

## The Correlation Between Static Fatigue Testing and the Quantitative Myasthenia Gravis Score and Activities of Daily Living Profile

Navdeep Lail, MD<sup>1</sup>; Gil I. Wolfe, MD<sup>1</sup>; Laura Herbelin, BS<sup>2</sup>; Sharon P. Nations, MD<sup>3</sup>; Barbara M. Foster, PhD<sup>3</sup>; Nicholas J. Silvestri, MD<sup>1</sup>; Lauren J. Peck<sup>4</sup>; Richard J. Barohn, MD<sup>4</sup>

<sup>1</sup>Departments of Neurology, Jacobs School of Medicine and Biomedical Sciences, Univ. at Buffalo/SUNY, Buffalo, NY

<sup>2</sup>University of Kansas Medical Center, Kansas City, KS

<sup>3</sup>University of Texas Southwestern Medical Center, Dallas, TX

<sup>4</sup>University of Missouri School of Medicine, Columbia, MO

### ABSTRACT

Fatigue is a common symptom in myasthenia gravis (MG), but both objective and subjective measures of fatigue are poorly studied in the disease. We conducted a pilot study of static fatigue testing (SFT) in a group of MG patients, using an isometric quantified muscle analysis computer system. Results from sustained isometric contraction of 5 muscle groups in 77 patients were correlated to the Quantitative MG Score (QMG) and the Activities of Daily Living Profile (MG-ADL), two commonly used outcome measures. Pearson correlation coefficients for the SFT were highest (0.33) for hand grip for both the QMG and MG-ADL. Correlations were quite poor for the proximal muscle groups and ankle dorsiflexion. More work is needed to develop objective and subjective measures of fatigue in MG.

**Keywords:** *myasthenia gravis, fatigue, disease outcomes*

### Introduction

Fatigue is a clinical manifestation of skeletal muscle weakness in myasthenia gravis (MG). Quantification of the fatigue in MG during isometric exercise has not been carefully studied and may be a useful measurement in clinical research trials. Interestingly, fatigue measurements have been reported in amyotrophic lateral sclerosis<sup>1</sup> and multiple sclerosis<sup>2</sup> but not in MG patients. Our goal was to study static fatigue testing (SFT) in MG patients using an isometric quantified muscle analysis (QMA) computer

system. As such, we analyzed a physiological measure of fatigue, that may or may not relate to actual muscle weakness and that differs from subjective assessments of fatigue such as the Fatigue Severity Scale.<sup>3</sup> We compared the results of the SFT to the Quantitative Myasthenia Gravis Score (QMG)<sup>4</sup> and the Activities of Daily Living Profile (MG-ADL).<sup>5</sup>

### Methods

Seventy-seven MG patients were evaluated, using the SFT, QMG<sup>4</sup> and MG-ADL.<sup>5</sup> SFT was performed on the dominant side (side of handwriting) on handgrip, elbow flexion, elbow extension, knee extension, and foot dorsiflexion. The isometric muscle testing was performed using standardized techniques developed in amyotrophic lateral sclerosis trials.<sup>6,7</sup> The hardware for isometric muscle testing and computer software for fatigue analysis were developed by Jim Fielding (the Computer Source, Gainesville, GA).

Patients were placed in gravity-eliminated positions with the limbs stabilized by the examiner (Table 1). They pulled against a standardized strap attached to a strain gauge that was connected to the computer system. For each SFT measurement, the patient performed maximum muscle contraction for 30 seconds. Isometric strength (kgs of force) was measured for 30 seconds and analyzed in 5 epochs. The 5 epochs were W1: 0-5 secs, W2: 2-7 secs, W3: 4-9 secs, W4: 25-30 secs, and W5: 0-30 secs. SFT results were assessed by comparing the maximum force generated in the 2-7 second epoch (W2) with the 25-30 second epoch (W4) (Figure 1). The W2 and W4 epochs were chosen for comparison to allow for the subject to build up to a full force in the first two seconds and then compare that value to the

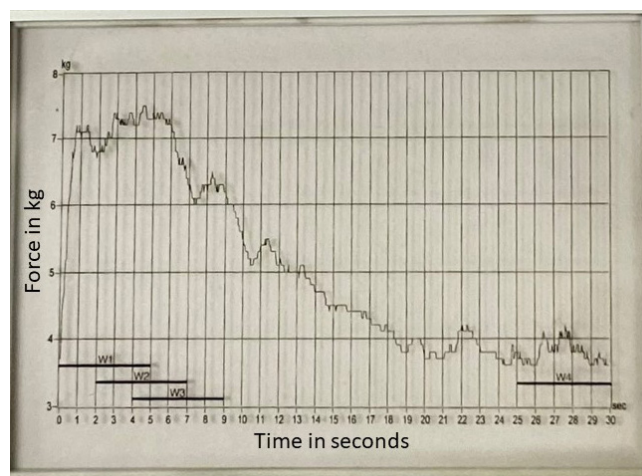


Figure 1. Static fatigue testing in a single MG subject demonstrating the decline in isometric strength across time epochs. Epochs W1 through W4 are noted by bars on the x-axis.

Table 1. Static fatigue testing procedures by muscle group

Muscle group	Test position	Limb stabilization
Hand grip	Sitting; elbow bent to 90 degrees	Support under forearm and under dynamometer <sup>6</sup>
Elbow flexion	Supine; elbow at 90 degrees with maximum contraction, forearm in neutral	Stabilizing at the shoulder and at the elbow (ulnar groove)
Elbow extension	Supine; elbow at 90 degrees with maximum contraction, forearm in neutral	Stabilizing at shoulder and over the biceps
Knee extension	Sitting over the edge of the bed; knee at 90 degrees with maximum contraction, towel under distal thigh to level femur	Pushing down on the shoulders
Foot dorsiflexion	Supine; ankle at 90 degrees dorsiflexion with maximum contraction	Pushing down distal to the knee

final five seconds of the 30-second contraction interval. Statistical analysis comparing SFT to the QMG and MG-ADL was performed using a Pearson correlation coefficient.

## Results

The Pearson correlation coefficient between the SFT and QMG was 0.33 for hand grip, 0.23 for elbow extension, 0.10 for elbow flexion, 0.15 for ankle dorsiflexion, and 0.16 for knee extension. The coefficient between the SFT and MG-ADL was 0.33 for hand grip, 0.06 for elbow extension, 0.03 for elbow flexion, 0.15 for ankle dorsiflexion, and 0.19 for knee extension.

## Discussion

Overall, correlation coefficients were low between SFT and two validated and commonly utilized measures of clinical status in MG. SFT measurements for hand grip demonstrated the best correlation with the QMG and MG-ADL. Possible explanations for the overall poor correlations include the fact that SFT assesses fatigue in only one muscle group at a time, whereas both the QMG and MG-ADL provide a more global picture of MG clinical status. Quantitative outcome measures in MG are often effort-dependent, and a subject's receptiveness to encouragement by the examiner can vary. In addition, the time epochs chosen to generate the SFT value may not have been optimized for the correlation. Perhaps comparison of the slope of the decline in isometric contraction at different time points would provide a stronger correlation with existing measures.

Even without a strong correlation to established outcome measures, SFT may capture other information of value in MG. Ten percent of the variance of both QMG and MG-ADL was accounted for by SFT. This indicates that the SFT is providing some additional information regarding overall MG clinical status to that provided by the QMG and MG-ADL. Further study would be needed to see if SFT or

a related strategy that objectively measures fatigue would provide a sensitive and reliable endpoint for interventional studies in MG.

Subjective measures of fatigue have been developed, most notably the Fatigue Severity Scale (FSS). The FSS has been applied to multiple sclerosis<sup>8</sup> and Parkinson disease<sup>3</sup> with variable correlation to established measures of disease severity, similar to our findings with SFT in MG. In neuromuscular conditions, the FSS demonstrated fair psychometric properties in congenital myopathies, but had little value in spinal muscular atrophy type 2.<sup>9</sup> The FSS has not been subjected to rigorous study in MG. Among existing subjective measures developed for MG, the chewing item in the MG-ADL does query subjects on their experience of fatigue with solid or soft food, but by no means provides a broad assessment of muscle fatigue.<sup>5</sup> Although some items in the MG Quality of Life 15 Score could be impacted by fatigue, the term "fatigue" does not actually appear on the questionnaire.<sup>10</sup> A recent study of a subjective fatigue measure in 779 Danish MG patients examined the association between the self-reported Multidimensional Fatigue Inventory (MFI-20) and a physical activity survey.<sup>11</sup> Of the five MFI-20 domains, general fatigue, physical fatigue, and reduced activity were most prominently impacted. Those MG subjects able to tolerate higher levels of physical activity reported lower levels of fatigue on the MFI-20 and also had more favorable MG-ADL scores, with correlation values in the 0.4 range.<sup>11</sup>

Objectively measuring for fatigue in MG or other disease states presents a considerable challenge. Further studies that include established clinical and electrophysiological measures in MG could determine how useful SFT or a related approach would be in MG clinical trials.

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### Corresponding Author

Gil I. Wolfe, MD, Department of Neurology, Univ. at Buffalo, 1010 Main St., Buffalo, NY 14202.

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