reference standard, both BOLD indexes performed comparably (area under the curve: 0.80 ± 0.04 vs. 0.73 ± 0.05; p = 0.24).

These data indicate that BOLD imaging detects anatomically and functionally significant CAD without the need for physiological or pharmacological stress. Our findings are pertinent to alternative imaging modalities with the potential to identify microvascular heterogeneity, and advance the concept of a functional assessment of CAD being performed at rest. The inability of resting MBF to discriminate the presence of CAD indicates that the favorable diagnostic performance of resting BOLD assessment is not dependent on changes in resting MBF. Although the observed change in resting BOLD SI is likely to reflect microvascular expansion, the underlying pathophysiological mechanism was not determined in our study: other factors may contribute to heterogeneous BOLD SI, including transit time heterogeneity, unequal hematocrit partition at bifurcations or myocardial hypertrophy leading to variations in regional demand. Similarly, coexisting microvascular pathology (e.g., diabetes, hypertension) may reduce diagnostic accuracy in CAD. Other limitations include the persistence of imaging artifact, which contributed to the limited specificity observed, and the use of a whole-slice index, which precluded assessment of the territory and extent of CAD. These issues may be addressed in future studies using absolute quantification of T2* and cardiac phase resolved imaging. Further study of resting microvascular function and oxygenation may offer valuable insights into the pathophysiology and pharmacotherapy of CAD.

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Early Phase ^{99}Tc-HMDP Scintigraphy for the Diagnosis and Typing of Cardiac Amyloidosis

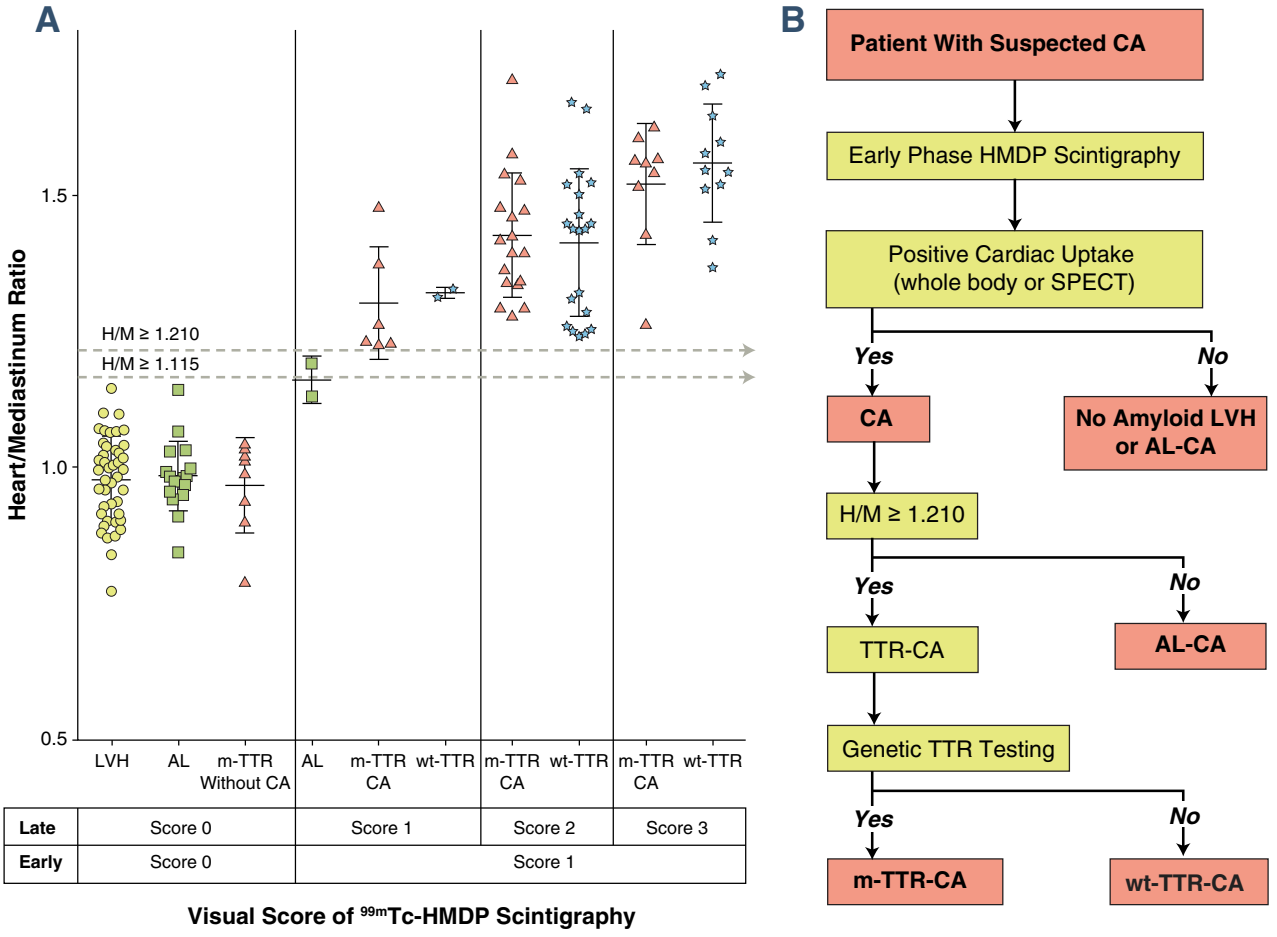
Although bisphosphonate scintigraphy has emerged as a valuable modality for cardiac amyloidosis (CA) diagnosis and typing with transthyretin CA showing strong cardiac uptake (1), the procedure in its current form is time consuming and may be regarded as inadequate especially in frail patients. In clinical practice, images are acquired at 10 min (soft tissue or early phase) and at 3 h (bone phase or late phase) following radiotracer injection. However, all studies have focused on late phase. Indeed, the Perugini's visual score, which is by far the most used to estimate heart retention is on the basis of late-phase images (2).

Little is known about the kinetic of bisphosphonates' cardiac uptake and the diagnostic value of the early phase scintigraphy in the 3 major forms of CA: light-chain (AL), hereditary transthyretin-related (m-TTR), and wild-type transthyretin-related (wt-TTR) amyloidosis (3). The aim of our study was to compare the accuracy of early (10 min) versus late (3 h) cardiac fixation of ^{99}mTc-hydroxyl-methylene-diphosphonate (HMDP) in diagnosing and typing CA.

A total of 135 patients referred for suspected CA were enrolled prospectively and consecutively. All patients had in addition to standard exams a ^{99}mTc-HMDP bisphosphonate-scintigraphy as part of their diagnostic work-up. The study protocol has been approved by local ethical committees. Written consent was obtained. The diagnosis of CA was performed as previously described (4).

^{99m}Tc-HMDP was performed after intravenous injection of 10 MBq/kg of the tracer (Cisbio International, Saclay, France). Planar images were acquired using a dual-head gamma camera (Philips-Precedence, Amsterdam, the Netherlands). Whole-body scans were acquired both at 10 min and 3 h. A single-photon emission computed tomography of the thorax was also performed immediately after the whole-body scan.

FIGURE 1 Early Phase ^{99}Tc-HMDP Scintigraphy for the Diagnosis and Typing of CA



(A) Agreement between (C/M) and Perugini's visual score. **(B)** Proposed diagnostic algorithm for patients with suspected cardiac amyloidosis (CA). AL = light-chain amyloidosis; C = cardiac; H = heart; H/M = heart-to-mediastinum; HMDP = hydroxyl-methylene-diphosphonate; LVH = left ventricular hypertrophy; m-TTR-CA = hereditary transthyretin-related cardiac amyloidosis; SPECT = single-photon emission computed tomography; TTR = transthyretin-related; wt-TTR-CA = wild-type transthyretin-related cardiac amyloidosis.

For the soft-tissue phase, radiotracer accumulation was graded as 0 (negative) if there was no visible myocardial uptake and 1 (positive) in case of tracer binding within the myocardium. ^{99m}Tc-HMDP cardiac uptake was evaluated semiquantitatively by 2 means: 1) early heart retention ratio was calculated by dividing the geometric mean of the left ventricular (LV) region of interest (ROI) by the geometric mean of whole-body counts; and 2) we calculated a heart-to-mediastinum (H/M) ratio on the anterior view of the whole-body scan by copying the LV ROI and placing it on the mediastinum at the large thoracic vessels level (middle of the chest, just above the left ventricle ROI).

Regarding the bone phase, visual scoring was performed according to Perugini's method (2): 0 = no cardiac uptake and normal bone uptake; 1 = slight cardiac uptake, less marked than bone uptake; 2 = moderate cardiac uptake with attenuated bone uptake; and 3 = strong cardiac uptake with slight/absence of bone uptake. Late heart retention (LHR), whole-body retention, and geometric mean in the skull were obtained as previously prescribed (4,5). LHR/whole-body retention and LHR/skull ratios were calculated.

Thresholds of early H/M to diagnose late-cardiac fixation and to discriminate TTR-CA versus AL-CA were determined using receiver-operating characteristic curve followed by Youden's test. We considered p values <0.05 statistically significant.

Of the 135 subjects referred for suspected amyloidosis and who underwent ^{99m}Tc-HMDP-scintigraphy, 93 were diagnosed as having amyloidosis or genetic *TTR* mutation. Nineteen had AL, 41 had m-TTR, and 33 had wt-TTR. Cardiac involvement was found in all patients with AL or wt-TTR amyloidosis. For subjects with m-TTR, 33 had CA, 3 were asymptomatic carriers and 5 had neurological symptoms with no evidence of CA. Thirty-one patients with LV hypertrophy and without amyloidosis served as controls. Interestingly, early phase ^{99}mTc-HMDP-scintigraphy cardiac uptake perfectly predicts late-phase finding, as it was found in 68 patients for whom late visual score was ≥1 and was undetectable in all the 57 patients with a null visual score at late phase.

As shown in **Figure 1A**, an H/M ratio ≥1.115 predicted late cardiac ^{99m}Tc-HMDP accumulation (visual score ≥1) with a sensitivity of 100% and a specificity of 97%, whereas an early H/M ratio ≥1.210 discriminated TTR-CA from AL with a perfect accuracy (100% sensibility and 100% specificity). Accordingly, we suggest a new algorithm to diagnose CA and TTR-CA on the basis of the early phase ^{99m}Tc-HMDP-scintigraphy (**Figure 1B**).

In conclusion, our study showed that early phase ^{99}mTc-HMDP-scintigraphy perfectly predicts late-phase finding. It is accurate to differentiate TTR- from AL-CA and from other causes of LV hypertrophy. This could be of particular benefit for frail patients and should increase availability of scintigraphy and cost effectiveness.

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Safety and Feasibility of Contrast Echocardiography for ECMO Evaluation

Transthoracic echocardiography and transesophageal echocardiography (TEE) are valuable for patients on extracorporeal membrane oxygenation (ECMO). These tools are used to perform “turn down” assessments, evaluate for cannula placement/position, and guide management. ECMO is a form of mechanical circulatory support using a pump and circuit for oxygenation and cardiac output. The multiple chest tubes, surgical incisions, mechanical ventilation, and restricted positioning required for ECMO patients can limit echocardiography quality. Even TEE images can be obscured by post-operative changes to the mediastinal structures and cardiac chambers.

Contrast echocardiography (CE) with perflutren microbubbles has been validated as a safe and effective method to evaluate cardiac chamber function and to rule out cardiac masses or thrombi in technically difficult studies (1). There is limited information on the utility and safety of CE in patients receiving ECMO (2). Potential issues include accelerated destruction of contrast microbubbles by the ECMO circuit (3) and concern for circuit interference because the systems are designed to detect bubbles (4). The purpose of this report is to evaluate our experience with the safety and feasibility of CE use in patients on ECMO.