

ATTR-CM AND AORTIC STENOSIS

MAKING A DIFFERENTIAL DIAGNOSIS

Aortic stenosis can coexist with ATTR-CM, leading to worse outcomes.¹ Learn more about when to suspect ATTR-CM.

ATTR-CM=cardiomyopathy of transthyretin-mediated amyloidosis.

SEVERE AORTIC STENOSIS MAY BE A SIGN OF ATTR-CM

~1 in 6 older adults with aortic stenosis (AS) undergoing TAVR may have ATTR-CM.
For those with low-flow, low-gradient AS, that number may be $\approx 2x$ higher.^{2*}

ATTR-CM vs AS

	ATTR-CM	Aortic stenosis
Etiology	Misfolding of TTR protein , possibly due to aging or due to an inherited genetic variant. TTR can aggregate in the heart, nerves, and GI tract, as well as other tissues, leading to multisystem manifestations ³⁻⁵	Calcification and/or stiffening of the aortic valve due to age-related degeneration, rheumatic fever, or congenital malformations ⁶
Age of onset	wtATTR: >60 years; hATTR: >30 years ⁷	50-70 years ⁶
Median survival, untreated	2.6-5.8 years ⁸⁻¹²	1.8 years ²



OVERLAPPING FINDINGS WITH AS AND ATTR-CM CAN CONFOUND DIAGNOSIS

Early identification and intervention are key to slowing ATTR-CM progression, but overlapping findings with AS can delay an accurate ATTR-CM diagnosis.^{1,4,13}

Overlapping findings with AS¹⁴

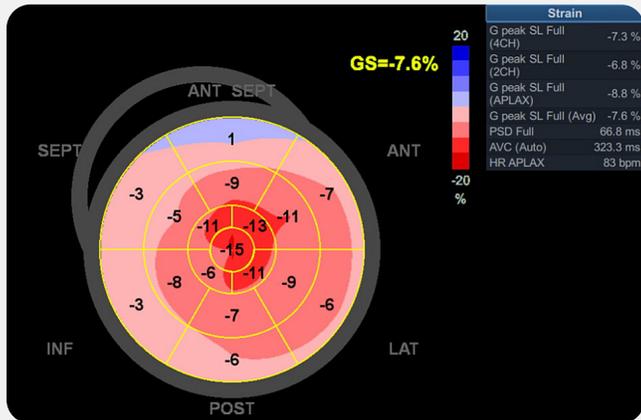
- LV hypertrophy
- HFpEF
- Conduction system disease
- Syncope
- Dyspnea
- Edema

*From a study of 151 patients (mean age 84 years \pm 6 years) with degenerative AS.²

GI=gastrointestinal; hATTR=hereditary transthyretin-mediated amyloidosis; HFpEF=heart failure with preserved ejection fraction; LV=left ventricular; TTR=transthyretin; wtATTR=wild-type transthyretin-mediated amyloidosis.

ECHO AND ECG FINDINGS MAY INDICATE ATTR-CM

ECHOCARDIOGRAPHY



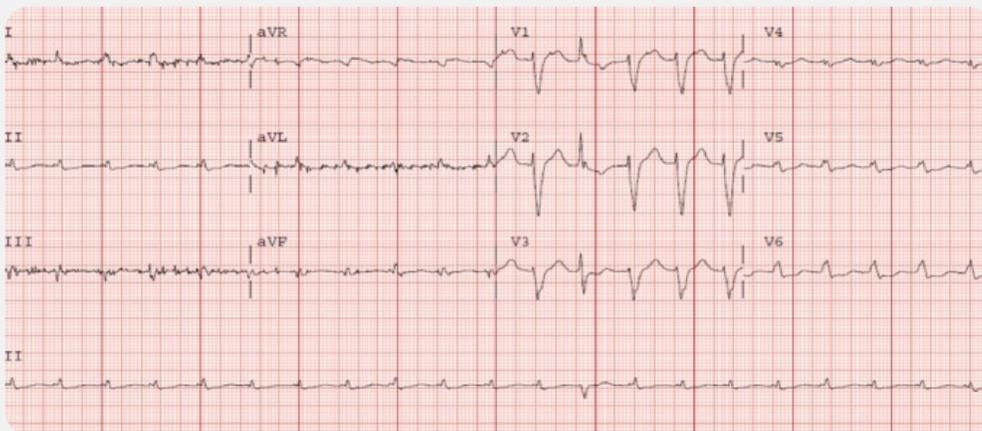
Longitudinal strain bull's-eye map¹⁵
Image reproduced with permission from Baptista et al.

Look for^{4,15-19}:

- Reduction in longitudinal strain with relative apical sparing (shown)
- Batrial enlargement
- Refractile myocardium

Findings of low-flow, low-gradient AS pattern should further raise suspicion of ATTR-CM.¹⁴

ELECTROCARDIOGRAPHY



Left bundle branch block with low voltage in limb leads²⁰
Image reproduced with permission from Taiwo et al.

Look for^{17,21,22}:

- Low QRS voltage compared to degree of LV wall thickening or relative to LV wall thickness
- Pseudo-infarction, AV conduction delays (e.g. atrial fibrillation)

In addition to these echo and ECG findings, **multisystem manifestations** and **intolerance to common heart-failure medications*** should be considered red-flag symptoms for ATTR-CM.^{2,4,13,17,22-25}

While echo and ECG may help raise clinical suspicion for ATTR-CM, they lack specificity to diagnose ATTR-CM alone.⁴

*Patients with ATTR-CM can have intolerance to standard medications for heart failure, including ARNi, ACEi, ARB, or beta blockers.⁴
ACEi=angiotensin-converting enzyme inhibitor; ARB=angiotensin receptor blocker; ARNi=angiotensin receptor-neprilysin inhibitor; AV=atrioventricular; ECG=electrocardiography; echo=echocardiography; QRS=Q wave, R wave, S wave.

TAKE ACTION TO IDENTIFY ATTR-CM

PATIENTS WITH BOTH AS AND ATTR-CM HAVE WORSE CLINICAL OUTCOMES COMPARED TO THOSE WITH AS ALONE¹:

↑90%

Increased risk of heart failure hospitalization

↑50%

Increased risk of death after an AVR

↑30%

Increased risk of death

Improved clinical outcomes start with a timely and accurate diagnosis

CONFIRMING AN ATTR-CM DIAGNOSIS^{4,13}

1

Rule out AL amyloidosis with simple monoclonal light-chain assays



2

Detect amyloid deposition in myocardial tissue with nuclear scintigraphy or cardiac biopsy



3

Once ATTR-CM is confirmed, **use genetic testing** to determine if it is hereditary

[Click here to learn more about suspecting ATTR-CM](#)

AL=light chain amyloidosis; AVR=aortic valve replacement.

References: 1. Masri et al. *J Am Heart Assoc.* 2025;14(2):e033251. 2. Castaño et al. *Eur Heart J.* 2017;38(38):2879-2887. 3. Maurer et al. *J Am Coll Cardiol.* 2016;68(2):161-172. 4. Kittleson et al. *J Am Coll Cardiol.* 2023;81(11):1076-1126. 5. Bezerra et al. *Front Mol Neurosci.* 2020;13:1-15. 6. Pujari et al. *StatPearls.* 2023. PMID: 32491560. 7. Ruberg et al. *J Am Coll Cardiol.* 2019;73(22):2872-2891. 8. Hawkins et al. *Ann Med.* 2015;47(8):625-638. 9. Aus dem Siepen et al. *Clin Res Cardiol.* 2018;107(2):158-169. 10. Gertz et al. *Mayo Clin Proc.* 1992;67(5):428-440. 11. Swiecicki et al. *Amyloid.* 2015;22(2):123-131. 12. Givens et al. *Aging Health.* 2013;9(2):229-235. 13. Kittleson et al. *J Am Coll Cardiol.* 2020;142(1):e7-e22. 14. Jaiswal et al. *Eur Heart J Open.* 2023;3(6):oead106. 15. Baptista et al. *Cureus.* 2023;15(1):e33364. 16. Dorbala et al. *Circ Cardiovasc Imaging.* 2021;14(7):e000029. 17. Dharmarajan et al. *J Am Geriatr Soc.* 2012;60(4):765-774. 18. Maurer et al. *Circulation.* 2017;135(14):1357-1377. 19. Falk et al. *Heart Fail Rev.* 2015;20(2):125-131. 20. Taiwo et al. *World J Clin Cases.* 2019;7(6):742-752. 21. Witteles et al. *JACC Heart Fail.* 2019;7(8):709-716. 22. Maloberti et al. *Int J Cardiol Cardiovasc Risk Prev.* 2024;21:200271. 23. Garcia-Pavia et al. *Eur J Heart Fail.* 2021;23(6):895-905. 24. Maurer et al. *Circ Heart Fail.* 2019;12(9):1-11. 25. González-López et al. *Eur Heart J.* 2015;36(38):2585-2594.