Improved Detection of Myocardial Involvement in Acute Inflammatory Cardiomyopathies Using T2 Mapping

Paaladinesh Thavendiranathan, MD, MSc; Michael Walls, MD; Shivraman Giri, MSBME; David Verhaert, MD; Sanjay Rajagopalan, MD; Sean Moore; Orlando P. Simonetti, PhD; Subha V. Raman, MD, MSEE

Background—T2-weighted cardiac magnetic resonance imaging is useful in diagnosing acute inflammatory myocardial diseases, such as myocarditis and tako-tsubo cardiomyopathy (TTCM). We hypothesized that quantitative T2 mapping could better delineate myocardial involvement in these disorders versus T2-weighted imaging.

Methods and Results—Thirty patients with suspected myocarditis or TTCM, referred for cardiac magnetic resonance imaging, who met established diagnostic criteria underwent myocardial T2 mapping. T2 values were averaged in involved and remote myocardial segments, both defined by a reviewer blinded to T2 data. In myocarditis, T2 was $65.2 \pm 3.2$ ms in the involved myocardium versus $53.5 \pm 2.1$ ms in the remote myocardium ($P<0.001$). In TTCM, T2 was $65.6 \pm 4.0$ ms in the involved myocardium versus $53.6 \pm 2.7$ ms in the remote segments ($P<0.001$). T2 values were similar across remote myocardial segments in patients and all myocardial segments in controls ($P>0.05$ for all). T2 maps provided diagnostic data even in patients with difficulty breath holding. A T2 cutoff of 59 ms identified areas of myocardial involvement, with sensitivity and specificity of 94% and 97%, respectively. T2 mapping revealed regions of abnormal T2 beyond those identified by wall motion abnormalities or late gadolinium-enhancement positivity. Conventional T2-weighted short tau inversion recovery images were uninterpretable in 7 patients because of artifact and unremarkable in 2 patients who had elevated T2 values. T2-prepared steady-state–free precession images showed areas of signal hyperintensity in only 17 of 30 patients.

Conclusions—Quantitative T2 mapping reliably identifies myocardial involvement in patients with myocarditis and TTCM. T2 mapping delineated a greater extent of myocardial disease in both conditions compared with that identified by wall motion abnormalities, T2-weighted short tau inversion recovery imaging, T2-prepared steady-state–free precession, or late gadolinium enhancement. Quantitative T2 mapping warrants consideration as a robust technique to identify myocardial injury in patients with acute myocarditis or TTCM. (Circ Cardiovasc Imaging. 2012;5:102-110.)

Key Words: myocarditis ■ tako-tsubo cardiomyopathy ■ T2-weighted imaging ■ T2-mapping ■ cardiac MRI

Cardiac magnetic resonance imaging (CMR) plays an important role in the diagnosis of acute myocarditis and tako-tsubo cardiomyopathy (TTCM).1-3 T2-weighted (T2W) imaging is an essential technique to make the correct diagnosis,4,5 particularly in cases in which late gadolinium enhancement shows no apparent injury. Unfortunately, traditional T2W-CMR techniques have limitations that affect diagnostic utility, with increased artifacts in patients with irregularities in cardiac rhythm or difficulties with breath holding.6 Surface coil intensity variation requires specialized normalization methods, bright signal from stagnant blood impairs recognition of adjacent myocardial T2 signal increase, and image interpretation remains mostly subjective. Semiquantitative approaches have been developed for T2W-CMR that, for instance, compute signal intensity relative to unaffected remote myocardium or adjacent skeletal muscle; however, these approaches perform poorly when there is diffuse myocardial involvement. Furthermore, these may be insensitive when there is concomitant skeletal muscle involvement, which has been reported in myocarditis.3

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Our group has developed a quantitative T2-mapping approach that overcomes many of these limitations.6 In this work, we sought to apply this technique to assess its utility and establish myocardial T2 cutoffs for diagnosis of acute myocarditis and TTCM and compare its diagnostic performance with traditional T2W–short tau inversion recovery (STIR) imaging and T2-prepared steady-state–free precession (T2p-SSFP) imaging.

Methods

Study Population

Consecutive patients referred for CMR assessment of acute myocarditis or TTCM between December 2009 and April 2011 who met established diagnostic criteria were prospectively enrolled for participation in an
institutional review board–approved human subject protocol. In addition, 30 healthy volunteers (control group) without a prior cardiovascular history were recruited from advertisements for an ongoing institutional review board–approved CMR technique development protocol to undergo myocardial T2 mapping in a single midventricular short axis (SAX) slice. For myocarditis, the following traditional diagnostic criteria were used: (1) symptoms and signs suggestive of cardiac disease (chest pain, dyspnea, and palpitations); (2) evidence of myocardial injury, as defined by ECG changes (ST-segment changes and conduction defects) and elevated serum markers, such as creatine kinase or troponin-I; and (3) exclusion of coronary artery disease by angiography and/or clinical criteria.3 For TTCM, the following proposed modified Mayo Clinic criteria were used7,8: (1) transient wall motion abnormality (WMA) of the LV mid segments, with or without apical involvement; WMA beyond single coronary distribution, usually preceded by a stressful trigger; (2) absence of obstructive coronary disease; (3) new ECG abnormalities or modest troponin elevation (reference upper normal limit, 0.11); and (4) absence of pheochromocytoma and myocarditis. Exclusion criteria included contraindications to CMR, hemodynamic instability, previous myocardial infarction, and previous episode of myocarditis. At the time of enrollment, medical history, ECG, and results of clinically obtained procedures, such as cardiac catheterization and serological markers, were recorded.

CMR Examination
All CMR studies were performed on a 1.5-T scanner (Avanto, Siemens Healthcare; Erlangen, Germany) using a 12-channel phased-array coil (6 anterior elements plus 6 spine coil elements). The following CMR protocols were used (typical parameters for the sequences are outlined in Table 1).

1. Balanced SSFP cine imaging in 3 long axis planes (horizontal, vertical, and 3 chamber) and 8 to 12 contiguous SAX planes to cover the LV. Real-time imaging with a time-adaptive sensitivity encoding (TSENSE) acceleration factor of 3 was used for subjects unable to breath hold.
2. T2 maps were acquired in basal, mid, and apical SAX and 3 long axis (horizontal, vertical, and 3-chamber) planes using a T2-prepared single-shot SSFP sequence, as previously described.6 Briefly, 3 T2p-SSFP images, each with a different T2p time (0, 24, and 55 ms, respectively; TR=3\times R-R, total acquisition time of 7 heartbeats) were acquired. All images were acquired with an attempted breath hold. To correct for residual cardiac and respiratory motion between images, a fast variational nonrigid registration algorithm was used, aligning all T2-prepared frames to the center frame.6 Finally, T2 maps were generated from these motion-corrected images by fitting a monoexponential decay curve at each pixel.
3. T2-weighted STIR images10 were obtained in basal, mid, and apical SAX and 3 long axis planes.
4. Late gadolinium-enhancement (LGE) imaging was performed in the same planes as SSFP cines using a segmented inversion-recovery gradient-echo sequence 10 minutes after 0.2 mmol/kg IV gadolinium diethylenetriamine penta-acetic acid (DTPA) administration. The inversion time was adjusted to null the myocardium. Non–breath-held single-heartbeat LGE imaging was performed for patients unable to breath hold.11

General Image Analysis
Left ventricular end-diastolic and systolic volumes were measured using the Simpson method and indexed to body surface area. A standardized 17-segment model13 was used to evaluate regional LV wall motion (1 indicates normal; 2, hypokinesis; 3, akinesis; 4, dyskinesis; and 5, aneurysmal); the wall motion score index was calculated as the sum of the segmental scores divided by 17.

Regional myocardial function was also assessed by analyzing peak circumferential and radial strain in each segment, including basal, mid, and apical SAX breath-held SSFP cines using vector-based feature-tracking software (Vector Velocity Imaging, Siemens; Mountain View, CA) that has been previously described.13–16 Briefly, contours were drawn along the LV endocardial and epicardial borders and automatically propagated through all frames. The ventricle is divided into 6 segments at each SAX view. By tracking the features within each voxel throughout the cardiac cycle (similar to speckle tracking in echocardiography), circumferential and radial strain values were obtained. Six basal, 6 midventricular, and 4 apical segments were analyzed, yielding strain values for a total of 16 segments.

T2-Weighted Inversion Recovery (T2W-IR) and T2-Weighted SSFP (T2p-SSFp) images were independently evaluated by 2 experienced reviewers (P.T. and S.V.R. for T2W-STIR and T2-MAPS and S.G. and S.V.R. for T2p-SSFp) and rated by consensus as negative, segmental, or global, for edema, or inadequate. To classify patients as having global edema, the signal intensity was visually compared with adjacent skeletal muscle. Late gadolinium hyperenhancement of each myocardial segment was rated visually as none, subepicardial, midwall, subendocardial, or transmural.

T2 Map Image Analysis
One experienced reviewer (M.W.) blinded to the results of T2 mapping and regional strain analysis reviewed only cine and LGE images to label each of 16 LV segments as either affected, if wall motion was abnormal and/or LGE was positive (involved myocardium), or spared (remote myocardium). Subsequently, strain values were averaged for the affected and remote myocardial segments for comparison.

T2 values were recorded from quantitative T2 maps for 16 LV segments by drawing regions of interest encompassing each myocardial segment; the apical apex (segment 17) was avoided because of inherently thin myocardium precluding accurate delineation of myocardium without partial volume error. To ensure that the regions of interest were within the myocardium and did not include epicardial fat or pericardial effusion, SSFP SAX cine and LGE images from the identical slice positions as the T2p-SSFp images were reviewed concurrently to help delineate the myocardial borders.

<table>
<thead>
<tr>
<th>Table 1. CMR Acquisition Parameters</th>
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<tr>
<td><strong>B-SSFP CINE</strong></td>
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<td><strong>T2W-STIR</strong></td>
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<td><strong>T2-MAPS</strong></td>
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<td><strong>LGE</strong></td>
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<td><strong>Sequence</strong></td>
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<td><strong>Breath Hold</strong></td>
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<tr>
<td>Parallel acceleration</td>
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<td>In-plane resolution, mm</td>
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<td>Slice thickness, mm</td>
</tr>
<tr>
<td>TR/TE, ms</td>
</tr>
<tr>
<td>Band width, Hz/pixel</td>
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<td>Flip angle, °</td>
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B-SSFP indicates balanced SSFP; GRAPPA, generalized autocalibrating partially parallel acquisitions; TSENSE, time-adaptive sensitivity encoding; TR, repetition time; TE, echo time. *Performed in patients with a limited respiratory capacity.

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**Table 2. Baseline Characteristics and General CMR Findings of the Study Population**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Myocarditis (n=20)</th>
<th>TTCM (n=10)</th>
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<tbody>
<tr>
<td>Age, y</td>
<td>38±16</td>
<td>60±10</td>
</tr>
<tr>
<td>Male/female ratio</td>
<td>9:11</td>
<td>0:10</td>
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<tr>
<td>White race, %</td>
<td>65</td>
<td>90</td>
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<tr>
<td>BMI, kg/m²</td>
<td>29.0±6.8</td>
<td>27.2±6.0</td>
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<tr>
<td>Cardiac risk factors, %</td>
<td>35</td>
<td>70</td>
</tr>
<tr>
<td>Time between admission and CMR, d</td>
<td>1.6±2.0</td>
<td>1.8±1.3</td>
</tr>
<tr>
<td>Peak troponin-I, mg/dL</td>
<td>16.3±14.1</td>
<td>3.4±2.8</td>
</tr>
<tr>
<td>Length of stay, median (range, d)</td>
<td>3 (1-25)</td>
<td>3.5 (1-23)</td>
</tr>
<tr>
<td>LV volume index, mL/m²</td>
<td>80.2±14.4</td>
<td>77.3±9.1</td>
</tr>
<tr>
<td>End diastolic</td>
<td>41.1±11.0</td>
<td>45.6±7.5</td>
</tr>
<tr>
<td>End systolic</td>
<td>50±9</td>
<td>40±9</td>
</tr>
<tr>
<td>LV mass index, mg/m²</td>
<td>61.1±7.1</td>
<td>60.5±10.4</td>
</tr>
<tr>
<td>Wall motion score index, median (IQR)</td>
<td>1.3 (1.1-1.6)</td>
<td>2.0 (1.8-2.1)</td>
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<tr>
<td>LGE HE present, %</td>
<td>75</td>
<td>0</td>
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<tr>
<td>LGE distribution when HE present</td>
<td>95% epicardial and/or midmyocardial and 5% transmural</td>
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Data are given as mean±SD unless otherwise indicated. BMI indicates body mass index; HE, hyperenhancement; IQR, interquartile range; LV, left ventricle; LGE, late gadolinium enhancement.

*Cardiac risk factors included diabetes, hypertension, hypercholesterolemia, and smoking history.

†The laboratory’s high-sensitivity troponin-I assay was deemed normal as <0.11 mg/dL.

Initial clinical experience afforded recognition of visually apparent increased T2 in regions beyond abnormal wall motion and LGE in patients with both myocarditis and TTCM. Such apparent regions of increased T2 signal intensity identified beyond a segment denoted as abnormal by the blinded reviewer were considered involved myocardium as well. The T2 of “involved myocardium” was the average of the affected segments defined by the blinded reviewer and additional areas of visual T2 abnormality not identified by abnormal wall motion or LGE by the blinded reviewer. The T2 of “remote myocardium” was the average of values in the remote segments defined by the blinded reviewer that also lacked a visually apparent T2 abnormality.

**Statistical Analysis**

Continuous data with a normal distribution are expressed as mean±SD, and non-normally distributed data are expressed as median and interquartile range. Categorical data are expressed as frequency or percentage. Paired or unpaired t tests, as appropriate, were used for comparison of normally distributed data. A 1-way ANOVA with Bonferroni post hoc analysis was used for comparison of T2 values between controls and both remote and involved segments in patients with myocarditis and TTCM. Receiver operating characteristic curves were used to identify the cutoff values of T2 values to differentiate abnormal myocardial segments from control or remote myocardial segments, as previously defined. Interobserver agreement was tested by Bland-Altman analysis. Statistical significance was set at a 2-tailed value of P<0.05. All statistical analyses were performed using MedCalc (version 11.5.0.0).

**Results**

**Clinical and Serological Findings**

The baseline characteristics of the 30 patients (20 with acute myocarditis and 10 with TTCM) are summarized in Table 2. In addition, T2 maps were acquired in 18 male and 12 female healthy volunteers (age, 28±6 years). None of the patients had a history of cardiovascular disease. The peak troponin-I level averaged 16.3±14.1 mg/dL in patients with myocarditis and 3.4±2.8 mg/dL in patients with TTCM. Seventeen of the 20 patients with myocarditis and all patients with TTCM underwent invasive coronary angiography before CMR; all angiograms showed absence of significant coronary stenosis. The 3 patients who did not undergo coronary angiography were aged <25 years. The cause of myocarditis was viral by serological findings in 4 subjects, giant cell myocarditis by endomyocardial biopsy in 1 subject, and cause not identified in 15 subjects.

**CMR Findings: LV Function and LGE**

CMR was performed at 1.7±1.8 days (median, 1 day; range, 0–7 days) after admission to the hospital. All patients and controls were in sinus rhythm at the time of the CMR examination. Routine CMR findings in the study population are summarized in Table 2. Among patients with myocarditis, real-time cines and/or single-heartbeat LGE imaging were used in 3 because of difficulty with breath holding. LV systolic function overall was mildly reduced, with LV ejection fraction averaging 50±9%. A WMA involving at least 1 segment was present in 80% of patients with myocarditis. There was no apparent myocardial hyperenhancement by LGE in 25% of patients with myocarditis. In the remaining LGE-positive patients with myocarditis, hyperenhancement was typically subepicardial or midmyocardial and most commonly involved the inferior and inferolateral walls. As expected, peak troponin values in patients with LGE positivity were higher than in those who were LGE negative (18.4±13.7 versus 4.8±7.6 mg/dL; P=0.003). No patient had subendocardial hyperenhancement on LGE, consistent with absence of coronary disease–related myocardial infarction.

In the patients with TTCM, LV ejection fraction averaged 40±5%. Real-time cine and/or single-heartbeat LGE imaging was necessary in 2 patients. All patients had at least 1 LV segment with abnormal wall motion. LGE showed no hyperenhancement in all patients with TTCM.

**CMR Findings: Regional Strain**

In the subset of patients with myocarditis and TTCM who had breath-held SSFP cines and at least 1 completely normal myocardial segment (n=23), the peak circumferential systolic strain in the involved segments was −13.7±6.3% versus −23.3±5.8% in the remote segments (P<0.001), and radial strain in the involved myocardial segments was 16.8±7.6% versus 38.5±6.7% in the remote segments (P<0.001).

**CMR Findings: T2 Mapping**

The quantitative results of T2 mapping are illustrated in Figure 1. The T2 measured in the involved myocardium in patients with myocarditis was 65.2±3.2 ms compared with 53.5±2.1 ms in the remote segments (P<0.001). The T2 measured in the involved myocardium in patients with TTCM...
was 65.6±4.0 ms compared with 53.6±2.7 ms in the remote myocardium. Myocardial T2 in controls was 54.5±2.2 ms. There was no significant difference in T2 values in the involved myocardium between patients with myocarditis and TTCM (P>0.05, Bonferroni post hoc analysis) or between the T2 values of controls and that of the remote myocardium in patients with myocarditis or TTCM (P=0.6, ANOVA).

Typical T2 maps versus other CMR techniques are shown in Figure 2 for myocarditis and in Figure 3 for TTCM.

Figure 4A and 4B illustrate the receiver operating characteristic curves for T2 values to identify segments of myocardium involved with myocarditis or TTCM when compared with controls or remote myocardial segments. A cutoff value of >59 ms had a sensitivity of 94% (95% CI, 91%–97%) and a specificity of 98% (95% CI, 94%–99%) to differentiate involved myocardium in patients from myocardium of healthy controls. When compared with remote segments, the same cutoff had a sensitivity of 94% (95% CI, 90%–96%) and a specificity of 97% (95% CI, 83%–100%).

We performed a power calculation to assess the use of 59 ms to differentiate remote from involved myocardial segments in patients with myocarditis or TTCM. The following parameters were used: mean T2 of remote myocardium (μ₀), 53.5 ms; SD, 2.1 ms; T2 cutoff value tested, 59 ms (μ₁); sample size, 30 patients; and α value, 0.05. This provided a power of >95% to differentiate abnormal myocardial segments from remote segments.

Among all patients studied, 17 of 30 had myocardial segments identified as abnormal based on visual inspection of T2 maps beyond regions identified as abnormal by the blinded reviewer (ie, beyond areas of LGE hyperenhancement and WMA). On average, 2.1 additional segments (range, 1–12 segments) were identified as abnormal in these patients. The T2 value for these segments alone was 64.5±2.4 ms (P<0.001 compared with remote myocardium and controls). Among these patients, 13 had segmented SSFP cines with at least 1 completely normal myocardial segment. Despite normal wall motion, the radial strain for these segments was abnormally reduced (27.1±8.3% versus 38.7±5.6% for the remote segments in the same patients; P=0.002). The circumferential strain was −19.7±6.2% versus −25.0±5.9% for the remote segments (P=0.013). These find-
ings underscore greater sensitivity of strain analysis for regional myocardial dysfunction, which occurred in regions with measurably abnormal myocardial T2, compared with visual appreciation of abnormal wall motion.

In the 14 patients with myocarditis whose LGE showed epicardial or midmyocardial hyperenhancement, T2 values were measured in the regions of myocardial hyperenhancement and in the subendocardial myocardium of the same segments (Figure 5). The T2 in LGE-positive regions was $67.7 \pm 7.3$ ms versus $57.8 \pm 3.6$ ms in the adjacent subendocardial myocardium ($P<0.001$).

### T2 Mapping: Influence of Heart Rate

There were 5 patients in whom measured T2 values were lower than the mean values for the remote and involvement myocardial segments for the overall population, with remote segments having values as low as 47 ms and involved segments having values as low as 54 ms. These patients were also included in our analysis. On further review, these were all patients with heart rates between 92 and 105 beats/minute during T2 mapping. This is consistent with tachycardia preventing adequate T1 recovery and, therefore, affecting T2 measurement. Of these 5 patients, 4 had diagnostic-quality T2-STIR images that also showed regional areas of increased signal intensity.

### T2W-STIR and T2p-SSFP Versus T2 Mapping

T2W-STIR imaging was successfully completed in 14 (47%) of 30 patients. In the remaining patients, diagnostic images could not be obtained or were uninterpretable (Figure 6C) because of respiratory motion artifact arising from patients’ inability to breath hold or because of cardiac arrhythmia. In the 14 patients who underwent successful T2W-STIR imaging, myocardial edema was detected as areas of signal hyperintensity in 12. In 2 patients with negative T2W-STIR results, both showed myocardial hyperenhancement by LGE and 1 had corresponding WMAs; myocardial T2 values were elevated in multiple segments in both patients (Figure 6A and 6B).

In an independent review of T2p time of 55 ms in SSFP images from all 30 patients, myocardial edema was detected as areas of signal hyperintensity in 17 patients (Figure 7). T2
mapping from the affected regions of patients with visually
negative SSFP cases averaged 65.3±2.7 ms compared with
53.6±2.1 ms in remote regions in these cases. Of 13 visually
negative T2p-SSFP images, 8 showed myocardial hyperen-
hancement by LGE.

Interobserver Agreement
Interobserver variability analysis was performed for all patients
and controls by 2 independent observers (P.T., S.G.) who
measured T2 values in each of the 16 myocardial segments. The
T2 values for the involved and remote myocardium (as previ-
ously defined) were then averaged separately and compared
between the 2 observers. For the controls, the T2 values were
measured by drawing a region of interest to include the entire
midventricular SAX slice by the same 2 observers, and the T2
values were compared. Bland-Altman analysis showed good
interobserver and intrasobserver agreement in the measured T2
values for the affected myocardium, remote myocardium, and
controls (Figure 8). The difference in T2 between the 2 readers
was 0.2±0.8 ms in involved myocardium, −0.1±1.2 ms in
remote myocardium, and 0.4±1.2 ms in control myocardium
(P=0.38, P=0.63, and P=0.08, respectively).

Discussion
In patients with the inflammatory conditions of myocarditis
and tako-tsubo cardiomyopathy, we found elevated myocardial
T2 values using quantitative T2 mapping that readily delineated
the presence and extent of myocardial involvement. Current
CMR protocols in these conditions have focused on detecting
WMAs, myocardial hyperenhancement by LGE, and increased
signal intensity by subjectively interpreted STIR images. Such
an approach may be problematic for limitations related to each
of the techniques. First, WMAs may not be visually apparent,
particularly in segments adjacent to those with grossly impaired
contractile function. Second, LGE may not identify mild in-
volved in myocarditis and may be particularly insensitive to
tissue abnormalities in TTCM. Third, the use of STIR imaging
to consistently identify myocardial edema is limited by numer-

Figure 5. T2 values measured in an area of myo-
cardium with epicardial delayed enhancement vs
subendocardial myocardium in the same regions.
A, Short axis delayed enhancement image. B,
Short axis T2 image from the same slice position.

Figure 6. T2 maps, T2-weighted short tau
inversion recovery (T2W-STIR), and late
gadolinium enhancement (LGE) images in
3 representative patients with myocarditis
with no obvious edema on T2 STIR imag-
ing. A, A 44-year-old man with chest pain
and a peak troponin level of 33.3 mg/dL.
T2 values in the involved and remote seg-
ments were 65 and 54 ms, respectively.
B, A 20-year-old woman with shortness
of breath and chest pain with a peak tro-
ponin level of 4.0 mg/dL. T2 values in the
involved and remote segments were 66
and 56 ms, respectively. C, A 39-year-old
man with gastrointestinal symptoms and
fever with a peak troponin level of 12.4
mg/dL. Involved and remote segment T2
values were 67 and 45 ms, respectively.
persistent LV dysfunction and adverse remodeling. A greater extent of abnormal T2 portends a higher risk of subsequent cardiomyopathy. Further investigations may determine whether a treatment, as a subset of patients with myocarditis progresses to dilated cardiomyopathy.

Visual assessment of T2p-SSFP fared better than T2-STIR, providing adequate images for review in all patients but without evident abnormality in just less than half of the patients in this cohort. Our findings suggest that T2 mapping is robust in patients with inflammatory myocardial diseases and adds insights into the extent of myocardial involvement in these conditions. Abnormal T2 extended beyond areas of WMAs and LGE positivity in more than half of patients. The clinical significance of abnormal T2 values beyond segments of LGE and wall motion is unknown. It is intriguing to consider that distinguishing those with versus those without abnormal T2 values beyond areas of LGE and wall motion is possible even in patients with diffuse myocardial involvement, our experience suggests that, even in these patients, a segment of “normal” myocardium, composed of at least 15 pixels, can usually be identified.

The detection of myocardial edema using T2W-STIR has been feasible in patients with acute myocarditis and TTCM, although the routine clinical use of T2W-STIR imaging has been challenged by widely recognized limitations. The relative insensitivity of the T2-mapping technique to motion artifacts is a result of its use of a single-shot image acquisition and automatic correction of motion between images. This strategy has been previously described and is an important benefit, especially in patients with acute cardiopulmonary disease. Although motion artifacts are also reduced in the T2p-SSFP technique, a global increase in the T2 signal may be difficult to appreciate visually in any T2-weighted image, whereas globally elevated T2 values are easily recognized. Although our study demonstrated a clear advantage of T2 quantification over T2W-STIR and T2p-SSFP, we did not compare with T2-acquisition for cardiac unified T2 edema (ACUTE), another recently introduced method for T2-weighted imaging of myocardium. Based on results in the literature, we expect the performance of this technique to be similar to that of T2p-SSFP. In nearly three fourths of patients with myocarditis with hyperenhancement on LGE, T2 mapping identified abnormal T2 values beyond the typical pattern of involved segments may be a more useful criterion than LGE negativity to diagnose TTCM. In patients with myocarditis and TTCM, we identified 59 ms as a sensitive and specific cutoff to detect abnormal myocardium by quantitative T2 mapping using this specific T2-mapping sequence. The mean difference in T2 values between affected segments and remote myocardium in patients with acute myocarditis was 11.7 ms, whereas in patients with TTCM it was 12.0 ms. This large difference, along with a narrow distribution around the mean, resulted in minimal overlap between involved and remote myocardial segments (Figure 1). As such, quantitative mapping allowed differentiation of segments with versus those without myocardial involvement in all patients in this study; our data support use of a 59-ms cutoff for clinical decision making. Rapid acquisition, lack of a breath-holding requirement, and excellent interobserver agreement in T2 measurement all make this approach appealing for clinical use to diagnose myocarditis and TTCM.

Globally reduced T2 values were observed in the T2 maps of 5 patients; on further review, all of these patients had high heart rates (92–105 beats/minute) during T2 map acquisition. At such high heart rates, the TR of 3RR intervals is insufficient for T1 recovery of magnetization between the 3 T2-prepared acquisitions, leading to an underestimation of myocardial T2 values. We suggest, based on our experience from agarose phantom studies (S.G., unpublished data, 2010), that a TR >2300 ms is necessary for consistent T2 estimation; accordingly, we modified our implementation of the T2-mapping pulse sequence for future studies. In this study, this limitation was overcome by differential analysis of T2 values between remote and involved myocardial segments. It is, therefore, prudent to adjust the sequence timing to allow for at least 2300 ms between images and to compare T2 values between remote and involved myocardial segments. Although this may not be possible in patients with diffuse myocardial involvement, our experience suggests that, even in these patients, a segment of “normal” myocardium, composed of at least 15 pixels, can usually be identified.
myocardial segments deemed abnormal by LGE alone. Among all patients with myocarditis and TTCM, T2 mapping identified areas of abnormality in segments beyond those with an LGE or WMA in 57% (17 of 30 patients). Radial and circumferential strain, measured in abnormal T2 segments with a visually normal wall motion, was lower than strain measured in remote myocardium, consistent with contractile dysfunction accompanying elevated myocardial T2.

### Study Limitations

The relatively small sample size, albeit comparable to those of several previous publications assessing the use of T2W-STIR imaging in patients with acute myocarditis and TTCM, reflects the uncommon nature of the conditions studied. In 30 patients with inflammatory myocardial disease, T2 mapping readily distinguished regions of involved myocardium from remote and normal myocardium, resulting in highly significant results. Also, there was a wider distribution of T2 values in regions of myocardial involvement. This may reflect heterogeneity in tissue changes, just as there is an epicardial predominance of injury by late gadolinium enhancement. We combined patients with acute myocarditis and TTCM in our study; although the inciting mechanisms of these diseases may differ, they likely share inflammatory pathways leading to tissue injury such that increased myocardial T2 reveals sequelae of a common pathophysiological construct. Both typically present with chest pain, elevated biomarkers of myocardial injury, and no significant coronary stenosis, and both may have diffuse myocardial involvement; thus, validation of T2 mapping in myocarditis and TTCM is an important step toward routine clinical use in accurately distinguishing these conditions from acute coronary syndrome (ACS). We did not use early post-gadolinium imaging, another technique used in some laboratories for the diagnosis of myocardial inflammation. Although subsequent work may explore T2 mapping’s performance amid such techniques, the goal of the study was to establish numeric cutoffs for myocardial involvement using T2 mapping and to compare its utility to T2-weighted myocardial imaging in myocarditis and TTCM. The implementation of T2 mapping in this work used TR=3RR intervals, a choice based on our earlier experience with healthy subjects and patients with ACS. This strategy is suboptimal for patients with elevated heart rates, in whom 3RR intervals are not sufficient for the magnetization to recover; the resulting T1 weighting in the raw images caused a reduction in the calculated T2. However, in these patients, a significant difference in T2 values still existed between involved and remote myocardium. Finally, the T2p-SSFP sequence used was a single-shot acquisition; the performance of a segmented acquisition would likely be better because of higher spatial resolution and coil intensity correction.

### Conclusions

T2 mapping is a robust alternative to T2W-STIR and T2p-SSFP for detecting myocardial involvement in patients with

![Figure 8. Bland-Altman plots for interobserver agreement in the measurement of T2 values for patients with myocarditis or tako-tsubo cardiomyopathy (TTCM). A, Involved myocardial segments. B, Remote myocardial segments. C, Controls. LOA indicates level of agreement, 1 SD.](image-url)
acute myocarditis and TTCM. Relative insensitivity to cardiac and respiratory motion affords successful detection of acute myocarditis and TTCM with this approach, even in patients with difficulty breath holding. T2 mapping in both myocarditis and TTCM identifies more extensive myocardial involvement than that suggested by late gadolinium enhancement, cine imaging, and T2W-STIR.

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**References**


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