

Letter to the Editor**Amyloidosis in the Era of Mass Spectrometry-based Proteomics**

Thong Huy Cao, MD, PhD

Affiliations

University of Leicester, Department of Cardiovascular Sciences
National Institute for Health Research Leicester Biomedical Research Centre
Glenfield Hospital
Leicester
United Kingdom

Funding

T.H.C. is funded by the John and Lucille van Geest Foundation and the National Institute for Health Research Leicester Biomedical Research Centre.

Disclosures

T.H.C. has no relationships with industry.

Other disclosures: T.H.C. is funded by the John and Lucille van Geest Foundation and the National Institute for Health Research Leicester Biomedical Research Centre.

Address for correspondence

Dr Thong Huy Cao
University of Leicester, Department of Cardiovascular Sciences
National Institute for Health Research Leicester Biomedical Research Centre
Glenfield Hospital
University Road
Leicester, LE1 7RH
United Kingdom
Email: tch10@le.ac.uk
Phone: +44 116 258 3031

I read the article by Kotecha et al. published in the Journal of the American College of Cardiology (JACC) with great interest (1). Certainly, the authors conducted a very valuable and exciting study that 286 patients were recruited, including 100 with systemic light-chain (AL) amyloidosis and 163 with cardiac transthyretin (ATTR) amyloidosis. The findings in this study by histology and cardiovascular magnetic resonance T2 mapping suggest that myocardial edema is a mechanism additional to amyloid infiltration in contributing to prognosis in amyloidosis (1). The accurate identification of the protein causing the amyloidosis plays a crucial role in the therapeutic strategy and prognosis of patients with amyloidosis that is relied on the treatment of the underlying etiology. To date, there are about 36 different proteins that are known to cause amyloidosis in human (2). The most common method has been used is immunohistochemistry, but this method has low specificity and sensitivity. Mass spectrometry-based approaches have been demonstrated to be a reliable technique to identify and classify amyloidosis. An approach with a combination of laser microdissection (LMD) and mass spectrometry (MS)-based proteomics is a highly specific and sensitive novel method for identifying types of amyloidosis in biopsy specimens. By the use of LMD-MS, Vrana et al. identified the amyloid type with 100% specificity and sensitivity in a training set of 50 patients with amyloidosis and with a success of 98% in an independent validation set of 41 patients (3). Furthermore, matrix-assisted laser desorption/ionization imaging mass spectrometry (MALDI-IMS) has been demonstrated being an independent analytical method for the identification and classification of amyloidosis in two recent studies (4,5). MALDI-IMS is a very young method in the field of amyloid diagnostics.

Mass spectrometry-based proteomics is an upcoming method for diagnosis and classification of amyloidosis in the era of omics. This is one of the most powerful techniques in protein identification and quantification for a large scale of proteins from biopsy

specimens. Theoretically, all known proteins causing amyloid types can be identified by a single analysis using a mass spectrometer. Therefore, this technique could replace 36 different antibody-based immunohistochemical tests that would be required to check all known amyloid types. This would bring far more benefits in term of cost effective. Furthermore, this technique has great potential for providing a comprehensive understanding of the complex pathogenesis in amyloidosis that would help develop novel biomarkers and new therapeutic targets in order to improve outcomes for patients with amyloidosis.

References

1. Kotecha T, Martinez-Naharro A, Treibel TA, et al. Myocardial Edema and Prognosis in Amyloidosis. *J Am Coll Cardiol* 2018; 71(25): 2919-31.
2. Sipe JD, Benson MD, Buxbaum JN, et al. Amyloid fibril proteins and amyloidosis: chemical identification and clinical classification International Society of Amyloidosis 2016 Nomenclature Guidelines. *Amyloid* 2016; 23(4): 209-13.
3. Vrana JA, Gamez JD, Madden BJ, et al. Classification of amyloidosis by laser microdissection and mass spectrometry–based proteomic analysis in clinical biopsy specimens. *Blood* 2009; 114(24): 4957-59.
4. Casadonte R, Kriegsmann M, Deininger SO, et al. Imaging mass spectrometry analysis of renal amyloidosis biopsies reveals protein co-localization with amyloid deposits. *Anal Bioanal Chem* 2015; 407(18): 5323-31.
5. Winter M, Tholey A, Kristen A, et al. MALDI Mass Spectrometry Imaging: A Novel Tool for the Identification and Classification of Amyloidosis. *Proteomics* 2017; 17(22).