Title: Longitudinal decline in functional performance in ambulatory boys with Duchenne Muscular Dystrophy

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Abstract Body:

Purpose/Hypothesis: Duchenne muscular dystrophy (DMD) is an X-linked recessive disorder, characterized by progressive muscle weakness. Carefully collected natural history information is needed in this progressive disease to facilitate clinical trials design. The aim of this study was to evaluate functional ability in a large cohort of ambulatory boys with DMD, using clinical outcome measures, and assess longitudinal functional decline.

Subjects: 126 ambulatory boys with DMD (5-12 yrs) and 33 age-matched controls participated. 1 yr follow-up data were collected in boys with DMD (n=107) and additional annual follow-up data were collected for up to 4 years for a subset of the subjects.

Materials/Methods: Subjects performed three timed functional tests: 10m walk/run, climbing four stairs, supine to stand (STS). They also completed the 6 minute walk test (6 MWT). Test instructions were standardized across 3 geographically distributed sites. Each timed functional test was performed three times and the fastest time for each test was recorded. The maximum time allowed to complete each test was set at 45 sec. Subjects were divided into four age groups- 5-6.9 yrs, 7-8.9 yrs, 9-10.9 yrs, and 11-12.9 yrs. To investigate loss of function in these subjects, we binned all annual visits into 1 year age groups. Data were analyzed using Mann Whitney tests for cross-sectional data; Kruskal-Wallis with post-hoc tests and Wilcoxon tests were done for longitudinal data.

Results: For all age groups, at baseline, boys with DMD required more time than controls to complete the timed tests and traversed a shorter distance during the 6 MWT. Even in the youngest age group, boys with DMD required over twice as long to climb stairs and complete the STS than controls. At 1 yr, 7-8.9, 9-10.9, and 11-12.9 yr old boys with DMD had significant functional decline in 10m walk/run and climbing four stairs time. Based on the 6 MWT, significant functional decline was only seen in 9-10.9 and 11-12.9 yr olds. In 5-6.9 yr old boys, no change in functional performance could be detected over 1 yr for any tests. Using all available data points, the number of subjects who were unable to perform each test increased with age. At age of 14, 70%, 60%, and 40% of subjects were unable to perform STS, climbing four stairs, and 10m walk/run tests, respectively. Subjects lost the ability to perform STS before any other functional test.

Conclusions: Ambulatory boys with DMD showed functional deficits compared to their peers at all ages tested (5-12 years). Starting at the age of 7 yrs functional decline over 1 yr could be detected except in 6 MWT. More than half of the subjects lost the ability to perform STS and climbing four stairs tests at age of 14 years.

Clinical Relevance: This observational natural history study in a large cohort provides important information on the functional decline in DMD and the timing of disease progression. This natural history data is valuable for clinical trial planning, both to appropriately power studies and to select the most appropriate cohort of subjects.