Expert Consensus Recommendations for Multimodality Imaging in Cardiac Amyloidosis

Adapted from the ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI

**INTRODUCTION**

• Despite recent advances, cardiac amyloidosis remains largely underrecognized or delayed in diagnosis
  - Clinical and diagnostic expertise is limited to a few expert centers
  - Evidence for imaging options are confined to small studies or limited multicenter experiences
  - No clear consensus on standardized imaging pathways exists

• The Expert Consensus Recommendations for Multimodality Imaging in Cardiac Amyloidosis reflects a multisocietal, international consensus document outlining:
  - Evidence base of imaging methods for cardiac amyloidosis and diagnostic criteria
  - Standardization of imaging techniques and appropriate utilization

• Societies that contributed to the development of the expert consensus recommendations
  - American Society of Nuclear Cardiology (ASNC)
  - American College of Cardiology (ACC)
  - American Heart Association (AHA)
  - American Society of Echocardiography (ASE)
  - European Association of Nuclear Medicine (EANM)
  - Heart Failure Society of America (HFSA)
  - International Society of Amyloidosis (ISA)
  - Society of Cardiovascular Magnetic Resonance (SCMR)
  - Society of Nuclear Medicine and Molecular Imaging (SNMMI)

**MULTIMODALITY APPROACH REQUIRED FOR DIAGNOSIS**

- **Echocardiography**
  - Major role in noninvasive diagnosis due to its assessment of structure and function and its pervasive use in patients with concerning cardiac symptoms.

- **Cardiac magnetic resonance (CMR)**
  - Important role due to its ability to provide tissue characterization, in addition to high-resolution morphologic and functional assessment.
  - Offers value in 2 clinical scenarios: differentiation of cardiac amyloidosis from other cardiomyopathies, and potentially early detection of cardiac amyloidosis.
  - CMR with late gadolinium enhancement (LGE) may be relatively contraindicated in patients with suspected cardiac amyloidosis and concomitant renal failure.

- **Radionuclide imaging**
  - Unique role in noninvasive diagnosis, as 99mTc-PYP (bone-avid) compounds can assist in the diagnosis of amyloid transthyretin (ATTR) cardiac amyloidosis with high sensitivity and specificity. Bone-avid radiotracers can definitively diagnose amyloid type when a plasma cell dyscrasia is excluded.
  - Single-photon emission computerized tomography (SPECT) imaging is necessary for studies that show planar myocardial uptake because it can help differentiate myocardial uptake from blood pool or overlying bone uptake.

*More details of these approaches can be seen on the reverse side of this sheet.

**99mTc-PYP is not FDA approved for the diagnosis of ATTR-CM (transthyretin amyloid cardiomyopathy). Please consult individual labeling for risks.**

Refer to the expert consensus statement for detailed recommendations for diagnosis.

The expert consensus recommendations were developed by the ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI. Pfizer is not responsible for their content.
## Recommendations for diagnosis

### THREE APPROACHES ARE RECOMMENDED FOR DIAGNOSIS OF CARDIAC AMYLOIDOSIS

#### 1 Histological diagnosis of cardiac amyloidosis: endomyocardial biopsy* (for amyloidogenic transthyretin [ATTR], amyloidogenic light chain [AL], or other subtypes)
- Endomyocardial biopsy positive for cardiac amyloidosis with Congo red staining with apple-green birefringence under polarized light; typing by immunohistochemistry and/or mass spectrometry at specialized centers

#### 2 Histological diagnosis of cardiac amyloidosis: extracardiac biopsy (for ATTR and AL)
- ATTR is diagnosed when the below criteria are met:
  - Extracardiac biopsy proven ATTR amyloidosis AND
  - Typical cardiac imaging features (as defined below)
- AL is diagnosed when the below criteria are met:
  - Extracardiac biopsy proven AL amyloidosis AND
  - Typical cardiac imaging features (as defined below) OR
  - Abnormal cardiac biomarkers: abnormal age-adjusted N-terminal pro-brain natriuretic peptide (NT-proBNP) or abnormal Troponin T/Hs-Troponin with all other causes for these changes excluded

#### 3 Clinical diagnosis of ATTR cardiac amyloidosis: 99mTc-pyrophosphate (PYP) (for ATTR)
- 99mTc-PYP Grade 2 or 3 myocardial uptake of radiotracer AND
- Absence of a clonal plasma cell process as assessed by serum free light chains (FLCs) and serum and urine immunofixation AND
- Typical cardiac imaging features (outlined below)

### TYPICAL CARDIAC IMAGING FEATURES OF ATTR AND AL

**Typical cardiac echo or CMR or PET features: ANY of the below imaging features with all other causes for these cardiac manifestations, including hypertension, reasonably excluded.**

#### Echocardiography
- Left ventricular (LV) wall thickness >12 mm
- Relative apical sparing of global longitudinal strain (LS) ratio (average of apical longitudinal strain/average of combined mid+basal LS >1)
- ≥ Grade 2 diastolic dysfunction†

#### Cardiac magnetic resonance (CMR)
- LV wall thickness > upper limit of normal (ULN) for sex on steady-state free precession (SSFP) cine CMR
- Global extracellular volume (ECV) >0.40
- Diffuse late gadolinium enhancement (LGE)‡
- Abnormal gadolinium kinetics typical for amyloidosis, myocardial nulling prior to blood pool nulling

#### Positron emission tomography (PET): 18F-florbetaben PET†
- Target to background (LV myocardium to blood pool) ratio >1.5
- Retention index >0.030 min⁻¹

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*Endomyocardial biopsy should be considered in cases of equivocal 99mTc-PYP scan. When 99mTc-PYP is positive in the context of any abnormal evaluation for serum/urine immunofixation or serum free light chain assay, or monoclonal gammapathy of uncertain significance (MGUS), this should not be seen as diagnostic for ATTR cardiac amyloidosis. In these instances, referral to a specialist amyloid center for further evaluation and consideration of biopsy is recommended.

These consensus recommendations were based on moderate-quality evidence from 1 or more well-designed, well-executed nonrandomized studies, observational studies, registries, or meta-analyses of such studies.

References:

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†Off-label use of FDA-approved commercial products.
‡18F-flutemetamol not studied systematically in the heart. 11C-Pittsburgh Compound B is not FDA approved and not available to sites without a cyclotron in proximity.

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