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Letters

TO THE EDITOR

Cardiac Biomarkers in Patients With Suspected Amyloid (Transthyretin) Cardiomyopathy

Which Cut-Offs?

We read with interest the paper by De Michieli et al,[1] who investigated high-sensitivity troponin T (hs-TnT) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) in patients undergoing ^{99m}Tc pyrophosphate scintigraphy for suspected cardiac amyloidosis (CA). The investigators propose threshold for hs-TnT of <6 ng/L and for NT-proBNP of <60 ng/L to rule out transthyretin CA. These thresholds are lower than those we previously reported (hs-TnT < 14 ng/L and NT-proBNP <180 ng/L).[2]

We agree that the lower pretest probability in the Mayo Clinic cohort likely contributed to these lower thresholds.[1] Heterogeneity in the diagnostic work-up may have also played a role. These include different scintigraphic tracers and positivity criteria ("diffuse tracer uptake" on tomographic imaging plus a heart-to-contralateral lung ratio ≥1.3[1] vs Perugini grades 2 and 3[2]). Furthermore, the European algorithm recommends both scintigraphy and testing for a monoclonal protein in all patients with suspected CA,[3] whereas the U.S. algorithm suggests testing for a monoclonal protein and performing scintigraphy only if no monoclonal protein is detected.[4] The investigators reasonably followed the U.S. algorithm, which explains the very low rate of amyloid light-chain (AL) CA.[1] Conversely, our study population consisted of patients with suspected CA. In the subgroup of patients in the validation cohort with increased wall thickness who did not have systemic AL amyloidosis, multiple myeloma, or smoldering myeloma, 11% were ultimately diagnosed with AL CA,[2] compared with only 0.6% in the Mayo cohort.[1] Thus, neither our full cohort nor the increased wall thickness subgroup is directly comparable with the Mayo cohort, given the higher prevalence of AL CA in our population. This discrepancy may help explain why we observed higher rule-out cutoffs, as cardiac biomarkers tend to be higher in AL CA.[5] Although our cutoffs also performed well in the subgroup with increased wall thickness and no monoclonal protein, we acknowledge that this subgroup was relatively small (n = 331 in the validation cohort vs n = 1,442 in the Mayo cohort).[1,2]

In summary, the study supports the potential use of very low circulating levels of cardiac biomarkers to rule out CA. Further studies using a standardized approach to patient selection and diagnostic evaluation are advised.

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The authors have reported that they have no relationships relevant to the contents of this paper to disclose.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

REFERENCES

1. De Michieli L, AbouEzzeddine OF, Abbasi MA, et al. Biomarkers to predict abnormal technetium-99m pyrophosphate scans in patients with suspected transthyretin amyloidosis. *JACC CardioOncol*. 2025;7:70-78.

2. Vergaro G, Castiglione V, Aimo A, et al. N-terminal pro-B-type natriuretic peptide and high-sensitivity troponin T hold diagnostic value in cardiac amyloidosis. *Eur J Heart Fail*. 2023;25:335-346.

3. Garcia-Pavia P, Rapezzi C, Adler Y, et al. Diagnosis and treatment of cardiac amyloidosis. A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur J Heart Fail*. 2021;23:512-526.

4. Writing Committee, Kittleson MM, Ruberg FL, et al. 2023 ACC expert consensus decision pathway on comprehensive multidisciplinary care for the patient with cardiac amyloidosis. *J Am Coll Cardiol*. 2023;81:1076-1126.

5. Castiglione V, Franzini M, Aimo A, et al. Use of biomarkers to diagnose and manage cardiac amyloidosis. *Eur J Heart Fail*. 2021;23:217-230.

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