CMR-Based Characterization of Cardiac Amyloidosis

Amyloidosis is a systemic disease caused by the deposition of misfolded proteins. Cardiac involvement is a major cause of morbidity and mortality, especially in the light chain (AL) and transthyretin (ATTR) forms. Amyloidosis usually presents as a restrictive cardiomyopathy with progressive systolic/diastolic dysfunction and arrhythmias but is often misdiagnosed as hypertrophic or hypertensive heart disease.

Recent evidence has supported the value of cardiac magnetic resonance (CMR) as a noninvasive diagnostic tool to detect cardiac amyloidosis, which is characterized by marked myocardial interstitial expansion leading to a typical early and diffuse contrast enhancement. Dungu et al. (1) wrote an interesting paper describing the differential CMR characteristics according to the amyloid type (46 AL, 51 ATTR, 2 serum amyloid A, 1 apolipoprotein A-I). Cardiac amyloidosis was confirmed by endomyocardial biopsy in 50 patients, whereas the other 50 patients had a positive extracardiac biopsy combined with echocardiographic criteria for cardiac amyloidosis (2). Contrast enhancement was present in 99 patients, was more extensive in ATTR amyloidosis than in AL amyloidosis, and was incorporated into a scoring system (Query Amyloid Late Enhancement) that independently differentiated ATTR amyloidosis from AL amyloidosis. Despite poorer left ventricular systolic function and worse biventricular hypertrophy, patients with ATTR amyloidosis experienced a better outcome than did those with AL amyloidosis.

Nevertheless, the study did not examine all possible parameters provided by a standard CMR scan. Right ventricular volumes, mass, and ejection fraction, which provide a more detailed characterization of right ventricular morphology and function than right ventricular wall thickness alone, were not measured. Moreover, the Query Amyloid Late Enhancement score did not include contrast enhancement of the atrial chambers, which is a common finding in patients with cardiac amyloidosis and in this study resulted in a difference between patients with ATTR amyloidosis and patients with AL amyloidosis. Finally, gadolinium kinetics in the myocardium and in the blood pool is significantly deranged in amyloid patients, but it was not taken into account when comparing patients with AL amyloidosis and patients with ATTR amyloidosis. As an example, blood pool early darkening after contrast administration is a typical feature of AL amyloidosis due to the rapid contrast washout from the blood pool into the systemic interstitial space, which is extremely enlarged by light chain deposition (3–5); similar indexes of contrast kinetics might have been investigated in the study.

Overall, CMR showed high diagnostic accuracy in detecting cardiac amyloidosis. In particular, contrast enhancement was present in all patients except 1 patient with AL amyloidosis with positive extracardiac biopsy and echocardiographic criteria for cardiac involvement but no proven cardiac involvement by endomyocardial biopsy. Similarly, 12 patients with a negative final diagnosis at CMR showed positive contrast enhancement, making contrast enhancement 100% sensitive to detect cardiac amyloidosis. On the other hand, there were only 6 patients with false-positive results, who presented cardiac hypertrophy with gadolinium contrast enhancement at CMR but interstitial collagen accumulation rather than amyloid deposition at endomyocardial biopsy (3 hypertensive, 2 hypertrophic, 1 alcoholic cardiomyopathy); a subtly different gadolinium kinetics (an earlier enhancement in amyloidosis vs. a later enhancement in fibrosis) could have been hypothetically disclosed by a careful analysis of gadolinium enhancement over time.

We agree with the authors that the increased availability of CMR has led to increased detection of cardiac amyloidosis, superior tissue characterization, and possible differentiation between interstitial diseases (inflammation, fibrosis, amyloid). The different biochemical properties of amyloid subtypes likely explain not only the variable imaging features but also the distinct prognosis. Further studies are needed to expand the results of the present study, possibly investigating the complexity of cardiac interstitial remodeling with novel T1 mapping techniques and correlating CMR findings with established biohumoral (natriuretic peptides, troponins), functional (peak oxygen consumption), electrocardiographic, and echocardiographic parameters.

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REFERENCES


REPLY: CMR-Based Characterization of Cardiac Amyloidosis

We thank Barison et al. for their interest in our paper (1). Cardiac amyloidosis is gaining significant exposure in the cardiac magnetic resonance (CMR) community because of the characteristic and near pathognomonic findings with the technique. We reported the first study that specifically aimed to differentiate between the light chain (AL) and transthyretin (ATTR) subtypes of amyloidosis through retrospective analysis of studies performed in multiple hospitals referring to a specialist amyloidosis center (1).

We did not include right ventricular volumes, mass, and ejection fraction in the analyses because not all studies included sufficient images to perform accurate analysis. Right ventricular morphology data (particularly right ventricular mass) are less reproducible, even in single center studies (2), and in this series axial data sets had rarely been routinely obtained (3). The Query Amyloid Late Enhancement score, a novel late gadolinium enhancement analysis, was designed to be a simple add-on to standard reporting. Various versions of the Query Amyloid Late Enhancement score were devised, incorporating other CMR variables, but we and the reviewers decided to report the score independently, without including potentially confounding factors, because it was a standalone predictor of amyloid type. The thinness of the atrial chambers precludes their use as a reliable measurement when assessing late gadolinium enhancement. Altered gadolinium kinetics, already widely reported in cardiac amyloidosis, appear very similar between amyloid types (4), but further quantitative assessment in this multiple center, multiple protocol study was not feasible.

Overall, the comments highlight the limitations of any retrospective study, but we would like to reinforce the view that our findings were actually strengthened by the study design. The data were derived from nonstandardized protocols performed on various scanners; however, despite this, an obvious difference between the amyloid subtypes was shown. Our results are therefore relevant to nonspecialist CMR centers, which often raise the possibility of amyloidosis for the clinicians who refer patients for CMR. Prospective studies with specialist amyloid protocols may seem ideal; however, in the real world, our results are applicable to all CMR operators.

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REFERENCES


