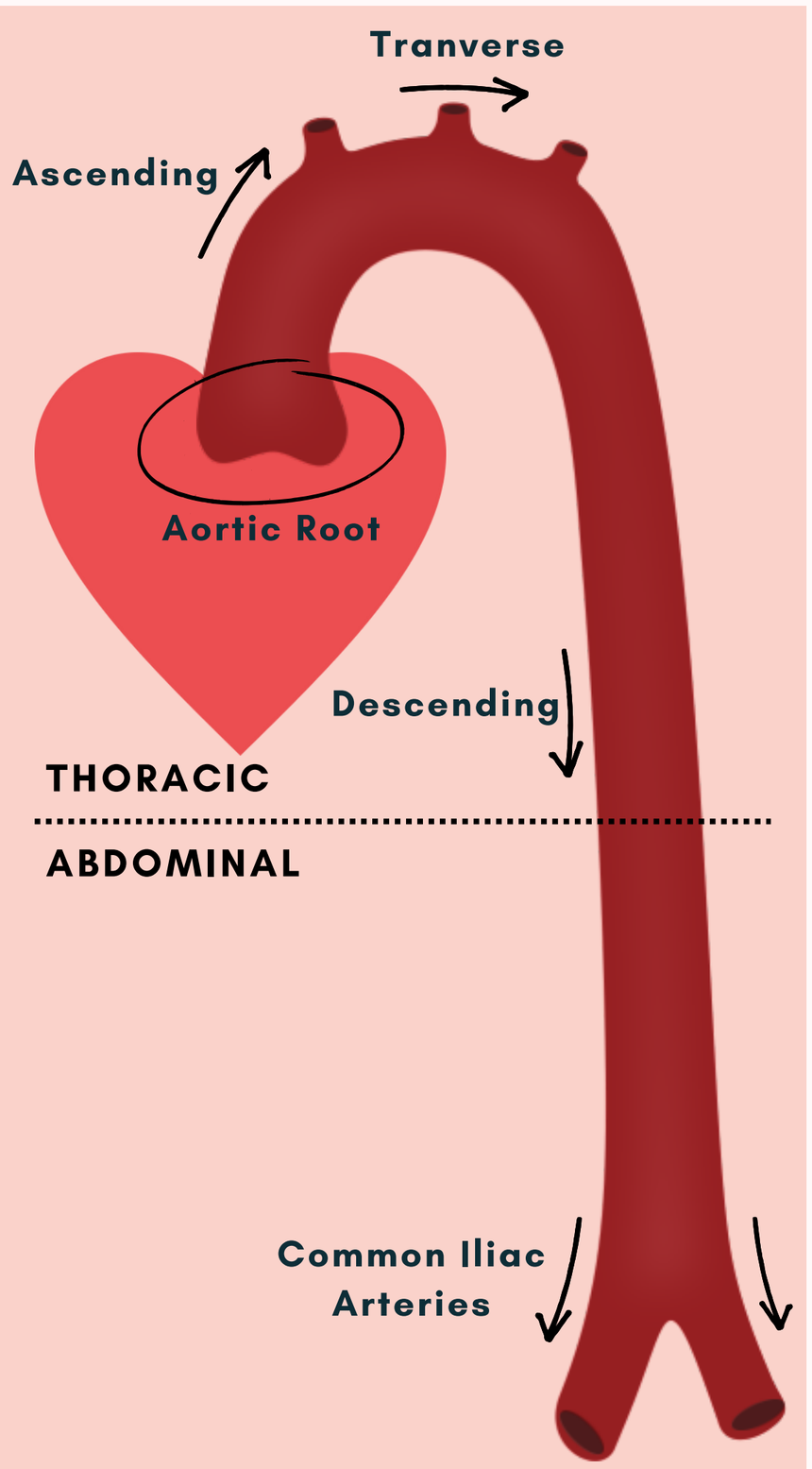
Heritable Thoracic Aneurysms and Dissections (H-TAAD)

OTTAWA CARDIO VASCULAR GENETICS



VASCULAR GENETICS DICTIONARY

Dilation: when a blood vessel stretches bigger than it should be.
Aneurysm: a dilation >50% larger than the blood vessel should be.
Dissection: a rip or tear in the inner lining of a blood vessel.
Degenerative: an aneurysm caused by the deterioration of a blood vessel over time, associated with risk factors such as high blood pressure, age, and smoking.
Familial or Heritable: a condition that runs in a family, or can be inherited.
Syndromic: a recognizable group of symptoms that are suggestive of a particular genetic condition.

Aneurysm Location

When there is a history of aortic aneurysm or dissection in a family, it is important to know **which part of the aorta** was affected.

Thoracic aneurysms can be degenerative (up to 75%), or heritable (roughly 25%). Of the heritable aneurysms, 5% of thoracic aneurysms are found in patients with "syndromic" presentations. These patients have a recognizable set of features, or "clues", that are suggestive of a particular genetic disorder. The most common conditions are Marfan syndrome, Loeys-Dietz syndrome, and Vascular Ehlers-Danlos syndrome.

Abdominal aneurysms are usually degenerative. They are much less likely to have a heritable component than thoracic aneurysms. Degenerative aneurysms occur over time, and are often related to factors like blood pressure, age, and smoking.

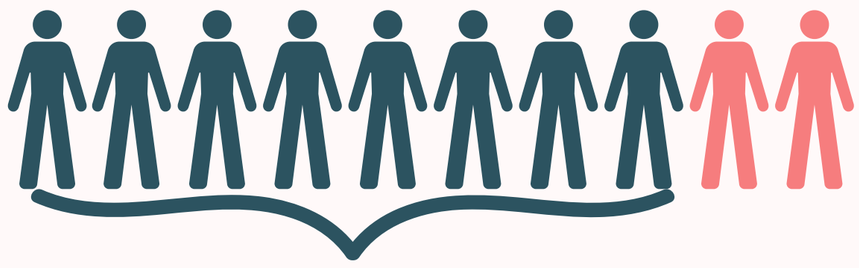
In the vast majority of individuals, aneurysms don't cause any symptoms unless they tear or rupture, which can be fatal. Therefore, screening and surveillance with imaging are important elements of treatment.

Genetic Testing

Condition	Genes	Detection Rate of Genetic Testing
Marfan Syndrome	FBN1	90-95%
Loeys-Dietz Syndrome	SMAD2, SMAD3, TGFB2, TGFB3, TGFBR1, & TGFBR2	Good to Very Good
Vascular Ehlers-Danlos Syndrome	COL3A1	Approx. 95%
Non-Syndromic Aortopathy	Several are known, many are yet to be discovered.	Approx. 20%

Heritable Non-Syndromic Aortpathies

Roughly 1/5 of all thoracic aneurysms occur in individuals who don't have other features suggestive of a particular genetic syndrome, but where there is clearly a familial component. In this population, we only identify a genetic cause in 20% of families.



For 80% of families with thoracic aneurysms that clearly run in the family, we don't find a genetic culprit. This doesn't mean that the aneurysms are not genetic, just that our technology couldn't find the culprit.

This reference is for educational purposes only.
If you have any questions, ask your health-care provider.

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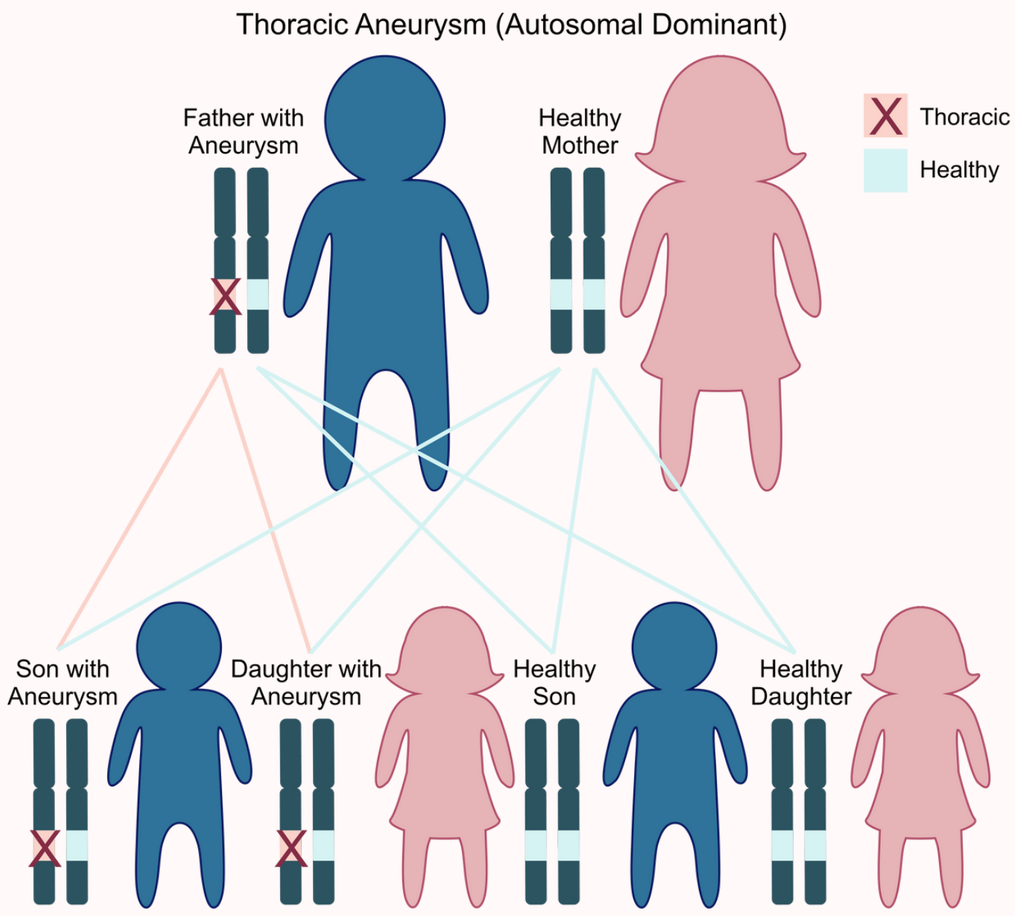

Inheritance

When thoracic aneurysms run in families, they are usually inherited in an "autosomal dominant" fashion. This means that each person with a thoracic aneurysm has a 50% chance of passing on a genetic risk factor for aneurysms to his or her children (both sons and daughters).

There can be significant variability in the severity of the condition even within the same family. **All first-degree relatives of an individual with an aneurysm (which is not believed to be degenerative) should have baseline imaging** of all the blood vessels that are affected in the family. First-degree relatives are parents, siblings, and children.

Genetic Testing Results

Genetic testing starts with an individual who has a thoracic aneurysm. If a disease-causing variant is found, it could help inform the individual's medical management (including informing when surgery should be performed), and family members can be offered genetic testing.

3 possible results from genetic testing:

Positive

Up to 20% of the time, a disease-causing genetic variant is found. This provides an explanation for the thoracic aneurysm or dissection.

- Additional imaging may be recommended.

→ Family members would have the option of genetic testing to find out if they are at risk for TAAD.

Negative

No disease-causing variant is found. The aneurysm can still be genetic, but the test did not find the cause.

→ Adult family members likely need repeat imaging every 5 years until age 65 to detect aneurysms early.

Indeterminate

We may find a variant of unclear significance, where we are not sure if it causes aneurysms.

- Additional imaging may be recommended.
- These patients should be referred to Genetics every 2-3 years for updated information.

→ This result can't be used to test family members, so adult family members likely need repeat imaging every 5 years until age 65 to detect aneurysms early.

Resources: www.ottawaCVgenetics.ca/patient-resources
www.cagc-accg.ca to find a genetic clinic

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