Resistance Strength Training Exercise in Children with Spinal Muscular Atrophy

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ABSTRACT

Introduction: Preliminary evidence in adults with spinal muscular atrophy (SMA) and in SMA animal models suggests exercise has potential benefits in improving or stabilizing muscle strength and motor function.

Methods: We evaluated feasibility, safety, and effects on strength and motor function of a home-based, supervised progressive resistance strength training exercise program in children with SMA types II and III. Up to 14 bilateral proximal muscles were exercised 3 times weekly for 12 weeks.

Results: Nine children with SMA, aged 10.4±3.8 years, completed the resistance training exercise program. Ninety percent of visits occurred per protocol. Training sessions were pain-free (99.8%), and no study-related adverse events occurred. Trends in improved strength and motor function were observed.

Conclusions: A 12-week supervised, home-based, 3 days/week progressive resistance training exercise program is feasible, safe, and well tolerated in children with SMA. These findings can inform future studies of exercise in SMA.

Key Words: spinal muscular atrophy, neuromuscular disorder, progressive resistance training exercise, home-based exercise program, strength training exercise.

INTRODUCTION

Spinal muscular atrophy (SMA) is a progressive neuromuscular disorder characterized by decreased muscle strength and motor function due to degeneration of motor neurons in the spinal cord and brainstem. [1] The clinical spectrum in affected individuals varies widely from severe generalized weakness (SMA types I and II) to modest proximal muscle weakness (SMA types III and IV). [2-4] In spite of considerable heterogeneity, most patients with SMA have markedly reduced muscle strength. [5, 6] A representative study demonstrated that SMA subjects have only ~ 5% of predicted age/gender reference values for knee extensor strength and ~ 20% of predicted strength for knee, elbow, and finger flexors. [7] Most studies in patients with SMA types II and III with a 12-month or shorter observation period show overall stability in measures of strength. [8, 9] However, studies with longer follow-up periods clearly demonstrate progressive muscle weakness and motor disability. [3, 4, 7, 10-13]

A number of studies have reported an association between strength and motor function in SMA. [7, 9, 14-16] At least 70% of patients with SMA type II and 40% of patients with type III require assistance with self-care, and 90% with type II and 60% with type III require assistance with mobility. [10] A wealth of data supports that strength and function decrease over time, muscle strength is associated with motor function, and change in strength correlates with change in function in individuals with SMA types II and III.

Historically, patients with neuromuscular disorders (NMD), including SMA, have been advised to avoid strenuous physical activity to avoid possible further muscle damage and to preserve their remaining strength. [17-20] However, over the past 2 decades, studies in both animal models and humans with motor neuron disease suggest that strength training is not only safe, but potentially beneficial. [21-34] Grondard et al. trained neonatal mice expected to develop an SMA phenotype to run on a wheel for

progressively longer durations and at faster speeds. [34] Exercise-trained mice, compared to those without such training, had a mean increase in survival, improved motor function, reduced muscle atrophy, and a lower rate of neuronal apoptosis and neuronal death in the ventral horn of the spinal cord. This study provided the first compelling evidence for the potential benefit of exercise on lifespan, motor function, and severity in the SMA phenotype. Clinical studies in human subjects are limited. However, 3 clinical studies that include adults with SMA (along with adults with other types of NMD) have reported improved muscle strength and motor function after resistance training exercise programs. [23, 27, 28] Muscle strength increased from 2%-83% without excessive soreness or fatigue, suggesting that resistance exercise was well tolerated and could result in increased strength in some subjects with NMD.

SMA has substantial morbidity and mortality, a significant effect on quality of life, and as yet, no proven disease-altering treatments. [35] Since individuals with SMA lose strength and function over time, younger patients with SMA have better strength and motor function than older ones. [3, 4, 7, 10, 11, 36] As a result, an earlier intervention is likely to be more effective than one later in the disease course. A progressive resistance training (PRT) exercise program has the potential to increase strength and improve motor function in children and young adults with SMA. PRT requires that muscles contract against an opposing force generated by some type of resistance (e.g., body weight, resistance bands, free weights) and involves a systematic increase in resistance training parameters to improve an individual's ability to exert force. [37, 38] Based on evidence from numerous medical, fitness, and sport organizations, PRT is a safe and effective form of exercise in healthy children as young as age 5 years. [37-42] In addition, a few studies have explored PRT in children with cerebral palsy [43] and Charcot-Marie-Tooth disease. [44] Widely accepted PRT recommendations in pediatrics include providing supervision,

targeting all major muscle groups, including a warm-up and cool-down period, and performing 2-3 sets of 8-15 repetitions. [37, 40, 41, 45]

Clinicians do not encourage patients with SMA to participate in PRT [46, 47] due to the lack of definitive literature disputing the long-standing concern of performing PRT in NMD. Therefore, further research is needed. The purpose of this pilot study was to examine the feasibility, safety, and effects of a PRT exercise program in a cohort of children and young adults with SMA. Our hypothesis was that children and adolescents with SMA types II and III could safely participate in and adhere to a 12-week, home-based, supervised PRT exercise program. Such preliminary data are a critical first step toward future studies to determine whether exercise programs such as PRT can help maintain or improve function in children with SMA.

MATERIALS AND METHODS

Participants

This was an observational study of a cohort of SMA patients recruited from an existing natural history database. Approval was provided by the Institutional Review Board at the University of Utah. Study inclusion criteria were: (1) ages 5-21 years; (2) diagnosis of SMA type II or III; (3) some antigravity strength in elbow flexors (EF), and (4) place of residence within a 60-minute, or 60-mile, drive of the University of Utah. (NCT01233817) Exclusion criteria were: (1) planned surgery or out-of-town trips during the proposed PRT intervention period; (2) inability to travel to study center for testing; and (3) neurological diagnosis other than SMA. Written informed consent (for participants ≥18 years), parental consent (for participants <18 years) and assent (for participants ≥7 years) were obtained from all participants.

Measures

Feasibility. Feasibility was assessed by measuring: 1) the number of patients

willing to participate (percentage of participants enrolled/participants recruited); 2) the fidelity of treatment (number of sessions that occurred according to study protocol/total number of sessions); 3) the ability for participants to achieve target perceived exertion levels using the Children's OMNI-Resistance Exercise Scale of perceived exertion [65]; and 4) the ability of participants to progress the exercise workload by calculating the change in resistance (weights secured at the ankle or at the wrist) from the first to last treatment during which target perceived exertion was achieved consistently. The Children's OMNI-Resistance Exercise Scale consists of pictorial and corresponding descriptors depicting a child “weight lifter” positioned along a 0-10 intensity gradient. It has demonstrated concurrent validity (r=0.72 to 0.88) in 10-14 year old females and males performing upper and lower body resistance exercise. [65]

Safety. Safety was assessed in the home setting by physical therapists administering the intervention and included: (1) monitoring strength every 2 weeks using hand-held dynamometery (HHD) of EF for all participants and KE for ambulatory participants; (2) monitoring pain with the Wong-Baker FACES Pain Scale during every session at 3 distinct times for each exercised muscle group (immediately after completing each set, at least 5 minutes after completing each set, and 2-3 days post exercise); and (3) recording caregiver responses to questions about adverse effects at every session. The Wong-Baker FACES Pain Rating Scale is among the most widely used and best-validated faces pain scale. The FACES scale is preferred by children, can be used for children as young as age 3 years, and has been validated in children with acute pain (Spearman correlation = 0.90). [66, 67]

Motor assessments were performed at baseline, 6-weeks, and 12-weeks. The majority of the assessments were performed by 2 physical therapists working in a hospital-based clinic, both of whom administer the outcome measures regularly as part

of an ongoing SMA natural history study and who administered the outcome measures as part of a previous clinical drug trial in SMA. [48] Strength assessment schedules varied depending on the measure collected. Quantitative muscle analysis (QMA) and HHD were administered twice at baseline; manual muscle testing (MMT) was administered only once at baseline. QMA was performed by a single physical therapist evaluator who was trained and supervised by an investigator (EG) with substantial experience using this technique in children with NMD. Two physical therapist evaluators who were trained and experienced in using HHD performed all HHD assessments. MMT was always carried out at the participants' homes by the physical therapists providing the home-based intervention. MMT definitions were reviewed with all therapists and included in their study binders.

Strength. Strength was assessed using 3 different measures: (1) QMA; (2) HHD; and (3) MMT. Maximum voluntary isometric contraction (MVIC), measured using both QMA and HHD, has been used to assess muscle strength quantitatively in clinical trials of NMD, including SMA. [6, 14, 49-58] MMT is a clinical tool performed as part of the routine neurological exam and does not require extensive training. It is a practical outcome measure in multicenter neuromuscular disease trials and has also been used in studies of SMA. [5, 11, 12, 15, 59-61]. Upper extremity strength of shoulder flexors (SF), shoulder extensors (SE), elbow flexors (EF), and elbow extensors (EE) was assessed in all participants. Additionally, ambulatory participants underwent lower extremity strength assessments of the hip flexors (HF), hip extensors (HE), and knee extensors (KE). Strength was assessed in all listed muscles with QMA [56] and MMT,[62] and in EF and KE with HHD, [49, 51] using previously described protocols. Inter-session reliability of QMA and HHD was assessed at baseline by measuring strength at 2 separate visits, 1 week apart to assure intra-rater reliability for the remainder of the study.

Motor Function. Motor function was assessed utilizing the Modified Hammersmith Functional Motor Scale-Extend (MHFMS-Extend). The scale has established validity (r=0.73), has a high intra-class correlation coefficient (ICC=0.93) demonstrating excellent test-retest reliability, and allows participation of higher functioning children with SMA in clinical trials. [51, 63] The MHFMS-Extend is designed for assessment of motor function specifically in the SMA population while incorporating typical gross motor development into the measurement tool. The scale consists of 20 original items (MHFMS) [64] plus 8 additional higher-level gross motor items (Extend), and each item is scored on a 3-point ordinal scale: 2 for unaided, 1 for assistance, 0 for unable. The total score can range from 0 if the child is unable to perform any of the items to 56 if the child can complete all tasks independently. All items are administered without thoracic or lower extremity orthotics and can be completed in 15 to 30 minutes. Scale administration and scoring criteria for the MHFMS-Extend are described in detail at www.smaoutcomes.org.

Intervention

Design of the study PRT exercise program adhered to widely accepted PRT recommendations for children. [37, 39-42, 68] In addition, the study followed the American College of Sports Medicine guidelines for an individualized PRT program for healthy adults; [69] incorporated NMD-specific recommendations for exercise study duration, supervision, and key outcome measures; [70] and compared favorably with the duration periods of previous resistance training exercise studies in NMD. [23, 27, 28] Participants began the PRT exercise program within 4 weeks following completion of baseline evaluations. The intervention was a 12 consecutive week, home-based program supervised by a physical therapist. Six physical therapists delivered the intervention. The study protocol was reviewed with all therapists, and each was provided a study

binder containing all necessary study materials for the duration of the study. Treatment integrity between the 6 therapists was evaluated by regular review of the session exercise logs by the study PI. Exercise sessions lasted 45-60 minutes, starting with a 5-minute warm up and ending with a cool down. Participants exercised 3 times weekly on non-consecutive days and performed 2 sets of 15 repetitions (reps). A recovery period of at least 5 minutes occurred between the first and second sets.

All participants exercised the SF, SE, EF, and EE. Additionally, ambulatory participants exercised lower extremity muscles including the HF, HE, and KE. Proximal muscles were exercised, as they are weaker in SMA. Resistance was achieved using ankle and wrist weights, body weight, or variation in the position or level of assistance provided. The physical therapist set up the appropriate exercise equipment and identified a location for the exercises. Strength of the muscle groups to be exercised was assessed using MMT on the first visit. The therapist choose an appropriate weight and exercise position based on MMT results and instructed the participant in the starting position for each exercise. Possible positions for exercises included supine, prone, side lying, sitting, and standing. Some exercises were modified using a sliding board for training of weaker muscles. The exercises were performed without weights first for at least 1 week. Once a participant was able to properly complete 2 sets of 15 reps, resistance was added. Free weights were attached to the distal limb at the wrist and ankle. Each exercise was progressed by adding a weight in as small as 0.08kg increments. Weight increased until the participant scored a 6/10 rating (somewhat hard) or 8/10 (hard) on the Children's OMNI-Resistance Exercise Scale of perceived exertion at the end of the second set. Therefore, a portion of the 12-week intervention was intended to identify the resistance, or weight lifted, that appropriately challenged the

participant per study protocol. The child continued to exercise that muscle group using the higher weight for at least 1 week prior to increasing the weight again.

The physical therapist recorded the weight lifted, position, sets, reps, and rest time for each muscle group exercised at each session. Physical exertion, and pre- and post-exercise pain score were reported after each set for each muscle. Compliance with the program and reports of any adverse events were also recorded at each session. The study coordinator and principal investigator followed up on all concerns and events. An independent data and safety monitor and principal investigator reviewed safety data regularly. A parent was present during all sessions for participants under age 18 years.

Outcome Measures

Feasibility and Safety. Treatment fidelity, the percentages of patients willing to participate, progression of exercise workload (weight lifted), reported pain, and perceived exertion were used to determine feasibility and safety. Change in exercise workload was calculated by subtracting the value of the weight used in the first session where the child lifted a weight that resulted in the target perceived resistance from the value of the weight used in the last session for each muscle exercised. One participant was not able to lift weights secondary to weakness, and thus changing the position from against gravity to gravity eliminated reduced the exercise workload and allowed participation. A second participant's perceived exertion was recorded incorrectly. Results from these 2 participants were not included in analysis of change in exercise workload. A composite weight progression score was calculated by adding the values from each exercise from both sides of the body. Counts of pain ratings and adverse events were used for statistical analysis. HHD of EF and KE were assessed in the participant's home

every 2 weeks by the physical therapists administering the exercise program, thus providing an additional safety measure.

Strength and Motor Function. An upper extremity composite score, a lower extremity composite score, and a total composite score were calculated for all strength measures. The upper extremity score was calculated by adding SF, SE, EF, and EE values from both sides. The lower extremity strength composite score was calculated by adding HF, HE, and KE values from both sides. The total composite strength score was calculated by adding the upper extremity and lower extremity composite scores. MMT scores that were not standard numbers were assigned the following numerical values prior to analysis to provide monotonic increasing equal intervals between scores: 2- = 1.67; 2+ = 2.33; 3- = 2.67; 3+ = 3.33; 4- = 3.67; 4+ = 4.33; 5- = 4.67. The average of 2 baseline values was used when more than 1 was available for QMA and HHD, and data from week 6 were used if any week 12 data were missing for participants.

Test-Retest Reliability of QMA and HHD. Participants completed baseline measures twice over 2 non-consecutive days prior to starting the study intervention. The second baseline evaluation occurred within 1.1 ± 0.6 weeks of the first. Having 2 baseline measurements from the same rater permitted calculation of the test-retest intra-rater reliability.

Statistical Analysis

A mixed effects linear regression model was used to analyze changes in composite measures of strength (HHD, QMA, MMT) and motor function (MHFMS-Extend) over time. The mixed effects model was specified with a random intercept, and unstructured correlation structure among the repeated measurements nested with participants. Change in exercise workload and perceived exertion from the first session

in which target exertion was reached using weights to the last session were compared using paired *t*-tests. ICCs were used to examine test-retest reliability of QMA and HHD. Data were analyzed using SAS 9.2 (SAS Inc., NC, USA). All *P*-values are from two-sided comparisons.

RESULTS

Participants. Sixteen children with SMA types II or III who lived locally were identified in the natural history database. Eleven children enrolled in the study. Two participants dropped out after completion of the baseline assessment and prior to start of PRT, one to undergo scoliosis surgery and the other due to lack of reliable transportation. Nine children (56% of those identified) completed the study. Demographic characteristics are described in Table 1.

Feasibility. All procedures were followed in accordance with the standards of the local institutional review board. Of 323 scheduled PRT sessions, 290 (90.4%) occurred per protocol, 24 (7.4%) did not occur, and 9 (2.2%) occurred but deviated from protocol. Reasons for missed PRT sessions included: participant out of town, participant or family sick, no physical therapist available, car problems, participant too busy, family did not hear doorbell, and physical therapist family emergency, in descending order of frequency. Reasons for deviations from protocol included: physical therapist forgot warm-up, shorter visit due to family schedule, participant refusal, and only 1 set performed due to patient fatigue.

An average of 4 weeks was needed to identify a starting weight that resulted consistently in target exertion level for each exercise. The average time period during which participants were using weights and reaching target exertion consistently was 8.1 (0.3) weeks. During this period, participants were able to progress the exercise workload

by increasing the weight lifted. (Table 2) The average amount of weight lifted by the participants as a group increased significantly (P<0.001) by 0.27 (0.05) kg, while the perceived exertion level remained unchanged (P=0.76).

Safety. Pain was perceived as a score of zero (absent) 99.5% of the time on the Wong-Baker faces pain scale. Nonzero scores ranging from 1/10 to 4/10 occurred on 8 exercise occasions. Seven of the nonzero scores occurred in the same study participant, with the remaining 1 nonzero score in a second participant. The EF and KE measured by HHD at home fluctuated from 1 measurement to the next but did not demonstrate loss of strength over time. Lastly, no study-related adverse events occurred during the PRT intervention period.

Strength. Strength was assessed using 3 measures, QMA, HHD, and MMT. A significant change was found in MMT total composite score, a non-significant increase in QMA, and no change in HHD. (Figure 1) Mean MMT scores at baseline ranged from an MMT score of 2 to 4- for non-ambulatory participants, and 2+ to 4+ for ambulatory participants. MMT upper extremity composite score increased by 2.7 (P=0.03), and MMT total composite scores increased by 3.3 (P=0.01). This significant change was attributed to increased strength of the SF, SE, and EF. QMA total composite score increased by 5.7 kg.

Motor function. MHFMS-Extend scores increased significantly (P=0.04). Mean baseline scores were 30.0 (SD, 17.7) and increased 2.0 (0.9) points to 32.0 (16.4) points at 12-weeks. Five participants had an increase in MHFMS-Extend scores, 2 had a decrease in scores, and 1 had no change in score from baseline to week-12.

Test-retest reliability of QMA and HHD. The test-retest reliability of QMA was high for all muscles (ICC=0.86 to 1.00 for 12 muscles) except for 2 lower extremity muscles (ICC=0.52 and 0.88) (Table 3). Test-retest reliability of HHD was high for

bilateral EE (ICC= 0.98 and 1.00), although it was not calculated for KE, since data were collected on only 2 participants.

DISCUSSION

Our purpose was to evaluate the safety and feasibility of a 12-week, home-based, supervised, 3 day/week PRT exercise program in children with SMA types II and III. All 9 participants who started the PRT exercise program completed it, with over 90% compliance to scheduled PRT sessions. This level of adherence is notable given the participants' time commitment as well as the large amount of coordination needed between participants, therapists, and study team members. Safety was a concern in performing a PRT program in children with SMA, since strengthening interventions have not been used in routine clinical practice and the effects of strengthening on children with significant weakness due to motor neuron disease was unknown. Therefore, we were pleased to find that PRT training was safe and well tolerated in this cohort.

Measures that supported exercise safety included: pain ratings (absent 99.5% of time), perceived exertion (unchanged throughout study), counts of adverse events (none noted), and the ability of participants to progress exercise load. There were no changes in HHD from pre- to post-PRT. While HHD was measured every 2 weeks by the physical therapist administering the PRT, there were several biases that likely influenced the usefulness of this data as a bi-weekly measure of safety. Biases included minimal training, lack of blinding, lack of reliability testing, technology malfunction, and variation in time, fatigue, and child effort. The perceptions of the parent, child, and therapist that strength did not decline could be validated with objective data in future studies. Limitations discovered in this study could be addressed with additional HHD training, mechanisms to minimize technical issues with the equipment, or by using a reliable measure such as QMA.

The most challenging part of the PRT intervention was to adapt the degree of resistance to the weakness of the pediatric SMA population. Healthy children work out with loads between 60% and 80% of the 1-repetition maximum (1RM). Training loads are usually determined by either taking a specific percentage of the 1RM, or by performing a multiple-RM testing. [37] However, obtaining an RM measure via repeated testing on children with weakness whose muscles fatigue was not feasible. Instead, we used the Children's OMNI-Resistance Exercise Scale to assess perceived exertion. This approach to quantifying effort in SMA proved feasible and resulted in achievement of an exertion level of at least *somewhat hard* 87% the time, and of *hard* 62% of the time during the weeks that the patients were increasing weights. In comparison, across the entire 12 weeks period, participants reached an exertion level of at least *somewhat hard* 79% the time, and of at least *hard* 55% of the time.

Additionally, we evaluated the effects of PRT on strength and motor function. There were no significant changes in strength between baseline and 12 weeks as measured by QMA and HHD. While the changes in muscle strength were relatively modest in these very weak patients, the trends toward small improvements in strength are not inconsequential. Therapists and other health care providers have been reluctant to recommend PRT due to concerns regarding potential loss of strength or injury. These findings are in contrast to decreases or stability in strength over time reported by others, [11, 12, 15] thus lending support to PRT as an intervention with promise. There was significant improvement in motor function with a small and variable mean increase of 2 points on the MFHSFS-Extend. These changes may have reflected variability in testing using the MHFMS, which can vary ± 2 points (SEM). Although an increase of 2 points on the MHFMS-Extend has questionable clinical relevance, some patients did achieve meaningful improvements in motor function. As an example, 1 ambulatory participant could not climb and descend 4 steps at baseline, and by week 12 of PRT the participant

achieved the ability to perform this task independently and safely. Since the intervention did not include functional task practice, the observed increase in motor function was not anticipated. KE and HF strength increased bilaterally in this participant on QMA, and increased strength may have contributed to improvement in stair walking. Although it is interesting to speculate, given these observations, clearly more studies are needed to evaluate for definite effects of PRT in this patient population, as well as possible correlations between improvements in strength and function.

This was a prospective pilot study with a number of potential limitations, including a small number of participants from a single geographic location, clinical variability (participants included children with both SMA types II and III), a lack of reported reliability and unbiased evaluators for MMT, and no control group inherent in a pilot study. We had a limited number of participants, but the specificity of the program, the close follow up, home visits, and high rate of completion are all strengths of this study. The increased attention and interaction with therapists on a weekly basis in this setting is also likely to have influenced performance. In addition, day-to-day and time-of-day variability in fatigue in this patient population may have affected energy and endurance at the time of PRT intervention. A larger group of subjects with SMA, follow-up over a period longer than 3 months, a control group, and further quantification of physiologic impact of exercise and exercise capacity in those with SMA are recommended to further validate our finding**s**. In typically developing children, a greater number of training sessions per week are associated with higher strength gains after resistance training, and longer training interventions are more beneficial than similar programs of shorter duration. [37] It is currently unknown how affected motor neurons and muscles of children with SMA react to exercise of varying duration and intensity. These issues are of considerable interest for future studies of exercise in SMA.

CONCLUSIONS

This study demonstrated feasibility and tolerance for progressive resistive exercise, without any evident decline in muscle strength or motor function, by a small group of children and adolescents with SMA. While the clinical significance of the limited improvements in strength and motor function observed in this pilot study remains unclear, the potential long-term benefit of any improvements in strength and motor function is clear. By providing additional reassurance that exercise can be performed safely without risk of harm, we hope this pilot encourages additional, larger studies on this important topic.

Table 1. Participant demographics (N=9).

Demographic	Count
Age mean (SD)	10.4 (3.8) years
Gender	Female = 5 Male = 4
Race	White non-Hispanic = 6 Other = 3
SMA Type	Type II = 6 Type III = 3

SD, standard deviation; SMA, spinal muscular atrophy

Table 2. Change in weight lifted (kilograms) and perceived exertion level (0-10 scale) between the first and last exercise sessions.

Muscle group	Weight Lifted mean (SD) [95% CI]	*P*-value	Perceived Exertion mean (SD) [95% CI]	*P*-value
R Shoulder Flexors	0.14 (0.14) [0.05, 0.27]	0.02	0.4 (1.0) [-0.5, 1.3]	0.29
L Shoulder Flexors	0.14 (0.18) [0.0, 0.32]	0.07	-0.4 (1.6) [-1.9, 1.1]	0.51
R Elbow Flexors	0.32 (0.18) [0.18, 0.45]	<.001	0.4 (1.9) [-1.2, 2.0]	0.6
L Elbow Flexors	0.36 (0.18) [0.23, 0.50]	0.001	0.9 (1.9) [-0.9, 2.6]	0.27
R Elbow Extensors	0.32 (0.18) [0.14, 0.45]	0.004	-1.0 (2.1) [-2.9, 0.9]	0.25
L Elbow Extensors	0.32 (0.23) [0.09, 0.54]	0.02	-0.7 (1.7) [-2.3, 0.9]	0.31
R Hip Flexors .and Extensors	0.18 (0.23) [-2.00 , 2.31]	0.5	-1.5 (0.7) [-7.9, 4.9]	0.2
L Hip Flexors and Extensors	0.36 (0.00) [0.36, 0.36]	NA	-1.0 (0.0) [-1.0, -1.0]	NA
R Knee Extensors	0.23 (0.18) [-1.22, 1.68]	0.3	0.0 (0. 0) [0.0, 0.0]	NA
L Knee Extensors	0.14 (0.18) [-1.32, 1.54]	0.5	-1.5 (0.7) [-7.9, 4.9]	0.2

SD, standard deviation; CI, confidence interval, R, right; L, left, NA = not available no variability in data.

Table 3. Test-retest reliability of QMA assessments from first to second baseline.

Muscle group	N	ICC
Shoulder Flexors	8	0.95 to 0.99
Shoulder Extensors	8	0.85 to 0.97
Elbow Flexors	9	0.86 to 0.96
Elbow Extensors	8	0.94 to 0.97
Hip Flexors	3	0.52 to 0.88
Hip Extensors	3	0.99 to 1.00
Knee Extensors	3	0.75 to 0.88

QMA, quantitative muscle analysis; ICC, Intra-class correlation coefficients.

Figure legend

Figure 1. The average change, with a 95% confidence interval, in muscle strength over time calculated using composite scores of quantitative muscle analysis (kilograms), hand-held dynamometry (kilograms), and manual muscle testing (numerical values), as well as average change in motor function over time using the Modified Hammersmith Functional Motor Scale-Extend (scores)

QMA, quantitative muscle analysis; HHD, hand held dynamometry; MMT, manual muscle testing; MHFMS-Extend, Modified Hammersmith Functional Motor Scale-Extend.

ABBREVIATIONS

1RM	One-repetition maximum
EE	Elbow extensors
EF	Elbow flexors
HHD	Hand-held dynamometry
HE	Hip extensors
HF	Hip flexors
ICC	Intra-class correlation coefficients
KE	Knee extensors
MHFMS	Modified Hammersmith Functional Motor Scale
MMT	Manual muscle testing
MVIC	Maximum voluntary isometric contraction
NMD	Neuromuscular disorder
PRT	Progressive Resistance Training
QMA	Quantitative muscle analysis
Reps	Repetitions
SE	Shoulder extensors
SF	Shoulder flexors
SMA	Spinal muscular atrophy
SD	Standard deviation

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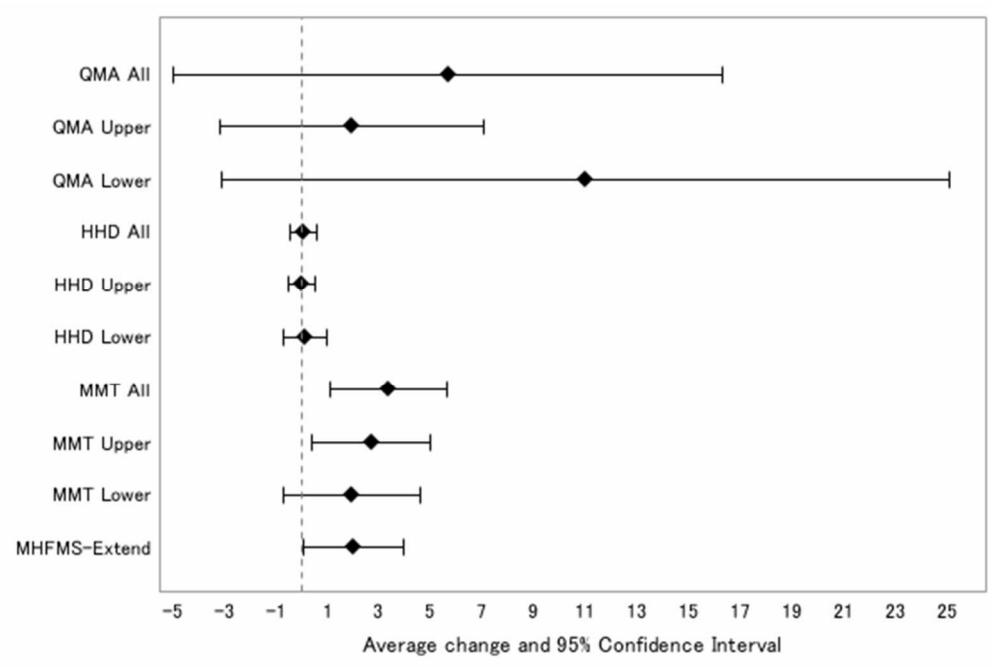

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