HHS Public Access

Author manuscript

*J Pediatr Rehabil Med*. Author manuscript; available in PMC 2015 May 20.

Published in final edited form as:

*J Pediatr Rehabil Med*. 2014 ; 7(4): 353–360. doi:10.3233/PRM-140305.

# Isokinetic Muscle Strength Differences in Patients with Mucopolysaccharidosis I, II, and VI

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## Abstract

**Purpose—**To determine muscular strength differences in patients with MPS-I, II, and VI versus age- and sex-matched healthy controls.

**Methods—**Dominant leg isokinetic knee extension strength was measured at 90 and 120 degrees per second (d/s) using a dynamometer in 30 subjects with MPS and 42 controls (5-16 yrs). MPSI was further divided into MPS-IA (attenuated) and MPS-IH (severe). Strength measures analyzed were peak torque (PkT), peak torque per unit body weight (PkT/BW) and per unit lean body mass (PkT/LBM), and average power (AP).

**Results—**Following adjusting strength measures for age, MPS-IH and MPS-II had significantly lower strength measures for all variables at both angular velocities. MPS-VI had significantly lower PkT, PkT/LBM, and AP compared to controls at 90 and 120d/s. In contrast, MPS-IA was not significantly different from controls for any strength variable at either angular velocity.

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Conflicts of Interest

PO and LEP have provided consulting support to and receive grant support from Genzyme. CBW has been a consultant and recipient of grants from Actelion, Amicus, BioMarin, Genzyme, Shire, and Synageva. NET, DRD, TCL, KDR, and JS have no relevant disclosures.

**Conclusion—**The results of this study suggest that decrements in skeletal muscle strength depend on MPS diagnosis and severity of disease. Children with MPS-IH demonstrate the greatest difference in muscular strength compared to healthy controls.

### Keywords

Mucopolysaccharidosis; Strength; Isokinetic

## 1. Introduction

Mucopolysaccharidoses (MPS) are rare genetic multisystem lysosomal storage disorders that are characterized by the inability to degrade specific complex carbohydrates called glycosaminoglycans (GAGs). MPS I is an autosomal recessive disorder caused by insufficiency of the lysosomal enzyme α-L-iduronidase. MPS I can be divided into two groups, the attenuated forms of MPS I (Hurler-Scheie and Scheie syndromes [MPS IA]) and the severe form of MPS I (Hurler syndrome [MPS IH]). Mucopolysaccharidosis II (Hunter syndrome [MPS II]) is an X-linked disease due to defects in the gene encoding the enzyme iduronate-2-sulfatase. The enzyme N-acetylgalactosamine-4-sulfatase (arylsulfatase B) is deficient in patients with MPS VI (Maroteaux-Lamy syndrome) [1-3]. These enzyme deficiencies result in an accumulation of GAGs in the cells of various body systems, including cartilage, bone, skin, heart valves, and blood vessels [1,4-8].

Studies that aim to evaluate the musculoskeletal system in MPS patients often focus on skeletal abnormalities [9-12]. Studies that have evaluated the impact of the disease on skeletal muscle have used functional tests such as the 6- or 12-minute walk test, 3-min stair-climb, and/or goniometric tests for joint mobility evaluation [2,6,7,13]. Cardoso-Santos and colleagues measured hand grip strength in MPS VI patients and reported that 23 out of the 26 patients tested could not generate enough pressure to activate the dynamometer resulting in a reading of zero pounds [13]. The other three patients' average grip strength was 0.1 pounds, well below normal values. To date, the present study is the only study to have directly examined leg strength in MPS patients.

Polgreen et al. [12] reported low bone mineral density (BMD), and following adjustments for height and pubertal status, higher muscle mass in children and adolescents with MPS. Muscle forces on bone are one of the most important factors influencing bone density. It is possible that despite having higher relative muscle mass, low muscular strength is contributing to low BMD in individuals with MPS. Additionally, muscular strength is an important contributor to functional independence and subsequent improvement in quality of life [14,15]. Therefore, we believe isokinetic muscle strength measures have the potential to be valuable, objective measures of the effect of new therapies for MPS on musculoskeletal disease.

The primary aim of this study was to evaluate skeletal muscle strength differences in patients with MPS I, II, and VI versus healthy controls. Despite the currently available therapies of hematopoietic cell transplantation (HCT) and/or enzyme replacement therapy (ERT), we hypothesized that all MPS subgroups studied would have decreased strength compared to the control group due to the involvement of the musculoskeletal system in MPS

disease progression. Based on the severity of the MPS IH phenotype, it was suspected that MPS IH would have the greatest difference in skeletal muscle strength [1,11,16], while MPS VI and MPS IA groups would have significantly less strength than controls but more strength than the MPS IH group as a result of less neurologic involvement [1,2,13]. Finally, as would be expected based on the mode of inheritance [1], all of our MPS II subjects are male. In addition, our patients were on the attenuated end of the spectrum for MPS II; for these reasons, MPS II was postulated to have the least skeletal muscle strength decrements compared to the control group.

## 2. Methods

### 2.1. Subjects

Thirty individuals with MPS IH, IA, II, or VI were recruited from a larger 5-year, observational study of bone and endocrine disease in children and adolescents with MPS. In addition, 42 age- and sex-matched, healthy subjects were recruited to serve as controls from a childhood cancer survivors study in which they also served as controls [17,18]. Informed consent was obtained from the parents or legal guardians of all subjects. Assent was obtained from all subjects whenever cognitively possible. All subjects included were between 5 and 16 years of age. Exclusion criteria for the MPS subjects were pregnancy, radiation exposure in the previous 12 months above 500 mrem, non-English speaking, or inability to comply with study procedures. Exclusion criteria for the control subjects were chronic illnesses including hypothyroidism and delayed puberty, risk for growth hormone deficiency, or incomplete strength data. The study protocols were approved by the University of Minnesota Institutional Review Board.

### 2.2 Anthropometric

Measurements for height and weight were taken at the start of the visit using a digital stadiometer. Body mass index (BMI) was calculated as weight in kilograms (kg) divided by height in meters-squared ($m^2$). Tanner stage was assigned according to pubic hair development in boys and breast and pubic hair development in girls. Measures of body composition (i.e., fat mass, lean body mass, and bone mineral mass) were made using dual-energy X-ray absorptiometry (DXA) (Lunar Prodigy DXA Scanner, pediatric software version 9.3; General Electric Medical Systems, Madison, Wisconsin). The healthy subjects were scanned on a different Lunar Prodigy scanner than that used for the MPS subjects; therefore all DXA measurements were standardized between machines as previously described [12]. Fat mass was expressed as a percent of total body mass; lean body mass (LBM) was expressed in kilograms.

### 2.3 Isokinetic strength evaluation

The present study employed the Biodex System 3 dynamometer (Biodex Medical Systems, Inc., Shirley, NY, USA), which has been used in both clinical and research settings. The dynamometer has been found to be mechanically valid and reliable for isokinetic strength testing [19] and has been used successfully in studies evaluating the isokinetic knee flexion and extension strength of individuals with cerebral palsy [20-22]. To our knowledge there have been no studies testing the validity and reliability of the Biodex System 3

dynamometer in cognitively and/or developmentally impaired populations. The angular velocities of 90 and 120 degrees/second (d/s) were chosen based on standardized research protocols. During testing, resistance is imposed at a constant velocity of motion through an electrically controlled servomechanism [19]. The use of an isokinetic dynamometer allows for the measure of torque (any force that results in a rotation about an axis) at the anatomical joint throughout the entire available range of motion, rather than at one particular point in the range of motion as in handgrip dynamometers [23].

Subjects were seated in the chair of the dynamometer. The chair was adjusted for correct alignment with the knee attachment, hip flexion at 85°, and the axis of the lever arm visually aligned with the knee's anatomical axis of rotation. Stabilization straps were placed around the waist and around the mid-thigh of the test leg. In subjects who were tall enough, stabilization straps were also placed across the torso so that the straps did not cross at the level of their neck. The range of motion at the knee, limb weight, and reference position (90° flexion) were determined using the dynamometer. Dominant leg isokinetic knee extension strength was measured at angular velocities of 90 and 120 degrees per second (d/s). Subjects were instructed to provide a maximal effort for 6 consecutive kicks at each angular velocity (extension then flexion being one kick).

All strength measures were evaluated for extension of the self-reported dominant leg only. The muscular strength variables included were peak torque (PkT), peak torque per 100 pounds body weight (PkT/BW), peak torque per 100 pounds lean body mass (PkT/LBM), and average power (AP) in watts. The variable PkT is an absolute measure (no adjustment for body size or mass) of the highest torque generated at any moment during a repetition, and represents the maximum strength ability of the exercised muscle [24]. Peak torque per unit body weight and PkT/LBM are relative measures of strength per size [24]. These relative measures are scaled by body weight or lean body mass of the participant [(Peak Torque/Body Weight) x 100 and (Peak Torque/Lean Body Mass) x 100, respectively]. Average power is the amount of total work divided by the time to complete that total work. The variable AP provides a measure of the work rate intensity and the time in which muscle can produce force [24].

### 2.4 Statistical analysis

Descriptive statistics were tabulated separately for the healthy control and MPS groups, including means and standard deviations for continuous variables and frequencies and percentages for categorical variables. For height and weight, standard deviation scores relative to age and gender from CDC growth data were also calculated [25]. Levene's test was used to test for homogeneity of variance. Due to unequal samples sizes and some variables having a significant Levene's test, a Welch's F test was used to test the null hypothesis. Comparisons between controls and the collective MPS group (All MPS) were made via an independent samples t-test with unequal variances. Demographic and strength variables with a significant Welch's F test were compared via a Dunnett's T3 post-hoc analysis (Table 1; demographic variables: sex, height, weight, LBM; strength variables: PkT, PkT/BW, PkT/LBM, AP) in order to determine statistical significance of differences between groups while controlling for multiple comparisons. Strength mean differences

adjusted for age, confidence intervals, and unadjusted P-values in Table 2 were based on linear regression with robust variance estimation for confidence intervals and P-values. Statistical significance after the Holm adjustment for multiple comparisons is also indicated. Linear regression was used to also evaluate differences on strength variables removing the influence of growth hormone use among MPS patients to explore the extent to which the differences between groups changed. All analyses were performed using either IBM SPSS Statistics 21 software (SPSS, Chicago, IL, USA) or R v2.152.

## 3. Results

### 3.1. Characteristics of the subjects

Table 1 contains descriptive characteristics of the MPS subjects (N = 30) compared to healthy controls (N = 42). Participants ranged from 5 to 16 years of age. Controls were significantly taller than the collective MPS group (All MPS; $t(49) = 8.21$, $p < 0.001$), MPS IH ($p < 0.001$), MPS II ($p < 0.01$), and MPS VI ($p=0.04$) cohorts (Welch's $F(4, 12.09) = 20.04$, $p < 0.001$). In addition, controls weighed significantly more than All MPS ($t(37) = 4.69$, $p < 0.001$), MPS IH ($p = 0.02$) and MPS VI ($p = 0.03$) patients (Welch's $F(4, 11.46) = 11.85$, $p < 0.001$). The MPS IA group also weighed significantly more than the MPS VI cohorts ($p = 0.03$). All MPS ($t(69) = 4.10$, $p < 0.001$), MPS IH ($p < 0.001$) and MPS II ($p < 0.01$) (Welch's $F(4, 13.03) = 12.84$, $p < 0.001$) had significantly lower LBM compared to controls. The MPS IH group ($p = 0.02$) also had significantly lower LBM compared to the MPS IA group. We have previously shown that the MPS group has deficits in whole body bone mineral content compared the healthy children [12]. There were no statistically significant ($F(4, 66) = 1.77$, $p = 0.146$) differences in percent fat mass between groups.

Of the MPS participants, 10% had growth hormone deficiency (1 with MPS IH, 2 with MPS II) and 33% were treated with recombinant human growth hormone (hGH) (5 with MPS IH, 3 with MPS II, 2 with MPS VI), 57% were on ERT (all MPS IA and MPS II, 3 with MPS VI), and all MPS participants had normal thyroid function tests (i.e., thyroid stimulating hormone and free thyroxine levels) at the time of the study. All 12 subjects with MPS IH and 2 subjects with MPS VI were treated with HCT previously; 2 subjects with MPS IH had also received peri-transplant treatment with ERT. No subjects within the MPS IA and MPS II cohorts had been transplanted.

#### 3.3. Strength measurements

Unadjusted means of all strength measures for each group are presented in Table 1. Of note, the collective MPS group and MPS IH had significantly lower strength measures for all variables at both angular velocities ($p < 0.001$ for all variables). At both angular velocities, MPS II had significantly lower PkT (90 d/s Welch's $F(4, 13.73) = 17.80$, $p = 0.003$; 120 d/s Welch's $F(4, 13.65) = 16.50$, $p = 0.018$) and AP (90 d/s Welch's $F(4, 13.46) = 24.51$, $p = 0.001$; 120 d/s Welch's $F(4, 13.77) = 19.27$, $p = 0.012$) compared to controls. At 90 d/s, PkT/BW was significantly lower in MPS II compared to controls (Welch's $F(4, 12.32) = 17.53$, $p = 0.029$); however, at 120 d/s the difference was not significant (Welch's $F(4, 12.46) = 14.58$, $p = 0.093$). At each angular velocity, PkT (90 d/s Welch's $F(4, 13.73) = 17.80$, $p = 0.013$; 120 d/s Welch's $F(4, 13.65) = 16.50$, $p = 0.024$) and AP (90 d/s Welch's

F(4, 13.46) = 24.51, p = 0.006; 120 d/s Welch's F(4, 13.77) = 19.27, p = 0.008) were significantly lower in MPS VI compared to the controls, but PkT was not significantly different after being scaled by LBM (PkT/LBM; 90 d/s Welch's F(4, 12.24) = 9.52, p = 0.630; 120 d/s Welch's F(4, 12.54) = 8.29, p = 0.502) or body weight (PkT/BW; 90 d/s Welch's F(4, 12.32) = 17.53, p = 0.830; 120 d/s Welch's F(4, 12.46) = 14.58, p = 0.746).

Age was a significant confounder for absolute measures of strength (PkT and AP). Therefore, age adjusted mean differences and confidence intervals were determined (Table 2). Again, MPS IH had significantly lower strength measures for all variables at both angular velocities ($p < 0.001$ for all variables). In contrast to unadjusted findings, nearly all strength measures were also statistically significantly lower in the MPS II cohort compared to controls (except PkT/LBM 120).

Because 33% of MPS subjects were being treated with hGH, all strength variables were also analyzed between control and MPS patients not using hGH at the time of testing. The significant differences across strength variables was not affected (data not shown).

## 4. Discussion

To our knowledge, the present study is the first to directly measure skeletal muscle leg strength in individuals with MPS. We observed that skeletal muscle leg strength differed between MPS groups, with MPS IH having the greatest strength decrements compared to controls. MPS II and MPS VI had similar strength decrements, while MPS IA participants demonstrated no statistically significant decrease in strength compared to controls. This observation in the MPS IA group was unexpected because although individuals with MPS IA are less severely affected compared to MPS IH, they do still have significant joint and musculoskeletal disease [26,27]. It is more likely that while MPS IA strength is not statistically significantly different from controls, the estimated deficits (ranging from approximately 20%-30% lower than the controls) suggest clinically significant strength deficits: a larger study with the same variability observed here would have been statistically significant.

Adjusting all strength measures for age accentuated differences in strength for all MPS groups. Despite magnifying the differences, adjusting for age did not alter the statistical significance of strength differences for the MPS IH and MPS IA groups. For MPS II and MPS VI, when strength measures were unadjusted, scaling PkT by body weight or LBM diminished the discrepancy observed in PkT; however, following adjustment for age, the difference in strength remained for PkT/BW (MPS II) and PkT/LBM (MPS II and MPS VI).

Peak torque, a measure of the maximum amount of force generated irrespective of body size or weight, is likely lower in MPS IH, MPS II, and MPS VI compared to controls due to their lower body weight and/or LBM. The persistence of strength deficits after scaling by body weight (PkT/BW) or LBM (PkT/LBM) and adjustment for age suggest either a problem intrinsic to the muscle or along the efferent motor pathway in these disease groups. Differences in cognitive function could contribute to these strength decrements, as well as if subjects were not able to give maximal effort. These findings do not appear to be related to

HCT because no MPS II patients were treated with HCT and they still exhibited strength deficits. In addition, in a study of childhood cancer survivors who were exposed to chemotherapy and radiation (which are used in preparatory regimens for HCT), these exposures were not associated with strength measured by Biodex [28].

The significant difference of AP between the MPS groups and controls suggests a possible difference in muscle composition. Increased power can relate to a greater proportion of fast-twitch motor units in the muscle; conversely, lower power can relate to a greater proportion of slow-twitch motor units [29-31]. It may be speculated that MPS IH, II, and VI patients have a greater proportion of slow-twitch motor units compared to controls based on our findings of lower AP in these individuals. Another possibility is that the decrease in power is a manifestation of the infiltration of GAGs into the muscle fiber. Unfortunately, neither of these theories can be tested in our study population because we do not have muscle biopsies. Lastly, joint stiffness and contractures are symptoms of nearly all MPS types [10,25] and thus pain due to joint stiffness may be a contributing factor in lower power production. However, following completion of the isokinetic strength testing, nearly all participants stated that they had very little to no discomfort during testing.

The observed differences in muscular strength between the forms of MPS I may be a result of time of onset and severity of the symptoms of MPS IH compared to the two phenotypes encompassed in MPS IA. Hurler syndrome (MPS IH) presents in infancy and is the most severe form of MPS I. For the attenuated forms, Hurler-Scheie typically manifests in childhood and is of intermediate severity; Scheie syndrome typically presents later, progresses more slowly, and is the most attenuated form of MPS I [1,32]. The differences in years of decreased activity and degree of limitation in activity likely contributed to the differences in strength we found between MPS IH and MPS IA. Additionally, Shapiro et al. [33] observed poorer neurocognitive function in MPS IH compared to MPS IA. Therefore, the combination of more severe skeletal disease and neurocognitive dysfunction may have resulted in MPS IH having lower strength measures. These measures of strength could thus be used as functional outcome measures of overall improvement in physical activity and decreased disease severity in MPS IH therapeutic studies.

Accumulation of GAGs in the brain is thought to contribute to the neuropathology affecting synaptic connectivity and plasticity of neurons [34-36]. There can be substantial neurological involvement in MPS IH and some forms of MPS II leading to cognitive impairment and motor control difficulties [1,37]. The degree of neurological involvement may play a significant role in the differences observed between MPS phenotypes. GAG storage has been demonstrated in the brainstem of MPS IH dogs [38], which is a noteworthy observation because the brainstem is the motor control center of the brain. Dusing and colleagues observed a possible manifestation of brainstem GAG storage in MPS IH patients who exhibited below-average gross motor abilities such as decreased locomotor abilities and a decreased gross motor quotient on the Peabody Developmental Motor Scales, 2nd edition [37,39]. These gross motor deficits may contribute to the significant decreased dominant knee extension strength we found in MPS IH subjects.

Spinal cord compression is also characteristic of MPS I, II, and VI [40-44] and can result in muscular weakness [45]. This may be a reason for the observed strength deficits in the present study and should be a focus of future investigations.

The present study is limited by the inability to address the contribution of neurological versus intrinsic muscular deficits in the strength decrements observed. In studies involving children, there is the concern of whether maximal effort is produced. Although participants were instructed to provide a maximal effort, no measurements of muscle activation (i.e. electromyography) were made which could potentially address these issues. However, analysis of the coefficient of variance (a measure of the duplicability of the test based on the amount of variation between repetitions) did not differ between groups at 90 d/s or 120 d/s (Welch's $F(4, 12.18) = 2.69$, $p = 0.08$ and Welch's $F(4, 12.66) = 1.78$, $p = 0.19$, respectively), suggesting internal validity of testing results [24]. Another limitation is the evaluation of strength being isolated to the dominant leg, as there may be differences in strength in other body regions. Additionally, the use of an isokinetic dynamometer may be limited in the clinical setting due to the cost and availability of the equipment, as well as the initiation of treatment in patients that are too young to feasibly complete isokinetic strength testing.

## 5. Conclusion

Children with MPS IH, II, or VI have significant decreased skeletal muscle strength unlike children with MPS IA. Although not statistically significant, children with MPS IA do showed decreased strength that is possibly clinically significant. Isokinetic muscle strength measures have the potential to be used as objective measures of the effect of new therapies for MPS on musculoskeletal disease.

## Acknowledgements

The authors would like to thank all the study participants and their parents, as well as the study coordinator Jane Kennedy, RN. The project described was supported by Grant Number K23AR057789 from NIAMS/NIH, Grant Number U54NS065768 from NINDS/NIDDK/NIH, a grant from the University of Minnesota Pediatric Foundation, and by the National Center for Advancing Translational Sciences of the NIH Award Number UL1TR000114. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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**Table 1**

Patient descriptive summaries across disease groups: values presented are mean (SD) or N (%) where indicated.

| Covariate | Control (N=42) | All MPS (N=30) | MPS IH (N=12) | MPS IA (N=6) | MPS II (N=8) | MPS VI (N=4) |
|---|---|---|---|---|---|---|
| Age (yr) | 12.3 (2.15) | 12.3 (3.04) | 11.1 (2.97) | 14.6 (2.48) | 11.0 (2.15) | 15.2 (2.13) |
| Female | 10 (23.8%) | 9 (30.0%) | 7 (58.3%) | 1 (16.7%) | 0 (0.0%) *† | 1 (25.0%) |
| Height (SDS) | 0.77 (1.2) | −2.5 (1.8) * | −3.1 (1.7) * | −0.87 (1.6) | −2.0 (1.3) * | −4.1 (1.6) * |
| missing height | 7 (16.7%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Weight (SDS) | 0.66 (0.85) | −1.1 (1.9) * | −1.5 (1.9) * | 0.36 (1.6) | −0.43 (1.1) | −3.2 (1.2) *† |
| Body Mass Index | 20.8 (4.41) | 20.9 (4.7) | 20.0 (4.06) | 24.6 (6.42) | 20.3 (4.17) | 19.2 (2.76) |
| missing Body Mass Index | 7 (16.7%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Lean Body Mass (kg) | 37.3 (11.0) | 27.1 (9.48) * | 20.7 (5.52) *† | 39.3 (9.09) | 27.1 (5.27) * | 27.8 (9.54) |
| missing Lean Body Mass | 1 (2.38%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Percent Fat Mass (kg) | 21.0 (9.92) | 22.7 (12.8) | 26.1 (13.0) | 27.9 (13.0) | 18.0 (11.9) | 13.8 (9.01) |
| missing Percent Fat Mass | 1 (2.38%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Pubic Tanner | 2.52 (1.47) | 2.79 (1.63) | 2.67 (1.67) | 4.0 (1.0) | 1.62 (1.19) | 4.0 (1.41) |
| missing Pubic Tanner | 2 (4.8%) | 1 (3.3%) | 0 (0.0%) | 1 (16.7%) | 0 (0.0%) | 0 (0.0%) |
| GH Deficient | 0 (0.0%) | 3 (10.0%) | 1 (8.3%) | 0 (0.0%) | 2 (25.0%) | 0 (0.0%) |
| GH Use | 0 (0.0%) | 10 (33.3%) | 5 (41.7%) | 0 (0.0%) | 3 (37.5%) | 2 (50.0%) |
| HCT Treated | 0 (0.0%) | 14 (46.7%) | 12 (100%) | 0 (0.0%) | 0 (0.0%) | 2 (50.0%) |
| ERT Treated | 0 (0.0%) | 19 (63.3%) | 2 (16.7%) [a] | 6 (100%) | 8 (100%) | 3 (75.0%) |
| PkT 90 | 79.5 (35.1) | 41.0 (29.7) * | 23.2 (12.1) * | 78.1 (41.5) | 40.1 (19.8) * | 40.5 (12.9) * |
| PkT/BW 90 | 52.9 (13.6) | 34.1 (13.5) * | 25.1 (7.91) * | 43.1 (15.2) | 37.1 (10.6) * | 41.5 (16.9) |
| PkT/LBM 90 | 70.0 (15.6) | 47.1 (19.8) * | 36.8 (13.8) * | 63.1 (23.5) | 48.5 (19.0) | 51.3 (18.9) |
| missing PkT/LBM 90 | 1 (2.38%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| AP 90 | 67.6 (30.0) | 31.3 (27.0) * | 13.8 (8.53) * | 64.3 (40.0) | 32.4 (16.1) * | 32.0 (10.5) * |
| PkT 120 | 73.8 (31.6) | 39.2 (27.2) * | 23.1 (12.4) * | 72.9 (34.3) | 38.3 (22.2) * | 38.6 (12.9) * |
| PkT/BW 120 | 49.6 (14.0) | 32.7 (12.6) * | 24.8 (7.42) * | 41.3 (14.3) | 35.0 (12.2) | 39.0 (13.6) |
| PkT/LBM 120 | 65.7 (16.0) | 45.2 (18.9) * | 36.2 (12.7) * | 59.9 (19.9) | 46.2 (22.7) | 48.3 (14.7) |

| Covariate | Control (N=42) | All MPS (N=30) | MPS IH (N=12) | MPS IA (N=6) | MPS II (N=8) | MPS VI (N=4) |
|---|---|---|---|---|---|---|
| missing PkT/LBM 120 | 1 (2.38%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| AP 120 | 81.2 (38.5) | 37.1 (30.1)* | 18.2 (12.2)* | 71.4 (40.8) | 38.6 (24.9)* | 39.4 (13.0)* |

SDS, standard deviation score; GH, growth hormone; HCT, hematopoietic cell transplantation; ERT, enzyme replacement therapy;

PkT, peak torque (N-m); PkT/BW, peak torque per unit body weight (%); PkT/LBM, peak torque per unit lean body mass (%); AP, average power (Watts). Body Mass Index = body weight(kg)/height-squared($m^2$)

*$p$<0.05 significantly different than controls

†$p$<0.05 significantly different than MPS IA

[a]Peri-transplant ERT, not at time of study visit.

**Table 2**

Differences in mean strength adjusted for age with robust variance estimates for 95% confidence intervals and P-values.

| Outcome | MPS IH - Control | P-value | MPS IA - Control | P-value | MPS II - Control | P-value | MPS VI - Control | P-value |
|---|---|---|---|---|---|---|---|---|
| PkT 90 | −56.3 (−69.2, −43.4) | <0.001* | −1.4 (−44.8, 42.1) | 0.194 | −39.4 (−58.1, −20.7) | <0.001* | −39.0 (−58.3, −19.7) | <0.001* |
| PkT/BW 90 | −26.6 (−32.6, −20.5) | <0.001* | −12.2 (−24.7, 0.3) | 0.056 | −14.4 (−22.0, −6.7) | <0.001* | −14.6 (−32.2, 3.0) | 0.104 |
| PkT/LBM 90 | −31.4 (−40.6, −22.3) | <0.001* | −10.3 (−27.7, 7.2) | 0.249 | −19.5 (−32.5, −6.6) | 0.003* | −23.1 (−43.3, −2.9) | 0.025 |
| AP 90 | −45.6 (−57.5, −33.7) | <0.001* | −19.2 (−47.7, 9.3) | 0.186 | −26.3 (−36.0, −16.6) | <0.001* | −56.3 (−74.4, −38.1) | <0.001* |
| PkT 120 | −50.7 (−62.9, −38.5) | <0.001* | −0.9 (−36.8, 34.9) | 0.226 | −35.5 (−55.4, −15.6) | <0.001* | −35.2 (−54.1, −16.2) | <0.001* |
| PkT/BW 120 | −24.0 (−29.8, −18.3) | <0.001* | −10.0 (−22.3, 2.3) | 0.112 | −13.7 (−22.6, −4.8) | 0.003* | −12.7 (−26.8, 1.4) | 0.077 |
| PkT/LBM 120 | −28.3 (−36.7, −19.9) | <0.001* | −8.1 (−23.8, 7.6) | 0.313 | −18.2 (−33.8, −2.6) | 0.022 | −20.3 (−36.0, −4.6) | 0.011 |
| AP 120 | −53.2 (−66.4, −40.0) | <0.001* | −28.8 (−62.1, 4.5) | 0.090 | −31.9 (−47.7, −16.0) | <0.001* | −66.4 (−89.3, −43.6) | <0.001* |

PkT, peak torque (N-m); PkT/BW, peak torque per unit body weight (%); PkT/LBM, peak torque per unit lean body mass (%); AP, average power (Watts)

*remained significantly different after Holm correction for multiple comparisons.