Cardiac Amyloidosis Imaging

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RATIONALE/INTRODUCTION

Differentiation between amyloid light-chain (AL) and amyloid transthyretin (ATTR) cardiac amyloidosis is critical because of the differences in treatment. AL cardiac amyloidosis is treated with chemotherapy or stem-cell transplantation. ATTR cardiac amyloidosis is treated with disease-modifying agents that silence, stabilize, or disrupt ATTR protein misfolding and by the management of heart failure symptoms. ATTR cardiac amyloidosis demonstrates avid uptake of ^{99m}Tc-pyrophosphate in the myocardium, whereas AL cardiac amyloid has minimal or no avidity. Although the binding mechanism of ^{99m}Tc-pyrophosphate is unknown, it is believed to bind in microcalcifications in amyloid fibrils. ATTR, compared with AL, amyloidosis has a higher density of microcalcifications related to the chronicity of the disease.

INDICATIONS

- Differentiation of ATTR from AL cardiac amyloidosis.
- Evaluation of patients with heart failure and an increased left ventricular wall thickness not due to other reasons.
- Evaluation of African-American patients more than 60 y old with heart failure and an increased left ventricular wall thickness greater than 12 mm not due to other reasons.
- Evaluation of patients more than 60 y old with unexplained heart failure and preserved ejection fraction.
- Evaluation of patients, particularly older men, with signs of heart failure in the presence of unexplained neuropathy, bilateral carpal tunnel syndrome, or atrial arrhythmias without typical risk factors.
- Evaluation of patients with a known or suspected family history of amyloidosis.
- Assessment for ATTR cardiac amyloidosis in patients with cardiac MRI or echocardiography findings consistent with cardiac amyloidosis.
- Evaluation of suspected ATTR cardiac amyloidosis in patients with contraindications to cardiac MRI, such as those with implantable devices or renal insufficiency.

CONTRAINDICATIONS/TECHNICAL CONSTRAINTS

- Pregnancy/breastfeeding (pregnancy must be excluded according to local institutional policy; if the patient is breastfeeding, appropriate radiation safety instructions should be provided).
- A recent nuclear medicine study (radiopharmaceutical-dependent).

PATIENT PREPARATION/EDUCATION

- There are no specific patient preparation requirements. The patient may eat and take medications as necessary before the study.
- A focused history containing the following elements should be obtained:
  - Past medical history: heart failure, heart failure with preserved ejection fraction (particularly in men), right heart failure (e.g., hepatomegaly, ascites, or lower extremity edema), unexplained atrial arrhythmias or conduction system disease, a pacemaker, concentric left ventricular wall thickening, hypertension that resolved over time, intolerance to angiotensin-converting enzyme inhibitors or β-blockers, bilateral carpal tunnel syndrome, lumbar spinal stenosis, previous orthopedic procedures, biceps tendon rupture, unexplained peripheral neuropathy, autonomic dysfunction (e.g., postural hypotension or alternating bowel pattern).
  - Family history of amyloidosis, cardiomyopathy, or polyneuropathy.
  - Signs and symptoms including shortness of breath during exercise or when lying down; swelling of the feet, ankles, and legs; dizziness, weakness, fatigue, irregular heartbeat, numbness or tingling in the hands or feet; skin thickening, easy bruising, enlarged tongue, diarrhea, constipation, frequent urination or incontinence.
  - Current medications.
  - Results of clinical laboratory tests, including serum κ/λ-free light chain ratio (abnormal if the ratio is <0.26 or >1.65), serum protein immunofixation (abnormal if monoclonal protein is detected), urine protein immunofixation (abnormal if monoclonal protein is detected), troponin levels and N-terminal pro–brain natriuretic peptide.
  - Results of other diagnostic tests, including echocardiography, cardiac MRI, and electrocardiography.

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TABLE 1
Radiopharmaceutical Identity, Dose, and Route of Administration

Identity	Dose	Route of administration
^{99m}Tc-pyrophosphate	370–740 MBq (10–20 mCi)	Intravenous

RADIOPHARMACEUTICAL IDENTITY, DOSE, AND ROUTE OF ADMINISTRATION

The radiopharmaceutical identity, dose, and route of administration are described in Table 1.

^{99m}Tc-pyrophosphate is primarily used for cardiac amyloidosis imaging in the United States. ^{99m}Tc-3,3-diphosphono-1,2-propanodicarboxylic acid (DPD) is used in Europe but is not approved by the Food and Drug Administration in the United States. ^{99m}Tc-hydroxymethylenediphosphonate (HMDP) can also be used for cardiac amyloidosis imaging. It is approved for use in the United States and may be substituted in times of ^{99m}Tc-pyrophosphate shortage. However, access to ^{99m}Tc-HMDP may be limited. Although no studies to date have directly compared the 3 tracers, published literature suggests they can be used interchangeably. When ^{99m}Tc-DPD and ^{99m}Tc-HMDP are used, whole-body scintigraphy in addition to planar and SPECT imaging is suggested to demonstrate other soft-tissue uptake.

^{99m}Tc-methylene diphosphonate, although widely available in the United States, has a lower sensitivity and should not be used for cardiac amyloid imaging.

ACQUISITION PARAMETERS: DYNAMIC/STATIC/PLANAR

The acquisition parameters are described in Table 2.

ACQUISITION INSTRUCTIONS

- After injection of the ^{99m}Tc-pyrophosphate, planar imaging is performed after a 3-h delay to allow blood pool clearance.

TABLE 2
^{99m}Tc-Pyrophosphate Cardiac Amyloidosis Imaging Parameters

Parameter	Characteristics	Standard, optional, or preferred
Camera type	Large-field-of-view γ-camera	Standard
	Cadmium zinc telluride	Optional*
Energy peak	140 keV	Standard
Energy window	15%–20%	Standard
Collimator	Low-energy, all-purpose	Standard
Patient position	Supine	Standard
Field of view	Heart/chest	Standard
Injection-to-imaging time	3 h	Standard
	1 h	Optional
Planar		
Acquisition type	Static	Standard
	Whole-body imaging	Optional†
Detector configuration	90°	Standard
Views	Anterior and left lateral	Standard
Number of views	2	Standard
Counts per view	750,000	Standard
Matrix	256 × 256	Standard
Magnification	1.46	
SPECT or SPECT/CT*		
Acquisition type	Step and shoot or continuous	Standard
Patient position	Supine	Standard
	Upright	Optional
Orbit	180°/90°	Standard
	360°/180°	Optional
Matrix	128 × 128 (minimum, 64 × 64)	Standard
Magnification	1.46 (180° orbit)	Standard
	1.0 (360° orbit)	Optional
Pixel size	2.3–6.5 mm	Standard
Projections/detector	40/32	Standard
Time/projection	20 s/25 s	Standard
CT attenuation correction	Heart	Preferred

*Parameters defined for γ-cameras as parameters for cadmium-zinc-telluride cameras have not been firmly established.

†Whole-body imaging is not performed when imaging with ^{99m}Tc-pyrophosphate. However, whole-body imaging is useful when imaging with ^{99m}Tc-HMDP or ^{99m}Tc-DPD to demonstrate soft-tissue uptake.

TABLE 3
SPECT Semiquantitative Visual Scoring

Grade	Description
0	No myocardial uptake and normal bone uptake
1	Myocardial uptake less than rib uptake
2	Myocardial uptake equal to rib uptake
3	Myocardial uptake greater than rib uptake with mild or absent uptake

- For planar imaging, the patient is placed supine with the arms above the head. For large-field-of-view cameras, the patient's shoulders are positioned near the top of the field of view to visualize the entire ribcage. Anterior and left lateral images are acquired for 750,000 counts.
- For SPECT imaging using a dual-head camera, the detectors are configured at 90° for a minimum of 32 stops at 25 s/stop. Absence of motion is verified before the patient is allowed to leave the facility.

COMMON OPTIONS

In times of ^{99m}Tc-pyrophosphate shortage in the United States, ^{99m}Tc-HMDP may be substituted for ^{99m}Tc-pyrophosphate. When ^{99m}Tc-HMDP is used, whole-body imaging (10–14 cm/min) in addition to planar and SPECT imaging is suggested to demonstrate extracardiac soft-tissue uptake (gluteal, shoulder, chest, and abdominal walls).

PROCESSING INSTRUCTIONS

- The anterior planar image is used to create a circular region of interest over the heart. Care must be taken to avoid including any extraneous activity outside the heart, such as in the sternum, the lung, or a hot rib due to previous injury.
- The heart region is mirrored (same size) by placing a second circular region on the opposite side of the chest on the flat area of the ribs (contralateral lung region), again ensuring there is no extraneous activity such as in the sternum, the spine, or a rib injury.
- The ratio of the heart to the contralateral lung is calculated by dividing the heart region by the contralateral lung region. A ratio of 1.3 or more is positive for cardiac amyloidosis.
- The SPECT data are reconstructed using filtered backprojection or iterative reconstruction and displayed in the coronal, sagittal, and transverse projections.
- The planar and SPECT images are visually assessed and assigned a grade of 0–3 based on myocardial uptake compared with rib uptake (Table 3). Grades 2 and 3 are considered abnormal.

PRECAUTIONS

Interpretation of ^{99m}Tc-pyrophosphate imaging and diagnosis of ATTR cardiac amyloidosis cannot be based on the planar and SPECT results alone. AL systemic amyloidosis must be excluded by serum and urine immunofixation and a serum-free AL assay in all patients with positive scan results.

SUGGESTED READING

1. ASNC cardiac amyloidosis practice points: ^{99m}technetium-pyrophosphate imaging for transthyretin cardiac amyloidosis. American Society of Nuclear Cardiology website. https://www.asnc.org/files/19110%20ASNC%20Amyloid%20Practice%20Points%20WEB(2).pdf. Published February 2016. Updated February 2019. Accessed January 31, 2023.
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5. Kittleson MM, Maurer MS, Ambardekar AV, et al. Cardiac amyloidosis: evolving diagnosis and management: a scientific statement from the American Heart Association. *Circulation.* 2020;142:e7–e22.
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