8-1-2023

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Recommended Citation
Hunn, Stephanie; Alfano, Lindsay; Seiffert, Michelle; and Weihl, Conrad C, "Exploring hand and upper limb function in patients with inclusion body myositis (IBM)." Neuromuscular Disorders. 33, 8. 643 - 650. (2023).
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Exploring hand and upper limb function in patients with inclusion body myositis (IBM)

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ABSTRACT

Inclusion body myositis (IBM) is an inflammatory myopathy characterized by progressive weakness of knee extensors and finger flexors. Many patients lose independence with fine motor tasks; however, a gap remains as to how these deficits correlate with performance on functional outcome measures. We describe functional hand impairments as measured by performance-based outcome measures in a cross-sectional sample of 74 patients with IBM. Subjects completed a series of outcome measures (Functional Dexterity Test (FDT), Performance of the Upper Limb (PUL), and Sollerman Hand Function Test (SHFT)) alongside a collection of patient reported outcomes (PROs). Assessments were compared to standard IBM measurements, including grip strength and IBM Functional Rating Scale (IBMFRS). FDT and SHFT demonstrated significant correlations to grip (p<0.001; Spearman correlations r=0.48–0.70). Significant correlation was found between all functional outcome measures and IBMFRS (p<0.001; Spearman correlations r=0.51–0.77), as well as PRO Upper Extremity Scale for IBM (IBM-PRO) (p<0.05; Spearman correlations r=0.55–0.73). Non-ambulatory patients demonstrated significantly weaker grip (p<0.001), resulting in lower PUL scores and increased FDT completion times (p<0.001). Collectively, these assessments may provide insight to understanding functional limitations of the hands and potentially allow for more inclusive clinical trials with future validation of hand assessments in IBM.

1. Introduction

Inclusion body myositis (IBM) is an inflammatory myopathy characterized by progressive weakness, specifically of the quadriceps and long finger flexors. The disease is more prevalent in males, with symptoms usually developing in adulthood and most individuals diagnosed after age 50 [1]. Historically, disease progression has been monitored by decline in IBM Functional Rating Scale (IBMFRS) scores and decrease in muscle strength testing, such as grip strength [2,3]. While these assessments are still utilized in both clinical and research settings, we continue to find limitations in capturing a more in-depth understanding of functional hand weakness in patients with IBM and the impact it has on daily activities.

Grip strength using a handheld dynamometry device measures maximum isometric strength of flexor muscles of the hand and forearm as one unit rather than measuring strength of individual muscles. Measuring pinch grip goes a step further to isolate targeted muscles, such as the flexor digitorum profundus and flexor pollicis longus [2]. With standard dynamometry testing, many patients with IBM have difficulty flexing their fingers to form a closed fist, often times requiring compensatory positioning (Fig. 1). This is one of the limitations with quantitative muscle testing or manual muscle testing, as our current strength measurements may not adequately represent the patient’s functional strength in the hands and fingers [4–6].

Measuring “power grip” by means of isometric grip strength testing has been able to detect disease progression through decline in strength over time as seen in previous longitudinal studies [1]; however, this grip is not considered to be one of the most common functional grips used in daily activities and often times is a measurement that IBM patients are having to use compensatory techniques to perform (i.e. only flexing at the metacarpophalangeal joints due to inability to make a closed fist). According to Sollerman and Ejeskar et al., the eight most common hand-grips are pulp pinch (20%), lateral pinch (20%),...
tripod pinch (10%), five-finger pinch (15%), diagonal volar grip (15%), transverse volar grip (14%), spherical volar grip (4%), and extension grip (2%) [7]. These grips require strength from a combination of intrinsic hand muscles and/or forearm muscles and may be assessed with isometric manual muscle testing of each individual muscle. Additionally, these intrinsic tasks require coordination and dexterity, which may be measured with dynamic movements such as observing whether or not a patient is able to complete a particular task (i.e. picking up coins).

Few studies have reported hand functional assessments in the IBM population [3], with common conclusions finding that standard outcome measures, such as peg board tests, are limited by the unique compensation techniques seen in patients with IBM [8]. Assessments using a composite scoring system, such as the Performance of the Upper Limb (PUL), take compensation into account; however, these assessments have not been validated in IBM. The ability to continue performing fine motor tasks using these compensation techniques may partly explain the discrepancy between perceived hand function captured in patient-reported outcomes (PROs) and weakness in distinct muscle groups.

As patients with IBM experience progression of hand weakness, quality of life can decrease with the progressive loss of independence with common activities of daily living [9]. With the lack of clinically validated upper extremity assessments in the IBM population and prior studies of hand function in IBM being mostly limited to grip and pinch strength, we attempt to broaden the understanding of utility of common upper extremity and hand assessments, previously validated in other diseases, including hand grip, the Functional Dexterity Test (FDT), Performance of the Upper Limb (PUL 2.0), and Sollerman Hand Function Test (SHFT), and patient-reported outcome measures.

2. Patients and methods

2.1. Patients

Patients with IBM, meeting a revised ENMC criteria (age of onset >40 rather than 45 years old) [6] were recruited from the Washington University School of Medicine IBM Multidisciplinary Clinic (WUSM) or at the 2022 Annual Patient Conference of The Myositis Association (TMA) (See Table 1). Written, informed consent was obtained on all patients enrolled at WUSM under an institutional review board (IRB) approved protocol. Patients enrolled via TMA were exempt from obtaining informed consent due to the lack of identifiable demographic and protected health information (PHI) being collected. Demographics recorded included the participant’s age, gender, diagnosis, hand dominance, age of symptom onset, and age of diagnosis. Additionally, 13 age-matched healthy control subjects were recruited specifically for the Functional Dexterity Test (FDT) to be used for comparative analysis under a separate IRB-approved protocol. These participants were exempt from obtaining a written consent as they were only asked to provide the participant’s age, gender, and hand dominance in addition to completing the FDT.

Each group completed a series of patient reported outcomes (PROs) and functional outcome measures. All patients completed the IBM-FRS, IBM-PRO, grip strength and Functional Dexterity Test (FDT), and clinic patients additionally completed the Performance of the Upper Limb (PUL) and/or Sollerman Hand Function Test (SHFT) along with the Disability of the Arm, Shoulder, and Hand (DASH) questionnaire.

2.2. Strength assessment

Grip strength was measured by a trained neuromuscular physician or physical therapist using a Jamar dynamometer. In both the clinic and conference settings, the patient was in a seated position with testing arm in line with trunk and elbow flexed to 90°. The participants arm and/or device was supported due to weakness, as needed. Both dominant and non-dominant hands were measured; however, only the dominant hand grip, defined as the patient’s preferred writing hand, was used for the analysis of this data as it was shown to have significantly greater grip strength than the non-dominant hand (p=0.001).

2.3. Functional outcome measures

2.3.1. Functional dexterity test (FDT)

The Functional Dexterity Test (FDT) uses a peg board with 16 wooden cylindrical pegs. Patients are seated and instructed to pick up each peg and turn them over as quickly as they can while trying to avoid supinating at the forearm or touching the board with the peg to turn it over [10]. Patients perform the task with both dominant and non-dominant hands; a maximum of 2 min per hand is allowed. The evaluator records the time it takes to complete the test, in addition to adding penalties for each use of restricted compensatory movements and each dropped peg.

2.3.2. Performance of the upper limb (PUL 2.0)

The Performance of the Upper Limb (PUL 2.0) is a 21-item upper extremity clinical outcome assessment that sums three dimensions into a composite score: high level shoulder dimension, mid-level elbow dimension, and distal wrist and hand dimension [11]. The test is performed with the patient in a seated position with back support and the table set ideally to a height that is level with the patient’s umbilicus. The PUL is performed with the dominant or preferred hand, though there are some items that require bilateral hand involvement to complete the task.

2.3.3. Sollerman hand function test (SHFT)

The Sollerman Hand Function Test (SHFT) is a 20-item test designed to assess a person’s ability to perform everyday tasks, such as opening jars, do up buttons, pour water, etc., using seven of the most commonly used handgrips—pulp pinch, lateral pinch,
tripod pinch, five-finger pinch, diagonal volar grip, transverse volar grip, and spherical volar grip [12]. This test is performed with both the dominant/preferred hand and the non-dominant hand. Each item is timed and scored on a 5-point scale from 0 (unable to perform task) to 4 (task completed without difficulty), with scoring based on time and use of an acceptable grip. A score of 80 points (maximum score) on the dominant hand and roughly 76-79 points on the non-dominant hand is indicative of typical performance [7-8].

The patient is instructed to begin the test in a seated position but is allowed to stand and reposition, as needed, for each item.

2.4. Patient reported outcomes

2.4.1. IBM functional rating scale (IBMFRS)

The IBMFRS is a 10-item questionnaire developed to assess common activities of daily living, such as fine motor tasks, dressing, hygiene, as well as ambulatory status and dysphagia in patients with IBM [13]. It was completed as an interview with the clinician scoring the patient’s functional level or as a self-reported questionnaire. The maximum is 40 points, with a higher score indicating a higher level of function and independence [13].

2.4.2. Disability of the arm, shoulder and hand (DASH)

The DASH questionnaire is a patient reported outcome measure that consists of 30 items assessing a patient’s ability to perform different upper extremity activities [14]. Specific sections related to work and extracurricular activities (such as playing a sport or instrument) are also included to assess the impact of upper extremity weakness and/or pain across multiple domains. A higher score indicates a greater level of difficulty or disease severity.

2.4.3. PRO upper extremity scale for IBM (IBM-PRO)

The IBM-PRO is a 12-item questionnaire designed specifically to assess a patient’s perceived level of difficulty with various daily activities involving hand and arm function [2]. Participants score each item on a 5 point scale (0- unable to 4- no difficulty) with a higher score indicating a higher level of function.

2.5. Data analysis

2.5.1. Descriptive statistics were performed for each cohort of patients that completed the functional outcome measures

Linear regression was used to determine whether or not there was statistical significance in performance of outcome measures as the disease progresses. Unpaired t-tests and Mann Whitney tests were used to analyze any differences in measurements and scoring between groups of subjects. Both parametric (Pearson R) and non-parametric (Spearman Rho) correlations were calculated to look for any relationships between the assessments and disease severity. Bonferroni correction test was also performed to reduce the potential for false positive findings within the data analysis.

3. Results

3.1. Demographics

Forty-six patients were enrolled from WUSM clinic and 29 from TMA. Of these 29 participants, one was excluded due to a self-reported disease history that was inconsistent with the typical progression of IBM, resulting in a total of 28 conference participants included in the final analysis. Our combined dataset included a total of 74 subjects (Table 1). The characteristics of our WUSM and TMA cohorts were very similar across age at enrollment, age of symptom onset, disease duration, and age at time of diagnosis. There was an average diagnostic delay of 4.8 years across our full cohort.

3.2. Relationship between upper extremity outcome measures, PROs and covariates

In our total cohort, grip strength significantly correlated with duration of the disease (p=0.01, Pearson r = -0.41) (Fig. 2). The other functional measures including FDT, PUL, and SHFT were not significantly correlated with disease duration (p>0.05) due to the heterogeneity of this patient cohort. The PROs were not found to have significant correlation with disease duration (p>0.05).

To further understand the heterogeneity of this patient sample, we divided the patients with IBM into sub-groups based on gender, ambulatory status, and the presence of anti-NT5c1A antibodies (See Table 2). Non-ambulatory patients, classified as non-walkers or full-time use of an assistive device, had significantly weaker grip than ambulatory patients (p=0.001). These patients required a significantly increased amount of time to complete the Functional Dexterity Test (p=0.001) and were found to have a lower total composite score on the Performance of the Upper Limb (p<0.001), indicating a higher level of upper extremity weakness or functional

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient demographics.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CLINIC COHORT</strong></td>
<td><strong>TMA COHORT</strong></td>
</tr>
<tr>
<td>n=46</td>
<td>n=28</td>
</tr>
<tr>
<td></td>
<td>(mean ± SD [range])</td>
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<tr>
<td>AGE</td>
<td>66.8 ± 8.3</td>
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<tr>
<td>[47 - 82]</td>
<td>[47 - 84]</td>
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<tr>
<td>AGE OF SYMPTOM</td>
<td>58.3 ± 8.1</td>
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<tr>
<td>ONSET</td>
<td>42 ± 76</td>
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<tr>
<td>AGE AT DIAGNOSIS</td>
<td>63.4 ± 8.0</td>
</tr>
<tr>
<td>[51 - 79]</td>
<td>[43 - 78]</td>
</tr>
<tr>
<td>DISEASE DURATION</td>
<td>8.3 ± 4.6</td>
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<tr>
<td>[1 - 25]</td>
<td>[2 - 19]</td>
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<tr>
<td>GENDER</td>
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<tr>
<td>Male= 31 (67.4%)</td>
<td>Male= 13 (46.4%)</td>
</tr>
<tr>
<td>Male= 15 (32.6%)</td>
<td>Female= 15 (53.6%)</td>
</tr>
<tr>
<td>NT5c1A (+/-)</td>
<td></td>
</tr>
<tr>
<td>Positive= 32 (69.6%)</td>
<td></td>
</tr>
<tr>
<td>Negative= 13 (28.3%)</td>
<td></td>
</tr>
<tr>
<td>Unknown= 1 (2.1%)</td>
<td></td>
</tr>
<tr>
<td>ENMC CRITERIA</td>
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</tr>
<tr>
<td>Clinically Defined</td>
<td></td>
</tr>
<tr>
<td>IBM: 30 (65.2%)</td>
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</tr>
<tr>
<td>Clinically Defined:</td>
<td></td>
</tr>
<tr>
<td>IBM: 10 (21.7%)</td>
<td></td>
</tr>
<tr>
<td>Probable IBM: 6 (13.1%)</td>
<td></td>
</tr>
</tbody>
</table>

limitation than the ambulatory group. There was no significant difference in performance between the ambulatory and non-ambulatory groups on the Sollerman Hand Function Test. No significant difference was found between gender or anti-NT5c1A antibody status in grip strength or performance of the three functional outcome measures.

3.3. Correlation of grip strength and upper extremity outcomes

Using Spearman and Pearson correlations, we compared performance of grip strength and the three functional outcome measures seen in Fig. 3. The SHFT demonstrated the highest correlation with grip (\(p<0.05\), Spearman correlation \(r=0.70\),
followed by the FDT ($p=0.001$, Pearson correlation $r=-0.48$). There was no significant correlation between grip strength and the PUL ($p>0.05$), which may be due to the PUL being multi-dimensional to quantify full upper extremity function in addition to functional hand strength.

3.4. Patient reported outcomes

Significant correlation was observed between the IBMFRS and all functional outcome measures, shown in Fig. 4. The IBM-PRO also demonstrated significant correlation with the functional outcome measures (See Table 3). The DASH was not found to have significant correlation with any of the functional outcome measures ($p>0.05$).

3.5. Comparison of IBM to controls

All patients in our cohort demonstrated grip strength lower than expected for their age range compared to healthy controls (males: mean 11.1 kgs [SD 9.0; range [0 – 43.1]), 47.6% predicted; females: mean 8.0 kgs [SD 4.6; range [1.8 – 19.5]), 47.9% predicted) [15]. Patients with IBM required increased time to complete the FDT compared to age-matched healthy control subjects, with a significant difference in performance between the two groups (healthy mean 29.6 s [SD 6.19]; IBM mean 75.9 s [SD 58.6]; $p=0.01$). The PUL demonstrated a ceiling effect in 15 patients (65%), similar to other patient cohorts without pronounced proximal upper extremity weakness [16].
While patients demonstrated adequate proximal upper extremity strength, distal weakness made it difficult to grip the weights and cans in a typical fashion. However, patients adapted by using alternative grip techniques to successfully complete high dimension PUL items, maintaining a high score in the presence of finger flexor weakness.

3.6. Exploration of individual grip and pinch techniques

Because the SHFT presented an opportunity to further analyze individual pinch and grip techniques, such as lateral pinch or volar grip, we attempted to determine if there was any trend in progression as to which grips or tasks are affected first. In Fig. 5-A, the transverse volar grip was found to correlate significantly with disease duration (p < 0.05). Fig. 5-B shows linear regression of each SHFT item with the mean and range of each item shown in the floating bar graph in Fig. 5-C. Item 7 (turn screwdriver), Item 10 (do up buttons), Item 17 (turn door handle), Item 19 (pour from container), and Item 19 (pour from jug) seeming to decline more rapidly as disease progresses. Items 17 and 19 both require use of the transverse volar grip. While we are unable to make any conclusions from this data given the small cross-sectional sample, these results provide insight to a more in-depth understanding of intrinsic hand techniques that may be worth exploring further in future research.

4. Discussion

Our study describes a cross-sectional sample of functional outcome measures to further our understanding of the utility of available clinical outcome assessments to quantify hand weakness and upper extremity function in patients with IBM and the impact of these on patient-reported outcomes. We evaluated a battery of clinical outcome measures along with patient reported outcome measures (PROs) in an attempt to improve the ability to quantify hand weakness in this population.

All strength and functional outcomes included were significantly correlated to patient-reported abilities as measured by the IBMFR5 and IBM-PRO. While grip strength does not account for modified, compensatory techniques, the scoring of the included functional outcome measures considers compensatory strategies and, therefore, may be representative of a more accurate measurement of the patient’s functional abilities. Using the battery of assessments described in this study, our data does suggest some differences in the amount of hand weakness based on ambulation status, with those patients that are considered non-ambulatory demonstrating greater progression of hand weakness, as seen in grip strength, the FDT and PUL. Our data does not suggest any differences between gender or the presence of anti-NT5c1A antibodies in the performance of these outcome measures.

Overall, the combination of performance-based testing shows potential of finding weakness and limitations in various ways that are not always captured through standard grip strength testing. While the intent to measure grip strength is to use a power grip, many of our participants used compensatory strategies in order to produce a measureable force. As patients lose the ability to flex the distal, and sometimes proximal, interphalangeal joints, they rely on flexion of the metacarpophalangeal joints and muscles of the thanar eminence to produce a detectable grip measurement. This becomes problematic when deciding at what point a modified grip should or should not be allowed and whether or not power grip is a true measurement of a patient’s grip strength. Additionally, with many clinical trials excluding patients who are no longer able to ambulate without an assistive device or rise from a chair independently, exploring performance-based hand functional assessments may have the potential to allow for more inclusive enrollment of IBM patients in future therapeutic trials. Further longitudinal data is needed to assess the ability of these outcome measures to detect change in function over the course of disease progression.

Exploring these performance-based measurements of hand function allowed for a more in-depth appreciation of the different types of modifications and compensatory techniques patients with IBM are able to utilize in order to complete a task. Additionally, it provides a foundation for understanding which tasks become difficult in earlier versus later stages of disease progression, which may be helpful in clinical evaluations. The Sollerman Hand Function Test (SHFT) offers closer evaluation of performing everyday tasks that patients commonly report as difficult, such as opening jars or picking up coins; however, the burden of testing time and equipment makes this assessment less feasible. Because the Performance of the Upper Limb (PUL) demonstrated challenges due to patients presenting with more distal weakness, it is not a suitable assessment for patients with IBM in its current format; however, there may be potential for a modified version of this test with special consideration given for modified grips to complete the shoulder dimension if the PUL were to be standardized in the IBM population.

With the limitations of current available strength and functional assessments, many methods of testing would need to be adapted to accommodate the particular phenotype of hand weakness in patients with IBM. Our study was able to observe various compensation techniques; however, not every functional assessment was able to be modified for this particular weakness pattern (i.e. the lack of grip strength to perform proximal shoulder items of the PUL). While manual muscle testing of individual intrinsic hand muscles may be useful for exploring each specific grip or pinch technique, these measurements may be limited in the ability to correlate with how each patient is able to compensate in order to continue performing activities of daily living. Additionally, function does not always equate with strength. Further collaboration is necessary to determine of existing outcome measures can be modified to meet the need of the IBM population or if there is a need for development of a novel assessment.

We acknowledge that our cross-sectional sample of convenience may impact generalizability of our findings. Of the patients included in the final analysis, those recruited from the TMA Patient conference had self-reported their diagnosis of IBM, along with self-report of disease onset and duration of symptoms. Other
limitations include the burden of equipment and time constraints when testing in the Washington University IBM Clinic. While strength measurements and the FDT can be quickly administered with minimal equipment, the SHFT and PUL require more time and space for completion. The SHFT was particularly cumbersome and may not be feasible in most clinics or future clinical research trials.

In conclusion, available strength and functional clinical outcome assessments are feasible for use to assess upper extremity ability in patients with IBM. The unique progression of weakness and compensatory strategies required to maintain independence are not explicitly quantified using available measures as designed. Adaptation of available tools, or development of a novel scale, may be warranted to sensitively and accurately assess progression of finger flexor and upper extremity weakness in patients with IBM across the spectrum of disease.

**Funding**

This work was supported by the National Institute of Health [grant K24AR073317], CureIBM, The Myositis Association, and Bill M. & Cecile Autrey Ham Charitable Foundation.

**Declaration of Competing Interest**

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:
Conrad Weihl reports a relationship with Sarepta Therapeutics Inc that includes: consulting or advisory. Conrad Weihl reports a relationship with MLbio that includes: consulting or advisory. Conrad Weihl reports a relationship with Abata that includes: consulting or advisory.

Acknowledgments

The authors would like to thank the Myositis Association for allowing the research team space and resources at the 2022 Patient Conference in order to enroll conference attendees in this research project.

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