Follow-up and screening of patients with Thoracic Aortic Disease (TAD) and their First-degree Relatives - Full Clinical Guideline

Reference no.: CG-CLIN/4202/23

Introduction

Thoracic aortic aneurysm (TAA) is a potentially life-threatening disorder with a strong genetic component. The number of genes implicated in TAA has increased exponentially over the last decade. Approximately 20% of patients with TAA have a positive family history. As most TAA remain asymptomatic for a long time; screening of at-risk relatives is warranted to prevent complications.

Aim and Purpose

The aim and purpose of this guideline is to ensure that patients with TAA are identified as soon as possible, and the first-degree relatives are screened appropriately. This is to prevent complications where possible.

Definitions, Keywords

TAA, TAD, Aorta, Aneurysm, Hereditary Thoracic Aortic Disease, Congenital, Hypertension, Atherosclerosis, Degenerative, Previous aortic dissection, Inflammatory aortitis, Infectious aortitis, Previous traumatic aortic injury, Aortic root, TTE, Transthoracic Echocardiogram, Bicuspid Aortic Valve

Cause of TAA

Hereditary Thoracic Aortic Disease (TAD) syndromic:

a) Marfan syndrome
b) Loeys-Dietz syndrome
c) Vascular Ehlers-Danlos syndrome
d) Smooth muscle dysfunction syndrome
e) Others: attribute to pathogenic variants in FLNA, BGN, LOX, HTAD (see Table 7)

Hereditary Thoracic Aortic Disease (TAD) non-syndromic:

a) ACTA2, MYH11, PRKG1, MYLK, and others
b) Familial thoracic aortic aneurysm without identified pathogenic variants in a known gene for HTAD.

Congenital conditions:

a) Bicuspid aortic valve
b) Turner syndrome
c) Coarctation of the aorta
d) Complex congenital heart defects (tetralogy of Fallot, transposition of the great vessels, truncus arteriosus)

Hypertension

Atherosclerosis

Degenerative

Previous aortic dissection

Inflammatory aortitis:

a) Giant cell arteritis
b) Takayasu arteritis
c) Behcet's disease
d) Immunoglobulin G4-related disease, antineutrophil cytoplasmic antibody-related, sarcoidosis

Infectious aortitis:

a) Bacterial
b) Fungal
c) Syphilitic

Previous traumatic aortic injury

Recommendations

1. In patients with aortic root/ascending aortic aneurysms or aortic dissection, obtaining a multigenerational family history of TAD, unexplained sudden deaths, and peripheral and intracranial aneurysms is recommended.
2. In patients with aortic root/ascending aortic aneurysms or aortic dissection and risk factors for hereditary TAD, genetic testing to identify pathogenic/ likely pathogenic variants (i.e., mutations) is recommended.
3. In patients with TAD who have a pathogenic/ likely pathogenic variant, genetic testing of at-risk biological relatives (i.e., cascade testing) is recommended. In family members who are found by genetic screening to have inherited the pathogenic/likely pathogenic variant, aortic imaging with TTE (if aortic root and ascending aorta are adequately visualized, otherwise with CT or MRI) is recommended.

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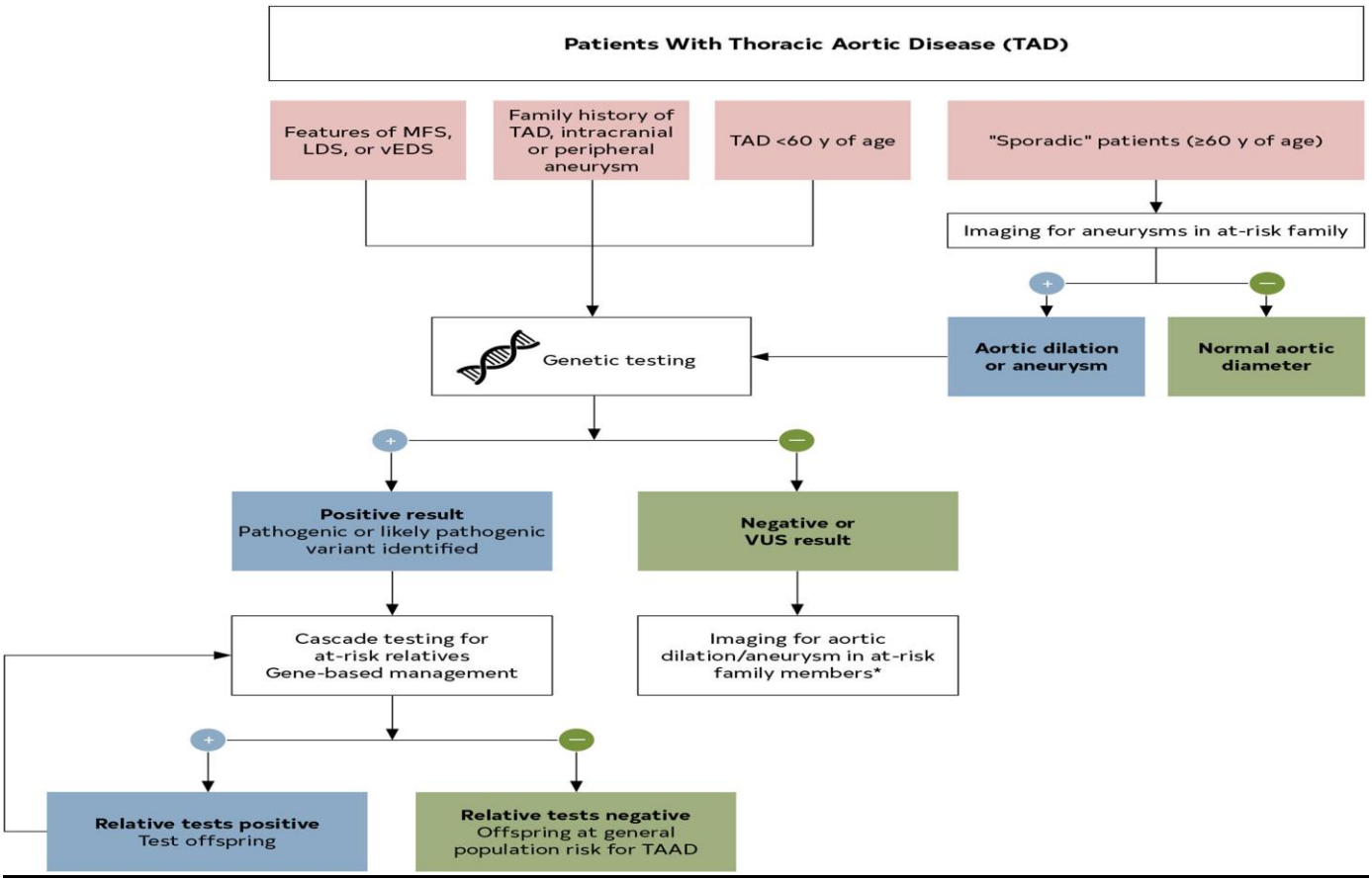
Diagnosed with TAA (indexed to height) or Family history TAA/Aortic dissection.

No family history of aortopathy and no identified syndrome or pathogenic genetic variant.	Positive family history of aortopathy, but no identified syndrome or pathogenetic variant.	Syndromic Heritable Thoracic Disease (HTAD) or non-syndromic HTAD with an identified pathogenic variant.	Bicuspid Aortic Valve
Single family screening If first screening <40 years, consider follow up >50 years.	Screening aortic imaging with Echo/CT/CMR of at-risk biological relatives (i.e., cascade testing) is recommended. Start at age of 25 years or 10 years before the youngest case of family. If normal, repeat every 5 years. Discontinue at age of 65 years, or if first screening >60years: ≥1 x follow-up.	Genetic testing of at-risk biological relatives (i.e., cascade testing) is recommended. In family members who are found by genetic screening to have inherited the pathogenic/likely pathogenic variant, aortic imaging with TTE (if aortic root and ascending aorta are adequately visualized, otherwise with CT or MRI) is recommended.	In patients with a BAV and a dilated aortic root or ascending aorta, screening of all first degree relatives by TTE is recommended to evaluate for the presence of a BAV, dilation of the aortic root and ascending aorta, or both; if the diameter and morphology of the aortic root, ascending aorta, or both cannot be assessed accurately or completely by TTE, a cardiac-gated CT or MRI of the thoracic aorta is indicated.

Genetic testing is recommended for individuals with syndromic features, family history of TAD, and/or early age of disease onset. Thoracic aortic imaging is recommended for first-degree relatives of all individuals with TAD, regardless of age of onset, to detect asymptomatic aneurysms. Positive genetic testing should trigger gene-based management and cascade testing of at-risk relatives. When testing is negative or reveals variants of unknown significance, first-degree relatives should undergo screening aortic imaging. Please see figure below: (Adapted from ACC/AHA guidelines 2022/2023)



Blue (+) indicates positive; green (–), negative; LDS, Loeys-Dietz syndrome; MFS, Marfan syndrome; TAAD, thoracic aortic aneurysm and dissection; TAD, thoracic aortic disease; vEDS, vascular Ehlers-Danlos syndrome; and VUS, variants of unknown significance. *Aneurysms are typically asymptomatic.

1. References (including any links to NICE Guidance etc.)

AHA/ACC guidelines 2022

2. Documentation Controls (these go at the end of the document but before any appendices)

Reference Number CG-CLIN/4202/23	**Version:** 1		**Status**	Final
Version / Amendment History	Version	Date	Author	Reason
	1	July 2023	Dr N Ahmed	New guideline
Intended Recipients: This guideline is intended for use by all clinicians managing patients for follow-up and screening of Thoracic Aortic Disease and their first-degree relatives.				
Training and Dissemination: This guideline is for all cardiology and medical staff.				
Development of Guideline: **Job Title:** Dr N Ahmed, Consultant Cardiologist and Assistant Clinical Director				
Consultation with: Consultant Cardiologists in University Hospital of Derby and Burton, UHDB				
Linked Documents: State the name(s) of any other relevant documents  				
Keywords: TAA, TAD, Aorta, Aneurysm, Hereditary Thoracic Aortic Disease, Congenital, Hypertension, Atherosclerosis, Degenerative, Previous aortic dissection, Inflammatory aortitis, Infectious aortitis, Previous traumatic aortic injury, Aortic root, TTE, Transthoracic Echocardiogram, Bicuspid Aortic Valve				

Business Unit Sign Off	**Group: SMBU2** **Date: 25.08.23**
Divisional Sign Off	**Group:Medicine Division** **Date:September 2023**
Date of Upload	September 2023
Review Date	September 2026
Contact for Review	Consultant Cardiologists