Amyloidosis is a condition in which misfolded proteins form insoluble deposits in the extracellular space of various tissues and organs, leading to interstitial expansion and disruption of structure and function. Light-chain (AL) amyloidosis is caused by an underlying plasma cell dyscrasia; cardiac involvement is common, is present in ≥50% of patients at presentation, and is a principal driver of morbidity and mortality. In practice, there has been reliance on ECG and echocardiographic features, as well as serum cardiac biomarkers, such as pro-brain natriuretic peptide and troponin T concentrations, for prognostic purposes and correlation to clinical response to treatment. However, these parameters can be of limited use because of concomitant etiologies for left ventricular (LV) hypertrophy and coexisting renal impairment. T1 relaxation time for hydrogen magnetization in the myocardium, an intrinsic characteristic of tissue, has been studied in a variety of pathologies with diffuse processes, including amyloidosis. Native, also known as noncontrast or precontrast, T1 mapping can be performed without the use of gadolinium-based contrast in patients with significantly reduced glomerular filtration rate. The technique of T1 mapping with cardiovascular magnetic resonance (CMR), in which T1 relaxation times for all pixels in the acquired image of the heart are measured, has been used for purposes of tissue characterization in regards to the diagnosis of cardiac involvement and prognosis in AL amyloidosis at single time point evaluations. Here we present a case using serial CMR native T1 mapping to assess treatment response of AL amyloidosis in a patient with renal failure.

A 60-year-old Caucasian woman with a past medical history of hyperlipidemia, chronic obstructive pulmonary disease, and chronic kidney disease experienced progressive symptoms of fatigue over the course of a year with ongoing declining renal function. As part of the work-up, a renal biopsy demonstrated AL amyloidosis, and a bone marrow biopsy demonstrated the presence of a plasma cell neoplasm. In addition, she had elevated beta-2 microglobulin (20.03 mg/L; reference range ≤2.64), immunoglobulin kappa-free light chains (58.10 mg/dL; reference range 0.33–1.94), and kappa:lambda-free light chains ratio (24.94; reference range 0.26–1.65) values, as well as abnormal troponin T (0.17 ng/mL; reference range <0.01) and pro-brain natriuretic peptide (70 000 pg/mL; reference range <300). The AL amyloidosis was treated with a course of cyclophosphamide, bortezomib, and dexamethasone for the first 8 months, followed by pomalidomide for maintenance therapy. She was referred for onco-cardiology evaluation and follow-up during chemotherapy treatment, given the cardiac findings of low-voltage ECG (Figure 1), LV hypertrophy, and diastolic dysfunction (Figure 2) on transthoracic echocardiography and abnormal cardiac biomarkers. Her ongoing renal failure with a glomerular filtration rate of <30 mL/min/m² led to the initiation of hemodialysis. As her renal failure precluded the use of gadolinium-based contrast in CMR imaging, we sought to assess potential cardiac involvement of amyloidosis with native T1 mapping for further tissue characterization. During the course of her treatment, she remained on hemodialysis and was serially followed with noncontrast CMR imaging.

The patient underwent 3 CMR studies, with baseline imaging near the initiation of chemotherapy treatment and follow-up imaging at 14 months and then again at 20 months after diagnosis. All the CMR studies were performed on a 1.5-Tesla clinical magnetic resonance imaging scanner (Aera; Siemens Healthcare, Erlangen, Germany). CMR cine imaging demonstrated biventricular hypertrophy, atrial thickening, preserved systolic function, and a small circumferential pericardial effusion, which are morphological and structural characteristics suggestive of cardiac involvement of amyloidosis in this case (Figure 3; Movie 1 in the Data Supplement). On each of the 3 studies, native T1 mapping was performed in short axis and 4-chamber views, using the Modified Look Locker Inversion Recovery (MOLLI) technique on the first study and the Shortened Modified Look locker Inversion Recovery (ShMOLLI) technique, which allows for acquisition of a T1 map with a shorter breath hold, on the subsequent studies. Good agreement has been demonstrated between these 2 techniques for T1 values under 1200 ms. The LV septum region of interest was manually contoured on the T1 map, each comprising an approximate area of 200 mm² in both short axis and 4-chamber views to determine the average T1 relaxation value.

T1 relaxation time on the initial study was in the range of previously published values compatible with cardiac amyloidosis. With treatment, she had symptomatic improvement that correlated with an interval decrease in T1 relaxation time.
This corresponded to a decrease in other markers of disease that were followed over the same time period, including kappa:lambda-free light chain ratio, pro-brain natriuretic peptide, and LV mass indexed to body surface area as measured on the CMR studies (Figure 5). This also correlated with transthoracic echocardiography parameters, suggesting improvement in diastology over the monitoring period, including increased medial E' (5.4–7.1 cm/s) and lateral E' (5.7–8.1 cm/s) velocities, decreased E/E' ratio (20.1 to 16.5), and increased deceleration time (292–352 ms). Additionally, maximum LV wall thickness decreased from 1.6 cm to 1.3 cm by both transthoracic echocardiography and CMR, and interatrial septal thickness decreased from 8 to 6 mm by CMR. Although significantly limited because of body habitus, retrospective strain analysis by 2D speckle tracking of the baseline transthoracic echocardiography images did suggest abnormal longitudinal strain in the basal and midventricular segments with relative preservation in the apical segments, with follow-up imaging demonstrating overall improvement in global longitudinal strain (−12% to −17%).

To our knowledge, this case is the first published report using serial native T1 mapping to follow treatment response in AL amyloidosis. This case demonstrated that the method could provide a noninvasive and noncontrast imaging method to monitor treatment progress in terms of cardiac involvement. It is unknown if and how variations in chemotherapy regimens, use of steroids, hemodialysis, or changes in serum protein or albumin levels may independently affect native T1 values. We posit that a decline in T1 relaxation values in this case, in conjunction with overall reduction in systemic and cardiac biomarkers in the setting of clinical improvement with treatment, may represent regression of amyloid deposition in the myocardium. Further study of serial imaging with additional patients and standardized protocols would need to be performed to test this hypothesis. This case demonstrates the promise of native T1 mapping for serial tissue characterization and its potential to become a future noninvasive, noncontrast imaging marker for cardiac amyloidosis surveillance monitoring that can perhaps contribute to the management of patients with this disease.

Disclosures
None.

References

Key Words: amyloid ◼ cardiovascular MRI ◼ noncontrast ◼ precontrast ◼ serial ◼ T1 mapping

Figure 1. 12-Lead ECG demonstrates sinus rhythm with low-voltage criteria in the precordial (<10 mm) and limb (<5 mm) leads.
Figure 2. Transthoracic echocardiography (TTE) diastology assessment demonstrates evidence of abnormal diastolic function with reduced tissue Doppler velocities (A, medial $E'$ 5.4 cm/s; and B, lateral $E'$ 5.7 cm/s) and mitral valve inflow velocity $E/A$ ratios (C, 1.0 at rest; and D, 0.8 with Valsalva maneuver).

Figure 3. Baseline study cardiovascular magnetic resonance (CMR) cine in the 4-chamber (4C) view demonstrates global extent of cardiac involvement, including biventricular hypertrophy, atrial wall thickening, preserved systolic function, and small circumferential pericardial effusion.
Figure 4. Serial native noncontrast T1 mapping of 3 studies of the patient in the short axis (SAX; A, D, and G) and 4-chamber (4C; B, E, and H) views. Manual contouring (approximate area of 200 mm² each) of the septum demonstrated decrease in averaged T1 relaxation values across the 3 studies (C, F, and I).
Figure 5. Timeline of clinical course and treatment, with correlating declines in biomarker and cardiovascular magnetic resonance (CMR) parameters, including native noncontrast T1 mapping values. BNP indicates brain natriuretic peptide; and LV, left ventricle.
Serial Native T1 Mapping to Monitor Cardiac Response to Treatment in Light-Chain Amyloidosis

David J. Hur, Demetrius L. Dicks, Steffen Huber, Hamid R. Mojibian, Judith L. Meadows, Stuart E. Seropian and Lauren A. Baldassarre

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SUPPLEMENTAL MATERIAL

Video Legend

Video Clip 1 (Figure 3): Baseline study CMR cine in the 4C view demonstrated global extent of cardiac involvement including biventricular hypertrophy, atrial wall thickening, preserved systolic function, and small circumferential pericardial effusion.