Clustering Trajectories of Ambulatory Function in the North Star Clinical Network Database

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Functional variability among boys with Duchenne muscular dystrophy (DMD) is well recognized and complicates the interpretation of clinical studies. To further understanding, we assessed whether boys with DMD could be clustered into groups sharing similar trajectories of ambulatory function over time, as measured by the North Star Ambulatory Assessment (NSAA) total score, and then explored associations with other factors. Using the North Star Clinical Network database (23 UK centres) we identified 337 genotyped patients with >1 NSAA assessment. Longitudinal NSAA was studied using latent class trajectory analysis, which produced evidence for at least four clusters of boys sharing similar trajectories vs. age: 25% in cluster 1 (lost NSAA function at age ~10y), 35% in cluster 2 (loss at ~12y), 21% in cluster 3 (loss at ~15y) and 19% in cluster 4 (loss > 15y). Ages at DMD diagnosis were similar across clusters (interquartile range 2.9 to 5.4 years). However, at first NSAA assessment, the following associations were observed with earlier- vs. later-declining clusters (means shown for clusters 1,2,3 and 4, respectively, all $p< 0.05$): younger age (6.3, 6.2, 6.9 and 7.7 years), worse NSAA (19, 22, 22 and 26), slower rise from supine (6.9, 6.1, 4.6 and 3.8 seconds), slower 10 meter walk/run (7.7, 6.9, 7.2 and 5.7 seconds) and younger steroid initiation (6.1, 5.8, 6.5 and 6.9 years). Dystrophin mutations amenable to skipping exons 44, 45, 51 and 53 (all >5% prevalence) were not significantly associated with clusters. Within this broad DMD population, four trajectory clusters were identified. Following similar ages at diagnosis, boys in faster vs. slower progressing clusters tended to initiate steroids earlier and to have worse function at their first assessment in the studied care centres. Identifying the extent to which other known factors (e.g., background genetics) associate with these clusters and explain variation in DMD disease progression is of high interest.

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