Published on *My46* (https://www.my46.org) 01/23/2022

My46 Trait Profile

Familial Thoracic Aortic Aneurysms and Dissections

Familial Thoracic Aortic Aneurysms and Dissections is a genetic condition characterized by problems with the aorta, the large blood vessel that carries blood from the heart to the rest of the body. It is caused by mutations in any one of many different genes.

Characteristics of Familial Thoracic Aortic Aneurysms and Dissections

Thoracic aortic aneurysm and dissections (TAAD) occur in the general population, with increasing frequency with age. The exact incidence is hard to estimate, as most people have no signs or symptoms. The aorta is the largest artery in the body and is responsible for blood getting from the heart to the rest of the body. Thoracic refers to the part of the aorta that is closest to the heart. Features of TAAD include dilation (stretching) of the aorta, which is caused by the aortic wall being weak. Dilation can progress and lead to aortic aneurysms (bulging out/ballooning of the aortic wall) and aortic dissections (tearing within the walls of the aorta). People with aortic aneurysms usually have no signs or symptoms. Individuals with an aortic dissection most commonly experience severe, sudden pain in their chest. They may also become pale, have a weak pulse or experience numbness and/or tingling. Aortic aneurysms may lead to life threatening aortic dissections or ruptures (partial or complete tearing open of the aorta), resulting in internal bleeding.

Risk factors for TAAD in the general population include, age (more commonly over 65 years), smoking, high blood pressure, and the build up of fat in the arteries of the heart. TAAD can also be associated with genetic syndromes including Marfan syndrome (see trait profile); Loeys-Dietz syndrome (see trait profile); Ehlers-Danlos syndrome, vascular type (see trait profile). These conditions often have other clinical features associated with them.

It is estimated that 20% of people with isolated TAAD have a familial form. Familial TAAD is a heritable condition that, like TAAD in the general population, mainly affects the thoracic aorta. Familial TAAD often occurs at a younger age than TAAD in the general population. Other vessels and arteries in the body can also be affected by familial TAAD. The aorta in the abdomen and the vessels of the brain and other parts of the body may become dilated or have aneurysms. Some types of familial TAAD are also associated with congenital heart defects, early onset heart attacks and occasionally bone, eye and skin findings. The age of onset for aortic dilation and progression, as well as other findings, is highly variable, even within the same family.

Diagnosis/Testing

TAAD is diagnosed clinically by different imaging of the aorta. This includes ultrasounds of the heart (echocardiogram) and other imaging of the heart (e.g., MRI or CT scan). For someone to be diagnosed with familial TAAD, they must have a clinical diagnosis of aortic dilation or dissection and not have been diagnosed with a genetic syndrome that is known to cause aortic dilation and dissection (e.g. Marfan syndrome, Loeys-Dietz syndrome or Ehlers-Danlos syndrome, vascular type). There must also be a family history of TAAD. It is important to note that it may not be possible to determine if there is a family history of TAAD unless all other first degree family members (siblings, parents and children) have had imaging to look at their aorta, as aortic dilation has no clinical symptoms.

Currently, there are at least eight genes associated with familial TAAD that are available to test on a clinical basis. These genes are: TGFBR1, TGFBR2, MYH11, ACTA2, MYLK, FBN1, SMAD3 and TGFB2. Approximately 20% of persons with a clinical diagnosis of familial TAAD will have a change or mutation identified in one of these eight genes. This means that in 80% of people with familial TAAD, a genetic cause cannot be determined. This may be because the

responsible gene has not been discovered yet or is not available to test on clinical basis.

Management/Surveillance

For individuals with a clinical diagnosis:

Individuals with aortic dilation are recommended to have frequent imaging of their aorta. Management of familial TAAD is aimed at slowing the progression of dilation, as well as preventing aortic dissection and ruptures. Exercise restrictions and blood-pressure lowering medications are often used to reduce stress on the aorta. When the progression of the dilation or the size of the aorta reaches a certain measurement, surgery can be considered to repair the aorta. Surgical management of aortic aneurysms can help prevent aortic dissections and ruptures, thus, early detection is important. These decisions can be influenced by the specific gene mutation in the family or if there is a family history of dissection with small aortic size. It is also recommended that affected individuals avoid the known risk factors of TAAD such as smoking.

For family members:

It is recommended that all first degree family members of a person with TAAD have imaging of their aorta. Family members that are found to have a TAAD-causing mutation should have periodic imaging of their aorta, as determined by their cardiologist. Depending on the specific mutation in the family, family members who have the mutation may also need imaging of other vessels in the body. Should a family member choose not to have genetic testing or if a genetic cause cannot be identified in a family, he/she should obtain a baseline cardiac evaluation and, if normal, repeat every two-five years, or as recommended by their cardiologist.

Mode of inheritance

Familial TAAD is mainly inherited in an autosomal dominant pattern. This means inheriting one mutation is enough for an individual to be at risk to develop TAAD. A mutation can be inherited from either parent or it can occur brand new (de novo) in an affected child.

Risk to family members

The risk to family members depends on whether or not the individual with TAAD has a mutation that was passed down from a parent. If a parent also has a mutation, the risk of having a child who also has the mutation is 50% with each pregnancy. If a parent does not have a mutation, the risk of other siblings being affected is very low.

Special considerations

Not everyone that inherits a mutation will develop TAAD. This is called reduced penetrance. Also, not every person that inherits a mutation will be diagnosed at the same age as other people with the same mutation, even within their own family. Some people may have aneurysms when they are very young, while others may be much older. This is due to variable expressivity. This may be due to other genetic or environmental factors that influence the progression of TAAD.

Resources

Genetics Home Reference: Familial thoracic aortic aneurysm and dissection
http://ghr.nlm.nih.gov/condition/familial-thoracic-aortic-aneurysm-and-dissection
TAD Coalition
http://www.tadcoalition.org/tad/
The John Ritter Research Program in Aortic and Vascular Diseases
http://www.johnritterresearchprogram.org/

References

Hiratzka, LF. et al. (2010)."2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the diagnosis and management of patients with thoracic aortic disease. A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine." Journal of the American College of Cardiology 55(14): e7-e129.

Milewicz DM, Regalado E. (Updated 12 January 2012). Thoracic Aortic Aneurysms and Aortic Dissections. In: GeneReviews at GeneTests Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle. 1997-2013. Available at http://www.ncbi.nlm.nih.gov/books/NBK1120/. Accessed [07/02/2013].

Created: 07/2013 **Created by:** Lindsay Meyers, MS, LCGC

Updated: mm/yyyy **Edited by:** Seema Jamal, MSc, LCGC