#959 DEVELOPMENT OF A PROGNOSTIC MODEL FOR 1-YEAR CHANGE IN TIMED 4 STAIR-CLIMB IN DUCHENNE PATIENTS

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Background

Longitudinal progression of disease is inherently heterogeneous among individuals with Duchenne muscular dystrophy (DMD). The resulting variation in outcome measures can complicate clinical trial design and potentially cloud interpretation of results.

The collaborative Trajectory Analysis Project (cTAP) is a pre-competitive coalition of academic clinicians, drug developers, and patient foundations; cTAP was formed in 2015 to identify biostatistical approaches to overcome the challenges of high variation in clinical trials in DMD.

We previously reported a prognostic score that explained 60% of variation in the change in 6 minute walk distance (6MWD) over 1 year, and significantly improved upon prognosis from baseline age, 6MWD and steroid use by also incorporating timed function tests, height and weight [Goemans N, vanden Hauwe M, Signorovitch J, Swallow E, Song J, Collaborative Trajectory Analysis Project (cTAP) (2016). Individualized Prediction of Changes in 6-Minute Walk Distance for Patients with Duchenne Muscular Dystrophy. PLoS ONE 11(10): e0164684. doi:10.1371/journal.pone.0164684]

The aim of the present study was to develop a prognostic model for 1-year change in 4-stair climb (4SC) among DMD patients, and to assess the additional predictive value of the model compared to commonly used factors (i.e., age, baseline 6MWD and steroid use).

Methods

Natural history data were collected from DMD patients approximately every 6 months over the course of 2 to 5 years during routine clinical practice at the Universitaire Ziekenhuizen pediatric neurology clinic in Leuven, Belgium.

Patient demographics, treatment experience and ambulatory outcomes were recorded at each visit.

Annualized changes in 4SC were studied between all pairs of visits separated by ~1 year (8-16 months). Prediction models were developed using multivariable regression for repeated measures. Generalized estimating equations (GEE) with an exchangeable covariance structure were used to account for the use of multiple pairs of visits from individual patients

Results

A total of n=235 ~1-year follow-up intervals from n=81 boys were included. Mean age was 9.1 years and mean 4-SC was 3.84 s at the start of these intervals; average duration of steroid use was 29.11 months. During the subsequent ~1-year, mean annualized change in 4SC was 0.71 s with a standard deviation (SD) of 2.20. Predictions based on age, baseline 4SC and steroid use explained 13% of variation in annualized 4SC changes (R-squared = 0.13). A broadened prognostic model, adding timed 10-meter walk/run, and rise from supine, as well as height and weight, significantly improved prediction, explaining 34% of variation in annualized 6MWD changes (R-squared=0.34).

In the broadened model, parameters that were most strongly correlated with 1 year change in 4SC were steroid use > 1 year ($p < 0.001$), baseline 4SC (s)($p < 0.001$), baseline rise from supine (s)($p < 0.001$) and baseline 10 meter walk run (s) ($p<0.05$).

Conclusion

A prognostic model incorporating timed function tests significantly improved prediction of 1-year changes in 4SC. Explained variation was more than doubled compared to predictions based only on age, baseline 4SC and steroid use, indicating significant potential for broader prognostic models to inform clinical trial design and interpretation in DMD

#Duchenne Muscular Dystrophy #Natural history #4-stair climb (4-SC) #prognostic model