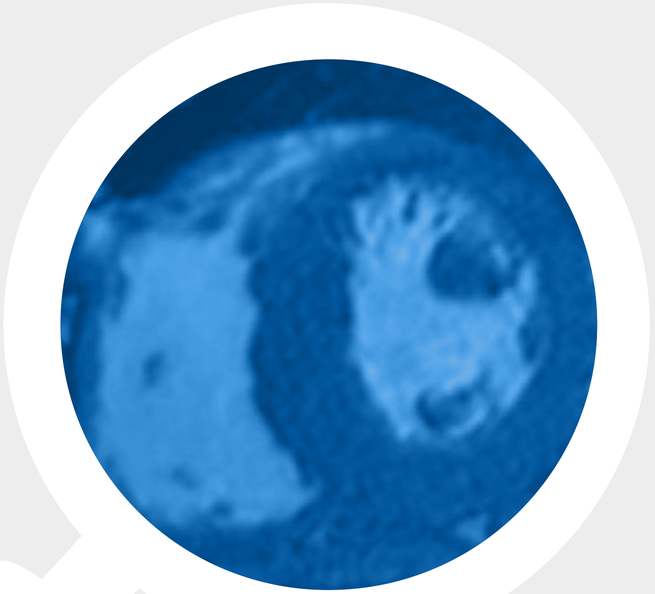
Using Cardiac Magnetic Resonance (CMR) to Suspect ATTR-CM



An Often Underdiagnosed Cause of Heart Failure[1-3]

Adapted from ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI* Expert Consensus Recommendations for Multimodality Imaging in Cardiac Amyloidosis: Evidence Base and Standardized Methods of Imaging and Diagnostic Criteria and Appropriate Utilization, Parts 1 and 2, including 2021 addendum.[4,5]

*The consensus report was written by a writing group of experts in cardiovascular imaging and amyloidosis assembled by the American Society of Nuclear Cardiology and endorsed by 8 societies including the American College of Cardiology, American Heart Association, American Society of Echocardiography, European Association of Nuclear Medicine, Heart Failure Society of America, International Society of Amyloidosis, Society of Cardiovascular Magnetic Resonance, and Society of Nuclear Medicine and Molecular Imaging.[4,5]

ATTR-CM Is an Underdiagnosed, Progressive, and Infiltrative Disease[6]

ATTR-CM Is Often Overlooked as a Cause of Heart Failure. Early Diagnosis and Treatment Are Critical to Extending Life[6,7]

Prognosis of **ATTR-CM worsens rapidly when left untreated,** resulting in continued amyloid deposition, organ dysfunction, and death.[6,8]

Once diagnosed, untreated patients with ATTR-CM have a **median survival of ~2 to 3.5 years**[6,8]

CMR, when used in combination with other imaging modalities, is an essential and noninvasive tool that can assist in the early detection of ATTR-CM.

The Role of CMR in Suspecting Cardiac Amyloidosis[4]

CMR may raise suspicion of cardiac amyloidosis in 2 scenarios:

- Differentiation between cardiac amyloidosis and other cardiomyopathic conditions with increased wall thickening
- Detection of early cardiac involvement in patients presenting with symptoms of systemic amyloidosis

When echocardiography findings are suggestive or indeterminate, or acoustic windows are poor, CMR may be advantageous:

- To characterize the right ventricle
- To characterize tissue based on the contrast-enhanced patterns of myocardial infiltration
- To precisely quantify cardiac chamber volumes and ventricular mass

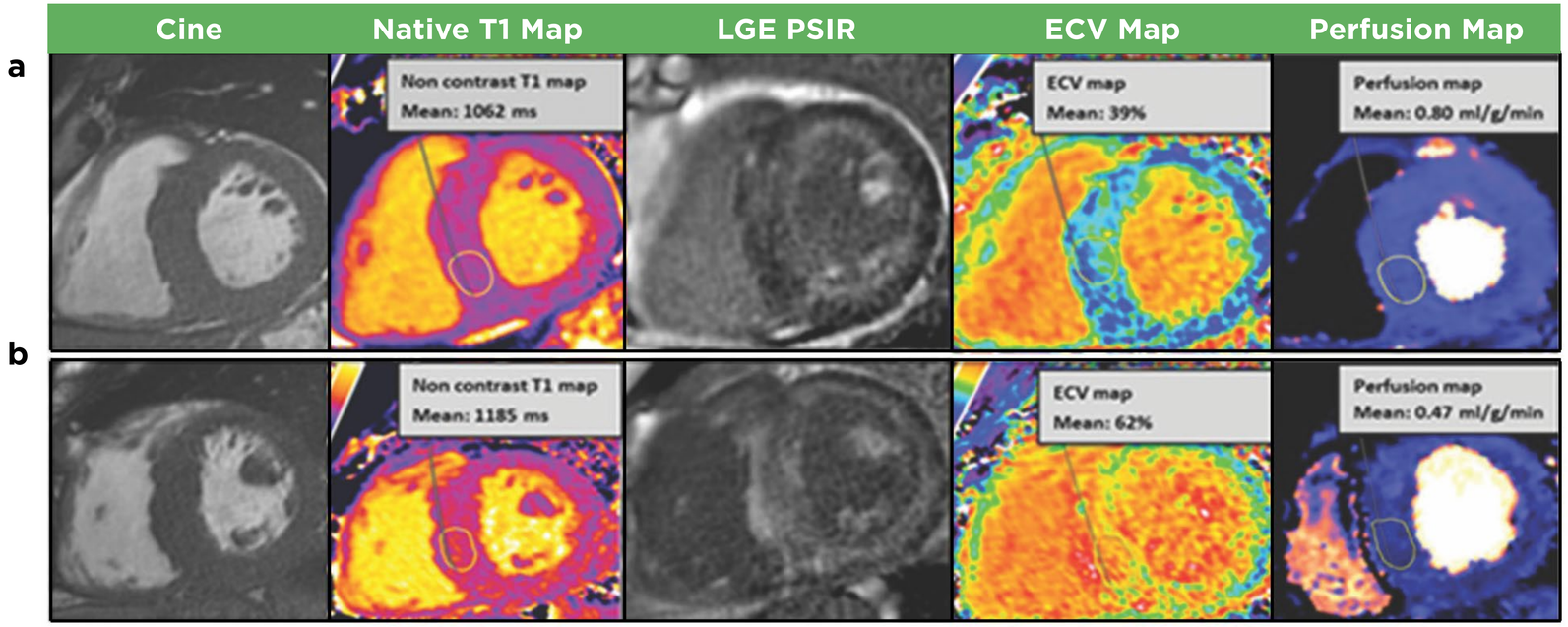
Certain findings on CMR are suggestive of Cardiac Amyloidosis but cannot definitively distinguish AL from ATTR

CMR may play a central role in the noninvasive diagnosis of cardiac amyloidosis due to its ability to assess cardiac structure, function, and tissue characterization.

Characteristic Imaging of Cardiac Amyloidosis With CMR[4]

Amyloid Burden

In the images below, CMR shows how **both patients a and b exhibit similar mass (cine)**—yet significantly different amyloid burden—with **patient b** showing a **significant higher amyloid burden** (higher native T1, transmural LGE, and higher extracellular volume [ECV]), and **lower myocardial resting perfusion** (after adjusting for ECV expansion).



Row (a) and row (b) represent two distinct patients with cardiac amyloidosis.

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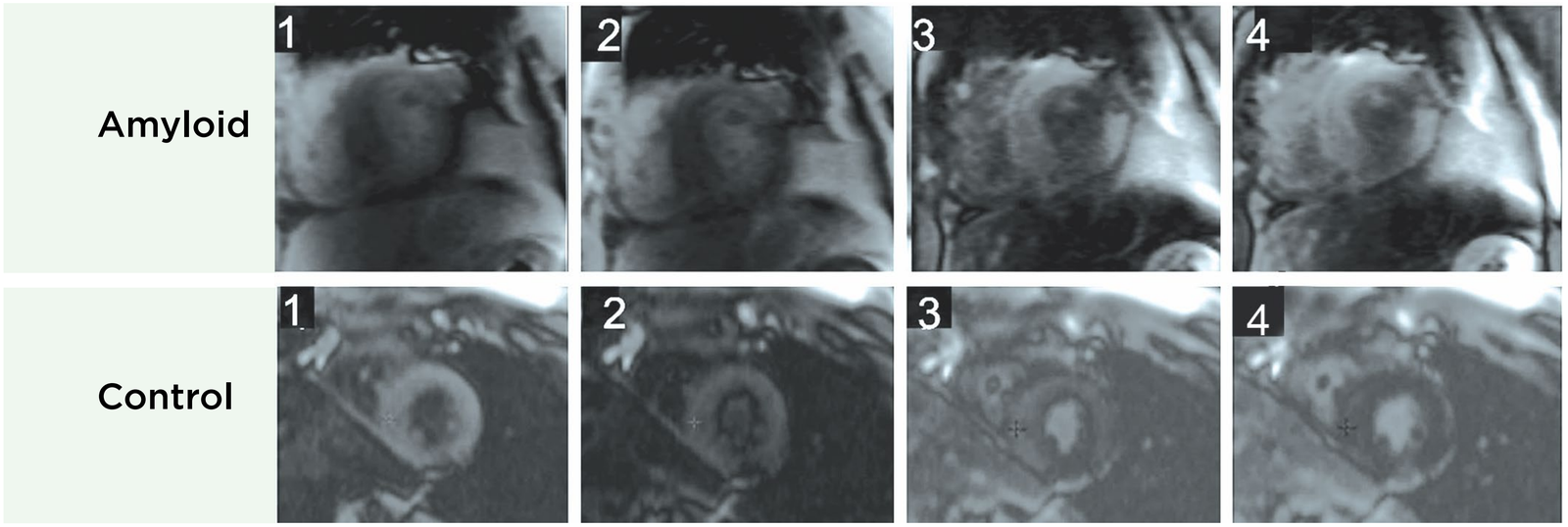
Characteristic Imaging of Cardiac Amyloidosis on CMR (continued)[4]

Myocardial and Blood Pool Nulling

The images below show a distinct pattern of myocardial and blood pool nulling. **In the amyloid patient** (top row), **the myocardium nulls prior to the blood pool, whereas in the non-amyloid control patient** (bottom row)**, the blood pool nulls prior to myocardium**.



Each row represents inversion scout images for two distinct patients: the upper row is an amyloid patient and the bottom row is a non-amyloid control patient.

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Recommendations for Standardized Interpretation and Reporting of CMR for Cardiac Amyloidosis[4]

LV Function and Morphology

CRITERIA FOR **REQUIRED** REPORTING:

- **Biventricular long-axis impairment** with relative apical functional sparing
- **Increased LV wall thickness**
  - >Laboratory ULN for sex on SSFP cine CMR and increased relative wall thickness >0.42 cm
- **LV stroke volume** index (<35 mL/m^2)
- **LV mass** ≥91 g/m^2 for men and ≥78 g/m^2 for women (with papillary muscle included as part of LV mass measurement)
- **Increased left atrial volume** >163 mL for men and >131 mL for women
- **Increased right atrial volume** >85 mL/m^2
- **Reduced atrial function** <29% for men and <35% for women
- **Pericardial effusion**

SSFP, steady state free precession; ULN, upper limit of normal.

Recommendations for Standardized Interpretation and Reporting of CMR for Cardiac Amyloidosis (continued)[4]

Amyloid imaging

CRITERIA FOR **REQUIRED** REPORTING:

- **Abnormal LGE pattern**
  - Diffuse LGE
  - Subendocardial LGE
  - Patchy LGE
  - Difficulty in achieving myocardial nulling over a range of inversion times
  - Dark blood pool signal

CRITERIA FOR **RECOMMENDED** REPORTING:

- Abnormal myocardial signal suppression pattern
- Myocardium nulls before blood pool on Look-Locker, Cine IR, or TI scout sequences

LGE, late gadolinium enhancement; IR, inversion recovery.

Recommendations for Standardized Interpretation and Reporting of CMR for Cardiac Amyloidosis (continued)[4]

Amyloid Quantitation

CRITERIA FOR **RECOMMENDED** REPORTING:

- **Abnormal TI mapping** (criteria may vary based on the sequence used [MOLLI, ShMOLLI] and the field strength of the magnet)
- **ECV >0.40** is highly suggestive of cardiac amyloidosis

MOLLI, modified Look-Locker inversion recovery; ShMOLLI, shortened modified Look-Locker inversion recovery; ECV, extracellular volume.

CMR Findings Related to Cardiac Amyloidosis Are **REQUIRED** to Be Reported as Follows[4]:

Strongly suggestive:

- Increased LV wall thickness
- Increased LV mass
- Biatrial enlargement
- Typical diffuse or global LGE pattern
- Difficulty achieving myocardial nulling
- Significantly increased ECV (>0.40),
- Small pericardial and/or pleural effusions

Not suggestive:

- Normal LV wall thickness
- Normal LV mass
- No ventricular LGE
- Normal atrial size

Equivocal:

Findings not described above

T2 mapping is currently not part of the standard clinical amyloidosis imaging protocol.
LGE, late gadolinium enhancement.

CMR Findings Related to Cardiac Amyloidosis Are **RECOMMENDED** to Be Reported as Follows[4]:

Interpret the CMR results in the context of prior evaluation

Provide follow-up recommendations:

- **Strongly suggestive CMR findings** cannot distinguish AL from ATTR cardiac amyloidosis
- **Endomyocardial biopsy is frequently unnecessary** in patients with strongly suggestive CMR findings and histologically defined systemic amyloidosis or diagnostic ^{99m}Tc-PYP/MDP/HMDP imaging
- **Consider evaluation to exclude:**
  - AL amyloidosis; evaluate for plasma cell dyscrasia (serum and urine immunofixation, serum FLC assay)
  - ATTR cardiac amyloidosis; consider imaging with ^{99m}Tc-PYP/MDP/HMDP

T2 mapping is currently not part of the standard clinical amyloidosis imaging protocol.

^{99m}Tc-MDP, ^{99m}technetium-labelled methylene diphosphonate; ^{99m}Tc-HMDP, ^{99m}technetium-labelled hydroxymethylene diphosphonate; ^{99m}Tc-PYP, ^{99m}technetium-labelled pyrophosphate; AL, immunoglobulin light chain amyloid fibril protein; ATTR, transthyretin amyloid fibril protein; FLC, free light chain.

SUMMARY

CMR May Help Increase Diagnostic Suspicion of ATTR-CM—an Underdiagnosed, Progressive, and Infiltrative Disease[1-3,5]

CMR may play a central role in the noninvasive diagnosis of cardiac amyloidosis, with the ability to[4]:

- **Assess cardiac structure**
- **Assess cardiac function**
- **Provide tissue characterization**

In patients with strongly suggestive CMR findings, imaging with nuclear scintigraphy, combined with blood and urine testing to rule out AL, should be considered as a next step for a definitive diagnosis of ATTR-CM.[4]

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