Longitudinal Assessment of Strength, Functional Capacity, Oropharyngeal Function, and Quality of Life in Oculopharyngeal Muscular Dystrophy

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Abstract

Objective
Oculopharyngeal muscular dystrophy (OPMD) is a late-onset, progressive muscle disease. Disease progression is known to be slow, but details on the natural history remain unknown. We aimed to examine the natural history of OPMD in a large nationwide cohort to determine clinical outcome measures that capture disease progression and can be used in future clinical trials.

Methods
Patients, invited by their treating physicians or from the national neuromuscular database, and invited family members, were examined twice, 20 months apart, using fixed dynamometry, MRC grading, maximum bite force and isometric tongue strength, Motor Function Measure (MFM), 10-step stair test, maximum swallowing-, chewing-, and speech-tasks and quality of life assessments.

Results
Disease progression was captured by 8 out of 18 measures over 20 months in forty-three genetically confirmed OPMD patients. The largest deterioration was seen in deltoid muscle strength (-27% (range -17 – -37%)), followed by the quadriceps (-14% (range -6 – -23%)), iliopsoas (-12.2%), tongue (-9.9%) and MRC sum-score (-2.5%). The 10-step stair test (-12.5%), MFM part D1 (-7.1%), and maximum repetition rate of /pa/ (-5.3%) showed a significant decrease as well (all p<0.05). Domain ‘Physical functioning’ of the SF-36 Health Survey significantly deteriorated (p=0.044). No relationship was found between disease progression and genotype or disease duration (p>0.05).

Conclusions
Despite the slow disease progression of OPMD, this study showed that several outcome measures detected progression within 20 months. The deltoid muscle strength, measured by fixed dynamometry, showed the greatest decline. This longitudinal data provides clinical outcome measures that can be used as biomarkers in future clinical trials.
Introduction

Oculopharyngeal muscular dystrophy (OPMD) is an autosomal dominant, late-onset muscle disease. The estimated prevalence is approximately 1:100,000, but several studies suggest that OPMD is underdiagnosed,\textsuperscript{1-5} mostly due to unfamiliarity among clinicians.\textsuperscript{3} The clinical characteristics of OPMD are ptosis due to weakness of the levator palpebrae muscle and dysphagia due to weakness of the pharyngeal muscles,\textsuperscript{6} both starting early in the disease course.\textsuperscript{7} Weakness of shoulder girdle and limb girdle muscles, even as an early sign,\textsuperscript{8-10} complete the clinical picture, but these symptoms are not always recognized as being part of OPMD, especially in the elderly.

There is no pharmacological treatment available for OPMD, but with recent developments in gene therapy, therapeutic trials in humans are forthcoming.\textsuperscript{11-14} Therefore, detailed information on the natural history and sensitive outcome measures to detect disease progression or therapy effect are urgently needed.\textsuperscript{15} Detailed analysis of the natural history will help to understand the variability in disease severity within families, which can possibly support therapy development. One small study including 8 OPMD patients investigated disease progression over a period varying from 8 to 16 months using magnetic resonance imaging (MRI) of the muscles and the Motor Function Measure (MFM) and showed disease progression in MRI, but no disease progression on the MFM.\textsuperscript{16} No other longitudinal clinical studies of OPMD are available.

This study aims to examine in detail the natural history in a large nationwide cohort of OPMD patients, to determine clinical outcome measures that capture disease progression and can be used in future clinical trials.
Methods

Patients

Patients were invited by their treating physicians or from the national neuromuscular database (Computer Registry of All Myopathies and Polyneuropathies, CRAMP)\textsuperscript{17} in the Netherlands. Approximately 80 patients are known to be diagnosed with OPMD by a neurologist (source: CRAMP database). Additionally family members of the patients were asked to participate through an information letter. Hereby, possible asymptomatic carriers and patients with subtle signs of OPMD could be included.

At baseline and at follow-up all patients were interviewed to identify complaints related to oropharyngeal tasks (swallowing, chewing and speaking) or related to functioning of the limbs.

Standard Protocol Approvals, Registrations, and Patient Consents

The study was approved by the local medical ethics committee (study nr. NL54606.091.15) and all patients gave signed written informed consent.

Clinical examination

All patients were clinically examined at baseline and after +/- 20 months by the same investigator (RK). The measurements are explained below.

Measurements of muscle strength

- **Fixed dynamometry** (Newton, N) was performed using the strength transducer KAP-S 2 kN (Angewandte System Technik GmbH) to measure the maximal isometric contraction of the shoulder abduction (deltoid muscle), hip flexion (iliopsoas muscle) and knee extension (quadriceps muscle). The best performance (maximum force) of the three measurements was used for analysis.

- **Manual muscle testing** was performed using the Medical Research Council (MRC) scale ranging from 0 (no muscle contraction) to 5 (maximal muscle strength)\textsuperscript{18} for neck extension and flexion, elbow extension and flexion, knee extension and flexion, hip abduction, hip flexion, foot dorsal flexion and foot plantar flexion, handgrip, wrist extension and flexion and shoulder abduction bilaterally (score 0 - 130).
- **Maximum bite force (MBF)** was measured using the Bite Force Gauge (Vrije Universiteit, Amsterdam). The best performance of three trials was used for analysis.

- **Maximum isometric tongue strength (MITP)** was performed using the Iowa Oral Performance Instrument (IOPI Medical LLC, Model 2.3). Patients were instructed to push the bulb with the anterior part of the tongue against the roof of the mouth as hard as possible. The best performance of three trials was used for analysis.\(^{19}\)

**Measurements of functional capacity**

- The **Motor Function Measure (MFM)** was performed which consists of three parts: D1, concerning stance and transfer tasks; D2, concerning tasks of axial and proximal muscles; D3, concerning tasks using distal muscles. The outcome ranges from 0 - 100%. A score of 100% implies no functional motor deficits.\(^{20}\)

- A timed **stair walking test** (10-steps) was measured in seconds.\(^{21}\) Patients were instructed to take the stairs as they normally would do. The stairs had one handrail. The patients decided themselves to hold the handrail or not.

- The **Test of Masticating and Swallowing Solids (TOMASS)** was performed by eating a cracker as fast as possible, in seconds.\(^{22}\)

- The maximum swallowing capacity was measured by the **maximum swallowing speed (MSS)** and **maximum swallowing volume (MSV)**. For the MSS, patients were instructed to drink 150 mL water as quick as possible.\(^{23,24}\) For the MSV, patients were instructed to swallow a maximal amount (mL) of water in one swallow.\(^{25}\)

- The maximum speech capacity was measured by the **maximum phonation time (MPT)** and **maximum repetition rate (MRR)**.\(^{26,27}\) MPT measures how long a patient can produce an /a/ in seconds. Norm values are available for several languages, also in Dutch.\(^{28-30}\) MRR is the number of syllables per second during the 5 first seconds (syllables/seconds) of producing the monosyllabic sequences /pa/, /ta/, /ka/ and a trisyllabic sequence /pataka/. The best score of three trials was used in the analysis.

- **Videofluoroscopy of swallowing** was performed with the Digital Swallowing Workstation (Swallowing Signals Lab, model 7120) to quantify the swallowing efficiency and safety using the Normalized Residue Ratio Scale (NRRS) and
the Penetration Aspiration Scale (PAS). For a detailed description of these measurements we refer to Kroon et al. (2020).

- Video-tapes were made of eye-movements and ptosis for off-line analysis by a neurologist (CH). Ptosis was scored both sides on a scale from 0 - 3 (0 = no ptosis, 1 = mild ptosis (above half of the pupil), 2 = severe ptosis (below half of the pupil), 3 = status after operative ptosis correction). Eye movements were scores as ophthalmoplegia present or absent.

Quality of life scales

For an assessment of patients’ quality of life, we used the International Quality of Life (INQoL) questionnaire and the SF-36 Health Survey.\textsuperscript{31, 32}

Statistical analysis

IBM SPSS Statistics (version 25) was used to conduct all statistical analyses and p-values of < 0.05 were considered statistically significant. The interviews and structured questionnaires were analysed by counting the number of patients who reported any (worsening of) subjective complaint in any of the domains. Individual scores on the INQoL and SF-36 Health Assessment were calculated according to their requirements and mean scores were estimated per domain. The results of all clinical measures at baseline and follow-up were compared using paired sample t-tests to calculate the mean differences with their 95% confidence intervals. Differences of measures that were not normally distributed at baseline were also tested using the Wilcoxon signed-rank test. The mean differences and confidence intervals were converted into percentages of worsening. The correlation between patient characteristics (disease duration and GCN-repeat size) and disease progression on all tasks was analysed by calculating Spearman’s rho correlation coefficients.

Data Availability

The anonymized data that support the findings of this study are available from the corresponding author upon reasonable request.
Results

Patients

Forty-four OPMD patients were invited by their treating physicians or from the national neuromuscular database. Nineteen family members of these patients, that were therefore putative OPMD patients, were asked to participate as well. Fig. 1 shows the flowchart of participant recruitment and inclusion. After genetic testing, it appeared that two family members did not have a mutation in the PABPN1 gene. Therefore, these two participants were excluded. The demographic and genetic details of the 43 OPMD patients are summarized in Table 1. Four patients did not have any complaints at baseline and these are further referred to as asymptomatic carriers. The mean time between the two visits was 20 months (median 20 months, range: 17 - 24 months).

At follow-up two out of four asymptomatic carriers reported subjective complaints and became symptomatic carriers; one reported ‘tired legs and difficulty climbing stairs’ and the other reported ‘a hoarse voice and difficulty with simultaneous tasks like eating and walking’.

Clinical measures

Nine of the 21 measures were not normally distributed with three having a p-value smaller than 0.05, however when using the Wilcoxon signed-rank test instead, the significance of the p-values did not change. Table 2 shows the mean percentages of worsening on the 21 measures of which ten proved statically significant.

Muscle strength

Fixed dynamometry

Fixed dynamometry of the deltoid muscle (left side), quadriceps (left side) and iliopsoas muscle (both sides) was performed in 39 patients. Thirty-eight patients underwent fixed dynamometry of the deltoid muscle and quadriceps (right side). Some patients were not able to perform the tasks due to injuries or technical errors.

All dynamometry measures showed a statistically significant decline over 20 months (Table 2, up to 27% decline), except for the iliopsoas muscle of the left leg (mean decline: 8.7% (95% CI: -18.3 – 0.1)). The deltoid muscle showed the largest strength deterioration over time (Fig. 2A, left arm: mean decline: 24% (95% CI: -16.8 – -30.2); right arm: mean decline: 27% (95% CI: -16.7 – -36.9)).
Maximum isometric tongue strength

Maximum tongue strength showed a mean decline of 9.9% over 20 months (95% CI: (-5.6 – -14.9), Table 2, Fig. 2B).

Manual muscle testing (MRC-scale)

The MRC sum-score of all muscles showed a mean decline of 2.5% between baseline and follow-up (Table 2, 95% CI: (-0.9 – -4.1)). The MRC-grading also showed a small but significant decrease of 0.1 to 0.2 points at follow-up for three individual muscle groups: hip adduction (both sides, mean difference: 0.19, p = 0.010), elbow flexion (right side, mean difference: 0.11, p = 0.024, left side mean difference: 0.10, p = 0.044) and shoulder abduction (right side, mean difference 0.14, p = 0.032, left side, mean difference: 0.14, p = 0.013).

Functional capacity

Stairs walking test

Thirty-four patients showed a mean decline of 12.5% (Fig. 2C, (95% CI: -19.6 – -5.4)). Six patients at baseline and nine patients at follow-up were not able to perform the stair walking test due to severe muscle weakness in the legs.

Motor Function Measure

Part D1 of the MFM test, concerning stance tasks and transfers, showed a mean decline of 7.1% (95% CI: -2.4 – -11.7, Table 2, Fig. 2D). Part D2 and D3 of the MFM did not show a significant change over 20 months (p > 0.05).

Swallowing, chewing and speaking

Swallowing tasks (maximum swallowing speed and maximum swallowing volume) and chewing time did not worsen significantly during follow-up (Table 2). Five patients at baseline and ten patients at follow-up were not able to perform the TOMASS chewing test. Of the speech capacity tests, only the maximum repetition rate of the syllable /pa/ was significantly slower at follow-up (mean decline: 5.3% (95% CI: -1.1 – -8.8)).

Videofluoroscopy

Forty-two patients were able to perform the videofluoroscopy. The amount of abnormal pharyngeal residue of thin liquid (10 mL) in the valleculae increased
significantly during follow-up (mean NRRS ratio 0.24 versus 0.13, p = 0.007). The NRRS ratios for the valleculae and pyriform sinus of the other consistencies did not show a significant difference between baseline and follow-up.

Patients showed no aspiration of thick liquids at baseline, while at follow-up unsafe swallowing (PAS > 3) was seen during swallowing 10 mL in 8% of the patients (p = 0.119) and 20 mL in 3% of the patients (p = 0.324). When swallowing 10 mL thin liquid, unsafe swallowing was less frequent at follow-up (baseline: 21% of all patients, follow-up: 10% of all patients, p = 0.033). No change in aspiration rate was seen for swallowing 20 mL of thin liquid and solid food.

Ptosis and ophthalmoplegia

Ptosis analyses was done for 40 patients; measurements of three patients were missing, because of poor video quality. At baseline, 31 patients had ptosis. Ptosis had worsened at follow-up for three patients: one patient went from no ptosis to mild ptosis and two patients went from mild ptosis to severe ptosis. Seventeen patients underwent ptosis correction of the right or/and left eye at baseline; at follow-up that were 19 patients.

Ophtalmoplegia analyses were performed in 37 patients, measurements of six patients were missing due to poor video quality. Based on the examination of 2 independent clinicians, subtle ophthalmoplegia was present in 14 out of 37 patients at baseline and follow-up, especially in the upper vertical direction.

Quality of life scales

The highest negative impact on quality of life was scored in the INQoL domains ‘muscle weakness’, ‘activities’, ‘body image’ and ‘fatigue’ (mean at follow-up: 46.8; 37.1; 32.5; 29.6), but none of the domains of the INQoL showed a significant difference between baseline and follow-up. In the SF-36 Health Survey the domain ‘physical functioning’ showed a significant deterioration between baseline and follow-up (baseline mean (SD): 61.2 (30.9); follow-up: 57.6 (31.4), p = 0.044).

Asymptomatic carriers

Each asymptomatic carrier scored somewhat lower on various muscle strength tasks (dynamometry of upper and lower extremities, maximum isometric tongue strength
and maximum bite force) and functional capacity tests (maximum swallowing volume and motor function measure).

**Natural history**

The deltoid, quadriceps and iliopsoas muscles showed the largest disease progression, followed by the tongue muscle (Table 2). Strength decline of these muscles was seen across all patients regardless of the disease severity: i.e. in mildly and severely affected patients.

No relationship was found between patient characteristics (disease duration and repeat length (GCN)) and disease progression in muscle strength and functional capacity measurements ($p > 0.05$). Fast and slow rates of disease progression were found in asymptomatic as well as in severely affected patients.
Discussion

Although disease progression in OPMD is known to be very slow, the main finding of this nationwide longitudinal cohort study is that deterioration can be detected by eight different clinical measures, irrespective of disease severity, during a period of only 20 months. In the absence of comparable studies, this implies that these measures (dynamometry of the deltoid, quadriceps, and iliopsoas muscles, maximum tongue strength, MRC sum score, 10-step stair test, part D1 of the MFM and maximum speech repetition rate /pa/) could be used to detect disease progression within the timeframe of a therapeutic trial.

With dysphagia being the main feature of OPMD it is highly relevant that tongue strength is one of the features that significantly reduces over an average of 20 months with a mean of 10%. Indeed, the tongue muscle is the most affected oropharyngeal muscle in OPMD patients as seen in muscle MRI measures. Moreover, tongue strength is easy to measure with commercially available hand-held devices. However, muscle strength of the deltoid muscle showed an even greater mean decline over time (27%). This emphasizes that upper extremity involvement is an important and common feature of OPMD, and our results show that deltoid strength could be a valuable measure to detect disease progression or therapeutic effect in OPMD patients.

Disease progression could also be measured by muscle strength measures of the lower extremities. Although some studies reported that the anterior thigh compartment is less affected on muscle MRI measures than the posterior part, in our dynamometry measurements there was a significant decline in muscle strength of the quadriceps muscle over 20 months. This may suggest that the strength of the posterior compartment (i.e. hamstrings muscle) might be a sensitive measure of disease progression as well. In our study set-up however, dynamometry of the hamstrings was not possible, so this should be the subject of future studies.

The stair walking test showed the largest decline of all functional capacity tests. In other natural history studies of slowly progressive neuromuscular disorders, for example in facioscapulohumeral muscular dystrophy (FSHD), the step-stair test did not show any clinical progression after 1 year. Furthermore, the MFM detected disease progression in our cohort, in contrast to one earlier study that showed no
progression in the MFM in 8 OPMD patients over a follow-up period of eight to 16 months.\textsuperscript{16} 

Except for reduced tongue strength and maximum repetition rate of /pa/, no significant decrease was found in the functional capacity tests of chewing, swallowing and speaking. Even maximum swallowing speed, which at baseline with a mean of 10 mL/s was already far below normal (25 mL/s),\textsuperscript{35} was only slightly and insignificantly reduced after 20 months. Apparently, it is not sensitive enough to detect a decline within 20 months or swallowing is already so slow that further deterioration becomes less likely (bottom-effect). During videofluoroscopy only a few changes were seen. Unsafe swallowing occurred less frequently in those ingesting 10 mL thin liquid at follow-up, which may reflect compensatory actions preventing unsafe swallowing or a learnt response between baseline and follow-up measurements. However, a small deterioration in unsafe swallowing was seen following ingestion of thick liquids. Then, videofluoroscopy does appears to be a less appropriate technique to detect swallowing deterioration in OPMD over 20 months.

Typically, healthy people very slowly deteriorate on muscle-related tasks because of aging (normal age-related changes). Hence, in our previous paper\textsuperscript{35} we compared OPMD patients with age-matched Dutch healthy controls on swallowing, chewing and speaking tasks. OPMD patients scored significant lower on these tasks compared to age-matched healthy controls. Also for the stair step test, healthy controls with approximately the same mean age (58.4 years) as our OPMD group, showed much faster stair step times compared to our OPMD group (mean per step: 0.336 seconds vs. 0.56 seconds).\textsuperscript{36} OPMD is suggested to be an accelerated aging disorder,\textsuperscript{37, 38} so we expect that the disease progression on clinical outcome measures will be greater in OPMD patients than in age-matched healthy controls, however, to our knowledge, there are no longitudinal studies on the clinical outcome measures in healthy controls. The goal of this study was to detect changes on clinical outcome measures in OPMD patients, which will be caused by disease progression and aging. A direct comparison to controls would explain this further, but was not the scope of the current study.
At follow-up, two of the four asymptomatic carriers had become symptomatic. On an individual level, each patient scored lower on various measures at follow-up; and that measure corresponded to the subjective complaints of the patient (i.e. difficulty climbing stairs and tired legs). Larger cohorts of asymptomatic OPMD carriers may give more insights into the subtle signs of disease onset, but are difficult to perform due to the rarity of the disease and the difficulty to find asymptomatic carriers.

Future longitudinal studies with larger (international) cohorts can also observe the natural history of OPMD patients per age groups. In this study, analyses by age group was not possible due to the small number of cases per age. Also, within-family analysis were not feasible in our study. Although ten different families were identified within our study, five of them were very small (only 2 family members). Still, similarities between family members might overestimate the magnitude and precision of the estimated changes over time, suggesting that in future studies this should be taken into account as well. However as OPMD is a rare disease, it is hard to perform large studies to allow such analyses.

According to the INQoL, the quality of life of our OPMD patients was reduced by several factors, but mostly by ‘muscle weakness’ and ‘fatigue’, which is in coherence with previous studies on the quality of life in OPMD patients. Similar QoL scores were also found in other populations with muscular dystrophies. QoL was not further reduced at follow-up, except that patients’ health status was slightly reduced according to the SF-36 Health Survey, but only in the domain ‘physical functioning’. This resonates with our main finding that captured disease progression on eight of the strength and functional capacity measures. The overall QoL-scale does not seem to be useful to capture progression within 20 months.

Some of the changes in clinical outcome measures are small and not likely to have functional implications for patients. However, as the measure may be more sensitive than patients’ subjective sense of progression, it is relevant for therapy trials to detect small effects. For the MFM a minimal clinically important difference is defined as 2.5 to 5% change. In our study a change of 7.1% was seen in OPMD patients. For the other clinical measures no studies exist on the minimal clinically important differences. Future longitudinal studies with the focus on the minimal clinical
important differences of clinical outcome measures in OPMD patients are needed to confirm our findings.

No relationship was found between disease progression and disease duration or genotype. On the contrary, fast and slow rates of disease progression were found in both mildly and severely affected patients. There must be epigenetic or environmental factors that influence disease progression that are not known yet. Larger studies with repeated follow-up measures are needed to ascertain a pattern in progression rates.

The results of this study may be influenced by the following shortcomings. The maximum bite force was measured by a validated tool that measures the bite force with the front teeth, but not with the molar teeth. Bite force may have been underestimated by this, although it does not change the value of this longitudinal data. Another limitation is that we may have left relevant measurements out of the examination, despite the carefully composed study protocol. Dynamometry measurements to measure the strength of the hamstring muscles may be relevant, but also spirometry to measure vital force capacity (VFC) is suggested to be relevant in OPMD in relation to dysphagia and dysarthria. Furthermore, for two measures some patients were unable to perform the task (ten patients for TOMASS chewing time and nine patients for stairs walking test), which suggests underestimation. This could have implications for the magnitude of the differences. Furthermore, judging ophthalmoplegia on the video recordings was difficult and progression was not possible to reliably objectify. Finally, a third time point during follow-up was not feasible within our study design, but would allow more solid conclusions on the responsiveness of the outcome measures. Further research is needed to make statements whether the clinical outcome measures can detect disease progression over a shorter or longer timeframe of a therapeutic trial.

An unexpected observation was that although most patients showed disease progression in the muscle strength tests, a few patients performed better at follow-up. Some of them reported that they had developed a more active lifestyle by playing sports or having adapted a walking routine during the study period. We did not systematically ask patients about their daily activities and sports, but it would be
interesting to examine whether an active life style may affect muscle strength and functional capacity in OPMD patients as it did in myotonic dystrophy type 1 and FSHD.\textsuperscript{44, 45}

This study shows the feasibility to quantify disease progression in OPMD within 20 months, the time frame of a drug trial. This paves the way for reliable clinical trials in humans. Equally important is that our results show that weakness of the shoulder girdle and lower limb girdle are more sensitive to changes than the oropharyngeal measurements. However, further research is needed to confirm and explain these findings in larger (international) cohorts.
## Appendix 1: Authors

<table>
<thead>
<tr>
<th>Name</th>
<th>Location</th>
<th>Contribution</th>
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<tbody>
<tr>
<td>Rosemarie Kroon, MA</td>
<td>Radboud university medical center, The Netherlands</td>
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</tr>
<tr>
<td>Johanna Kalf, PhD</td>
<td>Radboud university medical center, The Netherlands</td>
<td>Study concept and design, acquisition, analysis, interpretation of data, revision of the manuscript</td>
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<tr>
<td>Bert de Swart, PhD</td>
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</table>
References

45. Voet NBM, Kooi ELvd, Riphagen II, Lindeman E, Engelen BGMr, Geurts ACH. Strength training and aerobic exercise training for muscle disease. Cochrane Database of Systematic Reviews 2013;vol. 7:CD003907.
Figure Legends

**Figure 1.** Flowchart of participant recruitment and inclusion.

**Figure 2.** Measurements of muscle strength and functional capacity at baseline and follow-up. **A.** Muscle strength of the left deltoid muscle using dynamometry (N). **B.** Tongue strength (kPa). **C.** 10-step stair test. **D.** Part 1 of Motor Function Measure (MFM). Each line represents a patient. Red line = mean score.
Table 1. Patient characteristics

<table>
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<tr>
<th>Patient characteristics (n = 43)</th>
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<td>23</td>
</tr>
</tbody>
</table>

*No differences in the clinical phenotype and pathological expression between the recessive and dominant cases were found, therefore we did not exclude the recessive (GCN)11/(GCN)11 cases.46
Table 2. Mean (SD) at baseline and follow-up and percentage of decrease of the muscle strength and functional capacity measurements.

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD) baseline</th>
<th>Mean (SD) follow-up</th>
<th>% of decrease (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Muscle strength</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dynamometry of deltoid right arm (N)*</td>
<td>178.7 (85.2)</td>
<td>130.8 (73.2)</td>
<td>- 26.8 (-16.7 – -36.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dynamometry of deltoid left arm (N)**</td>
<td>173.4 (84.4)</td>
<td>132.6 (65.0)</td>
<td>- 23.5 (-16.8 – -30.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dynamometry of quadriceps left leg (N)**</td>
<td>333.6 (162.6)</td>
<td>285.8 (165.4)</td>
<td>- 14.3 (-6.0 – -22.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Dynamometry of quadriceps right leg (N)*</td>
<td>334.9 (167.5)</td>
<td>292.4 (170.3)</td>
<td>- 12.7 (-3.7 – -21.7)</td>
<td>0.007</td>
</tr>
<tr>
<td>Dynamometry of iliopsoas right leg (N)**</td>
<td>211.6 (92.0)</td>
<td>185.7 (82.7)</td>
<td>- 12.2 (-5.5 – -18.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Maximum tongue strength (kPa)</td>
<td>32.2 (13.9)</td>
<td>29.0 (13.7)</td>
<td>- 9.9 (-5.6 – -14.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dynamometry of iliopsoas left leg (N)**</td>
<td>208.8 (87.7)</td>
<td>190.7 (85.3)</td>
<td>- 8.7 (-18.3 – 0.1)</td>
<td>n.s.</td>
</tr>
<tr>
<td>MRC sum score (0 - 130)</td>
<td>122.0 (12.9)</td>
<td>119.0 (17.5)</td>
<td>- 2.5 (-0.9 – -4.1)</td>
<td>0.003</td>
</tr>
<tr>
<td>Maximum bite force (kg)</td>
<td>15.2 (7.2)</td>
<td>14.9 (8.0)</td>
<td>- 0.3 (-10.5 – 5.3)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Functional capacity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-step stair test (sec)***</td>
<td>5.6 (1.5)</td>
<td>6.3 (2.1)</td>
<td>- 12.5 (-19.6 – -5.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Motor Function Measure D1 (%)</td>
<td>79.3 (28.7)</td>
<td>73.7 (31.3)</td>
<td>- 7.1 (-2.4 – -11.7)</td>
<td>0.004</td>
</tr>
<tr>
<td>Maximum phonation time (s)</td>
<td>15.7 (8.2)</td>
<td>14.8 (7.7)</td>
<td>- 5.7 (-15.3 – 3.8)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Maximum repetition rate /PA/ (syl/s)</td>
<td>5.7 (0.6)</td>
<td>5.4 (0.8)</td>
<td>- 5.3 (-1.1 – -8.8)</td>
<td>0.014</td>
</tr>
<tr>
<td>Maximum swallowing volume (mL)</td>
<td>29.6 (18.9)</td>
<td>28.1 (17.6)</td>
<td>- 5.1 (-13.9 – 3.4)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Maximum swallowing speed (mL/s)</td>
<td>4.1 (0.6)</td>
<td>4.0 (0.6)</td>
<td>- 2.4 (-4.9 – 4.9)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Maximum swallowing speed (mL/s)</td>
<td>10.0 (7.2)</td>
<td>9.6 (7.2)</td>
<td>- 4.0 (-13.0 – 4.0)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Motor Function Measure D3 (%)</td>
<td>98.1 (4.4)</td>
<td>96.9 (8.6)</td>
<td>- 1.2 (-3.3 – 0.7)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Motor Function Measure D2 (%)</td>
<td>96.8 (8.4)</td>
<td>95.8 (10.6)</td>
<td>- 1.0 (-2.6 – 0.4)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Maximum repetition rate /PATAKA/ (syl/s)</td>
<td>5.4 (0.6)</td>
<td>5.4 (0.7)</td>
<td>0 (-3.7 – 1.9)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Maximum repetition rate /KA/ (syl/s)</td>
<td>5.0 (0.8)</td>
<td>5.0 (0.6)</td>
<td>0 (-4.0 – 2.0)</td>
<td>n.s.</td>
</tr>
<tr>
<td>TOMASS chewing time (sec)****</td>
<td>59.4 (28.4)</td>
<td>53.9 (25.8)</td>
<td>9.3 (-2.4 – 20.9)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Measurements are arranged in order of the degree of disease progression (% decline). Statistically significant worsening is given in bold.

*N = 38, **N = 39, ***N = 34, ****N = 33.
# Longitudinal Assessment of Strength, Functional Capacity, Oropharyngeal Function, and Quality of Life in Oculopharyngeal Muscular Dystrophy

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