

Predictors of clinical evolution in prehypertrophic Fabry Disease

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Background: In prehypertrophic Fabry Disease (FD), low myocardial T1 values, reflecting sphingolipid storage, are associated with early structural and ECG changes. The correlations between T1 values and functional parameters have not been explored. Furthermore, the potential prognostic role of T1 in predicting disease worsening is still unknown.

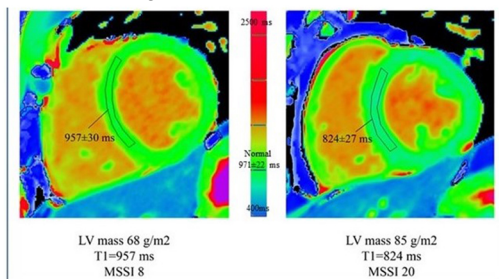
Aim: to study the association between T1 values and cardiac function (systo-diastolic function, arrhythmias, exercise capacity) and to explore the prognostic significance of T1 values in predicting disease worsening.

Methods: ECG, 2D-Echocardiography, Cardio-pulmonary test and CMR were performed in 44 Fabry patients with no left ventricular hypertrophy (35.7 ± 14.5 y, 68.2% F). Disease severity was quantified using Mainz Severity Score Index (MSSI). Study population was compared with a gender, age and BSA matched cohorts of 22 healthy volunteers. After 12 months follow up, clinical stability was evaluated using FASTEX, a recently developed severity scoring systems.

Results: FD patients were divided into 2 groups according to the presence of normal or low T1 values (normal T1, n = 18, 40.9%; Low T1, n = 26, 59.1%) (Figure 1). At baseline, T1 values showed a negative correlation with left ventricular mass ($r=-0.79$, $p < 0.0001$), maximum wall thickness (LVWT) ($r=-0.79$, $p < 0.001$), Sokolof-Lyon Index ($r=-0.54$, $p < 0.001$), left atrial volume ($r=-0.49$, $p < 0.0002$) and MSSI ($r=-0.61$, $p < 0.001$). No significant differences in systo-diastolic function and exercise capacity were observed comparing normal and low T1 Fabry patients. Arrhythmias were reported in 2 females with low T1 values and late gadolinium enhancement. After a 12 months follow up, 5 patients (40.0 ± 12.4 y, 2 females) showed clinical worsening (FASTEX $>20\%$). Higher LVWT (OR = 2.61, CI = 1.04-6.57, $p = 0.04$), left atrial volume (OR = 1.24, CI = 1.02-1.51, $p = 0.03$) and lower T1 values (OR = 0.98, CI = 0.96-0.99, $p = 0.03$) at baseline were independently associated with clinical worsening at follow up.

Conclusions: In prehypertrophic FD, low T1 values correlate with early electrocardiographic, morphological cardiac changes and worsening of global disease severity but are not associated with functional abnormalities. The presence of low T1 values is a risk factor for disease worsening, thus representing a potential new tool in prognostic stratification and therapeutic approach.

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Native T1 mapping in Fabry disease using ShMOLLI at 1.5 T. Both FD subjects in left and right pictures had normal LV mass and LV wall thickness, however patient with lower native myocardial T1 value (right) had greater LV mass and more severe global disease score compared to patient in left picture.