Clinical Application of T1 and T2 Mapping in Cardiac Magnetic Resonance Imaging for Nonischemic Cardiomyopathy: A Case-Based Review

Lulu Said Fundikira¹, Yoo Jin Hong², Pan Ki Kim², Sang A Lee², Kyung Sun Nam², Dong Jin Im³, Chul Hwan Park³, Hye-Jeong Lee², Jin Hur², Young Jin Kim², Tae Hoon Kim³, Byoung Wook Choi²

¹Department of Radiology and Imaging, Muhimbili University of Health and Allied Sciences, Dar Es Salaam, Tanzania
²Department of Radiology and Research Institute of Radiological Science, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
³Department of Radiology and Research Institute of Radiological Science, Gangnam Severance Hospital, Yonsei University Medical Center, Seoul, Korea

Cardiac magnetic resonance imaging is instrumental in diagnosing various cardiovascular diseases. Recently introduced T1 mapping and T2 mapping sequences have enabled quantification of the T1 and T2 relaxation times of the myocardium and associated cardiovascular structures, which are intrinsic properties of tissues. These sequences have been increasingly used to diagnose cardiomyopathy based on changes in the T1 and T2 relaxation times and to objectively quantify the severity of cardiomyopathy. As reference values in T1 and T2 mapping sequences are influenced by specific techniques or magnetic field strength, they are limitations. However, parametric imaging with native T1, T2, and extracellular volume fraction (%) values yields a higher diagnostic accuracy than conventional MRI and is useful for diagnosis, treatment, and risk stratification of cardiomyopathy.

Key words  T1 mapping · T2 mapping · Extracellular space · Magnetic resonance imaging · Cardiomyopathies.

INTRODUCTION

Cardiac magnetic resonance imaging (MRI) provides excellent assessment of myocardial function and anatomy and is used in diagnosis of cardiac diseases, including nonischemic cardiomyopathy [1-3]. Cardiac MRI is considered the gold standard for evaluating ventricular mass, volume, and ejection fraction, as well as for detection of focal myocardial fibrosis using late gadolinium enhancement (LGE). However, LGE has limited value in nonischemic myocardial disease, as the observed disease tends to be diffuse [4]. Moreover, LGE employs qualitative assessment of the myocardium and is susceptible to inter-patient and inter-image variability [5]. Recent innovations in cardiac MRI with the introduction of T1 mapping and T2 mapping sequences, including quantification of the T1 and T2 relaxation times of the myocardium and associated cardiovascular structures, have emerged as promising alternatives [4]. Mapping sequences allow for a per-voxel calculation of the absolute relaxation time of T1 and T2 values in milliseconds, as well as parametric reconstructed images of high spatial resolution [6].

The pixel signal intensity is based on the relaxation of hydrogen nucleus protons in a static magnetic field. T1 relaxation time depends on the molecular environment of the water molecules in the tissue and therefore characterizes each tissue very specifically. T1 relaxation time varies among tissues, but also
within the same tissue, depending on its pathophysiological status and the presence of inflammation, edema, fat, fibrosis, etc. [7].

T2 relaxation time is also a tissue-specific time parameter used to differentiate between normal and abnormal myocardial tissue. Increased water content is the main cause of longer T2 relaxation times. Thus, an increased T2 value is mainly noted in myocardial edema [8].

Cardiac MR mapping techniques have an advantage over LGE imaging by eliminating the influences of variations in signal enhancement by directly measuring the underlying T1 and T2 relaxation times [5]. Moreover, mapping enables quantification of the proportion of extracellular volume (ECV). ECV is calculated using a formula that combines native T1 and post-contrast times with hematocrit value. An increased ECV is a marker of myocardial remodeling and is most often due to excessive collagen deposition (in the absence of amyloid or edema) [9,10].

At a fixed magnetic field strength and in the absence of exogenous contrast agent, such as gadolinium chelate, the native T1 value of normal tissue falls within a predictable range (e.g., at 1.5 T, normal myocardium has a T1 relaxation time of 940–1000 ms) [11]. Normal myocardial T2 values acquired using steady-state free precession MRI have been reported to be 52.18±3.4 ms at 1.5 T [12] and 45.1 ms at 3 T [13].

Kellman and Hansen [14] reported myocardial ECVs in healthy volunteers to be similar at field strengths of 1.5 T (0.25±0.04) and 3 T (0.26±0.04). A “bolus only” injection is sufficient for ECV measurement, while a minimum delay of 15 min is recommended to reach a state of dynamic equilibrium for post-contrast T1 mapping and acquisition of time point data [6,15].

Studies have shown variability of native T1 relaxation times based on the sequence used, the magnetic field strength (higher native T1 values at higher strength), the image acquisition plane, and the region of myocardium being sampled, as well as the patient’s heart rate, age, and sex [8]. The Modified Look-Locker inversion recovery (MOLLI) sequence used for T1 mapping is characterized by data acquisition at a fixed point in the cardiac cycle over successive heartbeats during a single breath-hold (approximately 16–20 s). Multiple Look-Locker image acquisitions are performed at different inversion times and then merged into one dataset to facilitate final analysis [16].

The purpose of this study is to present various cases of nonischemic cardiomyopathy evaluated in our institution using T1 mapping, T2 mapping, and ECV quantification for diagnosis.

**CASE SERIES DISCUSSION**

**Dilated cardiomyopathy**

Dilated cardiomyopathy (DCMP) is the most common form of nonischemic cardiomyopathy and is characterized by a dilated and poorly functioning left ventricle. Half of the cases are idiopathic in nature, with the rest secondary to previous infection, alcohol and drug abuse, or toxicity [17,18]. Cardiac MR LGE shows patchy or diffuse midwall enhancement, which usually does not correspond to any coronary artery distribution, and represents fibrosis in the setting of chronic myocardial remodeling [17-19].

Buss et al. [20] noted that patients with DCMP usually show increased ECV compared with those in a control group, even in early stages of disease before a significant change in left ventricular (LV) function. Native T1 and ECV values are increased in DCMP (Fig. 1) and are correlated with reduced wall thickness [21].

**Hypertrophic cardiomyopathy**

Hypertrophic cardiomyopathy (HCMP) is the most common inheritable cardiac disorder. It is characterized by abnormal thickening of the LV wall in the absence of dilatation. HCMP commonly involves the interventricular septum in an asymmetric manner. Fibrosis occurs through intercellular deposition of collagen fibers and can be diffuse or present as focal scarring [22].

---

**Fig. 1. Dilated cardiomyopathy.** A 62-year-old woman was admitted to the hospital with dyspnea and pitting edema for one month. She underwent cardiac magnetic resonance imaging (Siemens 3 T); her left ventricle was dilated (LV end-diastolic dimension=7.3 cm, volume=235.3 mL/m²) and showed global diffuse hypokinesia; the measured LV ejection fraction was 25%. (A) Subtle LGE was noted at the mid-layer of the interventricular septum of the left mid-ventricle (arrows). (B-E) On the T1 mapping sequence, global native LV T1 was increased (B) (native T1=1434.4 ms, reference value=1203 ms), ECV was increased (D) (30.6%, reference=25%), and T2 was slightly increased (E) (56.2 ms, reference value=48.5 ms; reference values are the same in the following cases). (A) LGE image, (B) native T1 map, (C) post T1 map, (D) ECV map, and (E) T2 map. LV: left ventricular, LGE: late gadolinium enhancement, ECV: extracellular volume.
LGE has been reported in up to 75% of patients with HCMP in whom the clear majority have patchy midwall-type enhancement, which is typically most pronounced within the segments most severely affected by hypertrophy [23]. Native T1 sequences can depict the presence and pattern of myocardial fibrosis even in fibrotic areas that are undetected by LGE. Significant increases in native T1 and ECV values are observed in regions affected by HCMP [24] (Fig. 2).

**Myocarditis**

Inflammation of the myocardium can have a variety of etiologies, which are commonly viral, but is also caused by toxins, drugs, and autoimmune processes [25].

Findings on MRI include myocardial edema, wall motion abnormalities, and patchy subepicardial (96%) and midwall LGE (84%). The typical location of LGE is the lateral and inferior walls (73%), followed by the anterior wall [26].

T1 mapping provides improved detection of edema in acute myocarditis and subclinical low-grade myocardial inflammation compared to that with conventional T2 and LGE imaging [26].

T1 mapping has also shown sensitivity in identifying myocardial abnormalities caused by inflammation and fibrosis. T2 mapping specifically detects increased myocardial water content [19].

Both native T1 mapping and ECV are superior to the Lake Louise criteria for the diagnosis of myocarditis, although native T1 mapping can be influenced by the time between the onset of symptoms and MRI scanning [27].

A previous study involving patients with suspected systemic lupus erythematosus myocarditis demonstrated significantly increased native T1 and T2 values compared to those in normal control subjects. T1 and T2 mapping provides effective, noninvasive, and radiation- and contrast-free evaluation of myocarditis [28] (Fig. 3).

**Peripartum cardiomyopathy**

Peripartum cardiomyopathy (PPCM) is defined as the onset of heart failure in the last month of pregnancy or up to five months postpartum without previous history of heart disease [29].

PPCM is probably associated with pregnancy-related reduced
suppressor T cell activity, which may trigger autoimmune myocardial inflammation or activation of myocarditis. Recovery usually occurs in 50% of patients within six months [30].

LGE is evident in the mid-myocardium, mainly in the anterior and anterolateral segments [31]. LGE parallels irreversible myocardial injury and may contribute to persistent myocardial dysfunction, hampering recovery in some cases. However, Schelbert et al. [32] noted that LGE was uncommon in PPCM.

T1 mapping will show increased values; this is especially useful in patients with unremarkable LGE. Patients with edema have increased native T2 values compared with those in normal subjects [33,34] (Figs. 4 and 5).

**Amyloidosis**

Amyloidosis is a systemic disease characterized by the extracellular deposition of pathologic, insoluble amyloid protein in organs and tissues throughout the body. Cardiac involvement is common, with an immunoglobulin light chain associated with B-cell dyscrasias and transthyretin types of amyloidosis, and is associated with a poor prognosis [8]. Myocardial thickening is an important finding in cardiac amyloidosis with a restrictive diastolic filling pattern. Systolic dysfunction is usually seen in the late phase of the disease [35]. Endomyocardial biopsy is the gold standard for diagnostic testing, revealing infiltration and expansion of the interstitial space by amyloid deposits. However, it is rarely performed due to procedural risks and the possibility of sampling error. Diagnosis is often dependent on non-invasive imaging [36].

LGE imaging typically shows global transmural or subendocardial enhancement with a thickened myocardium and without territorial distribution [29].

ECV expansion in cardiac amyloidosis reaches extremely high values (on the order of 0.5 to 0.6). The myocardial amyloid load also has a relatively strong effect on native T1, which extends the utility of T1 mapping to patients with contraindications to contrast agent [16] (Fig. 6).

**Fabry disease**

Anderson-Fabry disease is an X-linked metabolic disorder associated with alpha-galactosidase deficiency and intracardiac glycolipid accumulation [37]. The typical cardiac manifestations include concentric biventricular hypertrophy, which may result from increased myocardial sympathetic nerve tone [38]. Cardiac involvement is common, with an immunoglobulin light chain associated with B-cell dyscrasias and transthyretin types of amyloidosis, and is associated with a poor prognosis [8]. Myocardial thickening is an important finding in cardiac amyloidosis with a restrictive diastolic filling pattern. Systolic dysfunction is usually seen in the late phase of the disease [35].

Endomyocardial biopsy is the gold standard for diagnostic testing, revealing infiltration and expansion of the interstitial space by amyloid deposits. However, it is rarely performed due to procedural risks and the possibility of sampling error. Diagnosis is often dependent on non-invasive imaging [36].

LGE imaging typically shows global transmural or subendocardial enhancement with a thickened myocardium and without territorial distribution [29].

ECV expansion in cardiac amyloidosis reaches extremely high values (on the order of 0.5 to 0.6). The myocardial amyloid load also has a relatively strong effect on native T1, which extends the utility of T1 mapping to patients with contraindications to contrast agent [16] (Fig. 6).

**Fabry disease**

Anderson-Fabry disease is an X-linked metabolic disorder associated with alpha-galactosidase deficiency and intracardiac glycolipid accumulation [37]. The typical cardiac manifestations include concentric biventricular hypertrophy, which may result from increased myocardial sympathetic nerve tone [38]. Cardiac involvement is common, with an immunoglobulin light chain associated with B-cell dyscrasias and transthyretin types of amyloidosis, and is associated with a poor prognosis [8]. Myocardial thickening is an important finding in cardiac amyloidosis with a restrictive diastolic filling pattern. Systolic dysfunction is usually seen in the late phase of the disease [35].

Endomyocardial biopsy is the gold standard for diagnostic testing, revealing infiltration and expansion of the interstitial space by amyloid deposits. However, it is rarely performed due to procedural risks and the possibility of sampling error. Diagnosis is often dependent on non-invasive imaging [36].

LGE imaging typically shows global transmural or subendocardial enhancement with a thickened myocardium and without territorial distribution [29].

ECV expansion in cardiac amyloidosis reaches extremely high values (on the order of 0.5 to 0.6). The myocardial amyloid load also has a relatively strong effect on native T1, which extends the utility of T1 mapping to patients with contraindications to contrast agent [16] (Fig. 6).

**Fabry disease**

Anderson-Fabry disease is an X-linked metabolic disorder associated with alpha-galactosidase deficiency and intracardiac glycolipid accumulation [37]. The typical cardiac manifestations include concentric biventricular hypertrophy, which may result from increased myocardial sympathetic nerve tone [38]. Cardiac involvement is common, with an immunoglobulin light chain associated with B-cell dyscrasias and transthyretin types of amyloidosis, and is associated with a poor prognosis [8]. Myocardial thickening is an important finding in cardiac amyloidosis with a restrictive diastolic filling pattern. Systolic dysfunction is usually seen in the late phase of the disease [35].

Endomyocardial biopsy is the gold standard for diagnostic testing, revealing infiltration and expansion of the interstitial space by amyloid deposits. However, it is rarely performed due to procedural risks and the possibility of sampling error. Diagnosis is often dependent on non-invasive imaging [36].

LGE imaging typically shows global transmural or subendocardial enhancement with a thickened myocardium and without territorial distribution [29].

ECV expansion in cardiac amyloidosis reaches extremely high values (on the order of 0.5 to 0.6). The myocardial amyloid load also has a relatively strong effect on native T1, which extends the utility of T1 mapping to patients with contraindications to contrast agent [16] (Fig. 6).

**Fabry disease**

Anderson-Fabry disease is an X-linked metabolic disorder associated with alpha-galactosidase deficiency and intracardiac glycolipid accumulation [37]. The typical cardiac manifestations include concentric biventricular hypertrophy, which may result from increased myocardial sympathetic nerve tone [38]. Cardiac involvement is common, with an immunoglobulin light chain associated with B-cell dyscrasias and transthyretin types of amyloidosis, and is associated with a poor prognosis [8]. Myocardial thickening is an important finding in cardiac amyloidosis with a restrictive diastolic filling pattern. Systolic dysfunction is usually seen in the late phase of the disease [35].

Endomyocardial biopsy is the gold standard for diagnostic testing, revealing infiltration and expansion of the interstitial space by amyloid deposits. However, it is rarely performed due to procedural risks and the possibility of sampling error. Diagnosis is often dependent on non-invasive imaging [36].

LGE imaging typically shows global transmural or subendocardial enhancement with a thickened myocardium and without territorial distribution [29].

ECV expansion in cardiac amyloidosis reaches extremely high values (on the order of 0.5 to 0.6). The myocardial amyloid load also has a relatively strong effect on native T1, which extends the utility of T1 mapping to patients with contraindications to contrast agent [16] (Fig. 6).
tricular hypertrophy, thickening of the atrioventricular valves, and an inferolateral mid-wall pattern of LGE due to focal fibrosis [21,38].

The disease process involves intramyocyte accumulation of lipids, which shortens the native T1 time. The extracellular matrix is not altered; thus, ECV is found within a normal range, comparable to that in controls (Fig. 7).

**Iron overload**

Thalassemia is an inherited hemoglobin disorder that requires regular blood transfusions, which may lead to iron overload in tissues including the heart. Patients may develop cardiomyopathy, which is the principal cause of mortality. Most of the observed cardiac problems are reversible in the early stages of the disease through chelation therapy [39].

Voskaridou et al. [40] in a study involving 106 patients with
beta thalassemia, found that comparison of heart T2 and serum ferritin values showed a negative correlation. Thalassemia major patients showed a significant negative correlation between the above two parameters; however, T2-values of the myocardium were significantly lower in thalassemia major than in thalassemia intermedia patients. Sado et al. [41] performed T1 mapping in cardiac iron overload patients and noted that T1 values were lower in affected patients than in healthy volunteers (836± 138 ms vs. 968±632 ms, p<0.001). They concluded that myocardial T1 mapping is an alternative method for cardiac iron quantification, with potential for improved detection of mild iron loading and with superior reproducibility.

Another study involving 106 patients with thalassemia major compared myocardial T1 against T2 and T2* for myocardial iron characterization. It was observed that, in patients with myocardial iron overload, T1 values were shortened compared to those in normal volunteers, with linear correlations between T2 and T2* (r=0.82; p<0.001) and between T1 and T2* (r=0.83; p<0.001) [42] (Fig. 8).

Short summary of this manuscript

T1 and T2 mapping are useful techniques to diagnose various non-ischemic cardiomyopathies.

Conflicts of Interest

The authors declare that they have no conflict of interest.

Acknowledgments

This study was supported by a faculty research grant of Yonsei University College of Medicine (6-2016-0077).

REFERENCES


