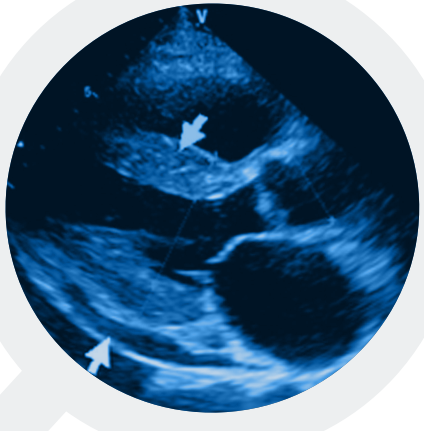
Cardiac Amyloidosis

Using ECHOCARDIOGRAPHY to Suspect Cardiac Amyloidosis



An underdiagnosed cause of heart failure[1]

Based on the Canadian Cardiovascular Society/Canadian Heart Failure Society (CCS/CHFS) Joint Position Statement on the evaluation and management of patients with cardiac amyloidosis

Pfizer

Cardiac amyloidosis is an underdiagnosed, progressive, and infiltrative disease that has the ability to disguise itself clinically as common cardiovascular disease states[1]

- **~10% of HFpEF patients** referred to a single centre had ATTR-CM confirmed by endomyocardial biopsy[2]*
- **~13% of hospitalized patients** with HFpEF and increased LV wall thickness had wild-type ATTR-CM confirmed by scintigraphy[3]†
- The annual incidence of AL is estimated at **10 per million** and increases with age[1]

AL = light chain amyloidosis; ATTR-CM = transthyretin-mediated cardiac amyloidosis; HFpEF = heart failure with preserved ejection fraction; LV = left ventricular

* Prospective analysis in 108 patients seen at the John Hopkins HFpEF Clinic who underwent endomyocardial biopsy to evaluate myocardial tissue histopathology.

† Prospective, cross-sectional, single-centre study at a tertiary university hospital in Madrid, Spain, that included 120 patients admitted for HFpEF, with LV ejection fraction ≥50% and LV hypertrophy ≥12 mm.

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

Cardiac imaging plays a critical role in the diagnostic evaluation of patients with suspected cardiac amyloidosis[1]

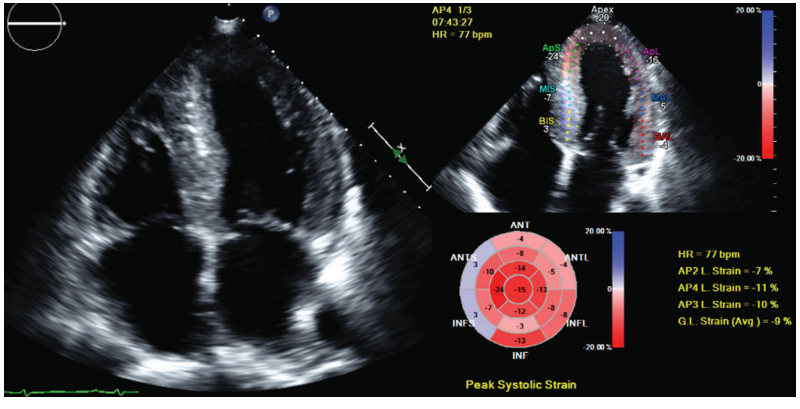
According to the 2020 CCS/CHFS Joint Position Statement, **echocardiography with longitudinal LV strain measurement is recommended to be performed in all patients with suspected cardiac amyloidosis to evaluate for characteristic features of cardiac amyloidosis** or alternative causes of heart failure.[1]

(Strong Recommendation, Moderate-Quality Evidence)

Although findings on echocardiography might be highly consistent with cardiac amyloid infiltration, in isolation, this test is generally not considered confirmatory of the diagnosis and cannot reliably differentiate sub-type.[1]

Echocardiographic findings that may be indicative of cardiac amyloidosis[1]

Apical 4-chamber view



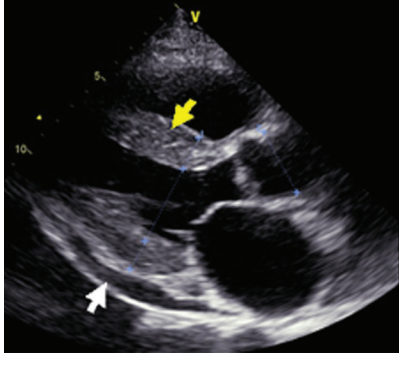
- Increased LV and RV wall thickness
- Preserved ventricular size, biatrial enlargement
- Diastolic dysfunction
- Increased valvular and interatrial septum thickness
- Small pericardial effusion
- Reduced LV global longitudinal strain, preserved apical strain (basal-apical gradient)

"Although findings on echocardiography and/or cardiovascular magnetic resonance imaging (CMR) might be highly consistent with cardiac amyloid infiltration, in isolation these tests are generally not considered confirmatory of the diagnosis, and neither test can reliably differentiate sub-type."[1]

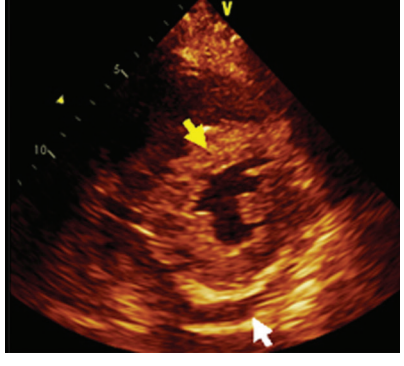
RV = right ventricular

Characteristic appearance of cardiac amyloidosis on 2D echo[1,4]

PARASTERNAL LONG AXIS



PARASTERNAL SHORT AXIS



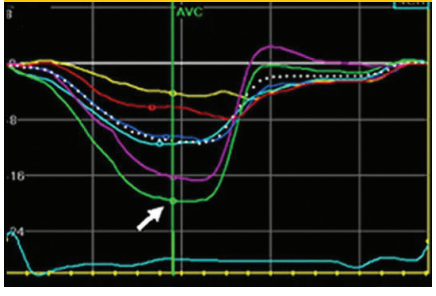
- **Increased LV wall thickness** with a sparkling texture of the myocardium (yellow arrows) in a patient with primary AL
- **Small pericardial effusion** (white arrows), often seen in patients with cardiac amyloidosis
- Both AL and ATTR cardiac amyloidosis patients demonstrate a typical pattern of distribution of STE-derived longitudinal strain in which basal LV segments are severely impaired while apical segments are relatively spared

STE = speckle-tracking echocardiography

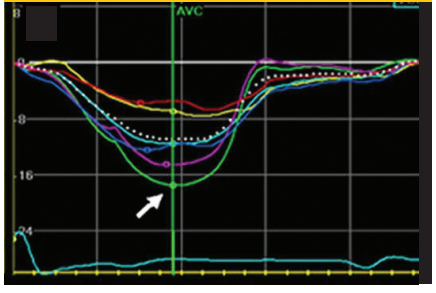
LV longitudinal strain abnormalities[1,4]

LV longitudinal systolic strain measurement using STE showing reduced global longitudinal strain with apical sparing (base to apical gradient) is a relatively more specific finding and can be helpful for differentiating cardiac amyloidosis from other causes of increased LV wall thickness.

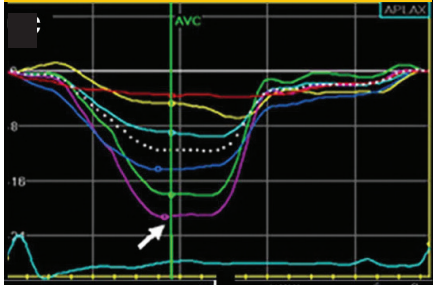
APICAL 4-CHAMBER VIEW



APICAL 2-CHAMBER VIEW

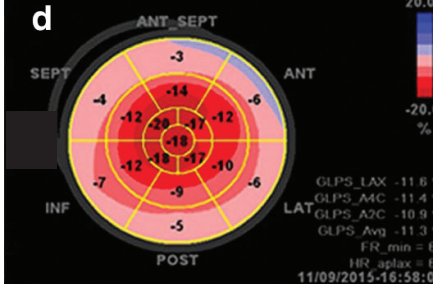


APICAL 3-CHAMBER VIEW



All images show abnormal longitudinal strain in the basal and mid segments with relative preservation in the apical segments (purple and green curves, white arrows) in a patient with hereditary ATTR-CM.

BULL'S-EYE MAP



- Corresponding bull's-eye map of the longitudinal strain pattern throughout the left ventricle with the "cherry-on-the-top" sign
- Red denotes preserved apical longitudinal strain
- Pink/blue denotes impaired longitudinal strain at the middle and basal segment values

Differential diagnosis of cardiac amyloidosis using nuclear scintigraphy or endomyocardial biopsy[1,5]

1. **Suspect ATTR-CM or AL**

2. **Differentiate AL amyloidosis**

Order the following tests:

- Serum kappa/lambda free light chain ratio (abnormal if ratio is <0.26 or >1.65)
- Serum protein immunofixation (abnormal if monoclonal protein is present)
- Serum and urine protein electrophoresis with immunofixation (abnormal if monoclonal protein is present)

Monoclonal protein absent

3. **Evaluate for cardiac involvement**

4. **Nuclear scintigraphy with ^{99m}technetium-labelled pyrophosphate**

or

Endomyocardial biopsy (EMB) with sub-type identification via mass spec or immunohistochemistry

Monoclonal protein present

3. **Hematology referral**

4. **Confirmation with biopsy of involved organ**

References

1. Fine NM *et al.* Canadian Cardiovascular Society/Canadian Heart Failure Society joint position statement on the evaluation and management of patients with cardiac amyloidosis. *Can J Cardiol* 2020;36:322-34.

2. Hahn VS *et al.* Endomyocardial biopsy characterization of heart failure with preserved ejection fraction and prevalence of cardiac amyloidosis. *JACC Heart Fail* 2020;8(9):712-24.

3. González-López E *et al.* Wild-type transthyretin amyloidosis as a cause of heart failure with preserved ejection fraction. *Eur Heart J* 2015;36(38):2585-94.

4. Dorbala S *et al.* ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI expert consensus recommendations for multimodality imaging in cardiac amyloidosis: part 1 of 2: evidence base and standardized methods of imaging. *J Nucl Cardiol* 2019;26(6):2065-123.

5. Maurer MS *et al.* Expert consensus recommendations for the suspicion and diagnosis of transthyretin cardiac amyloidosis. *Circ Heart Fail* 2019;12(9):1-11.

REVIEWED BY PAAB

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