# Measures of Person-Reported Outcomes and Clinical Functioning are Predictive of Strength in Facioscaphulohumeral Muscular Dystrophy

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## INTRODUCTION

FSHD is an autosomal-dominant disorder that asymmetrically affects the face, shoulders, and upper arms and later progresses to affecting the trunk and lower extremities. Symptoms usually begin before the age of 20 with a prevalence thought to occur around 4-10 per 100,000 people (1,2). The pathogenesis has been linked to the inappropriate expression of DUX4, a gene usually limited to the germline, that relaxes the chromatin either by a loss of macrosatellite repeats (D4Z4) or mutations in the structural maintenance of chromosome flexible hinge domain containing gene 1 (SMCHD1) (3).

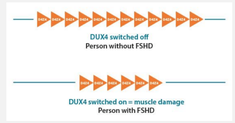


*Figure 1. Pathogenesis of FSHD (4)*

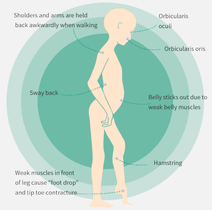


*Figure 2. Signs of FSHD (5)*

Much has yet to be done with validating clinical outcome measures that are sensitive to significant changes in disease progression and correlating these with patients' perception of the condition (6-8). The World Health Organization defines health-related quality of life as a multidimensional construct including physical, psychological, and social health dimensions (9,10). The need for easily-administered measures of health-related quality of life that are sensitive to changes in treatments across ages and disease severity are becoming increasingly apparent. The US Food and Drug Administration has strongly recommended including patient-reported outcome (PRO) measures as endpoints in all clinical trials (10, 11).

Prior studies have shown relationships between PRO measures may not be as expected at times. Instead of associations with weakness, PRO measures were found to be more associated with ADLs, pain, self-efficacy, and fatigue depending on the patient population (12). Furthermore, more patients have reported the *social role limitations* were of greater importance than those of facioscapulohumeral weakness (13).

## OBJECTIVES

- **Explore the relationship among clinical and person-reported measures of strength and function and health-related quality of life**
- **Evaluate magnitude of change in scores over time according to age or duration of symptoms.**

## MATERIALS & METHODS

This is a retrospective study of pre-existing data from the NIDRR-funded study entitled "State-of-the Art Clinical Endpoints versus Person-Reported Outcomes in Individuals with Neuromuscular Disease: Reliability, Validity and Responsiveness to Change" (PI: Craig McDonald, Co-I: Erik Henricson).

Patient's results will be from a de-identified data set from the REDCap data management system. There will be no access to identifiable PHI and it is anticipated that the study will be exempt from IRB review. They were assessed at initial visit and again one year later. 25 initial patients were assessed and 16 followed up in a year. An estimate of arm strength was created averaging elbow flexion and shoulder abduction and adjusting for weight.

Common descriptive, correlative, linear and non-linear statistical analysis techniques will be employed to explore relationships between strength, clinical function, and person reported mobility using parametric and non-parametric measures as appropriate using STATA. Estimates of clinically-significant change in individual measures over time, as well as scaling those estimates between pairs or combinations of measures were developed.

## RESULTS

Table 1. Descriptive statistics (n=41)

| Variable | Average | Standard Deviation | Minimum | Maximum |
|---|---|---|---|---|
| Age (years) | 53.2 | 18.4 | 13 | 76 |
| Height (cm) | 169.2 | 10.3 | 148.5 | 188.5 |
| Weight (pounds) | 178.2 | 41.7 | 72.4 | 265.1 |
| Weight-adjusted strength of elbow flexion and shoulder abduction | 0.15 | 0.07 | 0.04 | 0.28 |
| Average Pain | 4.07 | 1.90 | 1 | 8 |

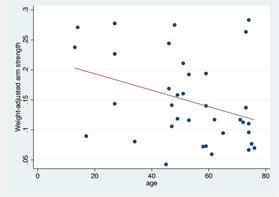


*Figure 3a.* On average a ten-year increase in age is associated with a 1.3 percent decline in arm strength as a percentage of overall body weight *(p=0.037) (n=36)*

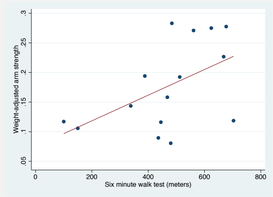


*Figure 3b.* On average a one hundred-meter decrease in six-minute walk distance is associated with a 2.2 percent decrease in arm strength as a percentage of overall body weight (p=0.049) *(n=15)*

*Table 2. Strong correlation among average pain, general activity, mood, walking ability, normal work, relations with other people, sleep, and enjoyment of life in Brief Pain Inventory (pr 0.01, st 0.001)*

| | Pain | General activity | Mood | Walking ability | Normal work | Relations with other people | Sleep | Enjoyment of life |
|---|---|---|---|---|---|---|---|---|
| Pain | 1 | | | | | | | |
| General activity | 0.74* | 1 | | | | | | |
| Mood | 0.68* | 0.77* | 1 | | | | | |
| Walking ability | 0.68* | 0.75* | 0.69* | 1 | | | | |
| Normal work | 0.71* | 0.80* | 0.66* | 0.92* | 1 | | | |
| Relations with other people | 0.66* | 0.76* | 0.88* | 0.66* | 0.69* | 1 | | |
| Sleep | 0.44 | 0.54* | 0.64* | 0.50 | 0.47 | 0.68* | 1 | |
| Enjoyment of life | 0.64* | 0.84* | 0.81* | 0.71* | 0.68* | 0.83* | 0.61* | 1 |

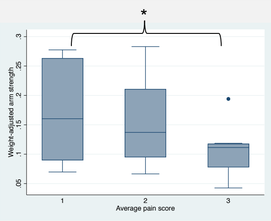


*Figure 4. Decline in strength with pain (1 low, 2 medium, and 3 high), *(p<0.05)*

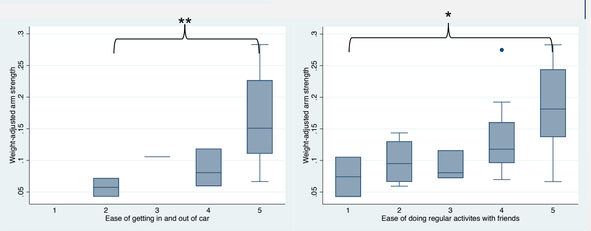


*Figure 5. Decline in strength with ability to get in and out of a car and doing regular activities with friends, * (p<0.05), ** (P<0.001)*

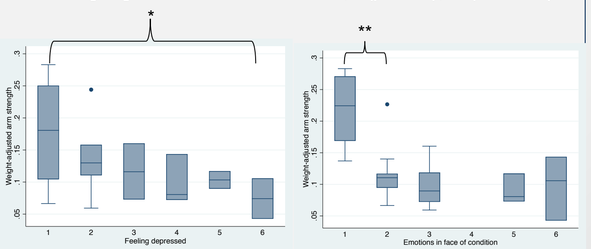


*Figure 6. Decline in strength with feeling depressed and ability to cope with condition, * (p<0.05), ** (p<0.0001)*

## CONCLUSIONS

- As expected, strength in arms and legs both decrease with age and disease progression when normalized for body weight
- Strong correlation with level of pain, general activity, mood, walking ability, normal work, relations with other people, sleep, and enjoyment of life provide an indication that these domains should be addressed from a psychosocial standpoint in regular management
- Declining strength is strongly associated with pain at later stages
- Questions regarding mobility and social activities are sensitive to changes in strength
- More work needs to be done to explore the relationships among weakness, pain, reduced social activity, and depression

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