Myocardial Deformation Analysis and Late-Gadolinium Enhancement: Important Markers of Cardiac Amyloidosis Involvement That Can Masquerade as a False-Negative Diagnosis — Reply —

We thank Dr. Di Bella and Dr. Pizzino for their interest in our article. They raised some important issues: (1) non-disease-specific impairment of myocardial strain analysis; (2) limitations of late gadolinium-enhanced (LGE) imaging; and (3) utility of advanced imaging techniques of myocardial T1 mapping for diagnosis of cardiac amyloidosis (CA). These issues are important for understanding the appropriate clinical use of myocardial strain imaging by cardiac magnetic resonance imaging (CMR).

As Dr. Di Bella and Dr. Pizzino mentioned, impairment of myocardial strain analysis is not disease-specific. In our study, we evaluated a total of 61 patients with systemic amyloidosis and demonstrated that myocardial strain analysis by CMR facilitated the detection of LGE-positive CA without using contrast agents. Further, CS parameters correlated with CA severity. Thus, myocardial strain analysis can be used for assessing cardiac involvement in patients with systemic amyloidosis or where CA is highly suspected. In addition, myocardial strain analysis by CMR has the potential to serve as a noninvasive imaging marker for disease surveillance, possibly contributing to the management of patients with CA. However, further research is warranted to determine the utility of characteristic strain findings, previously reported as the supra-normal CS, and the apical sparing of the LS for differentiation of CA and other cardiac diseases. Further, these strain findings may have high specificity to CA.

At present, LGE imaging is the most reliable method for identifying cardiac involvement in amyloidosis. However, it has certain limitations in the diagnosis CA. First, LGE manifests in the later disease stages, complicating early detection of the disease. Second, the use of gadolinium-based contrast agents is contraindicated in patients with severe renal dysfunction, a relatively common finding in patients with amyloidosis. Third, because LGE cannot be easily quantified, it is not reliable for following up on changes over time. Fourth, LGE findings are highly variable in patients with CA, and it is assumed that LGE findings vary according to cardiac amyloid progression over time. This atypical LGE pattern can contribute to false-negative interpretations in patients with CA. Lastly, traditional LGE imaging, using the inversion recovery sequence, poses technical difficulties that carry a serious risk of false-negative findings or of obtaining a mirror image of the true LGE pattern, potentially contributing to the described variable LGE patterns. This problem can be reduced using a phase-sensitive inversion recovery (PSIR) sequence that renders the LGE image far more accessible. In our study, LGE imaging was performed using a PSIR sequence. As Dr. Di Bella and Dr. Pizzino indicated, assessing the left atrial and right ventricular LGE is also imperative.

Myocardial T1 mapping, a novel approach to myocardial tissue characterization, can overcome the limitations of LGE imaging. It features high diagnostic accuracy for the detection of CA and may be more sensitive than LGE imaging for identifying cardiac involvement. For differentiating patients with transthyretin CA from those with immunoglobulin light-chain CA and those with non-amyloid cardiac diseases, cardiac uptake on bone scintigraphy with tracers (e.g., 99mTc-pyrophosphate, 99mTc-3,3-diphosphonate, 1,2-propanedicarboxylic acid, and 99mTc-hydroxymethylene diphosphonate) has high diagnostic performance. Using these advanced diagnostic imaging modalities, a more precise diagnosis of CA can be performed with appropriate management of patients with CA.

Finally, we again thank Dr. Di Bella and Dr. Pizzino for their careful review and thoughtful comments on our study.

Disclosures

The authors declare no conflict of interest.

References