T1 mapping and amyloid cardiomyopathy: how much better can it get?

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This editorial refers to ‘T1 mapping and survival in systemic light-chain amyloidosis’10, by S.M. Banypersad et al., on page 244.

Systemic light-chain (AL) amyloidosis carries a high risk of cardiac involvement and portends poor prognosis.1 Patients with cardiac AL amyloidosis have a median survival of 8 months compared with ~4 years when the heart is spared. Therefore, confirmation of cardiac involvement is critical for therapeutic decision-making and patient counselling. Furthermore, differentiation from other cardiomyopathies with left ventricular hypertrophy or features of restrictive physiology on echocardiography is frequently necessary.

Over the last decade, cardiovascular magnetic resonance (CMR), and particularly the late gadolinium enhancement (LGE) technique, has been validated as a means to identify cardiac involvement in AL amyloidosis.2–4 The appearance of global, subendocardial LGE in combination with a dark left ventricular blood pool is the hallmark for identifying cardiac involvement. However, LGE-CMR has some limitations in patients with amyloid disease. For example, the pattern of LGE may sometimes be atypical and patchy, even in patients with advanced disease. Furthermore, a significant subset of AL amyloid patients suffer from significant renal dysfunction, where gadolinium contrast administration is problematic due to the risk of nephrogenic systemic fibrosis.1

More recently, newer CMR tissue characterization techniques such as T1 mapping have emerged.5 Myocardial T1 mapping methods are used for native (i.e. without the use of gadolinium-based contrast agents) and also for post-contrast T1 measurements. In combination with haematocrit, pre- and post-contrast measurements enable the quantification of the extracellular volume fraction (ECV). Native myocardial T1 values reflect a composite signal from both the intracellular (predominantly myocytes) and extracellular compartments. Elevated native T1 times and expansion of ECV in the myocardium have been reported in several commonly encountered cardiac conditions including myocardial infarction, myocarditis, hypertrophic and dilated cardiomyopathy, cardiac involvement in systemic diseases, and aortic stenosis.6

As expansion of the extracellular space is its pathophysiological hallmark, cardiac amyloidosis has been intensively investigated using these newer T1 mapping methods (Figure 1). The first of these studies showed that native T1 mapping can accurately identify cardiac involvement in AL amyloidosis, exhibiting significantly elevated T1 values compared with normal or hypertrophy (due to aortic stenosis) controls.7 Native T1 values correlated with disease burden and, notably, showed the potential to identify patients with early disease. Subsequent post-contrast T1 mapping studies showed similar findings, with substantial increases in ECV, which correlated with the extent of amyloid burden.8,9

Banypersad and colleagues now provide evidence of the prognostic value of T1 mapping techniques in patients with systemic AL amyloidosis.10 The authors studied a cohort of 100 patients with histological proof of systemic AL amyloidosis, although only 7 patients had histological confirmation of disease in the heart from endomyocardial biopsy. Patients were grouped into three categories by echocardiographic criteria and biomarker data: approximately one-half with definitive cardiac involvement, one-quarter without, and another quarter with possible cardiac involvement. In addition, 54 healthy volunteers were studied. The CMR protocol included: cine CMR, pre-contrast (native) T1 mapping, LGE, and post-contrast T1 mapping. The ECV was calculated from post-contrast T1 after primed infusion as part of the equilibrium CMR technique (ECVi) and also based on post-contrast T1 at 15 min after bolus (ECVb). After a median follow up of 23 months, 25 patients died, most probably from cardiac causes. Importantly, the authors found that native T1 mapping and ECV (as measured by either the bolus or the equilibrium technique) were both significant predictors of mortality in AL amyloidosis. Comparison of the three predictive models, i.e. native T1 mapping, ECVi, and ECVb, showed that all three methods performed equally well with similar discriminative ability for cumulative mortality.

The authors should be commended for conducting the largest prognostic CMR study in cardiac amyloidosis to date. Their findings...
are significant because, although the role of CMR (including mapping techniques) in the diagnosis of cardiac amyloidosis was previously well established, outcome data were either conflicting for LGE or not available for T1 mapping techniques. We now have conclusive evidence that T1 mapping techniques have a strong predictive role in patients referred for suspected AL amyloidosis. Furthermore, it is important to note that native (non-contrast) T1 mapping provides practically the same diagnostic and prognostic information as ECV techniques, which involve the use of gadolinium contrast. This is important for the clinician, as native T1 mapping is a relatively quick and simple scan to perform and analyse, providing quantitative results with minimal subjectivity that are highly reproducible. Therefore, native T1 mapping can easily be added to a cardiomyopathy CMR scan protocol. Whether we should always proceed to post-contrast T1 mapping for ECV measurement in such cases is a matter of debate. In our view, if native T1 time is increased and the patient has either altered kinetics of gadolinium on inversion time scout (i.e. the myocardium reaches the null crossing before the blood pool) and/or the classical amyloid pattern of LGE is present, then post-contrast T1 mapping for ECV is probably redundant. As the authors point out, for patients with significant renal impairment who are at increased risk for nephrogenic systemic fibrosis with gadolinium administration, non-contrast T1 mapping is certainly the preferred option.

The study by Banypersad and colleagues has some limitations. The authors report T1 values and ECV measurements only based on a region of interest drawn in the basal septum in a four-chamber view. The opportunity exists to analyse whole-heart T1 or even native T1 time of the myocardium has a relatively narrow normal range with small variability (global myocardial T1 is 955 ms in the mid-ventricular slice image acquired with the shortened modified look-locker inversion recovery-ShMOLLI sequence). In cardiac amyloidosis, there is the same number of myocytes (so no real hypertrophy) but significant expansion of the extracellular space due to infiltration by amyloid fibrils (illustrated with green colour in this example) which is responsible for the significant myocardial thickening. Native T1 time is substantially increased due to the amyloid deposition (global myocardial T1 is 1098 ms in this example; image acquired with the ShMOLLI sequence). Similarly increased are extracellular volume measurements on amyloid heart disease (no extracellular volume maps shown here). Figure modified from JACC Cardiovasc Imaging 2013;6;488-497 with permission of the publisher.
amyloid heart disease—a fortunate and timely coincidence with the emergence of a series of novel drugs for the causal treatment of amyloid which are currently under investigation.15 Such novel therapeutic approaches, combined with the new quantitative imaging techniques discussed here, provide hope that in the future, prognosis of this currently deadly disease may be substantially improved.

Conflict of interest: none declared.

References