Letter by Porcari et al Regarding Article, "Association Between Atrial Uptake on Cardiac Scintigraphy With Technetium-99m-Pyrophosphate Labeled Bone-Seeking Tracers and Atrial Fibrillation"

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To the Editor:

Hussain et al[1] report the results of a single-center retrospective analysis investigating the presence of atrial uptake (AU) of technetium-99m-pyrophosphate (^{99m}Tc-PYP) and its association with atrial fibrillation (AF) in patients referred for suspected transthyretin (TTR) amyloid cardiomyopathy (ATTR-CM). The authors found a 20% prevalence of AU on single-photon emission computed tomography (SPECT/CT) imaging that was associated with any AF and with significantly lower freedom from incident AF at 1-year, independently of ATTR-CM diagnosis and sex. Fifty-eight patients (10% of the study population, 50% of those with AU) had evidence of isolated AU and did not fulfil noninvasive criteria for ATTR-CM.

We read this study with interest, but our enthusiasm was tempered by concerns surrounding the methodology of image evaluation. Given the thin atrial wall, accurate localization of tracer uptake to the atrial wall to diagnose AU is challenging, even with the use of SPECT/CT imaging. Scintigraphic images reported in the manuscript were evaluated by a single operator with supervision from a senior expert nuclear medicine physician for challenging cases. In view of the aforementioned challenges, we think that evaluation of all images by 2 independent readers and inclusion of some interoperator variability analyses would have provided more confidence in the reported findings.

Amyloid deposition has been demonstrated to occur in all cardiac chambers and tissues.[2,3] Even assuming that AU can reliably be assessed by SPECT/CT, it is unclear why ATTR amyloid would deposit only in the atria, sparing the ventricles. The authors hypothesize that AU reflects ATTR amyloid deposition in the atria and might serve as an early marker of disease, before development of ventricular involvement, although support for this hypothesis was only provided in 13 patients by way of histological identification of amyloid with no mention of the histological methods employed for identification and typing of amyloid; importantly, myocardial uptake of ^{99m}Tc-PYP cannot establish a diagnosis ATTR-CM without additional investigations which do not seem to have been performed in this cohort.[4]

It is unclear whether patients underwent a comprehensive diagnostic work-up for ATTR-CM, as recommended by international societies of cardiology,[4,5] and how the disease was ruled out in challenging cases. Hussain et al[1] considered a heart-to-contralateral ratio >1.3 to indicate ATTR-CM. However, Perugini grade is the only validated scintigraphic scale through which this diagnosis can be established. Additionally, the authors do not provide information on cardiac structure such as ventricular wall thickness assessed by echocardiography or CMR imaging. Surprisingly, the latter was performed only in 1.7% (n=10/580) of patients. Such data would be of interest to understand how many patients with isolated AU had a hypertrophic phenotype and/or other features consistent with a possible early amyloid cardiomyopathy. Finally, it seems that sequencing of the *TTR* gene was not performed in patients with ATTR-CM.

Identification of the earliest site of amyloid deposition in the heart is of great clinical interest with respect to timely diagnosis ATTR-CM. Our extensive experience of longitudinal follow up, including serial ^{99m}Tc-DPD scintigraphy, in carriers of pathogenic *TTR* mutations who develop clinical disease indicates that uptake of tracer is initially apparent in the basal segments of the left ventricle and interventricular septum. We think that further studies, supported by rigorous histological evaluation, are required to explore the applications of cardiac scintigraphy for early diagnosis of ATTR-CM.

ARTICLE INFORMATION

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Disclosures

None.

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