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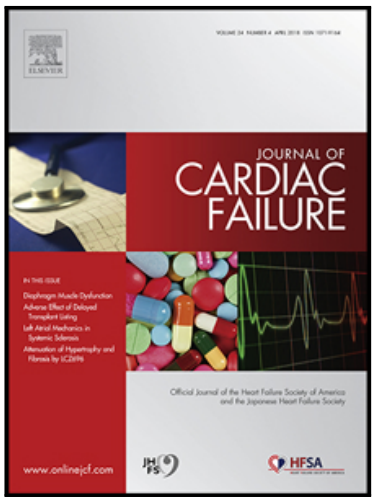

nAddendum to ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI expert consensus recommendations for multimodality imaging in cardiac amyloidosis: Part 1 of 2—evidence base and standardized methods of imaging

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Addendum to ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI expert consensus recommendations formultimodalityimaging incardiacamyloidosis:Part1of2—evidence baseandstandardized methodsofimaging

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THE NEED FOR AN ADDENDUM

There are two primary reasons for an addendum. The first is that the document reviewer list is being updated to include Dr. Richard Cheng and Dr. Roy John, who have critically reviewed the document, but were inadvertently not listed as reviewers. In addition, since the publication of this document and introduction of approved therapies for transthyretin cardiac amyloidosis (ATTR-CA), the clinical use of bone tracer cardiac scintigraphy has been extended to populations with lower prevalence of ATTR-CA. Numerous observations have raised concerns about (1) incorrect diagnosis of ATTR-CA based on ^{99m}Tc-pyrophosphate (PYP) planar imaging and heart-to-contralateral lung (H/CL) ratio without confirmation of diffuse myocardial uptake on SPECT imaging at some sites; (2) excess blood pool activity on the |-hour planar and SPECT images being 2 interpreted as positive scans; and (3) missed diagnosis of light chain (AL) amyloidosis, as serum-free light chain studies and serum and urine immunofixation electrophoresis studies may not be recommended in the °°MT ¢-PY P/-3,3-diphosphono- 1 ,2-propanodicarboxylic acid/hydroxymethylene diphosphonate (^{99m}Tc-PYP/DPD/HMDP) report. Incorrect diagnosis leads to inappropriate therapy and worse patient outcomes. SPECT and planar imaging performed at 3 hour maximize specificity. Additionally, technical parameters have been updated.

Accordingly, we are issuing this addendum to clarify the protocols, interpretation, and reporting of 2 MTc-PYP imaging:

1. Acquisition (Table 4):

a. The time between injection of ^{99m}Tc-PYP and scan is revised: 2- or 3-hour imaging 1s recommended, and |-hour imaging is optional (Table 4).

If excess blood pool activity is noted, 3-hour imaging is recommended. The timing between injection and scanning is now consistent for ^{99m}Tc-PYP, -DPD, and -HMDP. We recognize some experienced centers that have become proficient at 1-hour scanning; the recommendation for 2- or 3-hour imaging is particularly important for centers starting new ^{99m}Tc-PYP programs.

b. SPECT imaging is required in all studies (irrespective of time between injection and scan) to highlight the importance of directly visualizing tracer uptake in the myocardium.

c. 1-hour planar-only imaging is not recommended.

d. Emerging literature suggests that cadmium zinc telluride (CZT) SPECT can also be used for ^{99m}T¢-PYP/DPD/HMDP imaging.*”

2. Interpretation (Table 5):

a. Planar imaging and H/CL ratio alone are insufficient for diagnosis of ATTR cardiac amyloidosis. SPECT imaging is necessary to identify myocardial uptake of ??"Tc-PYP/DPD/HMDP.

b. Repeat imaging is recommended at 3 hours if excess blood pool activity is noted.

c. The steps in Table 5 clarify that visual grading on planar and SPECT imaging 1s the primary method for diagnosis of ATTR cardiac amyloidosis.

d. Recommendations are clarified for ease of interpretation.

3. Reporting (Table 6):

a. Diffuse myocardial uptake should be visualized to report a positive scan.

b. The criterion for H/CL ratio > 1.5 as strongly positive has been removed (consistent with diagnostic criteria listed in the ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI Expert Consensus Recommendations for Multimodality Imaging in Cardiac Amyloidosis: Part 2 of 2—Diagnostic Criteria and Appropriate Utilization, where H/CL ratio was not listed).

c. Conclusions have been clarified.

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Table 4. Recommendations for standardized acquisition of ^{99m}Tc-PYP/DPD/HMDP for cardiac amyloidosis. Adapted from Reference (207)

Imaging procedures	Parameters	Recommendation
Preparation	No specific preparation. No fasting required	Required
Scan	Rest scan	Required
Dose	^{99m}Tc-PYP: 10-20 mCi (370-740 MBq) intravenously	Recommended
	^{99m}Tc-DPD: 10-20 mCi (370-740 MBq) intravenously	
	^{99m}Tc-HMDP: 10-20 mCi (370-740 MBq) intravenously	Recommended
Time between injection and acquisition:°>?"Tc-PYP/DPD/HMDP	2 or 3h	Optional. If excess blood pool activity noted on 1-h images, 3-h imaging is recommended.
Time between injection and acquisition:°> ^{99m}Tc-PYP only	1h	See below regarding image type.
General imaging parameters' Field of view	Heart	Required
	Chest	Optional for planar
CT attenuation correction	Heart	Recommended
Image type: planar	Chest	SPECT/CT fusion images helpful to localize tracer uptake to the myocardium
	2 or3h	Recommended
Image type: SPECT Position	Heart	1-hour planar-only imaging is not recommended
	Supine	Required
	Upright	Required
Energy window	140 keV, 15-20%	Optional
Collimators	Low energy, high resolution	Required
Matrix-Planar	256 x 256	Recommended
Matrix-SPECT	128 x 128 (at least 64 by 64 is required)	Recommended
Pixel size	2.3-6.5 mm	Recommended
Planar imaging specific parameters' Number of views*	Anterior and lateral	Recommended
Detector configuration	90°	Required
Image duration (count based)	750,000 counts	Recommended
Magnification	1.46 for large field of view systems	Recommended
SPECT imaging specific parameter†	1.0 for small field of view systems	Recommended with goal of achieving recommended pixel

		size
Angular range/detector configur	180°/90°	Recommended
	360°/180°	Minimum Required
ECG gating	Off; Non-gated imaging	Optional, recommended if large FOV camera is available
Number of views/detector	40/32	Recommended
Time per stop	20 s/25 5	Recommended
Magnification	1.46 (180° angular range)	Recommended
	1.0 (360° angular range)	Recommended

ECG electrocardiogram, PYP pyrophosphate

*Anterior and lateral views are obtained at the same time; lateral planar views or SPECT imaging may help separate sternal from myocardial uptake

†Parameters for Nal SPECT scanners

Table 5. Recommendations for interpretation of ^{99m}Tc-PYP/DPD/HMDP for cardiac amyloidosis. Adapted from Reference (207)

Step 1: Visual interpretation	
Evaluate planar and SPECT images to confirm diffuse radiotracer uptake in the myocardium	
Differentiate myocardial radiotracer uptake from residual blood pool activity, focal myocardial infarct, and overlapping bone (e.g., from rib hot spots from fractures) on SPECT images. If excess blood pool activity is noted, recommend repeat SPECT imaging at 3 h	
If myocardial tracer uptake is visually present on SPECT, proceed to step 2, semi-quantitative visual grading. If no myocardial tracer uptake is present on SPECT, the visual grade is 0	
Step 2: Semi-quantitative visual grading to diagnose ATTR cardiac amyloidosis	
Examine planar and SPECT images for relative tracer uptake in the myocardium relative to ribs and grade using the following scale:	
Grade 0	No myocardial uptake and normal bone uptake
Grade 1	Myocardial uptake less than rib uptake
Grade 2	Myocardial uptake equal to rib uptake
Grade 3	Myocardial uptake greater than rib uptake with mild/absent rib uptake Step 3: Heart/contralateral lung uptake ratio assessment (when applicable)
A circular ROI should be drawn over the heart on the anterior planar images with care to avoid sternal overlap and with size adjusted to maximize coverage of the heart without inclusion of adjacent lung. This ROI (same size) should be mirrored over the contralateral chest without inclusion of the right ventricle, to adjust for background and rib uptake (see Fig. 6*). The heart and contralateral ROIs should be drawn above the diaphragm	
An H/CL ratio is calculated as the fraction of heart ROI mean counts to contralateral lung ROI mean counts.	
H/CL ratios of C 1.5 at 1 h can accurately identify ATTR cardiac amyloidosis if myocardial PYP uptake is visually confirmed on SPECT and systemic AL amyloidosis is excluded (114). An H/CL ratio of C 1.3 at 3 h can identify ATTR cardiac amyloidosis	
NOTE: Diagnosis of ATTR cardiac amyloidosis cannot be made solely based on H/CL ratio alone with PYP. H/CL ratio is not recommended if there is absence of myocardial uptake on SPECT. Additionally, if the visual grade is 2 or 3, diagnosis is confirmed and H/CL ratio assessment is not necessary. H/CL ratio is typically concordant with visual grade. If discordant or the visual grade is equivocal, H/CL ratio may be helpful to classify equivocal visual grade 1 versus 2 as positive or negative	
See Fig. 7.* Grade 2 or Grade 3 uptake is consistent with ATTR cardiac amyloidosis if a monoclonal plasma cell dyscrasia is excluded, as this degree of uptake can be seen in [20% of patients with AL cardiac amyloidosis.(3) Grade 0 and Grade 1 uptake may be observed in AL cardiac amyloidosis and warrants further evaluation to exclude AL amyloidosis.(3) The writing group would like to emphasize the importance of excluding a monoclonal process with serum/urine immunofixation and a serum-free light-chains assay in all patients with suspected amyloidosis	
Of note: ^{99m}Tc-PYP/DPD/HMDP uptake could be seen in other causes of myocardial injury, including pericarditis, myocardial infarction (regional uptake), and chemotherapy or drug associated myocardial toxicity	

* Fig. 6 and 7 refer to figures in the original document

AL amyloid light chain, *ATTR* amyloid transthyretin, *H/CL* heart/contralateral lung, *ROI* region of interest

Table 6. Recommendations for standardized reporting of ^{99m}Tc-PYP/DPD/HMDP imaging for cardiac amyloidosis. Adapted from Reference (207)

Parameters	Elements
Demographics	Patient name, age, sex, reason for the test, date of study, prior imaging procedures, biopsy results if available (required)
Methods	Imaging technique, radiotracer dose and mode of administration, interval between injection and scan, scan technique (planar and SPECT) (required)
Findings	Image quality
	Visual scan interpretation (required)
	Semi-quantitative interpretation in relation to rib uptake (required)
	Quantitative findings H/CL lung ratio (optional; recommended for positive scans)
Ancillary findings	Whole-body imaging if planar whole-body images are acquired (optional)
	Interpret CT for attenuation correction if SPECT/CT scanners are used (recommended)
Conclusions	1. An overall interpretation of the findings into categories of (1) not suggestive of ATTR cardiac amyloidosis; (2) strongly suggestive of ATTR cardiac amyloidosis; or (3) equivocal for ATTR cardiac amyloidosis after exclusion of a systemic plasma cell dyscrasia (required)
	(a) Not suggestive: A semi-quantitative visual Grade of O
	(b) Equivocal: If diffuse myocardial uptake of ^{99m}Tc-PYP/DPD/HMDP is visually confirmed and the semi-quantitative visual grade is 1 or there is interpretive uncertainty of grade 1 versus grade
	2 on visual grading
	(c) Strongly suggestive: If diffuse myocardial uptake of ^{99m}Tc-PYP/DPD/HMDP is visually confirmed, a semi-quantitative visual grade of 2 or 3
	2. Statement that evaluation for AL amyloidosis by serum FLCs, serum, and urine immunofixation is recommended in all patients undergoing ^{99m}Tc-PYP/DPD/HMDP scans for cardiac amyloidosis (required)
	3. Statement that results should be interpreted in the context of prior evaluation and referral toa hematologist or amyloidosis expert is recommended if either: (a) Recommended echo/CMR is strongly suggestive of cardiac amyloidosis and ^{99m}Tc-PYP/DPD/HMDP is not suggestive or equivocal and/or (b) FLCs are abnormal or equivocal (recommended)