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From HCM to ATTR-CM: Rethinking Unexplained Hypertrophy

Dr. Blevins:

Imagine you're seeing an older patient—maybe in their late sixties or seventies—with left ventricular hypertrophy that checks the boxes for hypertrophic cardiomyopathy. The diagnosis seems straightforward. But what if it isn't the whole story?

You're listening to *AudioAbstracts* on ReachMD. I'm Dr. Hallie Blevins, and today, I'll be talking about the TTRACK study, which took a closer look at how often transthyretin amyloid cardiomyopathy, or ATTR-CM, is hiding in plain sight among patients labeled as having hypertrophic cardiomyopathy, or HCM. And just as importantly, it asked whether the nuclear imaging tools we rely on every day are actually doing their job consistently in real-world practice.

The investigators enrolled 766 patients aged 50 years or older, all with left ventricular wall thickness of at least 15 millimeters and no clear cause for hypertrophy. Patients with known sarcomeric mutations, prior amyloidosis, or severe aortic stenosis were excluded. This was very intentionally a population where the diagnosis of HCM looked reasonable but wasn't fully explained.

Every patient underwent technetium-99m-labeled bone scintigraphy, using one of three tracers: DPD, PYP, or HMDP. Some patients also had SPECT imaging, though this wasn't mandatory. Nuclear scans were read by onsite experts and then reviewed centrally, using the Perugini grading system to assess myocardial tracer uptake. If uptake was present, monoclonal protein testing followed to separate ATTR-CM from light-chain amyloidosis.

Now, let's get into the results. 18.8 percent, so nearly one in five patients, ended up with a noninvasive diagnosis of ATTR-CM. That's a striking number for a group already carrying an HCM diagnosis. And it reinforces a point many clinicians are starting to appreciate, which is, in older adults, hypertrophy doesn't always mean hypertrophic cardiomyopathy.

About 90 percent of patients had planar scintigraphy alone, which reflects routine practice. Despite that, agreement between onsite readers and centralized experts was strong, with a kappa of 0.84. Clinically meaningful disagreements were rare and in only about half a percent of cases.

Planar imaging was remarkably consistent to SPECT, with a kappa of 0.93. The few discrepancies that did appear were limited to PYP imaging and involved only minor grade differences that didn't change diagnostic classification.

One of the more thought-provoking findings came from comparing radiotracers. ATTR-CM was identified in 26.9 percent of patients imaged with HMDP, compared with 11.7 percent using DPD and 6.4 percent using PYP. Whether that reflects tracer performance, regional practice patterns, or patient selection isn't entirely clear, but it does raise important questions about how tracer choice may influence detection rates.

When the investigators looked beyond nuclear imaging, they found patterns clinicians will recognize—but none that could stand alone. Patients with ATTR-CM had slightly lower ejection fractions, higher left ventricular mass indices, and more frequent preserved apical strain. Concentric hypertrophy was also far more common than asymmetric patterns.

On MRI, late gadolinium enhancement showed up in 85 percent of ATTR-CM patients, compared with about 55 percent of those without cardiac uptake. ECGs also differed, with longer PR intervals, lower Sokolow indices, and more conduction abnormalities.

The message from TTRACK is practical: ATTR-CM is common in older patients with unexplained hypertrophy, and nuclear imaging, especially planar scintigraphy, performs pretty reliably in everyday clinical settings. Imaging patterns and ECG clues can help, but they shouldn't be definitive.

But the real shift here is conceptual: for older patients, an HCM label should prompt deeper evaluation and not diagnostic closure.

This has been an *AudioAbstract*, and I'm Dr. Hallie Blevins. To access this and other episodes in our series, visit ReachMD dot com, where you can Be Part of the Knowledge. Thanks for listening!

Reference

Garcia-Pavia P, Del Moral FJH, Cappelli F, et al. Nuclear imaging and echocardiographic findings in hypertrophic cardiomyopathy with and without ATTR-CM. *ESC Heart Fail*. Published online October 13, 2025. doi:10.1002/ehf2.15440