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The cardiorespiratory response and physiological determinants of the assisted 6-minute handbike cycle test in adult males with muscular dystrophy.

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**Running Title:** Exercise in muscular dystrophy

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The cardiorespiratory response and physiological determinants of the assisted 6-minute handbike cycle test in adult males with muscular dystrophy.

Abstract (150 Words)

Introduction. Assisted six-minute cycle test (A6MCT) distance was assessed in adults with muscular dystrophy (MD).

Methods. Forty-eight males, including Duchenne (DMD), limb-girdle (LGMD), fascioscapulohumeral (FSHD), Becker (BMD), and non-MD (CTRL), completed handgrip strength (HGS), lung function (FEV\(_1\), FVC), body fat and biceps thickness assessments. During the A6MCT, ventilation (VE), oxygen uptake (VO\(_2\)), carbon dioxide (VCO\(_2\)) and heart rate (HR) were recorded.

Results. A6MCT and HGS were less in MD than CTRL. FEV\(_1\), FVC and biceps thickness were lower in MD than CTRL, lower in DMD than BMD, LGMD and FSHD, but not different between BMD, LGMD, and FSHD. A6MCT correlated with HGS, FEV\(_1\), FVC, body fat, VO\(_2\), VCO\(_2\), HR, and VE (r=0.455-0.708) in pooled BMD, LGMD, and FSHD participants.

Discussion. A lower A6MCT distance in adult males with MD was attributable to HGS and lung function. The A6MCT is appropriate for the assessment of physical function in adults with MD.

Key words. Muscular dystrophy, Six-minute assisted cycle test, grip strength, oxygen uptake, lung function.
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Introduction

Muscular dystrophy (MD) is a heterogeneous group of neuromuscular disorders characterised by a genetic predisposition to an absence or reduction in proteins within and around the sarcolemma. Duchenne muscular dystrophy (DMD), Becker muscular dystrophy (BMD), limb girdle muscular dystrophy (LGMD) and facioscapulohumeral muscular dystrophy (FSHD) all have distinct loci of impairments within the proteins of the sarcoglycan complex, which are reflected by distinct functional impairments in terms of location and severity of progression. They are however, all similar in that they are associated with a loss of physical function. Ambulatory status and walking speed are frequently used as indicators of progression and severity of various MDs. The association between timed walking tests and the progression of numerous neuromuscular conditions make them essential, yet simple means of monitoring and screening. Within MD, the 6-minute walk test (6MWT) is advocated based on its reliability, sensitivity and approximation to numerous physiological outcome measures, and its position as one of the best single measures of independence and function.

Although suitable for the early years of DMD, and some ambulatory MDs, the capacity to complete a 6MWT, is not possible in a large percentage of adults with MD. Indeed, the 6MWT although advocated as a test of functional capacity in MD, would be impossible in 55%, 18%, 36% and 100% of our previously-described adult participants with LGMD, FSHD, BMD and DMD, respectively. In search of an alternative functional test, Jansen, et al. validated the assisted 6-minute cycle test (A6MCT) against the 6MWT in children with DMD, and found a high degree of reliability and validity.

The A6MCT, was developed in children with MD as a submaximal endurance test for those who may be wheelchair dependent, or lack the confidence or capacity to
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complete timed walking tests. The use of a motor assisted device, set at minimal resistance and speed (7Hz) meant that even those with limited upper limb function could contribute some active torque, however minimal, over the 6-minute period. In contrast, those children who maintained upper limb function, even in DMD, could produce an active torque, and accelerate the arm crank to produce a good discriminatory test between the most impaired of those with MD.

At present, there are no normative A6MCT data from adults with MD. In non-ambulatory adults with MD, there is limited data on muscle function, particularly from a power-assisted task that would be sensitive to those who were most impaired. Unlike the 6MWT which is known to be associated with knee extension strength in children with DMD, and oxygen uptake (VO₂) and lung function in cardiorespiratory conditions, the A6MCT is yet to be presented alongside physiological parameters such as muscle size, strength and lung function in adults with MD.

The aim of the present study is therefore to: 1) compare A6MCT distance and cardiorespiratory function in adult males with MD; and 2) to identify whether A6MCT is associated with physiological outcomes such as muscle strength, size and lung function.

We hypothesise that A6MCT distance will reflect previous patterns of muscular and respiratory impairment such that all MDs will perform lower than CTRL, with DMD and BMD completing the lowest distance followed by LGMD and FSHD; consistent with data from 6MWT, we hypothesise that measures of muscle and respiratory function will correlate with A6MCT distance.

Methods
Forty-eight adult males volunteered for this study (Table 1), 38 of whom had previously been diagnosed with either FSHD, BMD, LGMD or DMD; the remaining 10 had no form of MD and formed a control group (CTRL). MD participants were classified as ambulatory, and were graded for arm and leg function using Brooke and Vignos scales, respectively, by a chartered physiotherapist. MD participants were recruited from, and tested at, The Neuromuscular Centre (Winsford, UK). All MD participants were receiving weekly physiotherapy treatment involving passive mobility activities lasting approximately 1 hour. Control participants (CTRL), free from neurological disorders and otherwise in good health, were recruited from the broader community of the Neuromuscular Centre (none were related to MD participants), or were staff/students of MMU. Control participants self-reported as being sedentary, undertaking less than 1 hour of recreational physical activity; none of the participants were undertaking any structured, or regular exercise training regimes. Two additional adult males with DMD and BMD, were unable to complete the testing protocol. Their reasons for withdrawal were 1) upper limb contractures making the hand cycle range of motion impossible to complete and 2) respiratory insufficiency to overcome the facemask used for expired gas analysis. The data presented here represents the 48 adult males who completed all procedures.

All procedures conformed to the standards set by the latest revision of the Declaration of Helsinki, and were approved by the local Ethics Committee of Manchester Metropolitan University. Written informed consent was obtained from all participants prior to inclusion.

Procedures
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All participants were tested on a single visit to the Neuromuscular Centre (Winsford, UK). The testing session was conducted in the following order: anthropometry, body composition assessment, lung function, grip strength, questionnaires, resting energy expenditure, and A6MCT. The same equipment was used for both population groups, with the exception of the seated scales for body mass measures in non-ambulatory MD participants.

Anthropometric measures

All participant heights were calculated as point-to-point arm span (index finger, elbow, shoulder and across midline), using a 2m tape measure. To account for the known discrepancy between standing height and arm span measures, a correction was applied using regression data from adult males, the known error of making this correction is 3.5% \(^\text{18}\). Participant height is presented as this corrected value. In a sample of MD participants who could complete arm-span and standing height (n=12), arm span was not different from height, with an error of 7.97cm (4.5%) and intraclass correlation, ICC=0.67, Estimating height from arm span within this sample, gave an error of 2.58 cm (1.4%), and ICC=0.66. In the Control group, body mass was measured by digital scales (Seca model 873, Seca, Germany). MD participants were weighed in seated scales (6875, Detecto, Webb City, Mo, USA). The weight of slings, shoes, splints etc. were subtracted from gross weight post weighing, separately.

Body composition

Fat mass and Fat Free Mass (FFM) were measured using Bioelectrical Impedance (BIA) (Body STAT, 1500) with adhesive electrodes paced on the right hand (between styloid process of ulna and radius) and foot (between the medial and lateral malleoli).
Body composition, FFM and fat mass were determined using the proprietary equations within the BIA device. The use of BIA has previously been used within DMD populations\textsuperscript{19}. BIA has been shown to be valid and reliable in comparison to DXA, in normal and overweight populations\textsuperscript{20,21}. In addition, the portability of the BIA makes it a viable alternative to DXA in participants with limited mobility\textsuperscript{22}.

\textit{Biceps thickness}

Biceps thickness was measured in all participants consistent with previously established methods\textsuperscript{23}. Participants were seated with their dominant arm hanging, relaxed to their side. The medial and lateral boundaries of the biceps were identified in the transverse plane using B-mode ultrasound (MyLab Gamma, Esaote, UK) with a linear array probe (7.5 MHz). Thickness measurements (the distance between the superficial and deep aponeurosis) were taken on the mid-sagittal line of the biceps at 60\% of the upper arm length (the distance from the acromion process of the scapular to the lateral epicondyle of the humerus). Three measurements were made at the proximal, middle and end of the displayed image, from three images of the biceps. The biceps thickness presented is the average of these measures.

\textit{Lung function}

Forced Vital Capacity (FVC) and Forced Expiratory Volume in one second (FEV\textsubscript{1}) were measured using an electronic spirometer (Pneumotrac, Vitalograph, Bucks, UK). All participants performed the measurements seated and wearing a nose clip. The best performance of three trials is reported. The validity of the electronic vitalograph is established in healthy and clinical populations\textsuperscript{24}.

\textit{Grip strength}
A digital handgrip dynamometer (Jamar plus, Patterson Medical, USA) was used to measure grip strength. Of those participants that could produce a measureable grip force (two DMD participants produced no grip strength), three maximal attempts were made. Participants performed the three, 5 second, maximal grip efforts, seated, with the dominant hand, and with the arm in a relaxed position by their side. All three tests were separated by one-minute, and the peak reading recorded. Test-retest reliability has been reported as high, with low measurement error\textsuperscript{25}.

**Physical activity questionnaire**

MD participants completed a disability specific physical activity questionnaire (PASIPD – Physical Activity Score for Individuals with Physical Disabilities)\textsuperscript{26}. This questionnaire encompasses a lower activity threshold and has been validated as a reliable outcome measure for physical activity in people with disability\textsuperscript{27}.

**Expired gas analysis**

Expired gas analysis was performed at rest and during the A6MCT using a facemask and volume sensor assembly (Metalyser, Cortex, Leipzig, Germany). Fractional concentrations of O\textsubscript{2} and CO\textsubscript{2} were measured via a capillary line from the facemask. The gas analyser and volume transducer were corrected for ambient conditions (pressure and temperature) and calibrated before each test. All participants were seated during resting and exercising measurements.

**Resting measures**

Resting measures were recorded for 1-minute, following 20 minutes of seated, facemask attached, rest. This duration was chosen as it allows a sufficient plateau in
respiration to acquire reliable data. Outcome measures for the expired gas analysis are described below.

**Assisted 6-minute cycle test**

The A6MCT was conducted in accordance with Jansen, et al., however only upper limb testing was performed as this allowed a wider range of participants to be recruited. Participants performed the A6MCT using a motor assisted, hand bike, mobility trainer (MOTOmed, Viva2, Reck, Germany), with a zero load speed of 7 RPM consistent with previously adopted methods. Participants were instructed to cycle as fast as possible for 6 minutes, whilst receiving verbal encouragement. Those MD participants who were unable to produce an active torque throughout the 6 mins, were encouraged to rest, allowing the hand bike to passively move their arms, until they were able to continue producing an active torque. The primary outcome measure of the A6MCT was cycle distance. Heart rate was monitored by short-range telemetry (Polar, Kempele, Finland) throughout the exercise test every 5 seconds and is presented averaged over each minute of exercise.

Blood lactate was assessed using fingertip, capillary samples (Accutrend plus, Roche Diagnostics Limited, UK) at 5 minutes pre (BLapre), and immediately post A6MCT (BLapost).

One-minute averages for rest, and for each minute of the A6MCT were taken from the breath-by-breath samples and are presented as standard temperature, pressure, dry volumes where relevant. Reported outcome measures include: pulmonary ventilation (VE), oxygen uptake (VO$_2$), carbon dioxide output (VCO$_2$), and respiratory quotient (RQ). VO$_2$ and VCO$_2$ are presented relative to body mass.
Statistics

All analyses were performed using IBM SPSS Statistics 24 software. Parametric assumptions of normal distribution were confirmed using Shapiro-Wilk’s test (P>0.05) in all dependent variables, except for Total A6MCT distance (P<0.05). Differences between the groups were analysed using a one-way ANOVA with post hoc. Post Hoc was either Tukey’s or Games-Howell depending on whether variance was homogenous (Levene’s P>0.05), or non-homogenous (Levene’s P<0.05), respectively. Variables that violated normal distribution were compared between groups using the Kruskal Wallis test, with post-hoc Mann-Whitney U pairwise comparisons, where appropriate.

Where comparisons were made at 1-minute intervals over the A6MCT, a 3 x 6 ANOVA was performed. Where group differences were observed, Tukey’s Post Hoc was conducted.

With all post hoc comparisons, unless otherwise stated, differences are denoted in one direction of comparison; i.e. if a group performed “worse” than any other, the P value is reported, or denoted with relevant superscript text.

Correlations were performed using grouped data (pooled FSHD, LGMD, and BMD) in the conditions that showed no between group differences for dependent variables; as this data was normally distributed, Pearson Correlation was performed.

All data are reported as means (SD). Statistically significant differences and/or associations were accepted at α≤0.05.

Results
Demographic, anthropometric and body composition measures

As shown in Table 1, DMD participants were younger than LGMD, BMD and FSHD groups. Compared to the control participants LGMD and FSHD were older. DMD and BMD showed no age difference from the CTRL participants. There were no differences in stature or body mass between groups. LGMD, BMD and DMD had higher body fat% than FSHD and control participants. Lean mass was less in DMD than CTRL, with no lean mass differences observed between other groups.

Biceps thickness

Compared to CTRL, DMD and BMD had smaller biceps thickness. There was no difference between MD populations for biceps thickness. LGMD and FSHD biceps thickness was not different from CTRL (Table 1).

Physical activity

Physical activity was less in DMD than LGMD (Table 1); there was no difference between the other MD groups.

Lung function

Compared to CTRL, FEV$_1$ was less in FSHD, LGMD and DMD. Compared to the other MD groups, DMD had a lower FEV$_1$. FVC was smaller than CTRL in all MD groups. DMD had a lower FVC than the other MD groups (Table 2).

Grip strength

Compared to CTRL, grip strength was less in all MD groups. The DMD participants had lower grip strength than LGMD and FSHD (Table 2).

A6MCT Distance
A6MCT distance was shorter in FSHD, LGMD, BMD and DMD than CTRL. The DMD A6MCT distance was shorter than FSHD, LGMD and BMD. There was no difference in A6MCT distance between BMD, LGMD and FSHD (Table 2).

**A6MCT VO\(_2\)**

Throughout the A6MCT, VO\(_2\) in DMD, BMD, LGMD and FSHD was lower than CTRL. VO\(_2\) during the A6MCT was lower in DMD compared to other MD groups. There was no difference in VO\(_2\) during the A6MCT at any time point between BMD, FSHD or LGMD (Figure 1A).

**A6MCT VCO\(_2\)**

Throughout the A6MCT VCO\(_2\) was lower than CTRL in DMD, BMD, LGMD, FSHD. Compared to the other MDs, DMD had lower VCO\(_2\) throughout the A6MCT. There was no difference in VCO\(_2\) during the A6MCT between BMD, FSHD or LGMD (Figure 1B).

**A6MCT HR**

Throughout the A6MCT, DMD had a lower HR than CTRL at minutes 2-6. In addition, DMD HR during the A6MCT was lower than LGMD at minutes 3-6, and lower than LGMD at minute 6. BMD had a lower HR than CTRL at minute 6. There was no difference in HR during the A6MCT between LGMD, BMD or FSHD (Figure 1C).

**A6MCT VE**

Compared to the CTRL, VE during the A6MCT was lower in DMD at all time points. In BMD and LGMD VE was lower than CTRL at minutes 2-6 of the A6MCT. FSHD...
VE was lower than CTRL at minutes 3-6 of the A6MCT. Within the MD participants, DMD VE was lower than BMD at minutes 1 & 4, and lower than LGMD and FSHD at all time points of the A6MCT (Figure 1D).

**A6MCT BLa**

Pre A6MCT BLa was not different between groups (Table 2). Post A6MCT BLa was lower in all MD groups compared to CTRL. Compared to FSHD and LGMD, post BLa was lower in DMD. Within group changes in BLa from pre to post were significant in all groups, except from DMD who showed no change in BLa pre to post.
Correlations

Within the pooled MD participants (BMD, FSHD and LGMD, n=29), A6MCT distance was correlated with handgrip strength \((r=0.609, P<0.05)\), \(\text{FEV}_1\) \((r=0.455, P<0.05)\), FVC \((r=0.518, P<0.05)\), body fat% \((r=0.571, P<0.05)\), and \(\text{BLaPost}\) \((r=0.437, P<0.05)\). In terms of cardiorespiratory measures during A6MCT, throughout the final minute of exercise (others are omitted for clarity), the A6MCT distance correlated with \(\text{VO}_2\) \((r=0.638, P<0.05)\), \(\text{VCO}_2\) \((r=0.636, P<0.05)\), Heart rate \((0.472, P<0.05)\), and VE \((r=0.708, P<0.05)\). No correlations were observed for A6MCT distance for other measures, of note these include PASIPD, body mass, BMI, stature, lean mass and biceps thickness.

In CTRL, A6MCT distance correlated with handgrip strength \((r=0.811)\), and biceps thickness \((r=0.634)\). No other correlations were observed for A6MCT distance in CTRL.

Discussion

The main finding in the present study was in agreement with our hypothesis, such that A6MCT distance was lower in adults with MD compared to CTRLs; in addition adult males with DMD had lower A6MCT distance than FSHD, BMD and LGMD. Within FSHD, BMD, and LGMD participants, the variance in A6MCT distance could be attributed to lung function (\(\text{FEV}_1\) and FVC), grip strength (consistent with our hypothesis) and cardiorespiratory measures of \(\text{VO}_2\), \(\text{VCO}_2\), HR and VE.
The A6MCT has previously been adopted in boys with DMD \textsuperscript{12,29,30}. Although different hand bikes were used, and previous data is presented as total revolutions \textsuperscript{29,12}, when estimated based on the distance achieved through 7 rpm passive cycling, the data in the present adults (CTRL = 687-781 revolutions) is similar to that presented previously (CTRL Boys \~800 revolutions). Of interest, is that boys with DMD previously achieved \~350 revolutions \textsuperscript{12}, the estimated value in the present adult DMD participants was lower than previous at 94 revolutions, consistent with the progressive nature of DMD.

The lower A6MCT distance in the present DMD participants, compared to FSHD, BMD, and LGMD can be attributed to the lower grip strength and lung function, and to lower HR, VO\textsubscript{2}, VCO\textsubscript{2} and VE throughout the A6MCT. Although speculative based on the present data, grip strength likely reflects the recruitable muscle mass available to produce cycle torque, and lung function reflects the ability for the respiratory system to respond to the demands of the exercise stress. In DMD, there was minimal grip strength and impaired lung function, and therefore lower A6MCT distance. Further evidence for the inability of adults with DMD to respond to an exercise demand was supported by the lack of any metabolic by-products, with no change in BLa from pre to post.

The correlations in the FSHD, BMD and LGMD participants and physiological parameters suggest that the A6MCT is a good measure of neuromuscular and cardiorespiratory function. It should be noted that, those measures with the highest correlation (grip strength, VE and VO\textsubscript{2}) could only explain \~40\% of the variance in A6MCT. The present correlations between the A6MCT and physiological measures, are however similar to those observed previously for the 6MWT and knee extension myometry\textsuperscript{7}. Indeed based on these previously reported correlations between
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myometry and walking tasks \( r=0.4-0.7 \), the 6MWT was advocated in MD as a valid single measure of “cardiac, respiratory, circulatory, and muscular capacity” \(^7\).

In terms of its appropriateness in adults with MD, none of the present adults with DMD, and only 48% of the other adult MD participants could start a 6MWT. Similarly, validation testing of the A6MCT (e.g. VO\(_2\)peak) could only be completed in a proportion of these participants, and beyond the grip strength measures presented here, there is presently no data comparing tests of upper limb function with A6MCT distance. Previously, the A6MCT and 6MWT were found to be in agreement \( r=0.65 \), with high retest reliability of the A6MCT \( \text{ICC}=0.89, 95\% \text{ CI 0.76–0.95} \)\(^{12}\). The A6MCT previously validated in children with MD, therefore represents an exercise test that can be completed by adults with MD who are non-ambulatory. Furthermore, in FSHD, BMD and LGMD, it represents a single measure that correlates well with grip strength and lung function.

We observed no correlations between bicep thickness and lean mass, and A6MCT distance in the pooled FSHD, LGMD and BMD participants; this is surprising as grip strength was correlated with A6MCT distance. The assessment of lean mass and biceps thickness may therefore not reflect the recruitable musculature in the MD participants. It is well established that there is substantial remodelling of muscle mass in MD \(^{31}\), with infiltration of non-contractile material, such that “pseudohypertrophy” is reported in some MD muscles \(^{32}\). It is likely that using more stringent measures of assessment (e.g. MRI or DXA), particularly in the upper limb, may have reflected more closely the muscle mass available for performing the A6MCT, as was reflected by the present grip strength results. Within the CTRL group, where one would assume the infiltration of non-contractile material is lower than MD, A6MCT distance correlated with biceps thickness \( r=0.634 \). The
associations in the MD participants between A6MCT distance, grip strength, VO$_2$ and Blapost, all suggest that recruitable muscle mass in the upper limb contributes to A6MCT, despite not being related to biceps thickness or lean mass in the present study. Although the use of ultrasonography may therefore be considered a limitation in the present study, due to lower limb contractures, and lack of mobility in some of our more impaired MD participants, MRI or DXA would have precluded their inclusion.

Although we have observed no difference between groups in the present study, we acknowledge that due to the heterogeneity (and associated measurement variance) of the participants within each category, a higher number of participants would be beneficial. The paucity of data from adult MD populations is such that the only previous data on the primary outcome measure (A6MCT) is in children with DMD vs CTRL $^{12}$, where the effect size ($d=2.42$) results in a recommended group size of $n=2$ (G*Power, Kiel, Germany). We do however, acknowledge a limitation in the present study that MD group differences may not be present in some outcome measures due to type 2 error associated with high variance. An example of this was grip strength, for which the CV was 55-65% in LGMD, FSHD and BMD, compared to 22% in CTRL. This heterogeneity of outcome measures is expected within MD, and is likely to have contributed to the correlational findings within the present study.

In conclusion, adult males with MD showed lower A6MCT distance than adult controls. Furthermore, adult males with DMD showed A6MCT lower than those with FSHD, LGMD and BMD. In adult males with BMD, LGMD, and FSHD, variance in the A6MCT was attributable to grip strength and lung function. The A6MCT can therefore be considered an inclusive and physiologically meaningful test of physical function for adults with MD.
Abbreviations

6MWT, Six-minute walk test
A6MCT, assisted six-minute cycle test
BMD, Becker's muscular dystrophy
BLa, blood lactate
CTRL, control
DMD, Duchenne muscular dystrophy
FEV₁, forced expiratory volume in 1s
FSHD, facioscapulohumeral dystrophy
FVC, forced vital capacity
HR, heart rate
LGMD, limb girdle dystrophy
MD, muscular dystrophy
PASIPD, physical activity score for individuals with physical disability
VE, pulmonary ventilation
VCO₂, carbon dioxide output
VO₂, oxygen uptake

References

Table 1 Participant Demographics

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<tr>
<th></th>
<th>CTRL</th>
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<th>LGMD</th>
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<td>9</td>
<td>11</td>
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<td>Age (yrs)</td>
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<td>45.1 (9.2)</td>
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<td>Mass (kg)</td>
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<td>24.0 (5.0)</td>
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<td>Biceps thickness (mm)</td>
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CTRL = Control, LGMD = Limb Girdle, FSHD = fascioscapulohumeral, BMD = Becker’s, DMD = Duchenne. PASIPD = Physical activity score for individuals with physical disability. \(^C\) denotes significant difference from CTRL, \(^F\) denotes significant difference from FSH, \(^B\) denotes significant difference from BMD and \(^L\) denotes significant difference from LGMD.
significant difference from LGMD (P<0.05). Data are presented as Mean (SD), except for Brooke and Vignos scales, which are presented as mean (range).
Table 2 Muscle, respiratory and exercise performance.

<table>
<thead>
<tr>
<th></th>
<th>CTRL</th>
<th>FSHD</th>
<th>LGMD</th>
<th>BMD</th>
<th>DMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grip strength (Kg)</td>
<td>44.9 (9.9)</td>
<td>25.9 (15.5) C</td>
<td>17.8 (9.8) C</td>
<td>9.7 (6.3) C,F</td>
<td>2.0 (2.6) C,L,F</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>4.12 (0.70)</td>
<td>2.79 (0.70) C</td>
<td>2.28 (0.79) C</td>
<td>3.21 (1.15)</td>
<td>0.88 (0.54) C,B,L,F</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>5.14 (0.95)</td>
<td>3.49 (0.92) C</td>
<td>2.95 (1.07) C</td>
<td>3.80 (1.42) C</td>
<td>1.13 (0.68) C,B,L,F</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>0.81 (0.08)</td>
<td>0.81 (0.10) C</td>
<td>0.78 (0.08) C</td>
<td>0.85 (0.04)</td>
<td>0.82 (0.19)</td>
</tr>
<tr>
<td>A₆MCT distance (Km)</td>
<td>3.53 (0.11)</td>
<td>2.54 (0.44) C</td>
<td>2.39 (0.82) C</td>
<td>2.13 (0.80) C</td>
<td>0.45 (0.54) C,B,L,F</td>
</tr>
<tr>
<td>BLₐ pre (mmol/L)</td>
<td>1.99 (0.90)</td>
<td>2.22 (0.70) C</td>
<td>2.15 (0.79) C</td>
<td>2.44 (1.80)</td>
<td>1.93 (0.58)</td>
</tr>
<tr>
<td>BLₐ post (mmol/L)</td>
<td>8.40 (3.02)</td>
<td>5.02 (2.10) C</td>
<td>5.03 (2.49) C</td>
<td>3.71 (1.38) C</td>
<td>2.17 (0.75) C,L,F</td>
</tr>
</tbody>
</table>

CTRL = Control, LGMD = Limb Girdle, FSHD = fascioscapulohumeral, BMD = Becker’s, DMD = Duchenne, FEV₁ = forced expiratory volume in 1s, FVC = forced vital capacity, BLₐ = blood lactate, A₆MCT = assisted six-minute cycle test. C denotes significant difference from CTRL, F denotes significant difference from FSHD, B denotes significant difference from BMD and L denotes significant difference from LGMD (P<0.05). Data are presented as Mean (SD).
Figure legends

Figure 1: Cardiorespiratory measures recorded during the assisted 6-minute cycle test. A = Oxygen uptake (VO₂), B = Carbon dioxide output (VCO₂), C = Heart rate (HR), D = ventilation (VE). * denotes significant difference from all other groups (P<0.05). C denotes significant difference from CTRL, F denotes significant difference from FSHD, B denotes significant difference from BMD and L denotes significant difference from LGMD (all group differences are P<0.05). For clarity, significant differences from CTRL only are shown on the ventilation figure. Data are presented as Mean (SD).
Figure 1: Cardiorespiratory measures recorded during the assisted 6-minute cycle test. A = Oxygen uptake (VO$_2$), B = Carbon dioxide output (VCO$_2$), C = Heart rate (HR), D = ventilation (VE). * denotes significant difference from all other groups (P<0.05). # denotes significant difference from CTRL, $^\ddagger$ denotes significant difference from FSHD, $^\$' denotes significant difference from BMD and $^¥$ denotes significant difference from LGMD (all group differences are P<0.05). For clarity, significant differences from CTRL only are shown on the ventilation figure. Data are presented as Mean (SD).