11.0%; $P = 0.812$) (Figure 1). From our study cohort, 8 randomly selected patients were re-analyzed pre- and post-revascularization. There was a high level of reproducibility for OS-CMR ΔSI values. The intra-observer coefficient of variation was 3.0%, whereas that of the interobserver coefficient of variation was 5.9%.

To the best of our knowledge, this is the first study to assess myocardial oxygenation in hibernating myocardium. This study shows that OS-CMR ΔSI is impaired in chronic LV dysfunction and improves after revascularization. This is even more pronounced in hibernating segments. Myocardial oxygenation is not downregulated in hibernating segments. Based on our findings, we propose that hibernating myocardium is not an adaptive reduction of contractile function in response to reduction of resting blood flow as originally proposed by Rahimtoola,[4] but rather, it reflects a state of ischemic myocardium. The data from our pilot study must be validated in larger multicenter studies.

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Comparison of ^{99m}Tc-DPD Scintigraphy, CMR Imaging, and Echocardiography in Patients With V30M-Associated Hereditary Transthyretin Amyloidosis

Variant transthyretin amyloid cardiomyopathy (ATTRv-CM) is most frequently associated with 3 transthyretin variants; V122I (p.[Val142Ile]), T60A (p.[Thr80Ala]), and V30M (p.[Val50Met]), the latter typically accompanied by ATTR amyloid polyneuropathy. ATTR-CM was, until recently, diagnosed histologically, usually via an endomyocardial biopsy. More recently, nonbiopsy diagnosis of ATTR-CM was established, enabling ~99% patients with ATTR-CM who do not have a confounding incidental monoclonal gammopathy to be diagnosed without recourse to endomyocardial biopsy.[1] Nonbiopsy diagnosis relies heavily on technetium-99m labelled radionuclide bone scintigraphy using the bone tracers 3,3-diphosphono-1,2-propanodicarboxylic acid (^{99m}Tc-DPD), hydroxymethylene diphosphonate or pyrophosphate, which is known to be extremely sensitive for detecting ATTR-CM. However, according to some investigators, V30M-ATTRv-CM is associated with less intense cardiac uptake on ^{99m}Tc-DPD scintigraphy than would be expected for the degree of myocardial amyloid infiltration or with complete absence of cardiac uptake despite presence of cardiac amyloidosis, thus risking misdiagnosis.[2]

We sought to establish the diagnostic performance of radionuclide scintigraphy in V30M-ATTRv-CM by analyzing a cohort of 64 patients with histologically proven V30M-ATTRv who had undergone ^{99m}Tc-DPD scintigraphy and echocardiography within 3 months of one another, including 23 cases in which cardiac magnetic resonance (CMR) imaging was also performed. Whole body planar and single-photon emission computerized tomography images were acquired 3 hours after intravenous administration of ~700 MBq of ^{99m}Tc-DPD and categorized according to Perugini grade.[3] Echocardiograms were performed and categorized according to the validated inferior wall thickness (IWT) score as characteristic of (IWT score ≥8), inconclusive for (IWT score 2-7), or no evidence of (IWT score <2) cardiac amyloidosis.[4] CMR with late gadolinium enhancement imaging and T1 measurement were performed as previously described[5] and graded as follows: negative CMR—CMR normal or indicating nonamyloid diagnosis (eg, hypertensive heart disease); positive CMR—diffuse subendocardial or transmural late gadolinium enhancement, altered gadolinium kinetics, and/or diffusely elevated extracellular volume; inconclusive

TABLE 1 Comparison of ^{99m}Tc-DPD Scintigraphy, Echocardiography, and CMR in V30M-ATTRv[a]

^{99m}Tc-DPD Scintigraphy	Echocardiogram				Contrast CMR Findings			
Perugini Grade	No Evidence of Cardiac Amyloidosis	Inconclusive	Characteristic of Cardiac Amyloidosis	Total	No Cardiac Amyloidosis	Inconclusive	Cardiac Amyloidosis	Total
All patients								
0	22	12	0	34	–	–	–	–
1	4	1	0	5	–	–	–	–
2	4	9	9	22	–	–	–	–
3	0	2	1	3	–	–	–	–
Total	30	24	10	64	–	–	–	–
Subset of patients with CMR imaging								
0	4	1[b]	0	5	5	0	0	5
1	3[c]	0	0	3	0	0	3	3
2	2[c,d]	6[d]	5	13	0	0	13	13
3	0	2[d]	0	2	0	0	2	2
Total	9	9	5	23	5	0	18	23

[a]The concordance between ^{99m}Tc-DPD scintigraphy and CMR was 100%. [b]One patient with no cardiac amyloidosis by CMR or ^{99m}Tc-DPD scintigraphy had an echocardiogram that was inconclusive. [c]5 patients with evidence of amyloid by ^{99m}Tc-DPD scintigraphy and CMR, did not have echocardiographic evidence of cardiac amyloidosis. [d]Ten patients with a Perugini grade ≥2 ^{99m}Tc-DPD scintigraphy and cardiac amyloid by CMR, did not have conclusive echocardiographic evidence of cardiac amyloidosis.

CMR = cardiac magnetic resonance; ^{99m}Tc-DPD = technetium-99m labelled radionuclide bone scintigraphy using the bone tracers 3,3-diphosphono-1,2-propanodicarboxylic acid; V30M-ATTRv = the V30M variant transthyretin amyloid.

CMR—not meeting criteria for positive or negative. All imaging was interpreted by 2 independent readers who were blinded to all other imaging modalities; a single discrepant read was resolved by in-person review. Study approval was from Royal Free Hospital ethics committee (ref: 06/Q0501/42).

A negative ^{99m}Tc-DPD scan (Perugini grade 0) in 34 patients was accompanied in all cases by absence of a characteristic amyloid echocardiogram, although 12 of 34 (35%) echocardiograms were categorized as inconclusive for amyloid. Among 30 patients in whom there was abnormal cardiac uptake of ^{99m}Tc-DPD (Perugini grade 1, 2, or 3), the echocardiogram was characteristic in 10 (33%), inconclusive in 12 (40%), and showed no evidence of cardiac amyloidosis in 8 (27%). There was complete concordance between ^{99m}Tc-DPD scintigraphy and CMR findings in all 23 patients who underwent CMR. Among 5 patients in whom there was an absolute discrepancy between ^{99m}Tc-DPD scintigraphy (positive) and echocardiography (negative) and in whom CMR was also performed, the CMR findings corroborated ^{99m}Tc-DPD scintigraphy findings in 5 of 5 (100%) cases (Table 1). Among 18 patients with evidence of cardiac amyloid by both ^{99m}Tc-DPD scintigraphy and CMR, only 5 of 18 (28%) had a characteristic amyloid echocardiogram with echocardiograms categorized as inconclusive in 8 (44%) and no amyloid in 5 (28%). Results of ^{99m}Tc-DPD scintigraphy were consistent with the expected phenotypes in V30M-ATTRv with absence and presence of cardiac uptake respectively in early-onset Portuguese and Greek-Cypriot patients and in late-onset British patients.

This study indicates complete concordance between the diagnostic performance of ^{99m}Tc-DPD scintigraphy and CMR, albeit in a subset of 23 patients from the cohort. Our findings suggest that a negative ^{99m}Tc-DPD scan (with single-photon emission computerized tomography imaging) or CMR in patients with V30M-ATTRv all but rules out amyloid cardiomyopathy and a positive ^{99m}Tc-DPD scan (Perugini grade 1, 2, or 3) or CMR indicates cardiac amyloid infiltration. Our data also appears to corroborate the previously reported limitations of echocardiography for diagnosing cardiac amyloid infiltration.

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