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Inflammatory cardiomyopathy in Fabry disease

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Topic(s):
Infiltrative Myocardial Disease

Citation:

Background: Fabry disease (FD) is an X-linked lysosomal storage disorder caused by mutations in α-galactosidase A. Cardiovascular magnetic resonance (CMR) has helped unveil the pathogenesis of Fabry cardiomyopathy: sphingolipid storage (low T1 mapping values), left ventricular hypertrophy (LVH) and myocardial fibrosis with late gadolinium enhancement (LGE) characteristically present in the basal inferolateral (BIFL) wall. Recent evidence has suggested that the LGE may be inflammation and oedema as part of this pathogenic process.

Purpose: To assess the presence of inflammation in patients with FD using T2 mapping (for oedema/inflammation) supported by blood troponin levels (showing myocyte death and by inference inflammation).

Methods: A multi-centre international study in gene positive FD patients using CMR and blood biomarkers. All participants underwent CMR at 1.5 T. Native T1 and T2 mapping were performed. The T1 mapping sequence was MOLLI with sampling scheme in seconds. LGE used a phase sensitive inversion recovery sequence. Global longitudinal 2D strain (GLS) values were obtained using feature tracking analysis. Blood high-sensitivity troponin T (hsTnT) was measured on the same day.

Results: 100 FD patients (age 43.8±1.3 years, 42% male) were included. 45% had LVH, 35% LGE. Low T1 mapping (normal <943ms) was found in 49% and 33% had high hsTnT values (normal <15ng/L). Mean T2 mapping values were 52.6±0.6ms in the BIFL wall and 49.5±0.3ms in the remote myocardium/septum (p<0.001, normal <53ms). T2 values in the BIFL wall were significantly higher among patients with LGE (58.2±6.1ms vs 49.2±3.1ms, p<0.001, Figure 1). In a per-segment analysis of 1600 segments, higher T2 values correlated positively with percentage of LGE per segment (r=0.262, p<0.001), T1 values (r=0.205, p<0.001), maximum wall thickness (r=0.253, p<0.001) and GLS values (r=0.212, p<0.001). HsTnT values were higher among patients with LGE (median of 31 vs 3ng/L in patients without LGE, p<0.001). There was a strong positive correlation between T2 values in the BIFL wall and ln(hsTnT) (r=0.776, p<0.001, Figure 2). The strongest predictor of increased hsTnT in multivariate analysis (age, sex, LVH, septum T1, T2 in the BIFL, GLS, LGE) was T2 in the BIFL wall (β=0.4, p=0.001).

Conclusions: Cardiac involvement in FD goes beyond storage (low T1 values). When LGE is present, this is almost always associated with a high T2 and troponin elevation supporting FD as a chronic inflammatory cardiomyopathy. Initial reports of LGE being fibrosis are too simplistic – LGE in FD appears to have a significant chronic inflammation/oedema component.
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Figure 1. Box-plot graph showing T2 values in remote and BIFL (LGE) areas

Figure 2. Scatter-plot graph illustrating a positive correlation between T2 values in the BIFL wall and blood hsTnT