

A limitation of this study is that coronary CTA was performed within clinical workup, which could implicate referral bias. Possibly, clinical information known to the reader might have influenced coronary CTA assessment as well. The nonsignificant difference in event rate between men and women with normal coronary CTA might be due to differences in risk factors or referral patterns, which this study did not have the power to detect.

In conclusion, obstructive CAD significantly predicted events in both men and women. Despite the small numbers and hypothesis-generating nature of our study, these findings further validate the role of coronary CTA to effectively risk stratify women and men.

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Left Atrial Volumes

Should We Reset the Reference Standard?

Left atrial (LA) volume has been shown to be a prognostic indicator of cardiovascular (CV) events and a marker of diastolic dysfunction (1,2). Normative values for indexed LA volume (LAV_i) have been established to be 22 ± 6 ml/m² (3). Yet, these values are on the basis of small sample size studies, from a period with different imaging technology and using inconsistent measurement techniques.

We aimed to re-examine the normal reference standards for LAV_i in a contemporary healthy population. We searched our institutional database for a 1-year period to identify healthy subjects with normal echocardiograms. Medical records were comprehensively reviewed to select healthy patients (no CV risk factors, pulmonary or renal disease). LA volume was calculated by the

biplane area-length method (3). Diastolic parameters were assessed. Furthermore, a healthy validation subset of 20 subjects was examined prospectively.

From June 2009 to June 2010, 285 healthy subjects were identified and LA volumes measured. The mean LAV_i was 30.3 ± 6 ml/m² (mean age 38.3 ± 14.8 years, 61.4% women) with no difference observed between men and women (30.3 ± 7.0 ml/m² vs. 30.5 ± 6.0 ml/m², $p = 0.81$) and no age differences in absolute or indexed LA volumes in the entire healthy cohort or by sex.

Mean diastolic parameters were normal. Thirty percent of subjects had a LAV_i ≥ 34 ml/m²—a cutoff used to identify those with abnormal diastolic function (1). E/A, average E', and E/E' were not significantly different between this group and those with a LAV_i < 34 ml/m². The prospective cohort of 20 healthy subjects, matched to age (38.3 ± 7.0 years), sex (60% women), and body surface area (1.8 ± 0.2 m²) had similar mean LAV_i to the retrospective cohort (31.7 ± 6.0 ml/m² vs. 30.3 ± 7.0 ml/m²; prospective vs. retrospective $p = 0.35$).

Reassessment of LAV_i in a contemporary healthy cohort suggests that normative reference ranges of LAV_i should be higher than previously reported. In the present study, the mean LAV_i in healthy subjects was 30.3 ± 6.5 ml/m², 38% higher compared with current reference values for mean normal LAV_i (22 ± 6 ml/m²) (3) (Fig. 1).

Various factors may account for the discrepancy between previously reported values and our results. Current reference values are on the basis of relatively small sample size studies and obtained from a period with different imaging technology. With improved spatial resolution in current imaging systems, measurement of LA boundaries may be more accurate. The confluence of the pulmonary veins may also be better

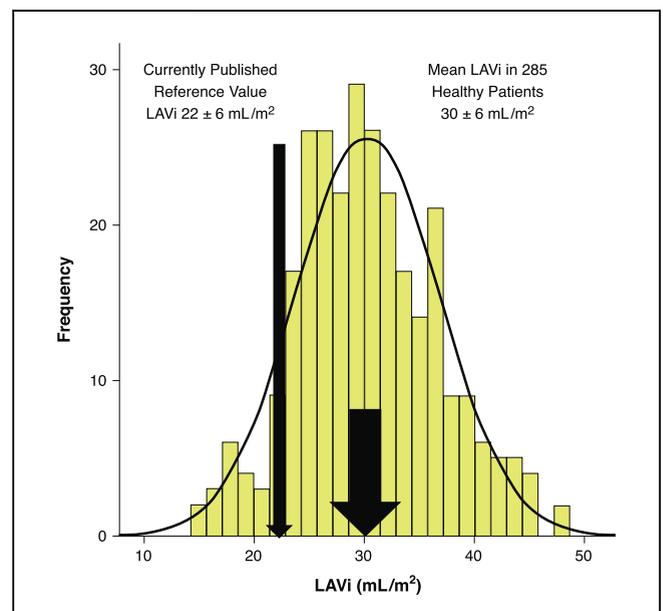


Figure 1. Distribution of LAV_i in Healthy Subjects (N = 285)

The **short black arrow** points to the mean indexed left atrial volume (LAV_i) of 30.3 ml/m², which is greater than the current published reference value of 22 ml/m² for normal (**long black arrow**).

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/m² 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/m² 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;

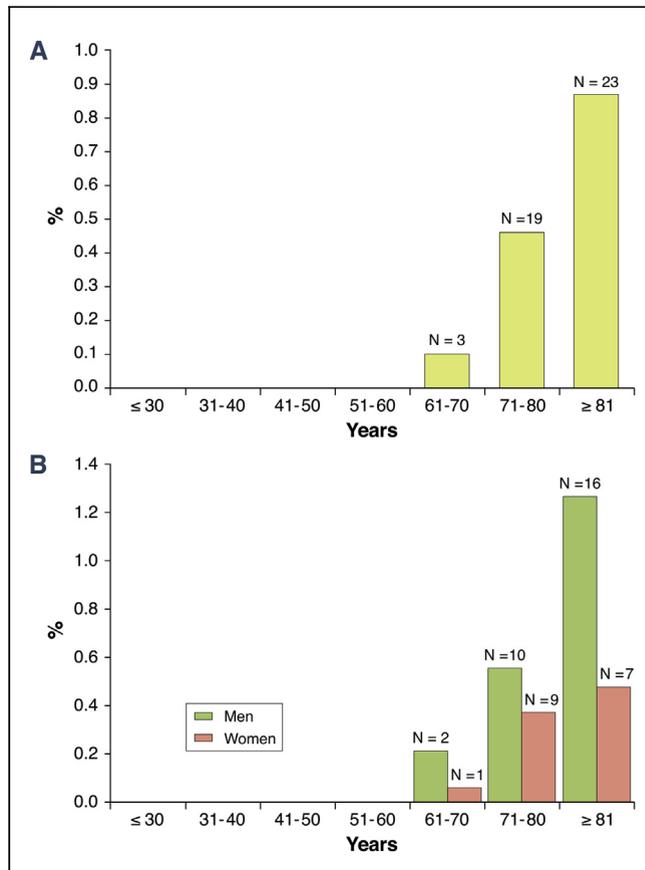


Figure 1. Frequency of Unexpected ^{99m}Tc-DPD Myocardial Uptake
Prevalence of myocardial tracer uptake according to age (A) and age and sex (B) among the 12,400 patients who underwent ^{99m}Tc-3,3-diphosphono-1,2-propanodicarboxylic acid (^{99m}Tc-DPD) scintigraphy.