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AMBULATORY FUNCTION IN DUCHENNE MUSCULAR DYSTROPHY (DMD): THE CHARACTERISTIC TRAJECTORY AND VARIATION ACROSS INDIVIDUALS

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OBJECTIVES: Clinical and economic research in DMD is complicated by heterogeneity in rates of progression through stages of ambulatory improvement, decline and loss. To aid the interpretation of DMD outcomes we described the typical pace of ambulatory progression and the variation across individuals.
METHODS: Serial assessments of the North Star Ambulatory Assessment (NSAA; ranging from 0 [non-ambulatory] to 34 [best function]) were analyzed in the UK NorthStar database using linear mixed effects (LME) models with subject-specific random splines for the effect of time. Key features of the fitted trajectories were summarized across individuals.
RESULTS: Totals of n=323 patents and n=2007 NSAA assessments were studied, with ages ranging from 2 to 22 years (median=8.6 years), and median follow-up of 3.3 years. The LME model explained 92% of the variability in NSAA scores. Across individuals, fitted NSAA trajectories exhibited medians (interquartile ranges) of 6.8 (5.9 to 7.8) years of age at peak NSAA, scores of 27 (23 to 30) at peak and 4.0 (3.6 to 4.6) years from peak to 50% loss. Ninety-five percent of patients reached peak NSAA between the ages of 5 and 9 years. Age at peak function, level at peak function, and time to 50% loss were weakly to moderately correlated with each other. Compared with age at peak NSAA, age at peak 10 meter walk/run speed was similar; age at peak rise from floor speed was earlier by 1.3 (0.7 to 1.8) years.
CONCLUSIONS: Despite variability across individuals, ambulatory progression in DMD follows common patterns. Different functional abilities peak at different ages, suggesting that they reflect different aspects of disease. Characterization of progression can help inform the design and interpretation of clinical studies, e.g., by enrichment for certain disease stages, and can serve as a reference point for much needed further research in DMD disease modeling.