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Which Equation Best Predicts Energy Expenditure in Amyotrophic Lateral Sclerosis?

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ABSTRACT

Objective The purpose of this study was to compare measured resting energy expenditure (REE) with estimates from three common prediction equations with the goal of determining which equation best estimates REE in amyotrophic lateral sclerosis (ALS).

Design Cross-sectional measurements of REE from indirect calorimetry were compared to calculations from the Harris Benedict, Mifflin-St Jeor, and Ireton-Jones equations. Additional measurements to identify predictors of REE included pulmonary function tests, fat-free mass by bioelectrical impedance, and anthropometrics.

Subjects/setting Participants were 56 men and women with ALS. For comparison, subjects were categorized by disease progression into three groups.

Statistical analyses Pearson correlations and paired *t* tests were used to compare measured REE with predicted REE from each equation, and the accuracy of each equation was quantified by the root mean squared prediction error and the percentage of REE estimates within 10% of measured values. Bias for each equation was calculated as the mean percentage difference between calculated and measured REE. Multiple linear regression was used to determine the best predictor variables for REE.

Results Across the disease spectrum, the Harris Benedict and Mifflin-St Jeor equations provided clinically acceptable estimates of REE, whereas the Ireton-Jones equations consistently overestimated REE. The best predictors of REE among this cohort were fat-free mass, sex, and age.

Conclusions When estimating energy requirements for patients with ALS, clinicians should choose prediction equations that incorporate sex and age as predictor variables, such as the Harris Benedict and Mifflin-St Jeor equations.

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Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease affecting upper and lower motor neurons and resulting in weakness and poor coordination of skeletal muscle. Although site of onset and rate of progression vary, most patients with ALS eventually experience some respiratory compromise when motor neurons innervating the diaphragm muscle become affected (1). Inadequate energy intake may exacerbate disease progression by accelerating muscle catabolism (2,3), but excessive energy intake may also pose detrimental effects to pulmonary function by increasing carbon dioxide production and ventilatory demand (4-6).

Despite the importance of appropriate energy intake for this patient population, currently there are no standards of care to assess kilocalorie requirements in patients with ALS. To determine an individual's energy requirement, the optimal, most direct method of measurement is determination of resting energy expenditure (REE) by indirect calorimetry (7). The expense and equipment required for indirect calorimetry preclude its application in routine clinical settings, so clinicians routinely use mathematical equations to estimate REE based on attributes such as height, weight, sex, and age to predict REE. Three commonly used prediction equations are the Harris Benedict (8), Mifflin-St Jeor (9), and Ireton-Jones equations (10).

Limited evidence suggests that energy requirements in ALS may correlate with severity of respiratory compromise so that REE estimates from prediction equations may underfeed some patients and overfeed others at different disease stages (11-14). However, most studies to date have only compared measured REE to REE estimates from the Harris Benedict equation. The specific

Table 1. Equations used to predict resting energy expenditure (REE) in kilocalories per day

Source	Equation[a]
Harris-Benedict (8)	Men: REE=66.47+13.75 (W)+5 (H)−6.76 (A)
	Women: REE=655.1+9.56 (W)+1.7 (H)−4.7 (A)
Mifflin-St Jeor (9)	Men: REE=(9.99×W)+(6.25×H)−(4.92×A)+5
	Women: REE=(9.99×W)+(6.25×H)−(4.92×A)−161
Ireton-Jones 2002 (10)	Spontaneously breathing REE=629−11 (A)+25 (W)−609 (O)
	Ventilator dependent REE=1,784−11 (A)+5 (W)+244 (S)+ 239 (T)+804 (B)

[a]Body weight (W) in kilograms (kg), height (cm), age (A) in years, sex (S, male=1, female=0), diagnosis of trauma (T, present=1, absent=0), diagnosis of burn (B, present=1, absent=0), obesity body mass index > 27 (present=1, absent=0).

aim of this study was to compare measured REE with calculations from three different prediction equations routinely used by registered dietitians at our North Carolina clinic (Table 1), with the goal of determining which equation best estimates REE in patients with ALS. An exploratory analysis was also performed to examine if the accuracy of each equation differed according to progressing stages of respiratory compromise.

METHODS

Subjects

Subjects were 25 women and 31 men, aged 35 to 74 years, with a diagnosis of probable, lab supported or definite ALS as defined by diagnostic criteria of the World Federation of Neurology (15). Exclusion criteria included body mass index (BMI; calculated as kg/m^2) <18 or >30, preexisting medical conditions known to influence REE (eg, impaired glucose tolerance, thyroid dysfunction, or infection within 30 days of testing), or concomitant diagnosis of any other neurologic disease. Informed consent was obtained, and the protocol was approved by the Institutional Review Board of Carolinas Healthcare System.

Procedures

All testing took place at an outpatient neurosciences clinic in Charlotte, NC. Height was obtained from medical records and verified by self-report. Weight was measured by a calibrated digital scale equipped with a hoyer-lift mechanism for those patients who were unable to stand. For each subject, the same investigator used Lange calipers (Cambridge, MD) to record triceps skinfold thickness in mm as the average of three successive measurements on the right side of the body.

Bioelectric impedance (BIA) was assessed by Quantum II BIA System (RJL Systems, Clinton Township, MI) according to standard protocol (16). Briefly, this method determines electrical impedance to a mild alternating current applied between a tetra-polar arrangement of electrodes on the wrists and ankles. Fat-free mass (FFM) in kilograms was estimated by incorporating this impedance value at a frequency of 50 Khz (Z_{50}) into a prediction equation that has been previously validated for patients with ALS (17):

$$\mathrm{FFM} = (0.436 \times \mathrm{W}) + (0.349 \times \text{mean } \mathrm{H}^2/\mathrm{Z}_{50}) - (0.695 \times \text{mean TSF}) + 9.245$$

Where W=weight in kilograms, H=height in centimeters, Z_{50}=impedance in Ohms, and TSF=triceps skinfold in millimeters.

REE

REE was assessed by indirect calorimetry via an open-circuit metabolic cart (Vmax Spectra V29N, SensorMedics Corporation, Yorba Linda, CA) according to standard protocol (18). Each morning, the gas analyzers of the metabolic cart were calibrated with two standard reference gas mixtures (16% oxygen/4% carbon dioxide/balance nitrogen and 26% oxygen/balance nitrogen), and the mass flow sensor was calibrated prior to each test. A trained research assistant monitored patients for the duration of the test, and for patients dependent on a ventilator, testing was conducted by a certified respiratory therapist. Oxygen consumption (vO_2) and carbon dioxide production (vCO_2) were recorded each minute for 30 minutes. Final analysis excluded the first 10 minutes of testing. The averages of vO_2 and vCO_2 were used to calculate REE by the equation of Weir (19). Respiratory quotient was recorded as the ratio of vCO_2/vO_2.

Assessment of Respiratory Function

Forced vital capacity (FVC), the most common indicator of respiratory function among patients with ALS (20), is defined as the maximum volume of air that can be exhaled after maximal inhalation (21). A trained technician used the Renaissance II Spirometry System (version 1.1, 2003, Tyco Healthcare, Gosport, UK) to measure FVC in liters for all nonventilated participants. In Table 2, FVC is expressed as percent predicted based on comparison to reference populations matched for age, sex, height, weight, race, and smoking status (22). For all patients attending our outpatient clinic, physicians routinely prescribe noninvasive ventilation when FVC declines to <50% per accepted guidelines (20,23). As the disease progresses and symptoms worsen, invasive mechanical ventilation by tracheotomy eventually becomes necessary to sustain pulmonary function (1,24).