

HIDDEN IN PLAIN SIGHT

SUSPECT ATTR-CM

The diagnosis of ATTR-CM is often delayed or missed. Routine heart failure assessments such as echo and electrocardiogram (ECG), along with advanced imaging techniques, can help identify clues on the diagnostic pathway. By increasing your suspicion of ATTR-CM, you can identify patients who may require further testing to make a diagnosis.¹⁻⁴



CONSIDER THE FOLLOWING CLINICAL CLUES, ESPECIALLY IN COMBINATION, TO RAISE SUSPICION FOR ATTR-CM AND THE NEED FOR FURTHER TESTING

HFpEF Heart failure with preserved ejection fraction (HFpEF) or other cardiac conditions (eg, severe aortic stenosis [AS],* arrhythmias) in patients typically over the age of 60⁵⁻⁷

INTOLERANCE to standard heart failure therapies, such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and beta blockers⁸

DISCORDANCE between QRS voltage on ECG and left ventricular (LV) wall thickness^{9,10}

DIAGNOSIS of orthopedic conditions, including carpal tunnel syndrome, lumbar spinal stenosis, biceps tendon rupture, and/or hip and knee arthroplasty¹¹⁻¹⁴

ECHO showing increased LV wall thickness⁹

NERVOUS SYSTEM dysfunction, including polyneuropathy and autonomic dysfunction, including gastrointestinal complaints and/or unexplained weight loss¹⁵

HFpEF: Heart failure with preserved ejection fraction (HFpEF) or other cardiac conditions (eg, severe aortic stenosis [AS],* arrhythmias) in patients typically over the age of 60⁵⁻⁷

- In ATTR-CM, diastolic function is impaired due to amyloid fibril deposition in the myocardium resulting in thicker and inelastic ventricles, thereby decreasing stroke volume. It is not until the later stages of ATTR-CM disease that ejection fraction drops^{16,17}
- Prevalence among older HFpEF patients:
 - ~10% of patients referred to a dedicated center had ATTR-CM confirmed by EMB^{18†}
 - ~13% of hospitalized patients with HFpEF and increased LV wall thickness had wtATTR-CM confirmed by scintigraphy^{5‡}
- In patients undergoing transcatheter aortic valve replacement for severe calcific AS, prevalence of ATTR-CM was 16% overall and 22% among men⁶

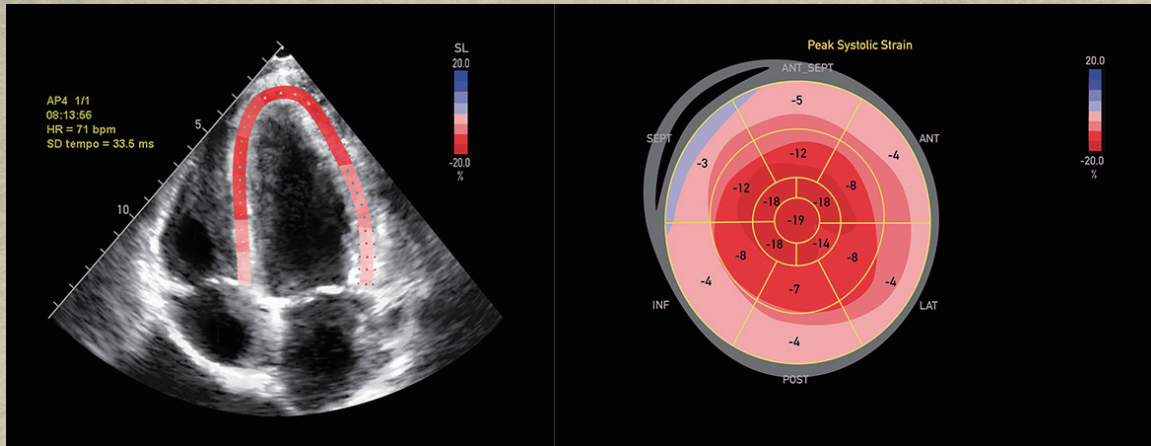
*Notably those with a low-flow, low-gradient AS pattern.⁶

†A prospective analysis in 108 patients (61% women, age range: 57-74 years) seen at the Johns Hopkins University HFpEF Clinic who underwent EMB to evaluate myocardial tissue histopathology.¹⁸

‡A prospective, cross-sectional, single-center study at a tertiary university hospital in Madrid, Spain. Included 120 patients ≥60 years of age (59% women, mean age: 82 ± 8 years) admitted for HFpEF, with LV ejection fraction ≥50% and LV hypertrophy ≥12 mm.

^{99m}Tc-labeled 3,3-diphosphono-1,2-propanodicarboxylic acid (^{99m}Tc-DPD) scintigraphy used to confirm ATTR-CM.⁵

Reduced longitudinal strain with apical sparing should raise suspicion of ATTR-CM^{1,17}



Illustrative representation.

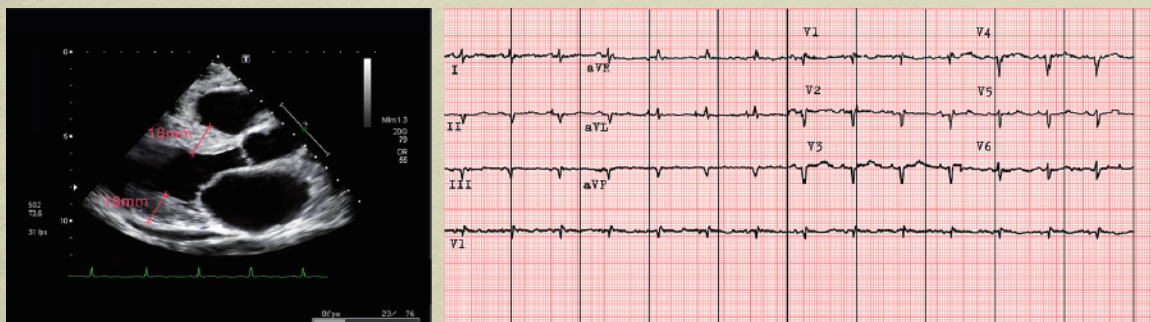
INTOLERANCE to standard heart failure therapies, such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and beta blockers⁸

- Intolerance to standard heart failure medications is common in patients with cardiac amyloidosis; such agents exacerbate symptomatic hypotension in the setting of concomitant autonomic dysfunction or by lowering heart rate and reducing cardiac output⁸

DISCORDANCE between QRS voltage on ECG and left ventricular (LV) wall thickness^{9,10}

- The classic ECG feature of ATTR-CM is a discordance between QRS voltage and LV mass ratio⁷
- The amplitude of the QRS voltage is not reflective of the increased LV wall thickness, because the increase is due to extracellular amyloid protein deposition rather than myocyte hypertrophy¹
 - Absence of a low QRS voltage does not, however, rule out amyloidosis, as low voltage can vary among cardiac amyloidosis etiologies^{9,19-22}

Discordance between LV wall thickness and QRS voltage



Illustrative representation.

DIAGNOSIS of orthopedic conditions, including carpal tunnel syndrome, lumbar spinal stenosis, biceps tendon rupture, and/or hip and knee arthroplasty¹¹⁻¹⁴

Bilateral carpal tunnel syndrome and lumbar stenosis

- Often seen in ATTR-CM due to amyloid deposition in these areas; lumbar spinal stenosis is principally seen in wtATTR-CM^{7,11,12}
- Bilateral carpal tunnel syndrome and lumbar spinal stenosis are known clinical predictors of ATTR-CM and may precede heart failure symptoms by several years^{7,12}
- Among patients undergoing carpal tunnel release surgery, 10.2% had amyloid deposits²³

Biceps tendon rupture

- Among patients with wtATTR-CM, biceps tendon rupture has been observed in 33% of patients, occurring in the dominant arm in 95% and bilaterally in 24% of patients¹³

Hip and knee arthroplasty

- In a study of 313 patients (172 with ATTR-CM), hip and knee arthroplasty surgeries were more frequent than in the general population, and on average, arthroplasty occurred 7.2 years before ATTR-CM diagnosis¹⁴

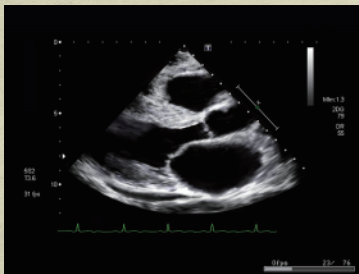
ECHOCARDIOGRAPHY showing increased LV wall thickness⁹

- Unexplained increased LV wall thickness (eg, hypertension) should raise suspicion for cardiac amyloidosis³

Transthoracic echocardiograms showing increased LV wall thickness

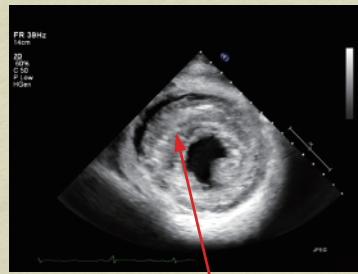
Parasternal long-axis view

ATTR amyloidosis heart

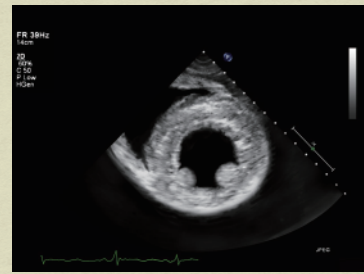


Parasternal short-axis view

ATTR amyloidosis heart



Normal heart



Illustrative representation.

Increased LV end diastolic
interventricular wall thickness

NERVOUS SYSTEM dysfunction, including polyneuropathy and autonomic dysfunction, including gastrointestinal complaints and/or unexplained weight loss¹⁵

- Gastrointestinal complaints due to autonomic dysfunction include chronic diarrhea, constipation, or both¹⁵
- Orthostatic hypotension due to autonomic dysfunction is another symptom that may occur with ATTR-CM¹⁵

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