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A Novel Approach to Predict 24-Hour Energy Expenditure Based on Hematologic Volumes: Development and Validation of Models Comparable to Mifflin-St Jeor and Body Composition Models

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ABSTRACT

Background Accurate prediction of 24-hour energy expenditure (24EE) relies on knowing body composition, in particular fat-free mass (FFM), the largest determinant of 24EE. FFM is closely correlated with hematologic volumes: blood volume (BV), red cell mass (RCM), and plasma volume (PV). However, it is unknown whether predicted hematologic volumes, based on easily collected variables, can improve 24EE prediction.

Objective The aim was to develop and validate equations to predict 24EE based on predicted BV, RCM, and PV and to compare the accuracy and agreement with models developed from FFM and with the Mifflin-St Jeor equation, which is recommended for clinical use by the Academy of Nutrition and Dietetics.

Design Participants had body composition measured by underwater weighing and 24EE by respiratory chamber. BV, RCM, and PV were calculated from five published equations.

Participants/setting Native American and white men and women were studied (n=351). Participants were healthy adults aged 18 to 49 years from the Phoenix, AZ, metropolitan area.

Main outcome measure Accuracy to within ±10% of measured 24EE and agreement by Bland-Altman analysis.

Statistical analysis Regression models to predict 24EE from hematologic and body composition variables were developed in half the dataset and validated in the other half.

Results Hematologic volumes were all strongly correlated with FFM in both men and women ($r \geq 0.94$). Whereas the accuracy of FFM alone was 69%, four hematologic volumes were individually more accurate (75% to 78%) in predicting 24EE. Equations based on hematologic volumes plus demographics had mean prediction errors comparable to those based on body composition plus demographics; although the Mifflin-St Jeor had modestly better mean prediction error, body composition, hematologic, and Mifflin-St Jeor models all had similar accuracy (approximately 80%).

Conclusions Prediction equations based on hematologic volumes were developed, validated, and found to be comparable to Mifflin-St Jeor and body composition models in this population of healthy adults.

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ACCURATE PREDICTION OF ENERGY EXPENDITURE (EE) is important for research and clinical care involving patients with overweight and obesity. In research, measurement of 24-hour energy expenditure (24EE) by whole-room indirect calorimetry is an important tool for studying obesity and metabolism.[1,2] Although studies involving the respiratory chamber rely on accurate prescription of energy intake (EI) to achieve a reasonable level of energy balance within the metabolic chamber, predicting the amount of food needed to match

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anticipated 24EE is challenging.[3] Achieving energy balance is especially important in studies of substrate utilization, as deviation from energy balance rapidly influences fuel selection (eg, shift to fat over carbohydrate oxidation during underfeeding).[4] Altered metabolism by under- or overfeeding undermines the assumptions for substrate utilization calculations.[5] Methods for prescribing EI are heterogeneous and prediction of EI to achieve energy balance have included equations based on anthropometrics (body mass index [BMI; calculated as kg/m^2] and body weight); body composition factors, such as fat-free mass (FFM) and fat mass (FM); and resting metabolic rate (RMR) adjusted for estimated physical activity level.[3,4,6] RMR may be measured by metabolic cart or predicted based on FFM and FM.[3] Improving energy balance has been achieved with 24EE measurements using predicted EI and subsequently prescribing the measured 24EE as EI in a second chamber,[7,8] but this adds time and expense. Adjustment of food provided at later times during the chamber, based on early EE measures, has been shown to improve accuracy but requires alteration in meal schedule and percentage distribution.[3]

In clinical settings, recommending goals for dietary intake requires knowledge of individual energy needs.[9] Although measurement by indirect calorimetry is ideal, this procedure is not feasible in most clinical settings and predicted energy needs can be used. For example, the 2016 position statement by the Academy of Nutrition and Dietetics[9] recommended (in the absence of indirect calorimetry to measure RMR) use of the Mifflin-St Jeor equation to estimate total energy needs,[10] which is based on anthropometric and demographic variables to estimate RMR, multiplied by a physical activity factor.

FFM and EE are closely correlated, but the physiologic basis for this linear association between FFM and 24EE is uncertain because FFM is a heterogeneous compartment composed of organs and tissues of different mass and of wide-ranging ability to consume oxygen.[11] However, there is an obligate relationship between oxygen consumption and supply,[12] and FFM is strongly related with total blood volume (BV), and closely related hematologic compartments, red cell mass (RCM) and plasma volume (PV).[13-17] The ratio of total body water to FFM is about 0.73, a ratio that applies to humans and other mammals.[18] The close relationship between hematologic volumes (BV, RCM, and PV) and FFM may be via total body water.[17,19,20] Gold standard assessment of BV, RCM, and PV requires injection of tracers[21] and is, therefore, invasive. Prediction equations for BV, RCM, and PV have been developed that are based on easily obtainable factors, such as age, sex, height, and weight.[22-25] To the authors' knowledge, the association between predicted BV, RCM, and PV, and directly measured FFM or EE measures has not been evaluated.

The goals of this study were to assess the degree to which these predicted hematologic volumes are associated with measured FFM and the usefulness of these hematologic volumes for predicting 24EE. In order to evaluate the association between FFM and these predicted hematologic volumes, BV,[22,24] RCM,[23,25] and PV[25] were calculated using five published prediction equations in a group of healthy adults who also had body composition measured by underwater weighing (UWW). Regression models based on these estimated hematologic volumes were developed to predict 24EE and were subsequently validated. The hypotheses that these estimated hematologic volumes were able to predict 24EE better than models involving FFM, body composition, and the Mifflin-St Jeor equation were evaluated.[10]

MATERIALS AND METHODS

Participants, Body Composition, and Energy Expenditure

Written informed consent was obtained before participation. The study was approved by the Institutional Review Board of the National Institute of Diabetes and Digestive and Kidney Diseases. Volunteers were adults recruited from the Phoenix, AZ, metropolitan area and admitted to the clinical research unit, who participated in an observational study investigating risk factors for obesity and type 2 diabetes as described previously,[2,26] and who had measurements of body composition by UWW and 24EE by whole-room indirect calorimetry (years 1985 to 1993). All participants were healthy by history, physical examination, and routine laboratory testing.

On admission, participants were provided a standard weight-maintaining diet (daily kilocalories: 20% protein, 30% fat, and 50% carbohydrates).[27] Height and weight were measured with the participant wearing light clothing. Body composition was assessed by UWW, with simultaneous determination of lung residual volume and percent body fat, FM, and FFM were calculated from the equation of Siri.[28] After at least 3 days on the weight-maintaining diet that started on admission, participants completed 24EE measurements by whole-room indirect calorimeter, described in detail previously.[29] Participants were directed not to exercise (eg, push-ups) while in the metabolic chamber, but they could otherwise move freely about the chamber. Prescribed EI in the respiratory chamber was based on equations developed from previously measured 24EE (men: 24 EI [kcal]=1,238+14.1 [body weight {kg}]−5.7 [BMI]; women: 24 EI [kcal]=951+19.3 [body weight {kg}]−18.2 [BMI]).[4] This prescribed EI in the chamber provided four balanced meals and is reduced approximately 80% to account for restricted physical activity inside the chamber, compared with the weight-maintaining diet provided to participants when they were outside the chamber.

Calculations for Hematologic Volumes

Five published prediction equations were used to calculate BV, RCM, and PV (Table 1). Two were chosen as they are the prediction equations recommended by the International Committee for Standardization in Haematology (ICSH) (RCM_{ICSH}, PV_{ICSH}).[25] Also selected were the formula for BV by Nadler and colleagues[22] (BV_{Nadler}) that is recommended by the National Blood Service of the United Kingdom to estimate BV to screen for blood donation eligibility,[30] and an estimate of red cell mass ($RCM_{Pearson}$) based on Nadler and colleagues' BV equation.[23] Preoperative estimate of BV is also important for patients undergoing surgery to guide fluid replacement. However, scaling based on actual body weight is problematic, particularly in patients with obesity,[24] prompting development of a BV formula ($BV_{Lemmens}$), based on BMI only and is more appropriate across a range of BMI.[24] $BV_{Lemmens}$ was therefore included for the analysis as well.

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