

## Clinical Studies

# Validation of the Energy Index Point Score to Serially Measure the Degree of Disability in Patients with Chronic Fatigue Syndrome

A. MARTIN LERNER<sup>1</sup>, SAFEDIN H. BEQAJ<sup>2</sup> and JAMES T. FITZGERALD<sup>3</sup>

<sup>1</sup>Departments of Medicine, Wayne State University School of Medicine and William Beaumont Hospital, Royal Oak, MI;

<sup>2</sup>DCL Medical Laboratories Indianapolis, IN;

<sup>3</sup>Department of Medical Education, University of Michigan School of Medicine, Ann Arbor, MI, U.S.A.

**Abstract.** *Background:* A simple quantitative accurate method for assessing the degree of fatigue in patients with chronic fatigue syndrome (CFS) is necessary for physicians and patients. Severity of the disease and recovery can, thus, be assayed. *Patient and Methods:* From February 1-27, 2007, fifty-six consecutive CFS patients at a single treatment center were simultaneously evaluated by the patient with the fatigue severity score (FSS), and by consensus of both patient and physician by the energy index (EI) point score. *Results:* The FSS and EI correlated well, 0.67,  $p < 0.001$ . *Conclusion:* The EI point score is a validated reliable method to assess fatigue in CFS patients.

The chronic fatigue syndrome (CFS) (US Centers for Disease Control and Prevention) is a worldwide public health problem of unknown cause and with no effective treatment (1, 2). CFS is a persisting or relapsing fatigue that reduces a person's activity level to below 50% of their normal activity level for a period of at least 6 months. CFS patients suffer prolonged generalized headaches, migratory arthralgia and sleep disturbance. Worsening, often prolonged fatigue occurs after levels of exercise that would have been previously easily tolerated. Symptoms include fever, chills, sore throat, painful lymph nodes (e.g. anterior or posterior cervical, axillary), muscle weakness and myalgias. Patients with established conditions that might produce similar symptoms are not diagnosed with CFS.

Among the physiological findings in patients with CFS are abnormal tilt-table tests (3), elevated 2-5A synthetase (4),

*Correspondence to:* A. Martin Lerner, MD, 32804 Pierce Road, Beverly Hills, Michigan 48025, U.S.A. Tel: +1 2485409866, Fax: +1 2485400139, e-mail: amartinlerner@yahoo.com

*Key Words:* Validation energy index point score, chronic fatigue syndrome.

oscillating flat and inverted abnormal T-waves on 24-h. ECG (Holter) monitors (5), abnormal cardiac wall motion (6) and elevated serum antibody titers to Epstein-Barr virus (EBV), cytomegalovirus (HCMV) and human herpesvirus type 6 (HHV6) (7-9). We hypothesized that CFS is persisting abortive herpesvirus (EBV, HCMV, HHV6) multiplication involving the heart (7) and have reported sustained benefit to CFS patients with long-term specifically directed pharmacokinetic antiviral therapy (10).

Fatigue is subjective and difficult to measure (11-15). We have developed a simple objective measure, the energy index (EI) point score, to assess a CFS patient's degree of disability. The fatigue severity score (FSS) (11) was compared with the EI score to validate EI.

## Patients and Methods

From February 1-28, 2007, 56 consecutive patients who met the CDC criteria for the diagnosis of CFS (1, 2) were included in this study. The EI was determined by consensus of physician and patient using an EI scoring scale for easy reference hung on the wall in each examining room. An EI point score of "0" is a bedridden patient. The patient at an EI point score of "1" may be out of bed, sitting, 30-60 minutes/day; "2" can sit, stand, walk 1-2 hours/day; "3" is out of bed sitting, standing, walking 2-4 hours/day; "4" out of bed, sitting, standing, walking 4-6 hours/day; "5" can perform with difficulty a sedentary job or its equivalent 40 hours/week; "6" the CFS patient can perform a sedentary 40-hour work/week, has limited housekeeping/social activities, daily rests, lying supine up to one-hour necessary; "7" up 7:00 a.m. to 7:00 p.m., sedentary 40-hour work/week plus light housekeeping, no supine rests (naps) necessary, "8" can work a full week, no naps, some social activities and light exercise; "9" may do all of above plus exercise 1/2 to 2/3 normal without excessive fatigue, awakens next morning refreshed and "10" the patient is normal. At an EI of 6-10, designated recovery, the patient no longer meets criteria for diagnosis of CFS. The FSS was simultaneously calculated by patient responses to the FSS questionnaire.

The FSS 9-item scale has a high degree of internal consistency as measured by Cronbach's alpha, an estimate of the reliability of a

Table I. Demographics and comparisons of EI and FSS Score in 56 consecutive CFS patients (US Copyright, 1999, Lerner AM and Deeter RJ).

	All patients (56)	Females (39 patients)	Males (17 patients)
Age, mean	48.3±1.7* years	47.1±1.8* years	51.2±3.8 years
EI, mean	5.4±0.2* units	5.2±0.3 units	5.8±0.4 units
FSS, mean	5.3±0.2	5.5±0.2	4.8±0.4
Bivariate fit, FSS by EI, normal ellipse	$p=0.950$	$p=0.950$	$p=0.950$
Correlation / probability	0.67; $p<0.001$	0.68; $p=0.001$	0.63; $p=0.0066$

\*Standard error of mean. EI, energy index point score; FSS, fatigue severity score.

scale, based on correlation of the individual items of a multi-item scale. FSS scores obtained by healthy controls on the FSS were compared with scores from patients with progressive multiple sclerosis and systemic lupus erythematosus (11).

## Results

The data are presented in Table I. The FSS and EI measured similar construct, thus supporting the validity of the EI point score. The correlation/probability was 0.67,  $p<0.001$ .

## Discussion

The simplicity, objectivity and quantitative quality of the EI, plus its ability to compare CFS patients of varying weights is highly useful. The EI point score can be expressed as kilocalories/day (10). The EI point score, therefore, is an accurate metric to follow the course of CFS patients from baseline to recovery (10, 16-18). The grading system accurately gauges the level of disability (EI point score, "severe, 0-3") or "moderately severe" (EI 4-5). The EI point score is best assessed at 6-week intervals with a resulting agreement by CFS patient and the physician. With pharmacokinetically administered antiviral therapy, significant improvement is usually seen only after 6-9 months (10, 16-18). The EI point score is not assessed if there is an intercurrent illness at any visit. The EI assessment is then delayed for two weeks at a special patient visit for this purpose. At an EI point score of >6, the diagnosis of CFS is no longer present. A significant metric in the recovery of the CFS patient occurs when the formerly CFS patient reaches an EI of 7, when no naps are necessary. A "nap" by definition here indicates the patient needs to lie supine during the day. They do not necessarily need to sleep during the "nap." We interdict exercise for the CFS patient until their EI is 8. Earlier exercise may initiate a CFS relapse.

Evaluation of CFS patients by symptoms is less accurate, more cumbersome and variable because of the unique individuality of every CFS patient. As the EI increases, the various symptoms such as syncope, chest pain, palpitations and muscle aches lessen and disappear. Earlier, a random sample of 22 non-CFS persons was compared with 20 CFS

patients (16). The non-CFS sample included 17 women and 5 men whose mean age was 35 years (median age, 38 years; range, 19-62 years). The mean EI of the non-CFS group was 9.9 (median EI, 10; range 7.5-10). The CFS patients included 17 women and 3 men whose mean age was 41 years (median age, 42 years; range, 16-53 years). The mean EI of the CFS group was 3.6 (median EI range 1-5). The gender and ages of the CFS and non-CFS groups were similar (Fisher's exact test and *t*-test). The EI's (CFS, 9.9 vs. non-CFS, 3.6) of the groups were different ( $p<0.0001$ ). The power of this data was 0.25. A small effect size is 0.2, a medium effect size is 0.5, and a large effect size is 0.8. The present comparison of the EI and FSS is a second confirmation of the EI point score, an accurate measure of the severity of illness of CFS patients.

It is facile to convert an EI score to kilocalories per day. We have performed this exercise several times (10, 17). We favor the EI, rather than kilocalories per day, for accuracy, facility and because the EI is not influenced by the different weights of CFS patients, while the measure kilocalories/day is influenced by weight. A more fatigued larger CFS patient may have a higher kilocalories expenditure than a more active smaller CFS patient. The EI is independent of patient weight. It objectively assesses what the CFS patient does daily.

Dr. Lerner owns patents concerning CFS diagnosis and treatment with antiviral agents.

## References

- 1 Holmes GP, Kaplan JE, Gantz NM *et al*: Chronic fatigue syndrome: A working case definition. *Ann Intern Med* 108(3): 387-398, 1988.
- 2 Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG and Komaroff H: The Chronic fatigue syndrome: a comprehensive approach to its definition and study. *Ann Intern Med* 121: 953-959, 1994.
- 3 Rowe PC, Bou-Holaigah I, Kan JS *et al*: Is neurally mediated hypotension an unrecognized cause of chronic fatigue syndrome? *Lancet* 345: 623-624, 1995.
- 4 Suhadolnik RJ, Reichenbach NL, Hitzges P *et al*: Changes in the 2-5A synthetase RNase L antiviral pathway in a controlled clinical trial with poly (1) - poly (Cu12) in chronic fatigue syndrome. *In Vivo* 8: 599-604, 1994.

- 5 Lerner AM, Lawrie-Hoppen C and Dworkin HJ: Repetitively negative changing T-waves at 24-h electrocardiographic monitors in patients with the chronic fatigue syndrome. Left ventricular dysfunction in a cohort. *Chest* 104: 1417-1420, 1993.
- 6 Lerner AM, Dworkin HJ, Sayyed T *et al*: Prevalence of abnormal cardiac wall motion in the cardiomyopathy associated with incomplete multiplication of EBV and/or CMV in patients with chronic fatigue syndrome. *In Vivo* 18: 417-424, 2004.
- 7 Lerner AM, Zervos M, Dworkin HJ *et al*: A unified theory of the cause of the chronic fatigue syndrome. *Infect Dis Clin Pract* 63: 239-243, 1997.
- 8 Lerner AM, Beqaj SH, Deeter RG *et al*: IgM serum antibodies to human cytomegalovirus nonstructural gene products p52 and CM2 (UL44 and UL 57) are uniquely present in a subset of patients with chronic fatigue syndrome. *In Vivo* 16: 153-160, 2002.
- 9 Beqaj SH, Lerner AM and Fitzgerald JT: Immunoassay with cytomegalovirus early antigens from gene products p52 and CM2 (UL44 and UL57) detects active infection in patients with chronic fatigue syndrome. *J Clin Path* 61: 623-626, 2007.
- 10 Lerner AM, Beqaj SH, Deeter RJ *et al*: Valacyclovir treatment in Epstein-Barr virus subset chronic fatigue syndrome with long-term thirty-six month follow-up. *In Vivo* 21: 707-714, 2007.
- 11 Krupp LB, La Rocca NG, Muir-Nash J *et al*: The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neuro* 46: 1121-1123, 1989.
- 12 Zachrisson O, Regland B, Jahreskog M *et al*: A rating scale for fibromyalgia and chronic fatigue syndrome (the fibro fatigue scales). *J Psychosomatic Research* 52: 501-509, 2002.
- 13 Wagner D, Niesenbaum R, Heim C *et al*: Psychometric properties of the CDC symptom inventory for assessment of chronic fatigue syndrome. *Population Health Metrics* 10.1186/1478-7954, 3-8, 2005.
- 14 Ware JT Jr and Grandek B: Overview of the SF-36 health survey and the international quality of life assessment (IQOLA) project. *J Clin Epidemiol* 51: 903-912, 1998.
- 15 Garratt AM, Ruta DA, Abdalla MI *et al*: The SF 36 health survey questionnaire; an outcome measure suitable for routine use within the NHS. *Br Med J* 306: 1440-1444, 1993.
- 16 Lerner AM, Zervos M, Dworkin HJ *et al*: New cardiomyopathy: pilot study of intravenous ganciclovir in a subset of the chronic fatigue syndrome. *Infectious Diseases in Clinical Practice* 6: 110-117, 1997.
- 17 Lerner AM, Beqaj SH, Deeter RG *et al*: *Drugs Today* 38: 549-561, 2002.
- 18 Lerner AM, Zervos M, Chang CH *et al*: A small, randomized, placebo-controlled trial of the use of antiviral therapy for patients with chronic fatigue syndrome. *Clin Infect Dis* 32: 1657-1658, 2001.

*Received April 2, 2008*

*Revised July 28, 2008*

*Accepted August 29, 2008*