ABSTRACT

OBJECTIVE: Experimental therapies under development for Friedreich's Ataxia (FRDA) require validated biomarkers. In-vivo reflectance confocal microscopy (RCM) of skin is a noninvasive way to quantify Meissner's corpuscle (MC) density and has emerged as a sensitive measure of sensory polyneuropathies. We conducted a prospective, cross-sectional study evaluating RCM of MCs and conventional peripheral nerve measures as candidate peripheral nerve markers in FRDA. METHODS: Sixteen individuals with FRDA and 16 age- and gender-matched controls underwent RCM of MC density and morphology, skin biopsies for epidermal nerve fiber density (ENFD), nerve conduction studies (NCS), and quantitative sensory testing (QST) including touch, vibration, and cooling thresholds. RESULTS: MC densities were measurable in all participants with FRDA, and were lower at digit V (hand), thenar eminence, and arch (foot) compared to controls. By contrast, sensory NCS showed floor effects and were obtainable in only 13% of FRDA participants. QST thresholds for touch, vibration, and cooling were higher at the hand and foot in FRDA than controls. Reductions in ENFDs were present in more severely affected individuals with FRDA (Friedreich's Ataxia Rating Scale (FARS) >60) compared to matched controls, although skin biopsies were not well tolerated in children. MC densities, ENFDs, and touch and vibration thresholds were associated with clinical disease severity (FARS and modified FARS) and duration since symptom onset. INTERPRETATION: MC density, ENFD, and QST thresholds provide structural and physiologic markers of sensory involvement in FRDA. Longitudinal evaluation is needed to determine whether these measures can identify changes associated with disease progression or treatment. © 2019 The Authors. Annals of Clinical and Translational Neurology published by Wiley Periodicals, Inc on behalf of American Neurological Association. PMID:31414727 DOI:10.1002/acn3.50865 Free full text