Quantitative Muscle Analysis Measurements in Low Disability Multiple Sclerosis

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INTRODUCTION

Multiple Sclerosis patients with minimal disability commonly experience motor fatigability not appreciated during standard neurological assessment, which can nevertheless be severely limiting. Quantitative Muscle Analysis (QMA) using strain gauges with computer-assisted technology can be used to sensitively measure strength and motor fatigue. Using similar methodology, people with MS and moderate disability have previously been shown to have significantly greater motor fatigue as compared to healthy volunteers (HV).

HYPOTHESIS

QMA will detect measurable differences in static fatigue between subjects with MS and low disability and HV.

Force vs Time of Grip/Knee Extension

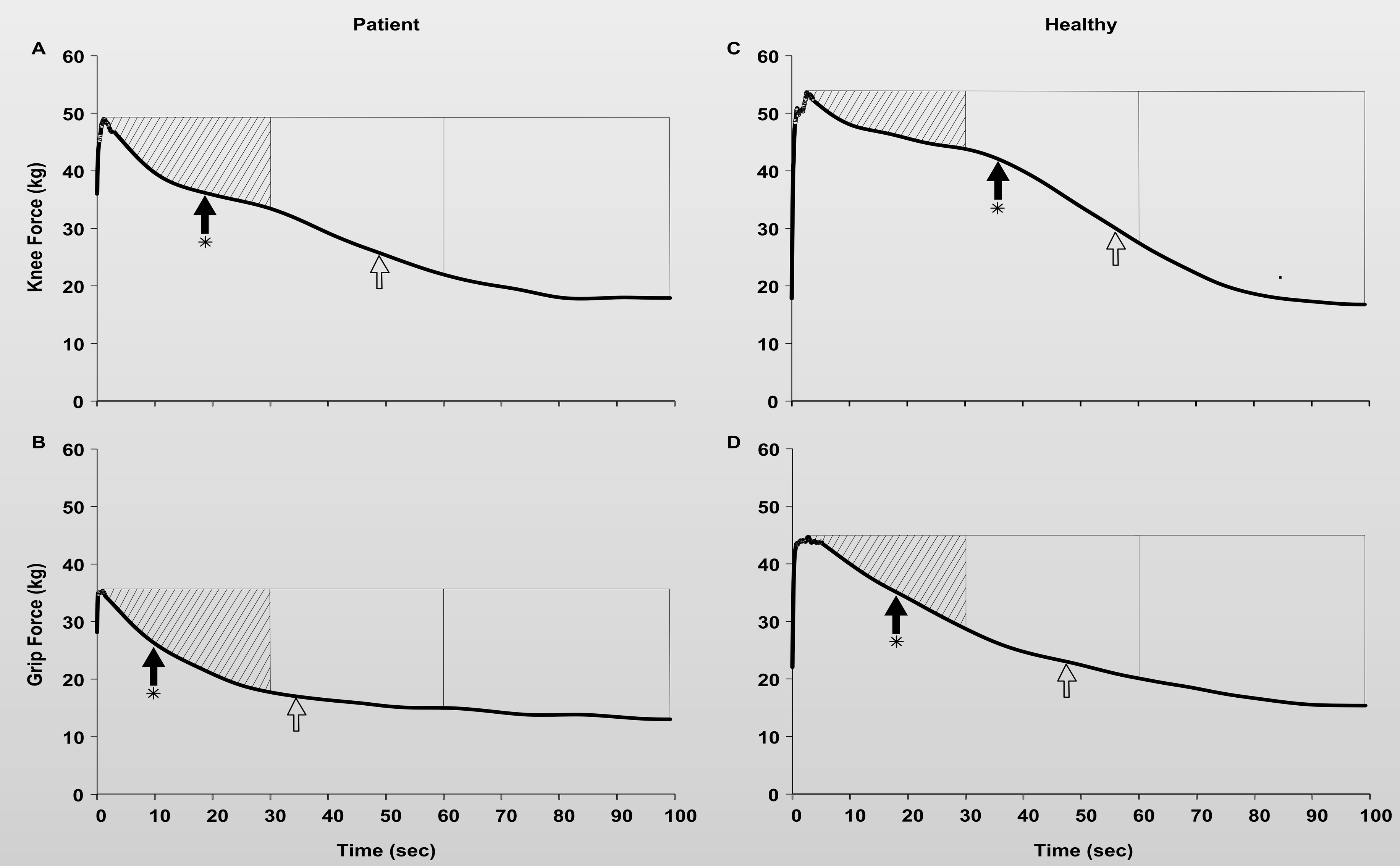


Figure 1: *Average force-versus-time curves generated during 100 second max SFT for knee extension and grip in patients and healthy controls. Dash markings (FI peak -30) and asterisks (exht 25,50) highlight significant differences between groups. The upward pointing arrows represent the 25% (black) and 50% (white) exhaustion times.*

Max Force/SFT of MS vs HV

Strength and effort measures	Patient	Healthy	P-value
Knee MVIC, kg	52.1 ± 12.8	54.8 ± 18.5	.718
Knee MVIC predicted, %	96.4 ± 21.6	102.4 ± 28.2	.609
Knee SFT effort, %	98.3 ± 8.2	104.9 ± 17.4	.323
Grip MVIC, kg	40.1 ± 6.9	47.5 ± 6.6	**.030**
Grip MVIC predicted, %	86.2 ± 14.0	101.0 ± 15.9	**.045**
Grip SFT effort, %	93.8 ± 14.2	98.6 ± 3.2	.317

Table 2: Maximum voluntary isometric contraction values, predicted values and static fatigue testing effort. Values displayed as average ± standard deviation.

Fatigue Index, Exhaustion Time, Slope

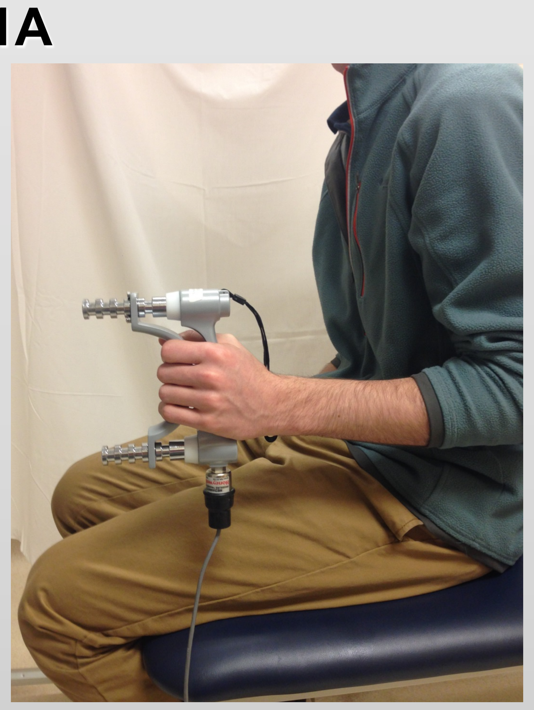
Fatigue-related measures	(Knee) Patient	(Knee) Healthy	(Knee) P-value	(Grip) Patient	(Grip) Healthy	(Grip) P-value
FI peak – 30	24.7 ± 5.4	15.7 ± 5.6	**0.002**	34.8 ± 6.8	22.5 ± 5.3	**0.000**
FI 5-30	27.1 ± 6.2	17.0 ± 6.3	**0.003**	38.9 ± 7.5	24.4 ± 6.4	**0.000**
FI 30-60	46.5 ± 9.3	34.5 ± 18.5	0.104	56.5 ± 8.9	49.4 ± 8.6	0.097
FI 60-100	62.1 ± 9.4	63.4 ± 14.8	0.818	62.4 ± 9.4	63.9 ± 7.0	0.695
Time to peak	1.52 ± 0.86	2.00 ± 1.14	0.310	0.67 ± 0.53	2.40 ± 1.85	**0.024**
Exht-25	17.9 ± 11.3	36.1 ± 18.6	**0.025**	9.6 ± 5.9	17.7 ± 5.8	**0.008**
Exht-50	49.3 ± 14.2	55.7 ± 15.0	0.384	33.7 ± 22.7	47.0 ± 13.0	0.143
Slope 5-30	-0.37 ± 0.18	-0.26 ± 0.39	0.415	-0.50 ± 0.22	-0.59 ± 0.21	0.371
Slope 30- 60	-0.39 ± 0.22	-0.57 ± 0.45	0.277	-0.09 ± 0.09	-0.27 ± 0.11	**0.001**
Slope 60-100	-0.10 ± 0.13	-0.26 ± 0.18	**0.032**	-0.05 ± 0.06	-0.13 ± 0.09	**0.029**

Table 3: Between group comparison of fatigue-related measures on grip and knee extensor muscle groups. Values displayed as average ± standard deviation.

METHODS

10 male subjects with MS and low disability (EDSS 1-2.5) and 10 age/gender-matched HV participated in this study. The subjects with MS were highly functioning and physically active but reported experiencing motor fatigue when performing intense physical activity. QMA was used to test participants' handgrip and knee extensor muscle strength on the dominant side. Maximal voluntary isometric contraction (MVIC), a measure of strength, and static fatigue test (SFT), a measure of motor fatigue, were calculated for each muscle group.

1A



1B

QMA testing for evaluating grip strength (1A) and knee extension strength (1B)

Study Participants

Participant characteristics	Patient (Average)	Patient (Range)	Healthy (Average)	Healthy (Range)	P-Value
Age, y	40.5 ± 8.9	(27 – 60)	41.0 ± 8.8	(25 – 58)	0.901
Disease Duration, y	8.1 ± 3.7	(2 – 12)	-	-	-
EDSS, median	1.8 ± 0.5	(1.0 – 2.5)	-	-	-
Height (cm)	176.0 ± 6.3	(170 – 192)	181.1 ± 7.1	(172 – 195)	0.091
Weight (kg)	84.8 ± 11.2	(69.5 – 103.0)	82.1 ± 14.7	(66.0 – 116.0)	0.657

RESULTS

- Grip strength in subjects with MS was weaker than matched controls, but within normal range compared to a normative reference group. There were no group differences in knee extension strength. These results indicate the individuals with MS were not weak. (Table 2)
- Motor fatigability was significantly greater in subjects with MS compared with healthy subjects for knee and grip during the first 30 seconds of sustained contraction. (Figure 1)
- Subjects with MS began to fatigue significantly earlier than healthy subjects during knee and grip contractions; 50% exhaustion time was reached earlier in subjects with MS however this did not reach statistical significance. (Figure 1)
- Initial time to reach maximum contraction was significantly shorter for subjects with MS compared to healthy subjects in the grip muscles, but not in knee extensors. (Table 3)
- No significant correlations were seen between MVIC and FI at the knee extensors (r= -0.38, p= 0.11) or at the grip muscles (r= -0.32, p= 0.18), indicating that, in our cohort, strength and fatigue were not associated.

CONCLUSIONS

Our findings suggest that static muscle fatigue measurements may be useful to detect motor impairments before substantial muscle weakness or disability emerges, potentially signaling an opportunity for earlier intervention. These subclinical motor deficits may explain the subjective difficulties in performing at previously attained levels reported by some patients. QMA-derived SFT may be a useful biomarker to predict functional prognosis or track disease progression as it relates to long-term disability. Such instrumented measures of function may prove useful for targeted rehabilitation interventions as well as outcomes measures in clinical trials.