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Original article

Cardiac magnetic resonance imaging in the follow-up of patients with Fabry cardiomyopathy

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ABSTRACT

Purpose: The purpose of this study was to evaluate the role of cardiac magnetic resonance imaging (MRI) in the follow-up of patients with Fabry disease. Our hypothesis was that LV functional parameters and native myocardial T1 and T2 values could be used to monitor treatment efficacy.

Materials and methods: This prospective, observational, multicenter study included patients with Fabry disease who underwent two cardiac MRI examinations performed at 1.5 T 24 months apart at five University Hospitals between March 2017 and December 2022. Changes in cardiac MRI parameters were compared between two groups of patients according to whether or not they were receiving specific treatment.

Results: Twenty-six patients with Fabry disease were enrolled. There were 17 women and 9 men, with a mean age of 45.3 ± 17.4 (standard deviation [SD]) years. Both treated and untreated patients showed an increase in native T1 values over time, but the T1 increase was higher in treated patients (global T1, +39.4 ± 28.9 [SD] ms) than in untreated ones (global T1, +14.5 ± 30.3 [SD] ms) ($P = 0.04$). T2 values decreased in treated patients (global T2, -2.11 [SD] ms ± 3.36 but increased in untreated ones (global T2, +0.57 ± 1.63 [SD] ms) ($P = 0.02$). No significant changes in extracellular cardiac volume, left ventricular functional parameters, late gadolinium enhancement or left atrial volume were observed. However, LV mass index increased in untreated patients and decreased in treated patients. Intra- and interobserver reproducibility of T1 measurements showed mean biases of -0.18 ms (limit of agreement:11.61, 11.24) and -0.64 ms (limit of agreement:23.82; 22.54), respectively.

Conclusion: Variations in native myocardial T1 values at cardiac MRI are significantly greater in patients with Fabry disease receiving treatment than in untreated patients, suggesting an effect of treatment on lipid storage. In addition, changes in T2 values suggest an anti-inflammatory effect of the treatment.

1. Introduction

Fabry disease (FD) is a rare X-linked disorder caused by a mutation in the GLA gene on chromosome Xq22. This mutation induces an enzyme deficiency in lysosomal alpha-galactosidase resulting in the accumulation of sphingolipids (particularly globotriaosylceramide [Gb3]) in the cells of many organs. Target organs include the kidneys, brain, heart, bowel, ears, and skin. The accumulation of sphingolipids triggers a series

Abbreviations: Δ, Delta (variation); Gb3, Globotriaosylceramide; MRI, Magnetic resonance imaging; ECV, Extra-cellular volume; FD, Fabry disease; LGE, Late gadolinium enhancement; LOA, Limits of agreement; LV, left ventricle; LVEF, Left ventricular ejection fraction; LVM, Left ventricular mass; M0, Month 0; M24, Month 24; SD, Standard deviation.

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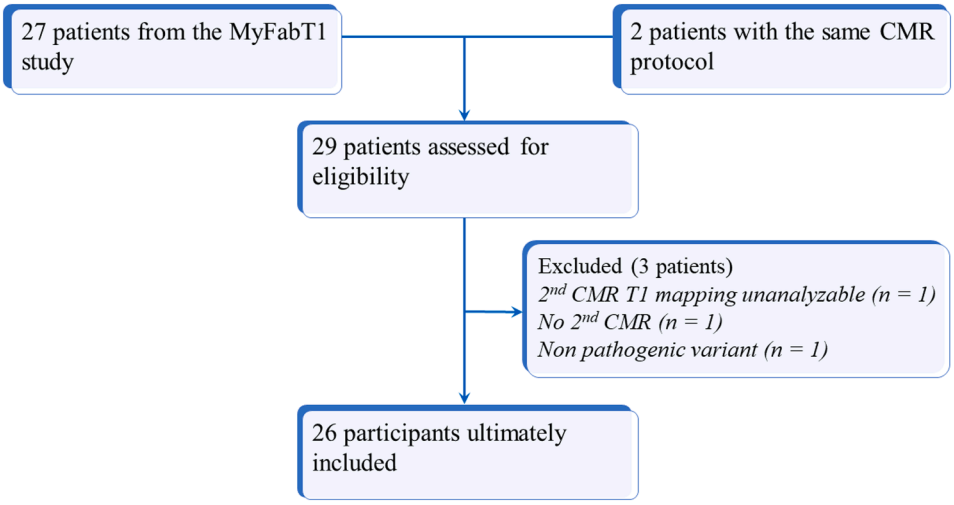

Fig. 1. Study flow chart.

of metabolic reactions that lead to tissue fibrosis [1].

Two main variants of FD have been described, including a multisystemic disease and the "late-onset" or cardiac variant in which myocardial lesions predominate or may even be isolated [1]. Cardiac damage is the leading cause of death in patients with FD [2]. Cardiac damage is characterized by a hypertrophy of the left ventricle (LV), which is not the consequence of an increased afterload and which may be asymmetric. Interstitial myocardial fibrosis may be present, typically developing initially in the basal lateral inferior segment. During the course of the disease, diastolic and then systolic dysfunction may develop in parallel with cardiac rhythm or conduction disturbances [3, 4]. These potential complications justify the treatment. Enzyme replacement therapy including agalsidase alpha and agalsidase beta [5, 6] and the oral chaperone (migalastat) [7] are the two families of drugs that are currently available.

In parallel with the monitoring of lyso Gb3 (the metabolite of Gb3) and troponins, the effectiveness of treatments in FD cardiomyopathy is generally determined on the basis of cardiac function parameters, notably left ventricular ejection fraction (LVEF), volume and mass (LVM), which do not directly reflect the accumulation of sphingolipids in the myocardium. Myocardial biopsy could be an option to quantify lipid storage, but the risk-benefit ratio would be unfavorable.

Cardiac magnetic resonance imaging (MRI) provides a comprehensive overview of the heart in terms of anatomy, function, and structure [8–10]. Myocardial native T1 values are typically decreased in FD and have been shown to correlate with myocardial sphingolipid storage [11–13]. Increased T2 values reflect inflammation [14] and have been described in early FD [15]. Finally, the increase in native T1 and extra-cellular volume (ECV) combined with late gadolinium enhancement (LGE) reflect myocardial fibrosis [16]. A study by Nordin et al. based on a one-year follow-up of patients with FD suggested that an increase in native T1 may indicate a response to enzyme replacement therapy [17].

The primary objective of the present study was to investigate the global and segmental changes in native T1 over a two-year period in patients with FD according to their therapeutic status (treated vs. untreated). LV functional parameters including myocardial mass, T2 and ECV changes over the same period were secondary objectives. We hypothesized that treated patients would exhibit significantly greater increases in native T1 values and decreases in T2 values compared to untreated patients, reflecting the beneficial effect of treatment on myocardial lipid storage and inflammation. In addition, we expected that these changes in myocardial parameters would correlate with improvements in left ventricular mass (LVM) and functional parameters, providing a comprehensive non-invasive marker of treatment efficacy in Fabry disease.

2. Materials and methods

2.1. Study design and population

This prospective, multicenter study was registered at clinicaltrials.gouv (NCT 02956954, MyFabT1). To be included, patients had to have a biochemical and genetic diagnosis of FD, and have undergone two multiparametric cardiac MRI examinations at 1.5 T 24 months apart, the second one before June 2023. At the time of enrollment, patients could be on a FD-specific treatment or treatment-naive. The choice of the treatment was left to the decision of a multidisciplinary team and was not influenced by the inclusion of the patient in the protocol. Nine patients were on agalsidase alpha (all being treated chronically, except one for whom treatment was initiated after M0). Three patients were on migalastat (all naive at M0) and one patient had been on agalsidase beta for two years. No patients had a change in treatment during the two years of follow-up. All patients gave informed consent and the study was approved by the institutional ethics committee.

The population consisted of 29 patients from five university hospitals. Two of them were not formally included in the MyFabT1 study, but they followed strictly the same protocol. Three patients were excluded: one patient had received an automatic implantable defibrillator after the first cardiac MRI examination. For this patient, the follow-up cardiac MRI was performed but could not be analyzed due to major artifacts. One patient did not undergo the follow-up cardiac MRI. Finally, a third patient with completely normal cardiac MRI examinations was finally considered as having a non-pathogenic variant (c.352C>T (p.Arg118Cys)).

A total of 26 patients were analyzed (Fig. 1). Patients were divided into two groups according to whether or not they were receiving a specific treatment for FD.

2.2. Cardiac MRI protocols

Three different MRI scanners were used (Magnetom® Sola and Magnetom® Aera, Siemens Healthcare, and Ingenia™ Ambition, Philips Healthcare) but all patients received their two examinations on the same equipment with same protocols in order to avoid inter-scan variations in measurements.

The cardiac MRI protocol was composed of conventional sequences including multiplanar CINE views, T1 maps (11 heartbeats variant (5 (3) 3) of modified Look-Locker inversion recovery (MOLLI) sequence), T2 maps (T2 prep), first-pass perfusion and LGE 10 min after intravenous

Table 1
Baseline characteristics of 26 patients with Fabry disease.

Variable	Total ($n = 26$)	Treated ($n = 13$)	Untreated ($n = 13$)	*P*-value
Age (year)	45.3 ± 17.4 [14–69]	50.9 ± 18.1 [14–69]	39.7 ± 15.3 [18–68]	0.10
Gender				0.10
Male	9 (9/26; 35)	7 (9/13; 54)	2 (2/13; 15)	
Female	17 (17/26; 65)	6 (6/13; 46)	11 (11/13; 85)	
Variant				0.43
Classic	12 (12/26; 46)	7 (7/13; 54)	5 (5/13; 38)	
Cardiac	14 (14/26; 54)	6 (6/13; 46)	8 (8/13; 62)	
Heart rate (bpm)	71.2 ± 12.1 [53–102]	72.0 ± 11.7 [53–88]	70.3 ± 12.9 [55–102]	0.73
Systolic blood pressure (mmHg)	128.2 ± 12.6 [108–150]	134.1 ± 12.6 [110–150]	120.9 ± 8.3 [108–136]	**0.01**
GFR (mL/min)	107.2 ± 29.0 [42–171]	98.5 ± 28.3 [42–143]	114.7 ± 28.6 [62–171]	0.17
BMI (kg/m^2)	26.6 ± 5.0 [19–39]	26.7 ± 4.7 [19–33]	26.6 ± 5.6 [20–39]	0.98
LVEF (%)	61.4 ± 7.0 [39–76]	62.0 ± 9.2 [39–76]	60.8 ± 4.1 [53–67]	0.67
EDV LVi (mL/m^2)	76.8 ± 12.8 [54–106]	75.8 ± 13.8 [57–98]	77.9 ± 12.2 [54–106]	0.69
ESV LVi (ml/m^2)	29.7 ± 7.4 [16–46]	28.8 ± 8.4 [16–46]	30.7 ± 6.3 [18–41]	0.52
LVMi (g/m^2)	65.1 (51.3; 107.1) [33–215]	113.2 (67.2; 134.1) [51–215]	51.4 (38.1; 54.2) [33–88]	< **0.001**
LAVi (mL/m^2)	35.0 (32.1; 45.3) [20–80]	43.3 (32.8; 47.3) [22–80]	34.2 (31.9; 39.3) [20–55]	0.51
GLS (%)	−14.8 ± 4.1 [−21–−6]	−12.8 ± 4.5 [−19–−6]	−16.9 ± 2.3 [−21–−12]	**0.01**
LGE				**0.03**
Yes	8 (8/26; 31)	7 (7/13; 54)	1 (1/13; 8)	
No	18 (18/26; 69)	6 (6/13; 46)	12 (12/13; 92)	
Global T1, (ms)	939 ± 58.3 [804–1023]	917.1 ± 60.6 [804–1016]	960.7 ± 48.8 [848–1023]	0.06
Global T2, (ms)	48.5 (46.9; 52.8) [44–55]	50.8 (47.4; 54.0) [45–55]	47.5 (46.8; 49.6) [44–55]	0.17
Global ECV (%)	27.6 (26.8; 28.9) [2–41]	28.5 (26.4; 31.3) [22–37]	27.5 (27.2; 28.4) [23–-41]	0.64

Qualitative variables are expressed as raw numbers followed by percentages into parentheses and were compared using χ^2 or Fisher exact test when appropriate.
Non normally distributed quantitative variables are expressed as medians followed by first (Q1) and third (Q3) quartiles into parentheses and ranges into brackets and were compared using the Wilcoxon test.
Normally distributed quantitative variables are expressed as means ± standard deviations followed by ranges into brackets and were compared using Student *t*-test.
Bold indicates significant *P* value.
BMI indicates body mass index; ECV indicates extra-cellular volume; EDV LVi indicates indexed end-diastole volume left ventricle; ESV LVi indicates indexed end-systole volume left ventricle; GFR indicates glomerular filtration rate; GLS indicates global longitudinal strain; LAVi indicates indexed left atrial volume; LGE indicates late gadolinium enhancement; LVEF indicates left ventricular ejection fraction; LVMi indicates indexed left ventricular mass.

administration of a gadolinium chelate injection. Two short axis views (basal and mid ventricular) were obtained to generate T2 and T1 maps. T1 maps were performed before and 12 mins after intravenous administration of a gadolinium chelate [18]. The ECV was calculated from the latter measurements and the patient's hematocrit.

Table 2
Variations (Δ) in myocardial native T1, ECV and T2 values after two years in 13 treated patients and 13 untreated patients.

Location	Treated ($n = 13$)	Untreated ($n = 13$)	*P* value
T1 Δ (ms)			
Global	39.4 ± 28.9 [8–105]	14.5 ± 30.3 [−41–81]	**0.04**
Septal	42.1 ± 28.7 [−3–103]	14.7 ± 29.4 [−25–93]	**0.02**
Lateral	34.5 ± 25.2 [5–81]	9.1 ± 31.1 [−46–88]	**0.03**
Extra-cellular volume Δ (%)			
Global	1.72 (−0.31; 2.96) [−8–7]	−1.68 (−2.17; 1.06) [−11–6]	0.19
Septal	0.50 (−2.06; 2.48) [−13–8]	−0.60 (−3.58; 1.48) [−18–5]	0.39
Lateral	2.19 ± 3.78 [−6–7]	0.17 ± 4.49 [−11–7]	0.25
T2 Δ (ms)			
Global	−2.11 ± 3.36 [−7–2]	0.57 ± 1.63 [−2–3]	**0.02**
Septal	−2.35 ± 3.97 [−8–2]	0.28 ± 2.21 [−3–5]	0.06
Lateral	−2.18 ± 2.96 [−7–2]	0.39 ± 2.28 [−5–3]	**0.03**

Non normally distributed quantitative variables are expressed as medians followed by first (Q1) and third (Q3) quartiles into parentheses and ranges into brackets and were compared using the Wilcoxon test.
Normally distributed quantitative variables are expressed as means ± standard deviations followed by ranges into brackets and were compared using Student t-test.
Bold indicates significant P value.

2.3. Image analysis

Images were analyzed using CVI42® (Circle CardioVascular Imaging Inc). Myocardial segmentation of the American Heart Association was used for regional analyses [18]. Segmentation was semi-automated using a 15 % offset on both epicardial and endocardial borders. It was firstly generated by AI and adjusted by the radiologist if needed. Three regions were analyzed: global including all 12 basal and mid segments, septal (segments 2, 3, 8 and 9) and lateral one (segments 5, 6, 11 and 12). Apical segments were not considered in order to avoid partial volume effect artifacts. In order to assess intra- and inter-observer reproducibility, T1 mapping of ten randomly chosen cardiac MRI examinations were processed twice by the same senior resident radiologist and once by a senior cardiac radiologist (respectively 3 and 30 years of experience in cardiac MRI).

Bi-ventricular volumes, left atrial volume and LVM were measured using automatic endocardial and epicardial contouring on cine sequences with a possible manual adjustment and LVM was drawn from muscle volume and density (excluding papillary muscles). Results were indexed to body surface aera derived from Boyd's formula.

LGE images were analyzed from both short axis and radially acquired long axis views, and classified as present or absent.

LV global longitudinal strain was measured using the tissue tracking mode of CVI42 after endo- and epicardial contouring of three long-axis CINE acquisitions of the LV (2-, 3- and 4 chamber-views).

2.4. Statistical analysis

The normality of the distribution of continuous variables was assessed by a Shapiro-Wilk test. Continuous variables were expressed as means ± standard deviations (SD) and ranges or medians, first (Q1) and third (Q3) quartiles and ranges according to the normality of the distribution [19]. Categorical variables were expressed as raw numbers, proportions and percentages. Statistical comparisons were performed using Student's *t*-test for normally distributed data, a Mann-Whitney U test for data with a skewed distribution, and the χ^2 and Fisher exact tests

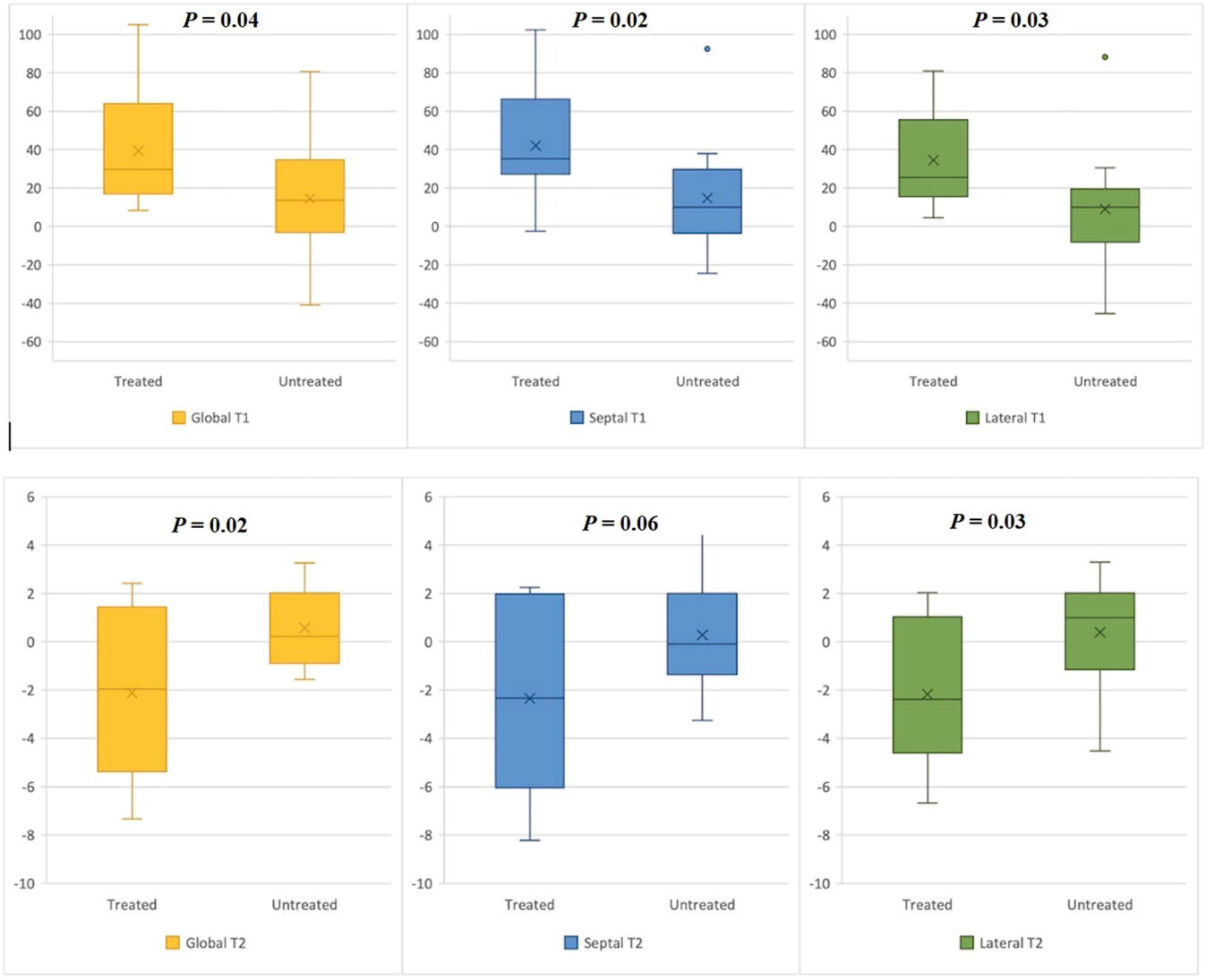

Fig. 2. Graphs show the results of the comparison of global, septal and lateral variations of native myocardial T1 and T2 values (ms) after two years of follow-up in treated *vs.* untreated patients. Box plots represent extreme values, median, first and third quartiles, and crosses represent mean values.

for categorical data. No multivariable analysis was performed due to the small sample size. A P value < 0.05 was considered to indicate statistically significant differences. Intra- and inter-observer reproducibility were assessed using Bland Altman plot, and presented as mean bias and limits of agreement (LOA). Data were analyzed using SPSS (Version 29.0.1.0; IBM).

3. Results

3.1. Study population

Population characteristics at baseline are presented in Table 1. The two groups were not different in terms of age, gender, type of variant, heart rate, glomerular filtration rate, body mass index, LVEF, indexed left ventricular end-systole volume, indexed left ventricular end-diastole volume, indexed left atrial volume and global T1, T2 and ECV.

Differences at baseline between the two groups were observed on median indexed LVM which was greater among treated patients (113.2 g/m^2; Q1, 67.2; Q3, 134.1) compared to untreated ones (51.4 g/m^2;Q1, 38.1; Q3, 54.2) ($P < 0.001$). Mean systolic blood pressure was greater in treated patients (134.1 ± 12.6 [SD] mmHg) compared to untreated ones (120.9 ± 8.3 [SD] mmHg) ($P = 0.01$). LGE was more frequent in treated patients (7/13 (54 %) compared to untreated patients (1/13; 8 %) ($P = 0.03$). Finally, global longitudinal strain was more impaired in the treated group (−12.8 ± 4.5 [SD] %) compared with the untreated group (−16.9 ± 2.3 [SD] %) ($P = 0.01$).

3.2. Global, septal, and lateral T1 relaxometry

Variations (deltas, Δ) in global, septal, and lateral native T1 values between month 0 (M0) and month 24 (M24) in treated vs. untreated patients are shown in Table 2 and Fig. 2. Individual global T1 evolutions are shown in Fig. 3. Both treated and untreated patients presented with an increase in native T1 values through time but T1 increase was greater in treated patients (+39.4 ± 28.9 [SD] ms) than in untreated ones (+14.5 ± 30.3 [SD] ms) ($P = 0.04$) (Fig. 4).

3.3. Global, septal, and lateral ECV

Global, septal, and lateral ECV Δ between M0 and M24 are shown in Table 2. No significant variation of ECV was observed in both groups.

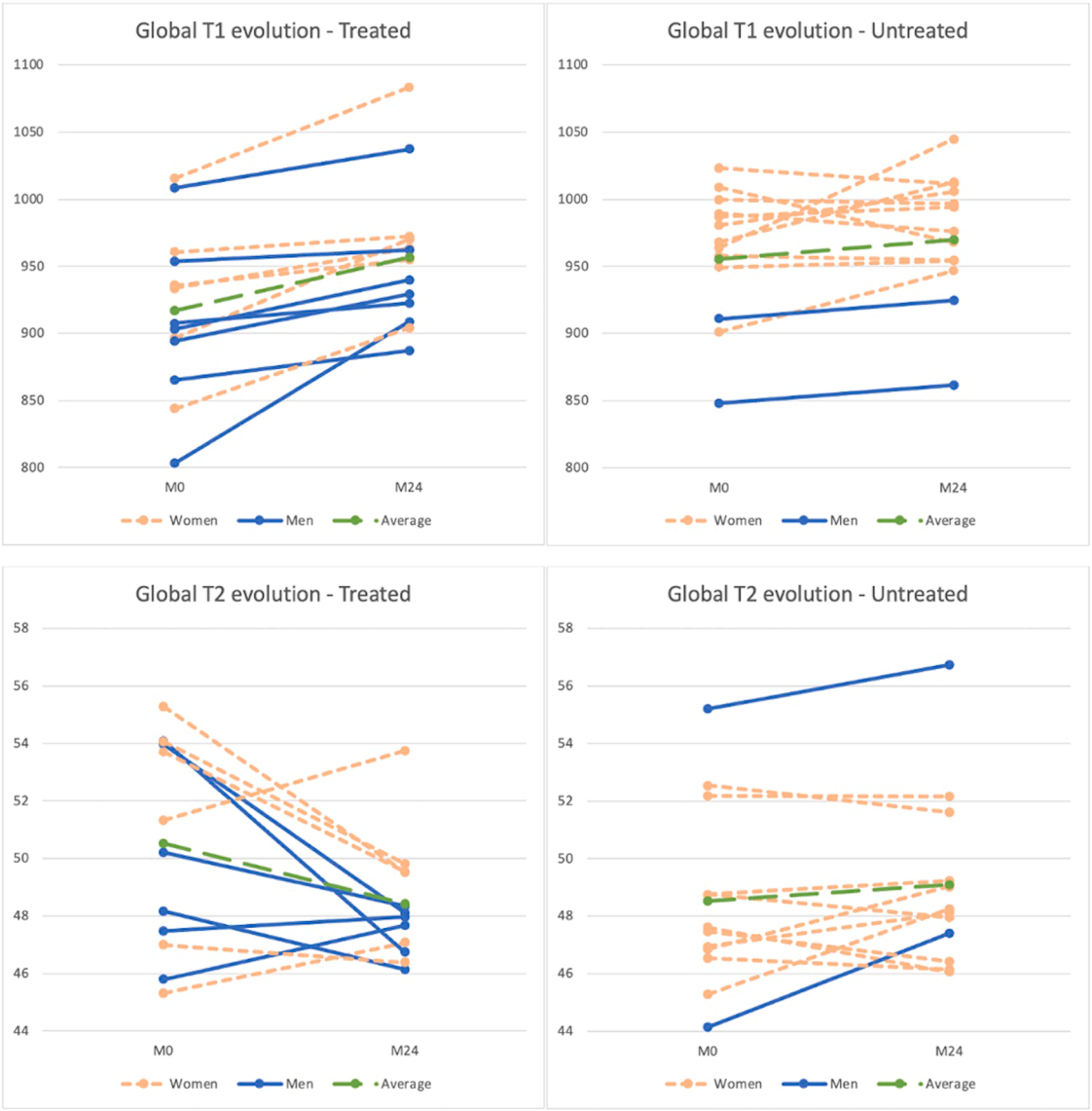

Fig. 3. Graphs show individual native myocardial T1 and T2 values (ms) variations in treated and untreated patients with Fabry disease after two years of follow-up.

3.4. Global, septal, and lateral T2 relaxometry

Global, septal, and lateral T2 Δ between M0 and M24 in treated and untreated patients are shown in Table 2 and Fig. 2. Individual global T2 evolutions are shown in Fig. 3. T2 values decreased in treated patients (global T2, −2.11 ± 3.36 [SD] ms) and increased in untreated ones (global T2, +0.57 ± 1.63 [SD] ms) ($P = 0.02$).

3.5. Left ventricular ejection fraction, volumes, mass, global longitudinal strain, left atrial volume end late gadolinium enhancement

Deltas in LVEF, indexed end-diastole and end-systole LV volumes, indexed LVM, global longitudinal strain and indexed left atrial volume between M0 and M24 are presented in Table 3. LGE was present in seven (7/13; 54 %) treated patients and one (1/13; 8 %) untreated patient at the time of inclusion and remained stable throughout the study. None of the six (6/13; 46 %) treated patients and 12 (12/13; 92 %) untreated patients without LGE at M0 developed it during the study.

3.6. Intra- and inter-observer reproducibility of T1 measurements

Intra- and inter-observer reproducibility showed respectively a mean bias of −0.18 ms, LOA [−11.61;11.24] and a mean bias of −0.64 ms, LOA [−23.82;22.54].

4. Discussion

In this study, we demonstrated that native myocardial T1 and T2 values, as assessed by cardiac MRI, can serve as valuable biomarkers for monitoring treatment efficacy in Fabry cardiomyopathy. Our findings indicate that treated patients showed significantly greater increases in native T1 and decreases in T2 values compared to untreated patients, suggesting that specific treatment may effectively reduce myocardial lipid storage and inflammation. These results are consistent with those of a previous study that had shown altered myocardial tissue characteristics in response to enzyme replacement therapy [17]. ECV, LV functional parameters, left atrial volume and LGE variations were similar between the two groups even if we noticed that the mean LV mass indexed increased in untreated patients while it decreased in treated patients.

As T1 values increase was more pronounced in treated patients than in their untreated counterparts, we speculate that it was the positive result of specific treatments of FD. Given their high cost and constraints, a biomarker of the effectiveness of FD treatments on cardiac structure

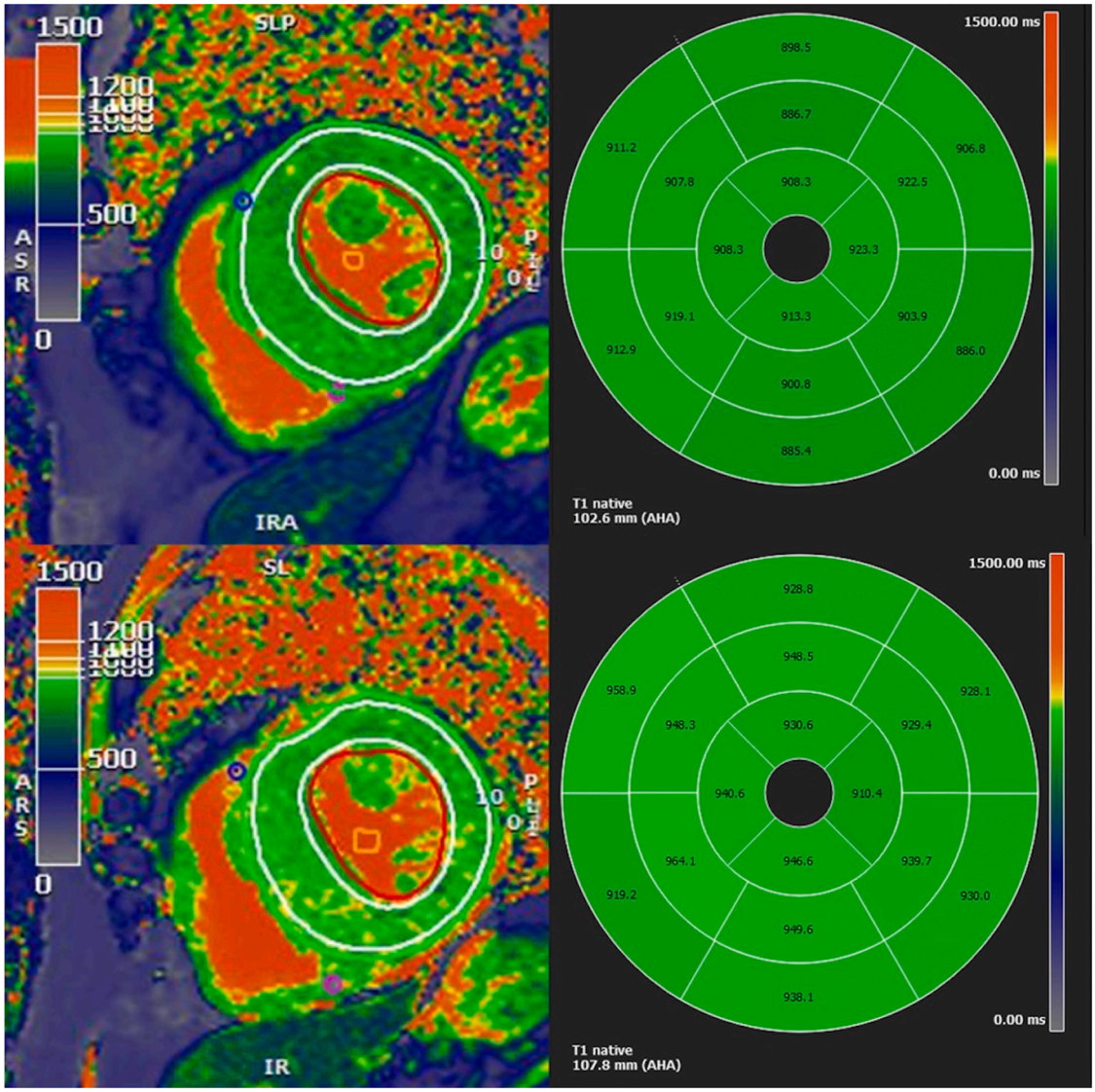

Fig. 4. The images show native T1 maps from cardiac MRI in a patient with Fabry disease who was treated with agalsidase alpha at M0 (top row) and M24 (bottom row). Note the global increase in T1 values in all segments.

Table 3
Variations in left ventricular functional parameters and left atrial volume after two years.

Variable	Treated patients ($n = 13$)	Untreated patients ($n = 13$)	*P* value
LVEF (%)	−0.99 ± 8.67 [−17–16]	+0.37 ± 6.42 [−9–14]	0.65
EDV LVi (mL/m^2)	+0.57 ± 8.07 [−12–18]	+2.31 ± 9.42 [−10–20]	0.62
ESV LVi (mL/m^2)	+0.45 ± 7.61 [−14–10]	+0.66 ± 5.41 [−8–9]	0.93
LVMi (g/m^2)	−1.88 ± 20.8 [−44–30]	+2.93 ± 8.77 [−9–27]	0.45
LAVi (mM/m^2)	+3.29 ± 10.03 [−12–20]	+2.39 ± 8.47 [−10–19]	0.81
GLS (%)	+0.64 ± 2.31 [−3–5]	+0.62 ± 1.40 [−2–3]	0.98

All variables are expressed as means ± standard deviations followed by ranges into brackets and were compared using Student *t*-test.
EDV LVi indicates indexed end-diastole volume left ventricle; ESV LVi indicates indexed end-systole volume left ventricle; GLS indicates global longitudinal strain; LAVi indicates indexed left atrial volume; LVEF indicates left ventricular ejection fraction; LVMi indicates indexed left ventricular mass.

would be useful parallel to plasmatic lyso-Gb3 and conventional transthoracic echocardiogram parameters such as LVM and LVEF. It is well known that myocardial T1 is significantly decreased in naive FD patients with cardiac involvement, possibly a consequence of the accumulation of lipids in the myocardium [11,12]. For this reason, native T1 seems to be a prime candidate for monitoring treatment and the regression of lipid overload. In the present study, the difference in native T1 variations between treated and untreated patients was significant globally as well as in septal and lateral segments. The increase in T1 values could be interpreted as the beneficial consequence of treatment reducing myocardial glycosphingolipid storage or, on the contrary, as the deleterious development of myocardial fibrosis [16]. However, myocardial fibrosis does not develop uniformly in all segments of the myocardium in FD. In advanced hypertrophic forms, LGE has been shown to develop primarily in the midwall of basal lateral segments, leading to segmental pseudo-normalization of T1 values. On the contrary, even in advanced forms, LGE and fibrosis seem to spare the interventricular septum, whose segments retain low T1 values [11,12,20,21]. Given in particular the results obtained in septal segments, it seems reasonable to think that the increase of T1 values was a real consequence of the treatment.

We had no definite explanation for the moderate increase in T1 values in untreated patients. However, the development of fibrosis

seems unlikely as ECV remained unchanged throughout the 2-years follow-up.

Although variations in myocardial T2 values appeared small in absolute values, significant differences were observed between the two groups in favor of the treated patients. In the context of FD, myocardial edema was shown to be associated with LGE [22] which itself was shown to be associated with poor prognosis [23]. The results of the present study argue in favor of treating patients with FD as early as possible in order to reduce inflammation and delay the development of fibrosis. Given the small variations observed, monitoring the effectiveness of the treatment using cardiac MRI could be an option, provided that the same equipment is used and the same protocol is followed.

Variations in ECV were similar between treated and untreated patients. This result is probably explained by the absence of modification of the ECV induced by sphingolipid myocardial storage, as suggested by previous studies [12,24]. The absence of difference in ECV variation and of any change in delayed enhancement questions the benefits of the administration of gadolinium chelate for every follow-up cardiac MRI in patients in the absence of clinical event.

Although not significant, the opposite trends in left ventricular mass variation in the two groups justify monitoring patients with Fabry disease using cardiac MRI, because of its long-standing known accuracy [25]. Variations in LVEF, indexed end-diastole and end-systole LV volumes, global longitudinal strain, indexed left atrial volume and LGE were similar in the two groups.

The major strength of this study was its two-year length of follow-up even if a longer period would probably be beneficial to check the validity of the present results given the very slow natural history of the disease. Another strength of the study was the good intra- and inter-observer reproducibility of T1 relaxometry measurements. This result is probably the consequence of the high quality of the AI-based contouring of epicardium and endocardium [26]. Given the slow natural history of the disease and the present results, it seems reasonable to suggest performing cardiac MR follow-up every two years for stable patients with FD. However, future studies with extended follow-up periods would be useful to evaluate the long-term prognostic value of MR biomarkers.

The study had several limitations. First of all, with only 26 patients, the study's sample size is relatively small which limits the statistical power and generalizability, especially when analyzing subgroup differences. The low number of patients did not allow to compare males and females. Secondly, no conclusion can be drawn regarding potential differences between specific treatments even if a large majority of patients were under agalsidase alpha. Nonspecific FD treatments were not evaluated either and could also induce a confusion bias. Third, both groups were not strictly comparable as patients of the treated group had a significatively higher indexed LVM and systolic blood pressure, an increased global longitudinal strain and more LGE. These differences are the consequence of therapeutic routines in our country which were targeting males more than females and severe forms rather than early ones although recent evidence showed that treating patients earlier and treating a greater proportion of females could be beneficial [27]. It can be assumed that better results would have been obtained with a selection of younger, treatment-naive patients without fibrosis. Fourth, CMR analyses were not realized blinded to the patient therapeutic status. Fifth, a correlation with biological parameters (*e.g.*, troponins, NT pro BNP, lysoGb3) was not included in the design of the study. Finally, because of missing data, we could not assess the FASTEX composite score [28].

In conclusion, our hypothesis was that myocardial native T1 and T2 relaxometry could monitor the efficacy of treatment in FD. The present two-year follow-up study performed with the same equipment and protocols showed that native T1 values were more increased in patients under specific treatment compared to untreated ones. In spite of the many limitations of the study, this increase in T1 values could be linked to the decrease of sphingolipid myocardial storage given the observation of septal segments which are known to be spared by fibrosis. Specific FD treatments also seem to be efficient on myocardial inflammation as shown by the comparative evolution of T2 values. Even though further investigations are needed, at best with a randomized double-blinded study, LV mass and myocardial native T1 and T2 values seem to be potential biomarkers of treatment efficacy.

Human rights

The authors declare that this work was performed in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patients.

Ethics

All patients gave informed consent and the study received validation from the institutional ethics committee.

CRediT authorship contribution statement

Jules Senlis: Formal analysis, Writing – original draft, Visualization, Formal analysis. **Fabien Labombarda:** Investigation. **Julien Burel:** Investigation. **Arthur Flouriot:** Formal analysis, Investigation. **Sébastien Normant:** Formal analysis. **Matthieu Demeyere:** Investigation. **Olivier Lairez:** Investigation. **Soraya El Ghannudi:** Investigation. **Alexis Jacquier:** Investigation. **Olivier Ghekiere:** Investigation. **Farah Cadour:** Writing – review & editing, Formal analysis. **Jean-Nicolas Dacher:** Formal analysis, Writing – review & editing, Methodology, Supervision, Conceptualization, Formal analysis.

Declaration of competing interest

Fabien Labombarda : Consulting fees from Takeda-Shire, Sanofi-Genzyme, Amicus Therapeutics, Chiesi; Research grants from Shire-Takeda.; Olivier Lairez : Consulting fees from Alnylam, Amicus Therapeutics, Astra Zeneca, BMS, Siemens, Pfizer; Research grants from NeuImmune, Novo Nordisk; Jean Nicolas Dacher : Consulting fees from Takeda-Shire, Amicus Therapeutics, Pfizer, Circle Cardiovascular Imaging; Research grant from Shire-Takeda; All other authors; no conflict of interest to disclose

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Further reading

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