Amyloidosis is a systemic infiltrative disorder in which insoluble protein fibrils are deposited in the extracellular matrix (ECM). The prognosis is predominantly determined by cardiac involvement because the amyloid depositions lead to a restrictive cardiomyopathy. Although endomyocardial biopsy is the gold standard for diagnosing cardiac amyloidosis, the associated risk for complications favors a noninvasive approach by using various cardiac imaging methods, whereas tissue diagnosis is made on a noncardiac biopsy. Accurate diagnosis of cardiac amyloidosis becomes difficult when a secondary cause of myocardial wall thickening (eg, hypertension) is present as well. Cardiac MRI is an excellent tool for assessment of systolic and diastolic function, myocardial thickness, and amyloid deposition with late gadolinium enhancement imaging. Late gadolinium enhancement imaging is a qualitative technique, which relies on the presence of normal myocardium to visualize infiltrated, enhanced tissue. Therefore, diffuse deposition of amyloid is difficult to highlight, because regional differences in signal intensities may be absent. T1-mapping is a cardiac MR technique, which allows absolute quantification of T1 values of the myocardium and enables assessment of ECM expansion present in cardiac amyloidosis.

A 71-year-old man with a medical history of hypertension presented with suspicion of congestive heart failure. A 12-lead electrocardiography showed atrial fibrillation and
low voltages in the extremity leads (Figure 1). Surprisingly, echocardiography demonstrated severe concentric hypertrophy with a preserved left ventricular systolic function (Figure 2). Due to the discrepancy between hypertrophy and low voltages, cardiac amyloid was suspected and cardiac MR imaging was performed using a clinical 1.5-T scanner (Avanto; Siemens, Erlangen, Germany). Despite atrial fibrillation, images were of diagnostic quality. Functional assessment showed a left ventricular ejection fraction of 53% and wall thickness of 16 mm. Both atria were dilated and small pericardial and pleural effusions were present (online-only Data Supplement movie).

To differentiate between hypertension-induced hypertrophy and increased myocardial mass due to amyloid depositions with subsequent increase in ECM, T1 mapping was performed before and at 5 and 10 minutes after 0.2 mmol/kg Gd-DOTA (Dotarem; Guerbet, Villepinte, France) contrast administration. This gadolinium-based contrast agent does not cross intact cellular membranes and distributes only in the extracellular space. T1 mapping was performed with a single short axis slice modified

Figure 2. Echocardiography (PSSAX) shows left ventricular hypertrophy. No evident granular sparkling of the myocardium was visible.

Figure 3. Late gadolinium enhancement shows difficulties in finding the correct inversion time with inversion of the blood pool signal and the myocardium at almost similar T1 relaxation times (slice thickness 8.0 mm, time of repetition 650 ms, field of view matrix 192×186; inversion time A: 200 ms, B: 225 ms).

Figure 4. Late gadolinium enhancement shows some midmyocardial patchy gadolinium enhancement in the lateral wall, likely representing more pronounced regional involvement (marked with an asterisk, inversion time 300 ms, slice thickness 8.0 mm, time of repetition 650 ms, field of view matrix 192×186).

Figure 5. T1 mapping was performed on a short axis slice by calculation of the T1 relaxation times for each of the 6 equiangular segments. Segmentation was performed by using the American Heart Association standard 17-segment model. LV indicates left ventricular; IS, inferoseptum; AS, anteroseptum; AN, anterior; AL, anterolateral; IL, inferolateral; IN, inferior; N/A, not applicable.
look-locker inversion-recovery sequence obtained during breath-holding. After T1-mapping, late gadolinium enhancement imaging was performed using an inversion recovery gradient echo sequence. Signal suppression of normal myocardial tissue was difficult (Figures 3 and 4). To assess whether the increased mass was due to an increase in ECM size or due to cellular hypertrophy, ECM size was estimated by assessing the myocardial distribution volume of Gd-DOTA. This myocardial distribution volume consists of both the extracellular, extravascular space and the tissue plasma space. This tissue plasma space fraction is in the order of 0.045 but cannot be separately assessed by MRI. T1 relaxation times were calculated for the blood pool and 6 isoangular segments of myocardium at the midventricular level (Figure 5). With the T1 relaxation times of myocardium and blood pool before and after contrast administration and correcting for hematocrit value (viz 0.37 l/L), the myocardial distribution volume was calculated. Analysis revealed a sharply increased myocardial distribution volume of Gd-DOTA in all segments (49%±5% of the myocardium; range, 44%–58%; Table) compared with previously described values of 24%±3% in normal and 34%±3% in hypertensive patients. These findings reinforced the suspicion of amyloidosis and subcutaneous adipose tissue biopsy was performed, confirming the diagnosis (Figure 6).

Using T1 mapping, we were able to show that myocardial amyloid deposition was not only limited to the enhanced areas on late gadolinium enhancement, but that it was a generalized process resulting in a diffuse increase in myocardial ECM volume. Figure 7 is an example of a different patient with cardiac amyloidosis. The cardiac tissue biopsy shows amyloid depositions giving rise to an increased ECM volume. T1 mapping has been used in patients with cardiac amyloidosis, although only for assessing T1 relaxation times. If cardiac amyloidosis is suspected and late gadolinium enhancement imaging is difficult due to diffuse infiltration, absolute quantification of myocardial distribution volume of an extracellular agent as an indication of ECM size may have additional value, especially if other causes for hypertrophy are present. Further analysis by comparison of T1 mapping and estimation of the ECM size in different pathophysiological processes causing myocardial wall thickening is necessary to assess the true applicability of this promising technique in clinical practice.

Acknowledgments

We thank the patient for his cooperation in providing us with the data and images.

Disclosures

Dr Hofman received a research grant from Research Support Siemens, Zoetermeer, The Netherlands. Dr Niessen received research grants from The Netherlands Organisation for Scientific Research. Dr van Rossum received research grants Medtronic, Heerlen, The Netherlands; Biotronic, Nijmegen, The Netherlands; and Abbott Vascular, Hoofddorp, The Netherlands.
References


Key Words: amyloid ▪ magnetic resonance imaging ▪ pathology ▪ T1 mapping ▪ tissue characterization
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Circ Cardiovasc Imaging, 2012;5:423-426
doi: 10.1161/CIRCIMAGING.112.973438

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