2- and 6-minute walk tests equally well assess walking capability in neuromuscular diseases

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Background

The 6MWT

• widely used to measure treatment efficacy and disease progression in patients with neuromuscular diseases.
• time-consuming
• often not tolerated by patients with severe lower limb muscle weakness.
Objective

• To investigate if the 2MWT can be a valid alternative to the 6MWT to describe walking capability in patients affected by neuromuscular diseases covering many phenotypes and disease severities.

• To measure walking speed in patients and healthy adults.
Inclusion/exclusion criteria

• **Inclusion criteria:** age ≥ 18 years, ability to walk ≥ 60 meters in a 6MWT and verified (genetically and/or biopsied proven) neuromuscular diagnoses

• **Exclusion criteria:** Medical conditions that could interfere with the interpretation of walking capability, e.g. heart failure and arthritis.
Methods

Walk test:
• Two test days: one 2MWT and one 6MWT separated by minimum 30 minutes rest.
• The order of the walk test was administrated randomly by pre-ordered sealed envelopes.
• The walk test followed the American Thoracic Society (ATS) guidelines.
• Habitual assistive devices permitted.

Additional measurements:
• Weight (kg), height (cm)
• Manual test of muscle strength bilaterally over hip, knee and ankle (MRC 0-5)
Subjects

115 patients with the following diagnosis:

- Dystrophia myotonica (n=20)
- Limb-girdle muscular dystrophy (n=18)
- Fasioscapulohumeral dystrophy (n=15)
- Kennedy disease (n=14)
- Charcot-Marie-Tooth (n=14)
- Sporadic inclusion body myositis (n=10)
- Mitochondrial myopathy (n=10)
- Becker muscular dystrophy (n=8)
- Mixed myopathies (n=6)

38 healthy adults – 6MWT
Weak vs. strong patients

• Weak patients: one or more muscle groups in the lower limb with a MRC score ≤ 4.

• Strong patients: muscle strength in the lower limb with a MRC score > 4.
Correlation between distance (m) walked in the 2MWT and the 6MWT

$r=0.99$

$P<0.001$
Walking speed (m/sec) – patients

2MWT is too short to capture fatigue - variable response in walking speed between first and second testday.
Walking speed (m/sec) - patients

First minute: 1.18
Last minute: 1.13

6MWT

P < 0.001
Walking speed (m/sec) – healthy adults

6MWT

First minute: 1.93
Last minute: 1.90

P=0.01
The absolute fall in walking speed did not differ between patients and healthy adults (p=0.10)
### Characteristics of study population

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Male/ Female</th>
<th>Age (years)</th>
<th>BMI</th>
<th>Height (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients</strong></td>
<td>11</td>
<td>75/40</td>
<td>52.6 (22-83)</td>
<td>25.2 (16.1-44.1)</td>
<td>173.9 (138-198)</td>
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<tr>
<td></td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Healthy adults</strong></td>
<td>38</td>
<td>19/19</td>
<td>47.6 (25-76)</td>
<td>25.1 (19.6-33.5)</td>
<td>175.6 (155-192)</td>
</tr>
<tr>
<td><strong>Weak patients</strong></td>
<td>84</td>
<td>55/29</td>
<td>54.3 (22-83)</td>
<td>25.9 (16.1-44.1)</td>
<td>174.1 (138-196)</td>
</tr>
<tr>
<td><strong>Strong patients</strong></td>
<td>31</td>
<td>21/10</td>
<td>48.1 (24-79)</td>
<td>23.5 (16.8-38.3)</td>
<td>173.2 (154-198)</td>
</tr>
</tbody>
</table>

### Correlation and walking speed for subgroups

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Correlation (p&lt;0.001)</th>
<th>First minute</th>
<th>Last minute</th>
<th>Decrease in speed (m/s)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DM</strong></td>
<td>20</td>
<td>r=0.99</td>
<td>1.39</td>
<td>1.34</td>
<td>0.05</td>
<td>0.01</td>
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<tr>
<td><strong>LGMD</strong></td>
<td>18</td>
<td>r=0.99</td>
<td>1.07</td>
<td>1.01</td>
<td>0.06</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>FSHD</strong></td>
<td>15</td>
<td>r=0.99</td>
<td>1.31</td>
<td>1.26</td>
<td>0.05</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Kennedy</strong></td>
<td>14</td>
<td>r=0.95</td>
<td>1.02</td>
<td>0.92</td>
<td>0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>CMT</strong></td>
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<td>r=0.96</td>
<td>1.2</td>
<td>1.18</td>
<td>0.04</td>
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<tr>
<td><strong>Mitochondrial</strong></td>
<td>10</td>
<td>r=0.99</td>
<td>1.18</td>
<td>1.11</td>
<td>0.07</td>
<td>0.03</td>
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<tr>
<td><strong>IBM</strong></td>
<td>10</td>
<td>r=0.98</td>
<td>0.73</td>
<td>0.73</td>
<td>0</td>
<td>0.53</td>
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<tr>
<td><strong>BMD</strong></td>
<td>8</td>
<td>r=0.99</td>
<td>1.43</td>
<td>1.36</td>
<td>0.07</td>
<td>0.04</td>
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<tr>
<td><strong>Mixed</strong></td>
<td>6</td>
<td>r=0.99</td>
<td>1.18</td>
<td>1.13</td>
<td>0.05</td>
<td>0.12</td>
</tr>
<tr>
<td><strong>Weak patients</strong></td>
<td>84</td>
<td>r=0.98</td>
<td>1.06</td>
<td>1.01</td>
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<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Strong patients</strong></td>
<td>31</td>
<td>r=0.99</td>
<td>1.51</td>
<td>1.45</td>
<td>0.06</td>
<td>&lt;0.001</td>
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</table>
Conclusion

The 2MWT is a valid alternative to the 6MWT to assess walking capability in patients with neuromuscular diseases.

2MWT is too short to capture fatigue.

Significant decrease in walking speed in the 6MWT in all subjects, showing that the 6MWT is suitable to capture fatigue in patients with different neuromuscular diseases.

Absolute drop in walking speed was similar among patients and healthy in 6MWT.
Reliability of 2- and 6-minute walk tests in neuromuscular diseases: Effect of heart rate correction

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Background

The 6MWT is a commonly used test to evaluate walking ability, but retest reliability is weakened by a well-documented learning effect.

Preliminary results indicate that the reliability of the 6MWT can be improved by correcting for heart rate (HR) during the test.

It is unknown whether the shorter 2MWT is also subject to a learning effect.
Objective

To investigate test-retest reliability of the 2-minute walk test (2MWT) and 6-minute walk test (6MWT) with and without heart rate correction.
Subjects

93 adult patients (32 females)
Mean age of 53 years (range: 22-83 years)
12 different neuromuscular diseases:

- Dystrophia myotonica (15)
- Limb-girdle muscular dystrophy (14)
- Kennedy disease (13)
- Charcot-Marie-Tooth disease (12)
- Facioscapulohumeral muscular dystrophy (11)
- Mitochondrial myopathy (9)
- Sporadic inclusion body myositis (8)
- Becker muscular dystrophy (5)
- Spinal muscular atrophy (3)
- Myotonia congenita (Thomsen disease) (1)
- Congenital myopathy (1)
- Polymyositis (1)
Inclusion/exclusion criteria

**Inclusion criteria:**
Age $\geq 18$ years and a walking distance $\geq 60$ meters.

**Exclusion criteria:**
Heart arrhythmias and drugs affecting the heart rate.
Methods

Order of tests was randomized.

The walk tests followed the American Thoracic Society (ATS) guidelines.

Habitual assistive devices were permitted.

Heart rate was monitored by a pulse-watch.
Results 6MWT

The mean walked distance in the 6MWT increased from test to retest by $11\pm26$ m (2.7 %) from 412 to 423 m ($p<0.001$).
Results 6MWT

When correcting for HR, the **learning effect was abolished** (3.79 vs. 3.80 m/HR, \( p=0.840 \)).
Results 2MWT

The mean walked distance in the 2MWT increased by $4\pm 9$ m (2.9 %) from 145 to 149 m ($p<0.001$).
Results 2MWT

When correcting for HR, the learning effect was maintained (1.38 vs. 1.41 m/HR, 2.2 %, $p=0.018$).
Results

6MWT (m)

6MWT with HR-correction (m/HR)

2MWT (m)

2MWT with HR-correction (m/HR)
Conclusion

Both the 2- and 6MWTs are associated with a learning effect.

The learning effect is eliminated when correcting for heart rate in the 6MWT, but not in the 2MWT.

We suggest to use heart rate corrected 6MWT to weed out day-to-day variation that is not due to a real change in a patient’s clinical condition.