visualized, thus avoiding inadvertent extension of the LA length measurement into the pulmonary vein—an error that results in smaller LA volumes. In addition, there has been a lack of consistency in methods used to calculate LAVi. Prior studies have reported LA volumes using biplane area-length, biplane Simpson's, and prolate ellipsoid methods (1,2,4).

LAVi is considered a marker of diastolic dysfunction (1), with a current cutoff value of 34 ml/m^2 used to indicate elevated left ventricular filling pressures in the setting of an E/E′ between 9 and 14. In our study, however, 30% of healthy subjects had a LAVi ≥34 ml/m^2 in the presence of normal echocardiographic indexes of left ventricular filling pressures.

This study is a retrospective analysis, and measurements were not performed blinded to the clinical data and thus are subject to selection and information bias.

In conclusion, reassessment of LAVi in a contemporary healthy cohort suggests higher normative reference ranges than previously published. Establishing normative values for LA volumes are important for clinical decision making, given the significant association that has been reported between increased LA volume and prognosis in a wide range of CV diseases.

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Identification of TTR-Related Subclinical Amyloidosis With ^{99m}Tc-DPD Scintigraphy

We have previously documented that ^{99m}Tc-3,3-diphosphono-1,2-propanodicarboxylic acid (^{99m}Tc-DPD) has a high affinity for transthyretin (TTR)-infiltrated myocardium, allowing a differential diagnosis with light-chain cardiac amyloidosis (1) and other non-amyloidotic cardiomyopathies with a hypertrophic phenotype (2). Notably, ^{99m}Tc-DPD allows an early diagnosis of TTR-related cardiac amyloidosis, even before the appearance of overt echocardiographic or electrocardiographic abnormalities (3). However, the potential role of this technique in the pre-clinical population screening has not been explored yet. We therefore evaluated prevalence and implications of incidental myocardial uptake among patients undergoing ^{99m}Tc-DPD scintigraphy for oncologic/rheumatologic reasons.

We retrospectively analyzed all ^{99m}Tc-DPD scintigraphies performed at our institution between 2008 and May 2013. Scintigraphy protocol and image analysis have been previously described (1).

During the study period, 12,521 patients underwent scintigraphy, including 121 with suspected cardiac amyloidosis: these patients were excluded. The study population therefore consisted of 12,400 patients with oncologic (95%) or rheumatologic (5%) indications to scintigraphy (37% men; mean age 74 years; range 65 to 82 years). Myocardial tracer uptake was present in 45 subjects (0.36%; 62% men; median age 81 years; range 77 to 84 years), and an associated localized area of bone metastatic activity was present in a single case. Specifically, myocardial uptake was strong in 40 cases (89%) and moderate in 5 (11%). The prevalence of incidental uptake increased progressively with age (Fig. 1).

Thirty-two of 45 patients showing myocardial uptake were contacted and offered a comprehensive cardiological evaluation including ECG, echocardiography, and endomyocardial biopsy in selected cases. Fourteen patients agreed to be evaluated (11 men;

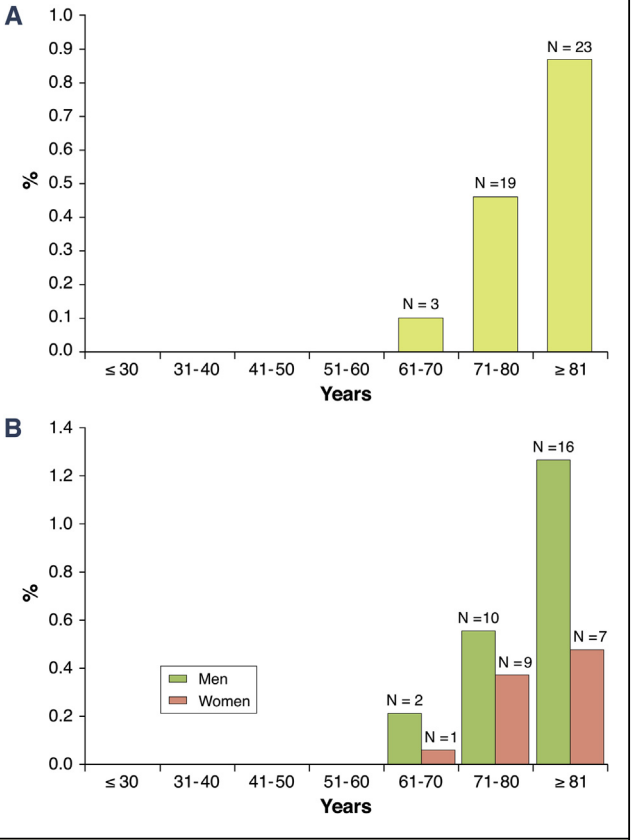

Figure 1. Frequency of Unexpected ^{99m}Tc-DPD Myocardial Uptake

Prevalence of myocardial tracer uptake according to age **(A)** and age and sex **(B)** among the 12,400 patients who underwent ^{99m}Tc-3,3-diphosphono-1,2-propanodicarboxylic acid (^{99m}Tc-DPD) scintigraphy.

median age 82 years; range 70 to 88 years). Four patients were symptomatic for dyspnea (New York Heart Association functional class II); 1 had a pacemaker; 2 were receiving antihypertensive therapy; carpal tunnel syndrome had been previously diagnosed in 3. None had overt neurologic symptoms. ECG was abnormal in all cases: atrial fibrillation in 3 cases, left anterior hemiblock in 2, isolated ST-T abnormalities in 4, abnormal Q waves in 3, and low QRS voltage in 2. Increased left ventricular (LV) wall thickness was detected in all patients (mean LV wall thickness, 14 mm; interquartile range: 13 to 15 mm), and LV ejection fraction was 58% (interquartile range: 54% to 67%). Other echocardiographic abnormalities included mild pericardial effusion (n = 6), A-V valve thickening (n = 5), and myocardial granular sparkling (n = 8). LV "hypertrophy" was completely unexplained in 10 patients and was out of proportion in 4 (moderate systemic hypertension with nondilated LV and ascending aorta). Genetic analysis was performed in 6 cases and documented an *Ile68Leu* TTR mutation in a single patient. Endomyocardial biopsy was performed in the remaining 5 patients and detected TTR-related amyloidosis in all, leading to a final diagnosis of wild-type TTR amyloidotic cardiomyopathy (senile systemic amyloidosis [SSA]).

In this large cohort of subjects undergoing ^{99m}Tc-DPD scintigraphy for different reasons, 45 (0.36%) showed unexpected myocardial tracer uptake. We cannot exclude a slight underestimation of the real prevalence because of the retrospective nature of the study. The subsequent cardiological evaluation revealed an unexplained increase of LV wall thickness in all the analyzed cases, and endomyocardial biopsy confirmed the diagnosis of TTR-related amyloidosis in all the patients who underwent the procedure. The impact of our study, albeit small, mainly relies on the possibility of an early (pre-clinical) identification of patients affected by TTR-related amyloidotic cardiomyopathy, mainly the form related to the deposition of wild-type TTR, a condition that is believed to be highly underdiagnosed. There are currently no reliable studies regarding the prevalence of SSA. If we consider all our patients with myocardial ^{99m}Tc-DPD uptake to be affected by TTR-related cardiomyopathy (mainly SSA), the prevalence of the disease would reach 1.4% among men in the ninth decade. It is noteworthy that although SSA is known to mainly affect elderly men, a relevant number of women showed asymptomatic myocardial tracer uptake. Finally, our data require confirmation through prospective studies, but, if confirmed, they would suggest the possibility of using ^{99m}Tc-DPD scintigraphy as a screening tool in populations at risk. With the advent of new drugs aimed at halting TTR deposition that are currently under clinical evaluation (4), an early diagnosis of the disease is highly encouraged and should be pursued.

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Diagnostic Problem of LV Hypertrabeculation/ Noncompaction?

With interest we read the article by Stacey et al. (1) about systolic and diastolic criteria for left ventricular hypertrabeculation/noncompaction (LVHT). Uniform diagnostic criteria for LVHT are a still unsolved problem in echocardiography as well as other imaging modalities like cardiac magnetic resonance (CMR). Whether the results of their investigations will lead to more clarification is questionable due to the following reasons: 1) No pathoanatomic gold standard is provided; thus, neither sensitivity nor specificity of the proposed criteria can be assessed. 2) It remains uncertain in how many patients LVHT was diagnosed by echocardiography. There is a need to calculate the percentage of LVHT patients in whom LVHT was diagnosed on echocardiography and CMR, on CMR but not on echocardiography and on echocardiography but not on CMR. 3) The duration and quality of follow-up remain uncertain. Were follow-up data obtained for each of the included patients? 4) Differentiation between LVHT on the one hand and papillary muscles, false tendons, and aberrant bands on the other is a difficult issue because these structures are seen frequently, and there is considerable anatomic variability (2,3). To our knowledge, the proposed "papillary muscle classification system" is not based on any pathoanatomic classification. Furthermore, it seems rather difficult to differentiate between papillary muscles and trabeculations when only short-axis views are considered. Only by using longitudinal views will it be possible to visualize the communication of the papillary muscles with the mitral valve leaflets via the chordae tendineae. Not to differentiate between LVHT and papillary muscles is not acceptable because LVHT diagnostic criteria definitions clearly exclude papillary muscles from the evaluation. 5) There is no need to distinguish between "myopathic LVHT" and "normal variants" because they are morphologically the same and have a similar complication rate and outcome. Normal variants may have subclinical myopathy or may have chromosomal abnormalities, which manifest only in the heart. This is why we recommend referring all LVHT patients to a myologist to also detect neurological abnormalities which are clinically inapparent for the cardiologist. As an initial step, the authors should provide information about how many of their patients had an elevated creatine kinase level and in how many patients was LVHT familial. Familial LVHT may suggest hereditary disease, including neuromuscular disorders.

Additionally, we have the following questions regarding the presented data. 1) It was previously reported that echocardiographically