

## Native Myocardial T1 Mapping by Cardiovascular Magnetic Resonance Imaging in Subclinical Cardiomyopathy in Patients With Systemic Lupus Erythematosus

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**Background**—Increased systemic inflammation has been linked to myocardial dysfunction and heart failure in patients with systemic lupus erythematosus (SLE). Accurate detection of early myocardial changes may be able to guide preventive intervention. We investigated whether multiparametric imaging by cardiovascular magnetic resonance can detect differences between controls and asymptomatic SLE patients.

**Methods and Results**—A total of 33 SLE predominantly female patients (mean age, 40±9 years) underwent cardiovascular magnetic resonance for routine assessment of myocardial perfusion, function, and late gadolinium enhancement. T1 mapping was performed in single short-axis slice before and after 15 minutes of gadolinium administration. Twenty-one subjects with a low pretest probability and normal cardiovascular magnetic resonance served as a control group. Both groups had similar left ventricular volumes and mass and normal global systolic function. SLE patients had significantly reduced longitudinal strain (controls versus SLE,  $-20\pm 2\%$  versus  $-17\pm 3\%$ ;  $P<0.01$ ) and showed intramyocardial and pericardial late gadolinium enhancement. SLE patients had significantly increased native myocardial T1 ( $1056\pm 27$  versus  $1152\pm 46$  milliseconds;  $P<0.001$ ) and extracellular volume fraction ( $26\pm 5\%$  versus  $30\pm 6\%$ ;  $P=0.007$ ) and reduced postcontrast myocardial T1 ( $454\pm 53$  versus  $411\pm 62$  milliseconds;  $P=0.01$ ). T1-derived indices were associated with longitudinal strain ( $r=0.37-0.47$ ) but not with the presence of late gadolinium enhancement. Native myocardial T1 values showed the greatest concordance with the presence of clinical diagnosis of SLE.

**Conclusions**—In patients with SLE who are free of cardiac symptoms, there is evidence of subclinical perimyocardial impairment. We further demonstrate that T1 mapping may have potential to detect subclinical myocardial involvement in patients with SLE. (*Circ Cardiovasc Imaging*. 2013;6:295-301.)

**Key Words:** late gadolinium enhancement ■ subclinical cardiomyopathy ■ T1 mapping ■ tissue characterization

Systemic lupus erythematosus (SLE) is a generalized inflammatory autoimmune disease, predominantly affecting young women.<sup>1,2</sup> Cardiovascular complications are a well-recognized complication of SLE and include inflammation of valves, myocardium, and pericardium, and they result in myocardial dysfunction and heart failure.<sup>1-7</sup> The underlying pathology includes immune complex- and complement-mediated injury with diffuse inflammation and myocardial fibrosis.<sup>3,4</sup> It is known that cardiac injury is accelerated through bouts of active disease; however, much of this process is thought to occur as a subclinical indolent process.<sup>1,7,8</sup> Although the high prevalence of cardiovascular complications in SLE, including myocarditis, has been recorded in autopsy studies, the detection of a subclinical process before the onset of symptoms and heart failure remains challenging.<sup>6-12</sup> Accurate detection of

early myocardial changes at the subclinical stage may be able to guide preventive intervention.

### Clinical Perspective on p 301

Several studies looked into detection of subclinical myocardial injury in SLE patients by echocardiography<sup>6,13,14</sup> and revealed no differences in global left ventricular (LV) systolic function but reported reduced longitudinal deformation and impaired diastolic relaxation. Echocardiography may suggest inflammation indirectly by detecting pericardial effusion, whereas cardiovascular magnetic resonance (CMR) can directly inform on inflammatory myocardial involvement.<sup>15,16</sup> In particular, T1- and T2-weighted imaging and high-spatial-resolution scar imaging (late gadolinium enhancement [LGE]) enabled CMR to discriminate between myocarditis

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and ischemic pathogenesis.<sup>15</sup> Few CMR studies performed in patients with systemic inflammatory disease recorded an increase in absolute and relative T1 and T2 signal intensity and also demonstrated LGE.<sup>8,17–19</sup> As LGE can differentiate differences between well-separated normal and abnormal tissues, it commonly misses uniform diffuse processes as expected in systemic inflammation.<sup>20</sup> Imaging with T1 mapping allows appreciation of diffuse myocardial processes.<sup>20–24</sup> In this study, we investigated whether multiparametric CMR can detect subclinical myocardial involvement because of systemic inflammation in patients with SLE who are free of cardiac symptoms.

## Methods

Thirty-three patients with an established diagnosis of SLE as per the American College of Rheumatology revised classification criteria<sup>25</sup> and no history of previous cardiac symptoms were recruited from the Louise Coote Lupus Unit, St Thomas' Hospital, London. All patients were in clinical remission<sup>26–28</sup> with stable blood results, and no change in medication was seen within the previous  $\leq 8$  weeks. **Twenty-one normotensive healthy subjects with low pretest likelihood for LV cardiomyopathy served as controls.** Additional exclusion criteria for both the groups included a history of cardiac events or known coronary artery disease or any general contraindication to contrast-enhanced CMR or adenosine stress and subsequently evidence of regional hypoperfusion on adenosine testing or ischemia-like LGE. Patient characteristics were recorded for all the subjects, including age, sex, body mass index, renal function, presence of cardiovascular risk factors such as hypertension, diabetes mellitus, dyslipidemia, and history of smoking, and therapy, including corticosteroids, antimalarials, and immunosuppressive agents. The study protocol was reviewed and approved by local ethics committee, and written informed consent was obtained from all the participants.

## Cardiovascular Magnetic Resonance

All subjects underwent a routine clinical scan protocol using a **3-T MRI** scanner (Achieva; Philips Healthcare, Best, the Netherlands). After standardized patient-specific planning,<sup>29</sup> volumetric cavity assessment was obtained by whole-heart coverage of gapless short-axis slices. Thereafter, **cine-images of 3 long-axis views** (4-chamber, 2-chamber, and 3-chamber views) and **transverse axial views were acquired.** All cine-images were acquired using a **balanced steady-state free precession** sequence in combination with parallel imaging (SENSitivity Encoding, factor 2) and retrospective gating during a gentle expiratory breath-hold (echo time/repetition time/flip angle, 1.7 milliseconds/3.4 milliseconds/60°; spatial resolution, **1.8×1.8×8 mm**). T2 imaging was performed by inversion recovery, T2-weighted spin-echo sequence with whole-heart coverage of short-axis slice acquisitions at a echo time/repetition time/flip angle of; TE/TR/flip-angle 60 milliseconds/2 beats/90° and interpolated voxel size of 0.6×0.6×8 mm. For myocardial perfusion imaging, 0.075 mmol/kg body weight of gadobutrol was injected as a peripheral bolus after 3 minutes of continuous adenosine infusion of 140  $\mu\text{g}/\text{kg}$  per minute, during the imaging of 3 short-axis slices per heartbeat using a k-t sense sequence, as previously described.<sup>30,31</sup> Steady-state free precession, single breath-hold–modified Look-Locker Imaging was used for T1 mapping and performed in a single equatorial short-axis slice before contrast administration and scar imaging, respectively (echo time/repetition time/flip angle, 1.57 milliseconds/3.3 milliseconds/50°; interpolated voxel size, 0.9×0.9×8 mm), phase-encoding steps  $n=166$ , heart-rate-adapted trigger delay, 11 phases (3+3+5), adiabatic prepulse to achieve complete inversion.<sup>21,32</sup> LGE imaging was performed in a gapless whole-heart coverage of short-axis slices  $\approx 15$  minutes after administration of a cumulative dose of 0.2 mmol/kg body weight gadobutrol using a mid-diastolic inversion prepared 2-dimensional gradient echo sequence (echo time/repetition time/flip angle, 2.0 milliseconds/3.4 milliseconds/25°; interpolated voxel size, 0.7×0.7×8 mm) with a patient-adapted prepulse delay. Imaging was repeated with changed fold-over direction, longitudinal views, and fat suppression.

## Image Analysis

All routine CMR analysis was performed on commercially available software. **Endocardial LV borders were manually traced at end-diastole and end-systole. The papillary muscles were included** as part of the LV cavity volume. LV end-diastolic and end-systolic volumes were determined using the Simpson rule. Ejection fraction was computed as LV end-diastolic volume–LV end-systolic volume/LV end-diastolic volume. All volumetric indices were normalized to body surface area. Edema ratio in T2-weighted images was obtained as the ratio between signal intensity of septal myocardium and skeletal muscle, as previously described.<sup>16</sup> The LGE images were visually examined for the presence of regional fibrosis showing as bright areas within the myocardium in 2 fold-over directions and corresponding longitudinal views and by exclusion of potential artifacts. Pericardial LGE was reconfirmed on the images with change in phase-encoding direction and fat suppression. Maximal pericardial thickness was then measured in LGE images in the short-axis views. T1 relaxation maps were obtained within single equatorial short-axis slices by placing the region of interest conservatively within the septal myocardium using a prototype tool (RelaxMaps, PRIDE; Philips, the Netherlands) with a prior image coregistration step for motion correction. Care was particularly taken to avoid contamination with signal from the blood pool. T1 values were then determined by fitting an exponential model to the measured data. In T1 algorithm, Look-Locker and noise correction were applied, as previously described.<sup>21</sup> In addition to the T1 values of native myocardium and blood pool, we calculated  $\lambda$  and extracellular volume fraction (ECV) according to the following formulas<sup>22,32</sup>:

1.  $\lambda = [\Delta R1_{\text{myocardium}}] / [\Delta R1_{\text{bloodpool}}]$  pre- and post-Gd contrast
2.  $\text{ECV} = (1 - \text{hematocrit}) \times \lambda$ ,

where  $R1=1/T1$ . Deformation analysis was performed by tracing the contours within the myocardium in the cine-images, using feature-tracking 2-dimensional prototype software (TomTec GmbH, Munich, Germany), as previously described and validated.<sup>33</sup> Radial and circumferential LV myocardial deformation was obtained in 3 SA slices for 16 standard segments. Longitudinal deformation was obtained in 3 long-axis views. Deformation is expressed as the average total peak systolic strain per measured direction.<sup>34</sup>

## Statistical Analysis

Normality of distributions was tested with the Kolmogorov–Smirnov statistic. Categorical data are expressed as percentages, and continuous variables as mean $\pm$ SD or median (interquartile range), as appropriate. Comparisons of the means were performed by Student *t* tests or  $\chi^2$  test, as appropriate for the type of the data. Associations were explored by single-variate and multivariate linear regressions. Univariate and multivariate binary logistic regression analyses were used to test for concordance with presence or absence of the SLE diagnosis. All tests were 2-tailed, and a value of  $P<0.05$  was considered significant.

## Results

Patients' characteristics are provided in Table 1. As expected, there was a predominance of women among the SLE patients. A small number of SLE patients had traditional cardiovascular risk factors, such as smoking, whereas none had diabetes mellitus, hypertension, or high cholesterol. The average time from SLE diagnosis to imaging was 7.4 years. Sixty percent of SLE patients were taking oral steroids and 49% disease-modifying therapies, predominantly mycophenolate mofetil ( $n=15$ ; 45%) and hydroxychloroquine ( $n=14$ ; 42%). Antiphospholipid syndrome was present in 17 patients (51%), of whom 15 had previous thromboembolic events requiring long-term anticoagulation. Twelve SLE patients (32%) had documented proteinuria.

**Table 1. Subjects' Characteristics, Including SLE Patients' Characteristics of Disease and Medication**

Variable	Controls (n=21)	SLE (n=33)	Significant P Value
Age, y	38±6	40±8	0.21
Male sex, n (%)	5 (23)	7 (21)	0.89
Body mass index	24±6	25±7	0.71
BP systolic, mm Hg	120±15	120±15	0.95
BP diastolic, mm Hg	75±11	78±12	0.21
Heart rate, bpm	65±10	65±11	0.84
Smoker, n (%)	3 (14)	5 (15)	0.91
SLEDAI	0 (0)	0 (0–3)	0.0
History of lupus nephritis, n (%)	0 (0)	15 (45)	0.001
Antiphospholipid syndrome, n (%)	0 (0)	17 (51)	0.001
RAS inhibitors, n (%)	0 (0)	11 (33)	0.002
Aspirin/clopidogrel, n (%)	0 (0)	7 (21)	0.004
Warfarin, n (%)	0 (0)	15 (45)	0.001
Current steroids, n (%)	0 (0)	20 (60)	0.001
Other anti-inflammatory, n (%)	0 (0)	16 (49)	<0.001
Hemoglobin, mg/L	13±1.2	12±1.6	0.27
eGFR, mL/min per m <sup>2</sup>	106±30	89±28	0.12
ESR	<7	24±9	...

BP indicates blood pressure; eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; RAS, renin angiotensin system; SLE, systemic lupus erythematosus; and SLEDAI, SLE Disease Activity Index.

Both groups had normal volumes, global systolic function, and LV mass (Table 2). The SLE group had significantly reduced longitudinal strain (controls versus patients:  $-20\pm 2\%$  versus  $-17\pm 3\%$ ;  $P<0.001$ ). Approximately two thirds of patients had myocardial LGE predominantly in the basal-midventricular, inferolateral-inferior, and inferoseptal segments (Figure 1). In the SLE group, there was no overt T2 enhancement, and T2 edema ratio was not different from controls. T1 mapping revealed significantly increased T1 relaxation time of native (T1myocardium<sub>native</sub>),  $\lambda$ , and ECV ( $P<0.01$  for all), whereas T1myocardium<sub>postcontrast</sub> was reduced ( $454\pm 53$  versus  $411\pm 62$  milliseconds;  $P=0.01$ ). Pericardial LGE was present in 20 patients (61%), most commonly enveloping the basal, midventricular lateral, and inferior LV segments. In few cases, pericardial enhancement was global (Figure 2). The mean pericardial thickness was  $4.1\pm 3.0$  mm.

In patients with SLE, there was a linear association between longitudinal strain and T1myocardium<sub>native</sub> ( $r=0.47$ ;  $P=0.006$ ; Figure 3), and T1myocardium<sub>postcontrast</sub> ( $r=-0.37$ ;  $P=0.04$ ), whereas associations with  $\lambda$  and ECV were not significant. The presence of overt myocardial LGE showed no association with strain values or above T1-derived indices. There were no differences between SLE patients with overt LGE and those without in terms of T1-derived indices (no LGE versus LGE: T1myocardium<sub>native</sub>:  $1148\pm 56$  versus  $1158\pm 48$  milliseconds,  $P=0.31$ ; T1myocardium<sub>postcontrast</sub>:  $424\pm 72$  versus  $410\pm 59$  milliseconds,  $P=0.29$ ;  $\lambda$ :  $0.49\pm 0.09$  versus  $0.50\pm 0.9$ ,  $P=0.39$ ; ECV:

**Table 2. Global Morphological and Functional Measures**

Variable	Controls (n=21)	SLE (n=33)	Significant P Value
LV-EDV index, mL/m <sup>2</sup>	77±14	79±12	0.45
LV ejection fraction, %	61±5	59±5	0.65
LV mass index, g/m <sup>2</sup>	44±12	47±11	0.38
LA area, cm <sup>2</sup>	20±5	20±5	0.82
Longitudinal strain	$-20\pm 2$	$-17\pm 3$	<0.0001
Radial strain	34±8	32±8	0.35
Circumferential strain	$-25\pm 6$	$-24\pm 5$	0.57
Myocardial LGE, n (%)			
Present	0 (0)	20 (61)	<0.0001
RV insertion points	...	12 (37)	...
Intramyocardial stria	...	13 (40)	...
Epicardial	...	5 (15)	...
Pericardial LGE			
Present, n (%)	0 (0)	20 (61)	<0.0001
Thickness, mm	...	$4.1\pm 3.0$	...
Pericardial effusion, n (%)	0 (0)	5 (15)	0.005
T2 edema ratio	$1.7\pm 0.5$	$1.9\pm 0.7$	0.27
T1myocardium <sub>native</sub> , ms	$1056\pm 27$	$1152\pm 46$	<0.0001
T1myocardium <sub>postcontrast</sub> , ms	$454\pm 53$	$411\pm 62$	0.01
$\lambda$	43±8	50±8	0.003
ECV, %	26±5	30±6	0.007

Student *t* test for differences from the control group. ECV indicates extracellular volume fraction; EDV, end diastolic volume; LA, left atrium; LGE, late gadolinium enhancement; LV, left ventricular; and RV, right ventricle.

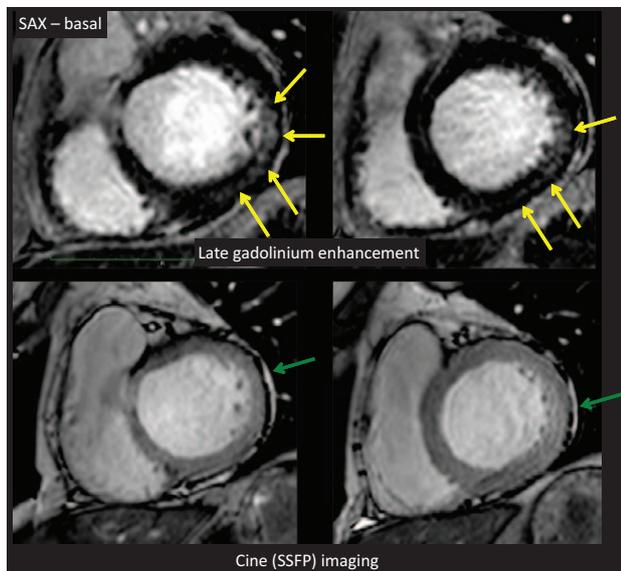
$P<0.05$  is considered significant.

$29\pm 6\%$  versus  $30\pm 6\%$ ,  $P=0.37$ ) or longitudinal strain ( $-17\pm 3\%$  versus  $-17\pm 3\%$ ;  $P=0.89$ ). There were no further associations with age, any medication, disease duration, estimated glomerular filtration rate, or proteinuria. Finally, the associations between  $\lambda$  and ECV were high in the cohort as a whole, as well as in subgroup analyses ( $r=0.96-0.99$ ).

We examined concordance between the presence or the absence of clinical diagnosis of SLE and myocardial imaging (Table 3). Because the presence of myocardial or pericardial LGE was always concordant with SLE diagnosis, the odds of nonconcordance were negligible. Longitudinal strain showed the greatest odds to yield discordant results with a misclassification rate of 32%. On the contrary, T1-derived measures showed a better concordance with the diagnosis of SLE, whereas myocardial T1<sub>native</sub> showed the greatest concordance with the clinical diagnosis and an 8% misclassification rate. In multivariate analysis including T1-derived measures, LV volumes, mass, and function, left atrial size, and myocardial and pericardial LGE, myocardial T1<sub>native</sub> was identified as the independent predictor of the underlying SLE diagnosis.

## Discussion

Using multiparametric CMR imaging, we demonstrate that patients with SLE and free of cardiac symptoms or history of cardiac disease have several subclinical abnormalities in cardiac structure and function despite apparently preserved global systolic function. We further demonstrate that among



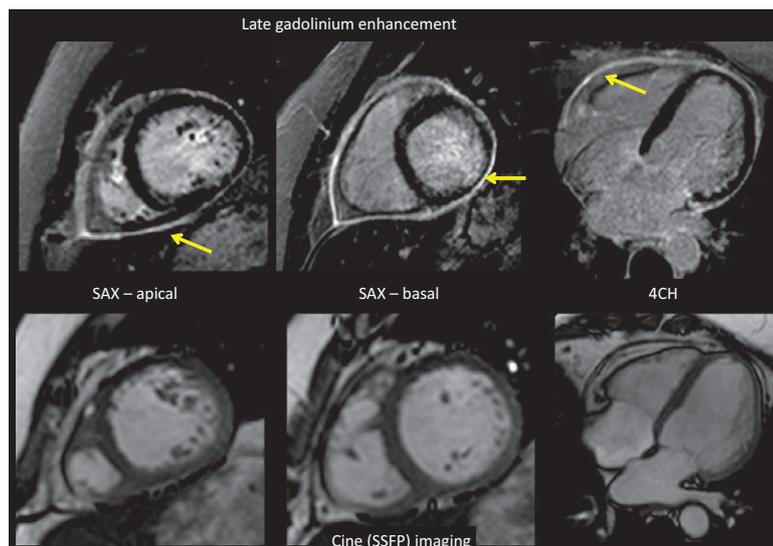
**Figure 1.** Representative images of myocardial enhancement. Visually detectable myocardial enhancement in the basal lateral segments (**yellow arrows**) and a rim of pericardial effusion (**green arrows**) on corresponding cine-images. T1 myocardium<sub>native</sub> value in this case: 1211 milliseconds,  $\lambda=0.56$ . SAX indicates short-axis slice; and SSFP, steady-state free precession.

these parameters, myocardial T1<sub>native</sub> is the best parameter to separate between normal subjects and SLE patients.

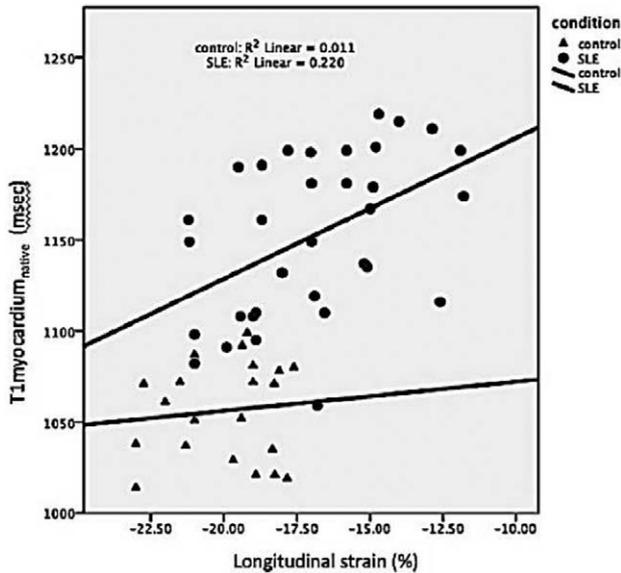
CMR is a technique that is sufficiently accurate and versatile to replicate the complexity of cardiovascular pathophysiology in patients with SLE. Detection of the small foci and striae of patchy myocardial fibrosis by LGE complements reduced longitudinal deformation and allows the detection of minimal changes in functional performance, which are not yet manifest to global systolic function. The observed findings are concordant with the existing knowledge of histopathologic changes and understanding of cardiovascular pathophysiology in SLE.<sup>1-4</sup> In a previous study using CMR in SLE patients, only ischemia-like pattern of myocardial LGE was found; however, patients included had cardiovascular symptoms.<sup>18</sup> In contrast, other studies set to interrogate subclinical cardiovascular

manifestations demonstrated patchy myocardial LGE patterns consistent with nonischemic regional fibrosis,<sup>8,17</sup> and our findings agree with the latter observation. Because the LGE appearances closely resemble the typical pattern found in patients with chronic stages of viral myocarditis<sup>35</sup> or early idiopathic cardiomyopathy,<sup>36</sup> these findings may represent a sequel to an indolent course of perimyocarditis. In further support of an inflammatory pathogenesis of LGE in SLE, Abdel-Aty et al<sup>8</sup> have shown a higher edema ratio in patients with active disease, indicating the presence of edema within the myocardial tissue, whereas in patients in clinical remission, this measure was not different from controls, indicating subsiding of an acute inflammation. Our results agree with these observation, and as edema ratio did not significantly contribute to discrimination between SLE and normal subjects, the observed differences in T1 are likely attributable to chronic changes such as diffuse fibrosis rather than edema, as expected in a state of clinical remission. Because of the absence of cardiac symptoms, biomarkers of myocardial injury or dysfunction, such as troponin or brain-natriuretic peptide (BNP), were not examined. The available evidence on the roles of these biomarkers amounts to few reports showing marginal increase in BNP<sup>37</sup> or N-terminal BNP in patients with evidence of carotids atherosclerosis.<sup>38</sup> In subjects >50 years of age and eligible for primary prevention (ie, high risk), combined BNP and troponin as a screening test for the presence of silent cardiac disease has been recently shown to offer a reasonable predictive value.<sup>39</sup> This population is, however, very different from our study cohort. In low-risk subjects, the combination of BNP and troponin showed no additional benefit beyond clinical parameters.<sup>40</sup> Because our patient population would be closer to this last example, we expect the addition of BNP to add negligible information about the cardiovascular risk. Systematic studies examining the value of these markers within the hypersensitive ranges may be warranted to identify the presence of ongoing myocardial injury.

Our findings expand on the previous evidence of diffuse myocardial involvement detected by T1 mapping in SLE patients. We found that patients with SLE have increased myocardial T1<sub>native</sub>, and this finding is concordant with a



**Figure 2.** Representative images of pericardial enhancement. Visually detectable myocardial enhancement with corresponding cine-images. T1 myocardium<sub>native</sub> value in this case: 1174 milliseconds,  $\lambda=0.46$ . SAX indicates short-axis slice; and SSFP, steady-state free precession.



**Figure 3.** Significant relationship between T1 myocardium<sub>native</sub> and longitudinal strain in patients with systemic lupus erythematosus (SLE).

single previous study using T1 mapping in SLE patients.<sup>17</sup> It is widely recognized that LGE can be challenging for visualization of diffuse myocardial process,<sup>20–24</sup> and hence, we used quantification of T1 relaxation in native and postcontrast myocardium to assist with assessment of myocardial involvement. We show that the composite T1 indices  $\lambda$  and ECV are also increased. ECV has been shown to correlate closely with histologically verified amount of replacement fibrosis on collagen staining<sup>21,22</sup>; however, the association between myocardial T1<sub>native</sub> and collagen content has been

less formally calibrated in the presence of myocardial disease. Previous phantom, animal, and human tissue-based studies lend insight into the effects on T1 signal by showing that T1 increases with increased water content and amount of extracellular fibrillar macromolecules.<sup>41,42</sup> Furthermore, in a normal human heart, a previous study showed significant correlation between T1 relaxation times with both percent of free water content and hydroxyproline concentration used to measure amount of collagen.<sup>43</sup> Messroghli et al<sup>44</sup> demonstrated that increased myocardial T1<sub>native</sub> corresponds to the areas of human myocardial infarction demonstrated on LGE. Because the range of ECV values in our study concurs with previously reported in subclinical myocardial disease,<sup>45</sup> we speculate that high variation of the longer native blood T1 values in high-field strength may in part explain the comparatively lower concordance of ECV. By detecting differences in T1-derived measures in asymptomatic population, we demonstrate for the first time that these indices may be able to discern a subclinical cardiomyopathic process. Our results may support development of novel methodology, which is noninvasive and radiation-free and allows detection of cardiac impairment before onset of symptoms and an advanced disease. Future studies looking at the longitudinal change in T1 values are required to ascertain whether disease progression reflects in worsening numbers or whether these are meaningful only as a binary information (normal/abnormal). Finally, it remains to be shown how these measures relate to patients’ outcome or whether they can be instrumental in guiding management toward an improved outcome.

A few limitations apply to this study. T1 sampling in the septum of a single short-axis slice is based on the assumption that it is representative of the diffuse myocardial involvement;

**Table 3. Uni- and Multivariate Binary Logistic Regression Testing Concordance With the Presence or the Absence of SLE Diagnosis**

Variable	$\chi^2$	Exp(B) (95% CI)	Significance (P Value)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Concordance Accuracy, % (95% CI)
<b>Univariate analysis</b>						
Longitudinal strain	4.3	1.8 (1.2–2.5)	<0.001	82 (73–94)	49 (30–63)	68 (57–73)
Myocardial LGE	17.4	...	<0.001	100 (84–100)	54 (45–56)	70 (59–70)
Pericardial LGE	21.2	...	<0.001	100 (84–100)	62 (37–62)	75 (63–75)
T1 myocardium <sub>native</sub>	42.9	1.1 (1.04–1.2)	<0.001	94 (86–98)	90 (74–97)	92 (81–96)
T1 myocardium <sub>postcontrast</sub>	6.2	1.0 (0.98–1.0)	0.01	82 (71–91)	65 (51–73)	71 (51–79)
Longitudinal strain	4.3	1.8 (1.2–2.5)	0.04	79 (67–89)	53 (34–68)	68 (54–81)
$\lambda$	21.5	1.1 (1.05–1.2)	<0.001	88 (78–94)	67 (53–72)	80 (72–89)
ECV	18.3	1.2 (1.06–1.4)	<0.001	83 (74–90)	72 (51–87)	80 (67–89)
<b>Multivariate analysis (forward stepwise)*</b>						
T1 myocardium <sub>native</sub>	38.3	1.1 (1.03–1.2)	0.004	94 (85–98)	90 (73–97)	93 (81–98)
Longitudinal strain			0.44			
Myocardial LGE			0.01			
Pericardial LGE			0.02			
T1 myocardium <sub>postcontrast</sub>			0.40			
$\lambda$			0.94			
ECV			0.87			

$\chi^2$  for Mantel-Haenszel tests; P values for Fisher exact tests. CI indicates confidence interval; ECV, extracellular volume fraction; LGE, late gadolinium enhancement; and SLE, systemic lupus erythematosus.

\*Multivariate model:  $\chi^2=50.7$ ,  $P<0.001$ ; Wald=8.7;  $-2$  Log likelihood=21.5, Nagelkerke  $R^2=0.83$ .

however, future studies with multiple slices are needed to determine any relevant regional variation. The small sample size may limit generalization of the present findings, and a predominantly female representation introduces a degree of bias; therefore, larger multicenter studies geared to link the present findings with the outcomes are required to validate this method for widespread clinical use. Because of the recruitment from a specialized unit for advanced rheumatologic care, our patient selection may be biased toward the population with severe disease. Whether detecting subclinical disease by T1 mapping can be used to guide management and improve outcome in SLE patients requires a confirmation in future studies. Also, the robustness and accuracy of measures for SLE patients need to be tested in a prospective cohort. Despite some early work on relating and validating the correlation of native T1 values to fibrosis, the current evidence is less strong in comparison to postcontrast T1 values or composite measures such as ECV. Limitations of spatial resolution may pose difficulty in measurements of pericardial thickness, especially in the submillimeter range. Because we used a high-spatial-resolution LGE sequence, used a high dose of contrast agent, and checked for pericardial fat, we believe we have controlled for most of the confounding factors. Even though we did not perform coronary angiography to formally exclude the presence of coronary artery disease, no patients showed regional hypoperfusion on adenosine testing, making significant myocardial ischemia a driver of observed changes unlikely.

Taken together, these findings show that patients with SLE and a history of long-term systemic inflammation have subclinical alterations in LV structure and function that are unrelated to significant myocardial ischemia. These changes include detectable perimyocardial LGE and reduced longitudinal strain, concordant with the previous observations. In addition, SLE patients show prolonged T1-derived indices, including T1myocardial<sub>native</sub>,  $\lambda$ , and ECV, potentially providing means to detect subclinical involvement in SLE patients.

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### Disclosures

None.

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### CLINICAL PERSPECTIVE

In this work, using multiparametric imaging with cardiovascular magnetic resonance, we were able to detect subclinical myocardial involvement in patients with systemic lupus erythematosus. We further demonstrate that among these parameters, myocardial T1 native is the best parameter to separate normal subjects from systemic lupus erythematosus patients. Our findings provide a proof-of-concept for noninvasive detection of subclinical cardiomyopathic involvement, which is beyond the detection threshold of current clinical diagnostic strategies. Whether detecting subclinical disease by T1 mapping can be used to guide management and improve outcome in systemic lupus erythematosus patients requires a confirmation in future studies.