

Amyloid-related heart failure now detectable with imaging test

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A type of heart failure caused by a build-up of amyloid can be accurately diagnosed and prognosticated with an imaging technique, eliminating the need for a biopsy, according to a multicenter study led by researchers at Columbia University Medical Center (CUMC).

The technique may also detect the condition—called transthyretin-related cardiac amyloidosis (ATTR-CA)—before it progresses to advanced heart failure, says study leader Mathew S. Maurer, MD, Arnold and Arlene Goldstein Professor of Cardiology and director of the Clinical Cardiovascular Research Laboratory for the Elderly at CUMC and a co-author of the paper.

The findings were published today in *JAMA Cardiology*.

"This is a huge advance for patients with ATTR-CA, which is under recognized and often misdiagnosed," said co-first author Adam Castano, MD, a cardiology fellow at CUMC. "This test will spare certain patients from having to undergo a biopsy in order to get a definitive diagnosis. Many people with ATTR-CA are frail and elderly, so being able to avoid a biopsy, even when it can be done with a less-invasive catheter-based procedure, is a significant step forward."

ATTR-CA is one of many types of amyloidosis, a condition in which a protein breaks down and forms fibrils that deposit in organs and tissues, eventually causing the organs to fail. In ATTR-CA, the transthyretin protein breaks down and forms amyloid fibrils, which mainly

accumulate in the heart, disrupting its function. Different types of amyloidosis require different treatments, so obtaining an accurate diagnosis is critical.

ATTR-CA was once thought to be rare, but it's now known that ATTR-CA resulting from a normal variant of the transthyretin protein has a prevalence of about 32 percent in patients with heart failure over age 75 years at autopsy. The prevalence in hospitalized patients with heart failure is about 13 percent. ATTR-CA can also result from a mutated form of the transthyretin protein, which can be inherited from one generation to the next. The prevalence of inherited ATTR-CA is not known, but the most common mutation in the United States is present in 3-4% of African Americans.

The diagnostic tool evaluated in the study is derived from bone scintigraphy, a form of single-photon emission computed tomography, or SPECT, that is conventionally used to detect bone cancer. In bone scintigraphy, patients are injected with a radioactive isotope with a particular affinity for bone that has remodeled due to bone cancer. Early on, researchers noticed that the isotope, technetium 99m pyrophosphate (Tc 99m PYP), also gravitates to amyloid deposits in the heart, a defining characteristic of ATTR-CA.

In this study, the researchers examined the diagnostic accuracy of the Tc 99m PYP test for ATTR-CA in a retrospective study of 179 amyloidosis patients (121 with ATTR and 50 with other types) who were evaluated at three leading amyloidosis centers (CUMC, the Mayo Clinic, and Boston University School of Medicine). The imaging scans were compared to tissue biopsy results, the gold standard for diagnosing ATTR.

The researchers found that the imaging test was able to correctly identify ATTR in 91 percent of those diagnosed with the disease, and was able to rule out ATTR-CA in 92 percent of those with other forms of

amyloidosis or no amyloidosis.

"In nonscientific terms, it's a very good test," said Dr. Castano.

The findings build on a recent international study, published in *Circulation*, showing that the test is highly reliable in diagnosing ATTR-CA, and when another form of amyloid called light-chain is ruled out with a blood test, a confirmatory biopsy is no longer needed. Drs. Castano and Maurer and most of the members of their research team also participated in that study.

The current study adds to these findings with the development of a computer algorithm that provides an objective analysis of the scans. Currently, radiologists assign a visual score of 0, 1, 2, or 3 to each scan, depending on the concentration of isotope that collects in the heart. The algorithm used in this study calculates a more quantitative score automatically, comparing the concentration in the heart to a similar area in the opposite side of the chest.

Using this algorithm, the team found that patients with a ratio of 1.6 or greater were about four times more likely to die from ATTR-CA over the median follow-up period of 1 year, compared to those with a ratio below 1.6.

At present, there are no effective treatments for ATTR-CA. However, several promising drugs for the disease are in phase 3 clinical trials.

"Ideally, we'll be able to use this imaging test to detect ATTR-CA well before it develops into advanced [heart failure](#), and then intervene with one of these new therapies, but further study of this test is required to determine how early in the natural history of this disease it can detect amyloid in the heart," said Dr. Castano.

More information: "Multicenter Study of Planar Technetium 99m

Pyrophosphate Cardiac Imaging: Predicting Survival in Patients with ATTR Cardiac Amyloidosis?" *JAMA Cardiology*, 2016.

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