Reliability and Validity of the Reachable Workspace Total Score with Wrist Weight in Facioscapulohumeral Muscular Dystrophy

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Conclusions:

- **The psychometric evidence supports the reliability and validity of the Reachable Workspace (RWS) as a measure of upper extremity function in FSHD (average for both arms Total Q1-Q5 score with 500g wrist weight).**
- **These findings support the use of the Q1-Q5 RWS with 500g wrist weights as an outcome measure in FSHD clinical trials. This is particularly important given the need for effective, well-validated methods to assess the impact of FSHD on patient functioning and outcomes, as well as the effects of new interventions.**

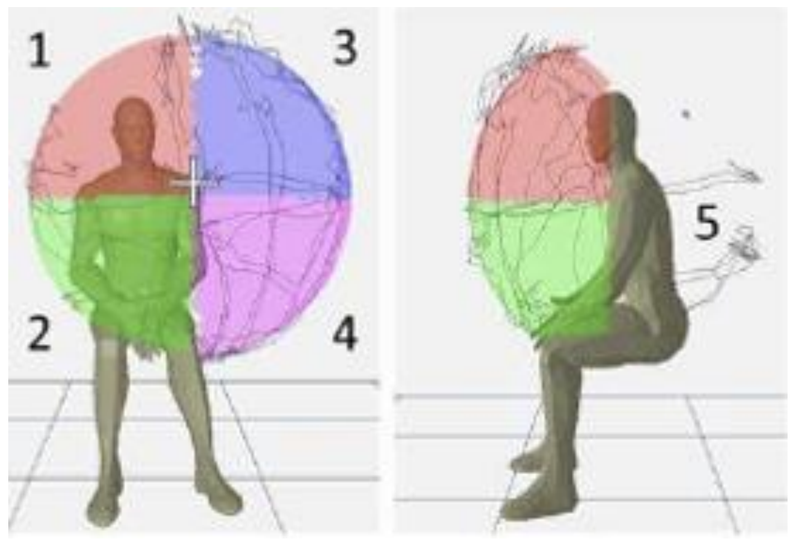
Background and Aim:

- Facioscapulohumeral Muscular Dystrophy (FSHD) is characterized by muscular degeneration leading to progressive weakness in the upper extremities, torso and legs, with approximately 20% of affected individuals eventually requiring a wheelchair.[1]
- FSHD significantly impacts daily functioning, health-related quality of life (HRQoL), and Activities of Daily Living (ADLs) due to reduced upper extremity (UE) function.[2-4]
- Patient-reported outcomes (PROs) are commonly used to assess limitations in function and ADLs. However, PROs may not fully capture real-world function due to factors like individual differences in ADLs and frequency of trial-based assessments. Thus, objective performance outcome (PerfO) measures can meaningfully complement PRO data.
- Reachable Workspace (RWS) evaluates shoulder and proximal arm mobility by utilizing a 3D motion sensor technology to calculate the reachable area (relative surface area (RSA)) across defined quadrants (originally Q1-Q4, Q5 was added later; Figure 1)[5] and is supported by psychometric evidence for RSA Q1-Q4.[6-11]
- **Aim: To extend existing evidence to demonstrate the reliability and validity of Reachable Workspace (RWS) average for both arms Total RSA Q1-Q5 with 500g wrist weight score (hereafter RSA score) in FSHD.[12]**

Methods:

- **Data sources:**
  - Baseline data from the Phase 2 ReDUX clinical trial was used to assess convergent and known-group validity, and Baseline to Week 4 data to assess test-re-test reliability.[12]
- **Outcome variables:**
  - Reachable Workspace (RWS), Timed up and go (TUG), FSHD TUG, Manual dynamometry, FSHD-Health Index (FSHD-HI) PRO, Patient's Global Impression of Change (PGIC), Ricci Clinical Severity Scale (CSS) and Musculoskeletal magnetic resonance imaging (MRI) were used for analysis.
- **Analysis:**
  - **Convergent validity:** Spearman's correlations were conducted between RSA score and all other outcome variables. Correlations were interpreted as weak ($|r|<0.3$), moderate ($|r|\geq0.3$ and $|r|<0.7$), or strong ($|r|\geq0.7$).[13]
  - **Known-groups validity:** Subjects were categorized as per Table 2. Group differences in RSA score were assessed using 2-way unpaired t-tests. Standardized effect sizes were estimated and interpreted as small (≥0.2 to < 0.5), medium (≥ 0.5 to < 0.8) and large (≥ 0.8).[14]
  - **Test-re-test reliability:** Among stable individuals (those reporting no change from baseline to week 4 on the PGIC) an intra-class correlation coefficient (ICC) was estimated to assess test re-test reliability. An ICC of ≥0.70 was considered an acceptable level of test-re-test reliability.[15]

Figure 1. Reachable Workspace (Q1 – Q5).



Results:

- **Sample characteristics:**
  - At baseline, 79 subjects were included. Subjects were on average 45.5 (SD=12.5) years old, and most subjects were male (67.0%) and white (87.0%).
- **Convergent validity:**
  - Overall, there were mostly moderate correlations between the RSA score and outcome measures (Table 1).

Table 1. Convergent validity: Correlations between average of both arms Total Q1-Q5 RSA with 500g wrist weight score and selected variables.

Outcome	N	r
FSHD-HI score		
Total Score	77	-0.28*
Subscore 2 Shoulder and Arm Function	76	-0.43***
Subscore 6 Activity Limitation	77	-0.28*
FSHD-HI items[1]	71 - 76	-0.49*** to -0.13
MRI scores		
LMV (all muscle average)	79	0.48***
MFF (all muscle average)	79	-0.54***
MFI (all muscle average)	79	-0.41***
FSHD-TUG		
Total (sec)	78	-0.66***
Supine-to-sit (sec)	78	-0.59***
Sit-to-supine (sec)	78	-0.60***
Sit-to-stand-walk-sit (sec)	78	-0.53***
Dynamometry		
All Muscles Total Average (kg)	78	0.55***
Upper Extremity Total Average (kg)	78	0.61***
Ricci CSS	79	-0.33**

*** p ≤ .05; ** p ≤ 0.01; *** p ≤ 0.001**

Key to correlation coefficients: weak: r<0.3; r>-0.3; moderate: r=0.3 to 0.7; r=-0.7 to -0.3; strong: r=0.7 to 0.9; r=-0.9 to -0.7

CSS, Clinical Severity Score; FSHD-HI, Facioscapulohumeral muscular dystrophy Health Index; LMV, Lean muscle volume; MFF, Muscle fat fraction; MFI, Muscle fat infiltration; N, Number of observations; r, Spearman's rank correlation coefficient

[1]The range of N and r are presented for the 16 FSHD-HI Items.

- **Known-groups validity:**
  - Known-groups with cell sizes > n = 10 were assessed (n = 15/16). Of those, twelve (80%) were nominally statistically different.
  - Nominally significant differences were observed for RSA score and FSHD-HI total score, and subscores.
  - Largest effect sizes were observed for MRI-based known-groups (Table 3).

Table 2. Known-groups definitions

Outcome measure	Known groups (n = 16)	
	Low severity	**High severity**
FSHD-HI Total Score/ Subscore Shoulder and Arm mobility/ Subscore Activities Limitations	Bottom 40% of observations Bottom 20% of observations < 50% items scored 4-5	Top 40% of observations Top 20% of observations ≥ 50% items scored 4-5
MRI MFF/MFI All muscles	Bottom 40% of observations Bottom 20% of observations	Top 40% of observations Top 20% of observations
MRI LMV All muscles	Top 40% of observations Top 20% of observations	Bottom 40% of observations Bottom 20% of observations
Ricci CSS	0 to 3	3.5 to 5

CSS, Clinical Severity Score, LMV, Lean Muscle Volume; MFF, Muscle Fat Fraction, MFI; Muscle Fat Infiltration

Table 3. Known-groups validity: Average of both arms Total RSA Q1-Q5 with 500g wrist weight score.

Known groups	ES	P Value*
FSHD-HI Total		
Bottom 40% (low severity) vs. top 40% (high severity) of observations	**0.67**	**0.011**
Bottom 20% (low severity) vs. top 20% (high severity) of observations	**0.68**	0.064
FSHD-HI Subscore 2 Shoulder and Arm Function		
Bottom 40% (low severity) vs. top 40% (high severity) of observations	**0.81**	**0.002**
Bottom 20% (low severity) vs. top 20% (high severity) of observations	**1.08**	**0.006**
<50% items scored 4-5 (low severity) vs. ≥50% items scored 4-5 (high severity)	**0.62**	**0.021**
FSHD-HI Subscore 6 Activity Limitations		
Bottom 40% (low severity) vs. top 40% (high severity) of observations	**0.63**	**0.02**
Bottom 20% (low severity) vs. top 20% (high severity) of observations	**0.94**	**0.01**
<50% items scored 4-5 (low severity) vs. ≥50% items scored 4-5 (high severity)	0.31	0.31
MRI LMV		
Top 40% (low severity) vs. bottom 40% (high severity) of observations	**1.02**	**<0.001**
Top 20% (low severity) vs. bottom 20% (high severity) of observations	**2.12**	**<0.001**
MRI MFF		
Bottom 40% (low severity) vs. top 40% (high severity) of observations	**1.39**	**<0.001**
Bottom 20% (low severity) vs. top 20% (high severity) of observations	**1.46**	**<0.001**
MRI MFI		
Bottom 40% (low severity) vs. top 40% (high severity) of observations	**1.14**	**<0.001**
Bottom 20% (low severity) vs. top 20% (high severity) of observations	**1.15**	**<0.001**
Ricci CSS		
0 to 3 (low severity) vs. 3.5 to 5 (high severity)	**0.58**	0.16

***P-value: nominally statistically significant at .05 level**
Purple = medium ES; Green = large ES; Red = Significant P-Value
CI, Confidence interval; FSHD-HI, Facioscapulohumeral muscular dystrophy Health Index; ES, Effect size; LMV, Lean muscle volume; MFF, Muscle fat fraction; MFI, Muscle fat infiltration; N, Number of observations; RSA, Relative surface area; RWS, Reachable workspace; SD, Standard deviation

Test-re-test reliability:

- Subjects with No change (4) on PGIC from baseline to week 4 (n=54) had a mean Q1-Q5 RSA score of 0.572 (SD=0.251) at baseline and 0.570 (SD=0.259) at week 4; the average difference was -0.002. The test-retest-reliability ICC for the Q1-Q5 RSA score was 0.98, suggesting almost perfect agreement.

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Disclosures:

LH and SHL are employees of Acaster Lloyd Consulting and may hold stock or stock options in the company. SA is a company director of Acaster Lloyd Consulting.
AEL and JJ are employees of Fulcrum Therapeutics and may hold stock or stock options of Fulcrum Therapeutics.
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