TITLE: A COMPOSITE PROGNOSTIC SCORE FOR TIME TO LOSS OF WALKING ABILITY IN DUCHENNE MUSCULAR DYSTROPHY (DMD)

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ABSTRACT

OBJECTIVES: Prediction of loss of ambulation (LoA) is a critical milestone in DMD. We assessed the extent to which combinations of patient characteristics help predict time to LoA across different data sources.

METHODS: Ambulatory boys (N=500; mean age=9.2 years) with DMD were drawn from two natural history databases (UZ Leuven and PRO-DMD-01 data provided by CureDuchenne) and three trial placebo arms (phase IIb and phase III trials of ataluren, phase III trial of tadalafil). Time to LoA, approximated as the inability to complete the six-minute walk test (6MWD), was analyzed using Cox proportional hazards models.

RESULTS: Eighty-five boys (17%) experienced LoA over 915 patient-years. A model including timed function tests ([TFT]; rise from supine, 4-stair climb and 10-meter walk/run), 6MWD, age, height, weight, steroid use and data source predicted time to LoA better than a model based only on age >7 years, baseline 6MWD <350m and data source (pseudo-R^2: 37% vs. 21%). Better TFT performance, deflazacort use (vs. prednisone), greater weight, lower height and lower BMI were significant predictors of longer time to LoA. Data source differences were present when adjusting only for age and baseline 6MWD ($p<0.05$), but were not significant after adjustment for the additional factors ($p=0.18$). Ad-hoc stratification of boys based on risk score percentiles produced good separation, with the highest risk groups having 1-year LoA risks of 64%, 28% and 3%, 2-year risks of 94%, 63% and 28%, and median times to LoA of approximately 1, 1.6 and 2.5 years, respectively. The median was not reached for lower-risk groups.

CONCLUSIONS: A composite prognostic score incorporating multiple measures of ambulatory function can improve prediction of time to LoA. Once validated, such a score can inform clinical practice and trial designs, and enable adjusted comparisons between patients receiving newer therapies (e.g., in extension trials) and natural history controls.

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