosis of Marfan syndrome to determine the aortic root and ascending aortic diameters and 6 months thereafter to determine the rate of enlargement of the aorta Annual imaging is recommended for people with Marfan syndrome if stability of the aortic diameter is documented. More frequent imaging should be considered based on clinical history
Surgical aneurysm repair	Surgical repair of the dilated aortic root/ascending aorta for patients with Marfan syndrome is usually performed when the diameter reaches a standard threshold per clinical guidelines
Control of hypertension	Beta adrenergic–blocking drugs should be considered for those patients confirmed to have Marfan syndrome and aortic aneurysm to reduce the rate of aortic dilatation unless contraindicated An angiotensin receptor blocker (losartan) should be considered for patients confirmed to have Marfan syndrome to reduce the rate of aortic dilatation unless contraindicated
Pregnancy	People with Marfan syndrome should be counseled about the risks and management options prior to pregnancy For people with Marfan syndrome who are contemplating pregnancy, it is reasonable to prophylactically replace the aortic root and ascending aorta if the diameter exceeds 4.0 cm

Patient conversation starters:

It's recommended that people with Marfan syndrome make a plan to monitor their health. This way, any health problems can be found as early as possible, and a treatment plan can be made.

If your genetic test result is confirmed, it's important to work with the right specialists, including a geneticist, to make a plan that's right for you.

See American College of Cardiology Foundation/American Heart Association for complete recommendations.[2] In addition, comprehensive Marfan syndrome management guidelines are available and have been extensively reviewed by experts.[1,3] Guidelines and recommendations may change over time.

If this result is confirmed, a specialist should be consulted for further clinical management. To locate a genetics center or specialty clinic, please visit the American College of Medical Genetics and Genomics or the Marfan Foundation.

Additional resources

The following advocacy groups have additional information and resources about Marfan syndrome:

The Marfan Foundation: Marfan.org
John Ritter Foundation: JohnRitterFoundation.org

References

1. Dietz H. FBN1-Related Marfan Syndrome. April 18, 2001. Updated February 17, 2022. In: Adam MP, Ardinger HH, Pagon RA, et al, editors. GeneReviews® [Internet]. University of Washington, Seattle; 1993-2022. https://www.ncbi.nlm.nih.gov/books/NBK1335/
2. Hiratzka LF, Bakris GL, et al. ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the diagnosis and management of patients with thoracic aortic disease. *Circulation.* 2010;121(13):e266-369. https://www.ncbi.nlm.nih.gov/pubmed/20233780
3. The Marfan Foundation. Healthcare Professionals. Management Overview. Accessed June 7, 2022. https://www.marfan.org/resources/professionals/management