LABupdate

Familial Aortopathy

Aortopathy is characterized by aortic dilation, which can lead to life-threatening aneurysms and/or dissections.[1-5] Early diagnosis is critical, since timely initiation of pharmacological treatment can slow aortic dilation, and prophylactic surgery may prevent aortic dissection or rupture.[1-5] Lifestyle adjustments may also help reduce the risk of catastrophic events.[1-4]

Thoracic aortic aneurysm and dissection (TAAD) may be seen in the context of several multisystem syndromes with overlapping symptoms, such as Marfan syndrome (MFS), Loeys-Dietz syndrome (LDS), and vascular Ehlers-Danlos syndrome (vEDS), but it can also occur in isolation.[2,4,6]

Approximately 20% of TAAD cases are familial.[4,6] Familial TAAD is typically associated with more aggressive disease progression than nonfamilial forms.[4,6]

Identifying the underlying cause of TAAD is important, since therapy and prognosis of different syndromic forms of TAAD may vary considerably. For example, prophylactic surgery is recommended for MFS[1], LDS[2], and isolated TAAD[4] but is generally contraindicated for vEDS due to the extreme tissue friability associated with that condition.[2,3]

In cases in which prophylactic surgery is recommended, the timing of surgery depends on the underlying genetic cause of the aortopathy. In particular, aortic aneurysms resulting from mutations in the genes *TGFBR1* and *TGFBR2* may require prophylactic surgery earlier and at smaller degrees of aortic dilation than aortic aneurysms resulting from other causes.[2,4]

The genetic mutations responsible for syndromic forms of aortopathy and TAAD are known. They typically show autosomal dominant inheritance; however, a family history may not always be clear, since type, severity, and age of onset of symptoms can vary even within families. In addition, MFS, vEDS, and LDS may be caused by de novo mutations.[1-3]

Genetic testing for familial aortopathy may[1-4,7]:

- Confirm a clinical diagnosis of Marfan syndrome, Loeys-Dietz syndrome, vascular Ehlers-Danlos syndrome, or TAAD.
- Identify close relatives of an index patient who carry the mutation and are thus at high risk for TAAD and may require continual screening and lifestyle adjustments.
- In some cases, predict the severity of disease based on the exact mutation found.

Relevant Assays*

Test Name	Test No.
GeneSeq®: Cardio Familial Aortopathy Profile	451432
FBN1 (Marfan Syndrome) Full Gene Sequencing	452028
GeneSeq®: Cardio Gene Specific Sequencing, NGS**	452053
Mutation-specific Sequencing, Whole Blood†	451382

* Visit the online Test Menu at **www.LabCorp.com** for more information, including a current list of included genes, test methodology, and specimen requirements. To request a sample shipping kit, please call 866-647-0735.
**Full Gene Sequencing for any gene(s) on any of the GeneSeq: Cardio panels
†Known mutation testing for any gene(s) on any of the GeneSeq: Cardio panels

References

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