HCM vs ATTR-CM: MAKING A DIFFERENTIAL DIAGNOSIS

~1 in 5 adults aged 50 years and older with HCM may actually have ATTR-CM.[1]*

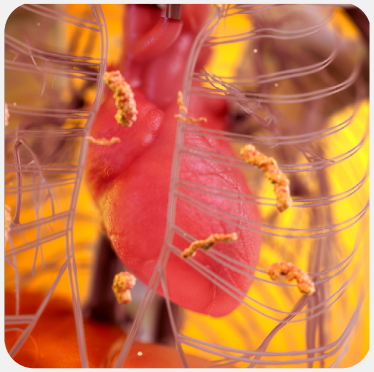
ETIOLOGY OF ATTR-CM AND HYPERTROPHIC CARDIOMYOPATHY

ATTR-CM

- **Misfolding of TTR protein**, possibly due to aging or due to an inherited genetic variant. Pathogenic TTR can aggregate in the heart, nerves, musculoskeletal system, and gastrointestinal tract, leading to multisystem manifestations[2-4]

HCM

- **Thickening of heart muscles** due to an inherited genetic variant or due to other nonfamilial causes[5-7]



Amyloid fibrils depositing into myocardial tissue

OVERLAPPING FINDINGS WITH HCM AND ATTR-CM CAN CONFOUND DIAGNOSIS

Early intervention is crucial to slowing ATTR-CM progression, but overlapping findings with HCM can delay ATTR-CM diagnosis.[3,8-11]

Signs that may be identified via echo, ECG, or cMRI[1,5,8,12]:

- LV hypertrophy
- Arrhythmias, including atrial fibrillation

Other clinical symptoms and biomarkers[1,5,8,12]:

- Elevated NT-proBNP and troponin I
- Shortness of breath
- Edema
- Fatigue
- Syncope

See reverse for more information on how to spot these signs via echo and cMRI

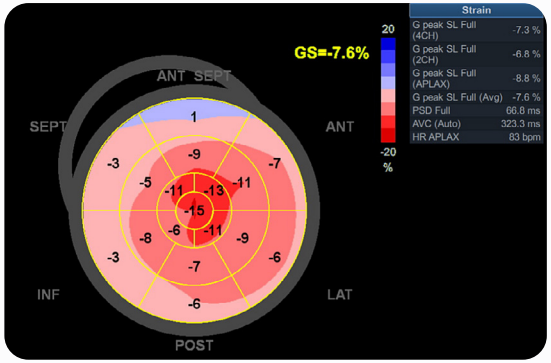
*Based on an epidemiological study of 766 patients with an HCM diagnosis.[1]

ATTR-CM=cardiomyopathy of transthyretin-mediated amyloidosis; cMRI=cardiac magnetic resonance imaging; ECG=electrocardiogram; echo=echocardiogram; HCM=hypertrophic cardiomyopathy; HF=heart failure; LV=left ventricular; NT-proBNP=N-terminal prohormone of brain-type natriuretic peptide; TTR=transthyretin.

SUSPICION AND DIAGNOSIS OF ATTR-CM

Signs on echo and cMRI that may increase clinical suspicion for ATTR-CM

ECHOCARDIOGRAPHY



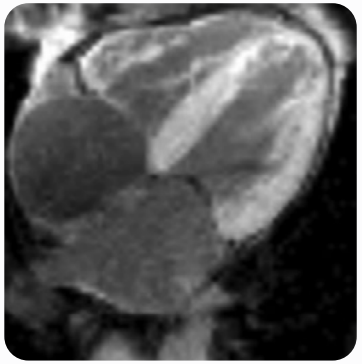
Longitudinal strain bull's-eye map

Image reproduced with permission from Baptista et al.[13]

Look for[3,13-17]**:**

- Reduction in longitudinal strain with relative apical sparing (shown)
- Biatrial enlargement
- Thickening of valves and septum
- Refractile myocardium

CARDIAC MRI



Late gadolinium enhancement

Image reproduced with permission from Quarta et al.[18]

Look for[8,15,16,18]**:**

- Diffuse, subendocardial or transmural late gadolinium enhancement (shown)
- Increased extracellular volume fraction

ADDITIONAL SIGNS OF ATTR-CM

- Electrocardiographic findings, including low QRS voltage relative to degree of LV wall thickness; pseudo-infarction; and AV conduction block[12,15,19]
- Intolerance to HF treatments*, bilateral carpal tunnel syndrome, and lumbar spinal stenosis[3,8,10-12,15,20-23]

Establish a diagnosis in 3 steps[3,8]

1. **Rule out AL amyloidosis** with simple monoclonal light-chain assays
2. **Detect amyloid deposition** in myocardial tissue with nuclear scintigraphy or tissue biopsy
3. **Use genetic testing** to determine if ATTR-CM is hereditary

Click here to learn more about suspecting ATTR-CM.

Diagnosis is based on the independent medical judgment of the healthcare professional.

*Patients with ATTR-CM can have intolerance to standard medications for heart failure, including ARNi, ACEi, ARB, or beta blockers.[3,8,10-12,15,20-23]

ACEi=angiotensin-converting enzyme inhibitor; AL=amyloid light chain; ARB=angiotensin receptor blocker; ARNi=angiotensin receptor-neprilysin inhibitor; HF=heart failure; QRS=Q wave, R wave, S wave.

References: 1. Garcia-Pavia et al. *Esc Heart Fail.* 2024;11:4314-4324. **2**. Maurer et al. *J Am Coll Cardiol.* 2016;68:161-172. **3**. Kittleson et al. *J Am Coll Cardiol.* 2023;81:1076-1126. **4**. Bezerra et al. *Front Mol Neurosci.* 2020;13:592644. **5**. Marian et al. *Circ Res.* 2017;121:749-770. **6**. Maron et al. *J Am Coll Cardiol.* 2022;79:372-389. **7**. Bonaventura et al. *J Am Heart Assoc.* 2023;12:e028974. **8**. Kittleson et al. *Circulation.* 2020;142:e7-e22. **9**. Rozenbaum et al. *Cardiol Ther.* 2021;10:141-159. **10**. Nativi-Nicolau et al. *Heart Fail Rev.* 2022;27:785-793. **11**. Maurer et al. *Circ Heart Fail.* 2019;12:e006075. **12**. Maloberti et al. *Int J Cardiol Cardiovasc Risk Prev.* 2024;21:200271. **13**. Baptista et al. *Cureus.* 2003;15:e33364. **14**. Dorbala et al. *Circ Cardiovasc Imaging.* 2021;14:e000029. **15**. Dharmarajan et al. *J Am Geriatr Soc.* 2025;60:765-774. **16**. Maurer et al. *Circulation.* 2017;135:1357-1377. **17**. Falk RH et al. *Heart Fail Rev.* 2015;20:125-131. **18**. Quarta et al. *Br J Radiol.* 2011;84(Spec Iss 3):S296-S305. **19**. Witteles et al. *JACC Heart Fail.* 2019;7:709-716. **20**. González-López et al. *Eur Heart J.* 2015;36:2585-2594. **21**. Castaño et al. *Eur Heart J.* 2017;38:2879-2887. **22**. Brito et al. *Glob Heart.* 2023;18:59. **23**. Mitter et al. ISA Congress 2020.

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