Harris-Benedict Equation and Resting Energy Expenditure Estimates in Critically Ill Ventilator Patients

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Background In routine practice, assessment of the nutritional status of critically ill patients still relies on traditional methods such as anthropometric measurements, biochemical markers, and predictive equations.
Objective To compare resting energy expenditure measured by indirect calorimetry (REE_{IC}) with REE calculated by using the Harris-Benedict equation with 3 different sources of body weight (from bed scale, REE_{HB1}; ideal body weight, REE_{HB2}; and predicted body weight, REE_{HB3}).
Methods This study included 205 critically ill patients (115 men, 90 women) evaluated within the first 48 hours of admission and undergoing mechanical ventilation. REE was measured by indirect calorimetry for 30 minutes and calculated by using the Harris-Benedict equation with the 3 sources of body weight. Data were compared by the Bland-Altman method.
Results The values based on ideal and predicted body weight (REE_{HB2} and REE_{HB3}) did not agree with REE_{IC}. Bland-Altman analysis showed that the limits of agreement varied from +796.1 kcal/d to -559.6 kcal/d for REE_{HB2} and from +809.2 kcal/d to -564.7 kcal/d for REE_{HB3}. REE_{IC} and REE_{HB1} (body weight determined by bed scale) agreed the best; the bias was -18.8 kcal/d. However, REE_{HB1} still overestimated REE_{IC} by +555.3 kcal/d and underestimated it by -593.0 kcal/d.
Conclusion For measuring REE in critically ill patients undergoing mechanical ventilation, calculation via the Harris-Benedict equation, regardless of the source of body weight, cannot be substituted for indirect calorimetry. (*American Journal of Critical Care.* 2016;25:e21-e29)

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Methods that help to assess the nutritional status of critically ill patients must be accurate, precise, easily applicable, and reproducible.[1] Physicians have not reached a consensus on the amount of energy they should prescribe to critically ill patients,[2] but experts from the European Society for Clinical Nutrition and Metabolism and the American Society for Parenteral and Enteral Nutrition agree that it is easier to optimize nutritional support prescription on the basis of indirect calorimetry.[3,4] Hence, indirect calorimetry is the reference standard for calculating the energy required by patients admitted to intensive care units (ICUs).[5] This noninvasive method provides relevant data such as volume of oxygen, volume of carbon dioxide, respiratory quotient, and resting energy expenditure (REE).[6-9] Indirect calorimetry also furnishes more specific and objective hemodynamic variables, such as cardiac output, in a noninvasive way.[10]

In routine practice, assessment of the nutritional status of critically ill patients still relies on traditional methods such as anthropometric measurements, biochemical markers, and predictive equations. Among predictive equations, the Harris-Benedict (HB) equation is the most often employed. However, in the case of critically ill patients, no consensus has been reached on which would be the best source of body weight to calculate the REE by the HB equation. Indeed, literature studies have employed real body weight, ideal body weight, and adjusted body weight.[11-14] Another issue concerning the HB equation is that researchers have developed it for a heterogeneous population consisting of healthy individuals, so it does not take account of personal characteristics such as body mass index (BMI, calculated as weight in kilograms divided by height in meters squared), age, presence of diseases, surgical procedures, and other variables that could interfere in metabolism during severe illness.[15] In other words, the traditional tools available to evaluate nutritional status are imprecise for critically ill patients. Among these tools, indirect calorimetry stands out because it actually measures REE in these individuals.[16]

Traditional tools available to evaluate nutritional status are imprecise for critically ill patients.

In an attempt to substitute for indirect calorimetry, more than 30 predictive equations have been proposed. The precision of these equations varies between 37% and 65% of the actual values measured by indirect calorimetry, which provides many patients with predicted energy demand that is around 40% above or below the physiological target. There are reasons for this discrepancy. First, most predictive equations require a precise measure of the real body weight, which is difficult to achieve in critically ill patients because of their health status and stress-related water retention. Second, most of the clinical assays determine REE upon patient's admission to the ICU; however, during the ICU stay, the patient may experience clinical alterations that can significantly modify REE with time (eg, fever and sepsis, sedation, paralysis, exercise, surgery, and food consumption).[5] In this scenario, REE measurement deserves particular attention, to ensure that nutritional support will meet the recommendations listed in nutritional guidelines.[4] To date, no literature study has compared REE measured by indirect calorimetry (REE_{IC}) with REE determined by the HB equation (REE_{HB}) on the basis of the predicted body weight. This weight is routinely used in the ICU to calculate the current volume in critically ill patients, and its use in the HB equation would be a novelty.

Bearing these issues in mind, in the present study, we compare REE_{IC} with REE_{HB} calculated on the basis of 3 different sources of body weight: body weight determined by bed scale (REE_{HB1}), ideal body weight(REE_{HB2}), and predicted body weight(REE_{HB3}).

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Methods

This observational transversal study conducted at the adult ICU of the University Hospital of Ribeirão Preto Medical School, University of São Paulo, from February 2011 to June 2012 and from April 2013 to November 2013. All the patients and/or relatives agreed to participate in the study and signed a written informed consent, approved by the research ethics committee (process number 8227/2011).

Patients

The sample comprised 205 patients (115 men, 56.1%; 90 women, 43.9%) admitted to the ICU, receiving mechanical ventilation, with a fraction of inspired oxygen less than 0.6 within the first 48 hours of admission. Patients with air leak, aerial fistula, very high positive end-expiratory pressure, or brain death and patients who did not provide the signed informed consent were excluded.

Indirect Calorimetry and Predictive Equations

The patients underwent indirect calorimetry on a portable calorimeter DELTATRAC II Metabolic Monitor (Datex-Ohmeda) for 30 minutes in stable condition in a calm environment, with no manipulation of the upper airways or of the ventilator settings for at least 30 minutes. Gas exchange measurements should be enough to ensure correct interpretation of the results obtained, avoiding periods of unstable conditions, such as alterations of settings on the mechanical ventilator and tracheal aspiration.[9] In this context, we considered that the steady state is often defined as 5 consecutive minutes during which oxygen consumption and carbon dioxide production vary by ±10% as validated previously.[17] The protocol was initiated after the DELTATRAC II equipment had warmed up for 30 minutes. The gas and pressure had been calibrated according to the manufacturer's instructions. All the patients were undergoing mechanical ventilation via multiprocessed ventilators (Savina or Evita XL, Drägermedical).

During the first 48 hours of admission to the ICU, REE was calculated with the HB equation; 3 different sources of body weight were employed: body weight determined by bed scale, ideal body weight, and predicted body weight.

The versions of the HB equation for men and women are as follows, with W equal to weight in kilograms, H the height in centimeters, and A the age in years: $66.47 + (13.75 \times W) + (5 \times H) - (6.75 \times A)$ for men and $665.1 + (9.563 \times W) + (1.85 \times H) - (4.676 \times A)$ for women. The ideal body weight was calculated from the height in meters: $22.5 \times H^2$ for men and $21.5 \times H^2$ for women. Predicted body weight was calculated from the height in centimeters: $50 + 0.91\,(H - 152.4)$ for men and $45.5 + 0.91\,(H - 152.4)$ for women.

After these data were obtained, the sample was divided according to the following criteria: age, sex, and BMI. In all the groups, the values achieved by using the HB equation (REE_{HB1}, REE_{HB2}, and REE_{HB3}) were compared with values for REE_{IC}. Stratification by age afforded 3 groups: 18 to 30 years, 31 to 60 years, and more than 60 years old. For BMI, 5 groups were formed on the basis of the World Health Organization's BMI table: less than 18.5, 18.5 to 24.9, 25.0 to 29.9, 30.0 to 39.9, and 40 or greater.

The study population was also divided into 3 subgroups, according to REE_{IC}: less than 1200 kcal/d, 1200-1800 kcal/d, and greater than 1800 kcal/d. The REE_{IC} obtained for these subgroups was compared with REE_{HB1}, REE_{HB2}, and REE_{HB3}. Because the group REE_{HB1} was the only group that provided slightly better agreement with REE_{IC}, it was subdivided to investigate whether this trend would remain in the subgroups.

Statistical Analysis

Data distribution was evaluated by D'Agostino Pearson, Kolmogorov-Smirnov, and Shapiro-Wilk normality tests. Considering that the distribution of all variables was nonparametric, the Wilcoxon test was used at a significance level lower than .05 ($P < .05$). Data for all the variables are presented as the median (minimum-maximum).

After this analysis, the data were compared by the Bland-Altman method,[18,19] which allowed us to describe the agreement between 2 quantitative measurements obtained by different methods. The Bland-Altman method is used to analyze the difference between 2 paired measurements with respect to the mean of 2 measurements. For better agreement, it is recommended that 95% of the data be included in ±1.96 SD of the mean of the difference and that the bias be close to zero. Analyses of limits of agreement were conducted for each predictive equation, stratified for sex, age, and BMI, to identify the different levels of agreement between these individual groups.

> The sample was divided according to age, sex, and body mass index.

All the analyses were conducted with the aid of MedCalc Statistical Software Version 12.2.

Results

The sample comprised 205 critically ill patients (115 men and 90 women) undergoing mechanical ventilation, with a median age of 57 (18-89) years, median weight of 71 (29-131) kg, and median height of 165 (145-188) cm. The median score on the Acute

Table 1
Clinical and demographic data of the 205 patients studied

Characteristic	Value
Sex, No. (%) of patients	
Male	115 (56.1)
Female	90 (43.9)
Age, median (minimum-maximum), y	54 (18-89)
Weight, median (minimum-maximum), kg	71 (29-131)
Height, median (minimum-maximum), cm	165 (145-188)
APACHE II score, median (minimum-maximum)	24 (4-47)
Death risk, median (minimum-maximum), %	53 (4-98)
Comorbidity, No. (%) of patients	
Sepsis	90 (43.9)
Pneumonia	55 (26.8)
Postsurgical	31 (15.1)
Traumatic injury	7 (3.4)
Neoplasm	6 (2.9)
Others	14 (6.8)
Body mass index (BMI),[a] No. (%) of patients	
< 18.5	11 (5.4)
18.5-24.9	86 (42.0)
25.0-29.9	58 (28.3)
30.0-39.9	44 (21.5)
≥ 40.0	6 (2.9)

Abbreviation: APACHE, Acute Physiology and Chronic Health Evaluation.
[a] Calculated as weight in kilograms divided by height in meters squared.

Physiology and Chronic Health Evaluation II[20] was 24 (4-47), and the median death risk was 53% (4%-98%). Diagnoses of sepsis (n = 90, 43.9%) and pneumonia (n = 55, 26.8%) predominated in this population (Table 1). Of the 205 evaluated patients, 120 (58.5%) were discharged from the ICU and 85 (41.5%) died.

Considering all the variables (sex, age, and BMI), comparison between REE_{IC} and REE_{HB} by the nonparametric Wilcoxon test did not reveal any differences between REE_{IC} and REE_{HB1}. The exception was the group of patients aged between 18 and 30 years—in this group, the difference between REE_{IC} and REE_{HB1} was significant ($P = .02$). All the groups showed a significant difference ($P < .05$) between REE_{IC} and REE_{HB2} and REE_{HB3}, except for the group of patients aged between 18 and 30 years ($P = .24$ for REE_{HB2}; $P = .24$ for REE_{HB3}) and the group of patients with a BMI between 18.5 and 24.9 ($P = .90$ for REE_{HB2}; $P = .86$ for REE_{HB3}).

The sample comprised 205 critically ill patients being treated with mechanical ventilation.

Subdivision of the population into 3 groups on the basis of REE_{IC} ($REE_{IC} < 1200$ kcal/d, REE_{IC} between 1200 and 1800 kcal/d, and $REE_{IC} > 1800$ kcal/d) showed that, compared with indirect calorimetry, the HB equation overestimated REE for most of the patients in the group with an REEIC less than 1200 kcal/d (n = 51, 96%). In the group with an REEIC greater than 1800 kcal/d (n = 32, 82%), the HB equation underestimated REE for most patients. Finally, in the group with an REEIC between 1200 and 1800 kcal/d, overestimation and underestimation also occurred, but the difference between REE_{IC} and REE_{HB} was no greater than 10%, the lowest among the 3 REE_{IC} groups. Figures 1 and 2 illustrate the aforementioned subgroups.

The median REE_{IC} was 1430 (540-2420) kcal/d, whereas the median REE_{HB1}, REE_{HB2}, and REE_{HB3} were 1463 (873-2486) kcal/d, 1325 (911-1877) kcal/d, and 1313 (869-1917) kcal/d, respectively.

The differences between the median REE_{IC} and the median REE_{HB1}, REE_{HB2}, and REE_{HB3} were -33 (2.3%), 105 (7.34%), and 117 (8.18%) kcal/d, respectively. If the median REE_{IC} (reference standard) is considered as 100%, the median REE_{HB2} and REE_{HB3} were approximately 92% of the median REE_{IC}.

According to the Bland-Altman analysis, REE_{HB2} and REE_{HB3} did not agree well with REE_{IC}; the limits of agreement varied between +796.1 kcal/d and -559.6 kcal/d for REE_{HB2} and between +809.2 kcal/d and -564.7 kcal/d for REE_{HB3} (Figure 3). Considering the studied population (n = 205), REE_{IC} and REE_{HB1} agreed the best: the bias was -18.8 kcal/d, which was the value closest to 0. Nevertheless, REE_{HB1} was still overestimated by +555.3 kcal/d and underestimated by -593.0 kcal/d.

Comparison of the results for the subgroups stratified according to sex, age, and BMI demonstrated that, in the case of stratification by sex, REE_{IC} and REE_{HB1} agreed better.

Stratification of the study population into 3 subgroups according to age—between 18 and 30 years (12.68%), between 31 and 60 years (45.37%), and more than 60 years (41.95%)—showed that agreement between REE_{IC} and REE_{HB1} was better for patients aged between 31 and 60 years, with bias of 8.5 kcal/d. With respect to the limits of agreement, patients aged between 18 and 30 years presented positive values of +403.3, +559.9, and +582.2 kcal/d, and negative values of -691.2, -736.8, and -751.7 kcal/d for comparison of REE_{IC} with REE_{HB1}, REE_{HB2}, and REE_{HB3}, respectively. Patients aged between 31 and 60 years displayed positive limits of agreement of 608.2, 839.8, and 849.2 kcal/d, and negative limits of agreement of 591.2, 515.5, and 521.1 kcal/d for comparison of REE_{IC} with REE_{HB1}, REE_{HB2}, and REE_{HB3}, respectively. Patients more than 60 years old had positive limits of agreement of 529.8, 783.5, and 796.9 kcal/d and negative limits of agreement of 550.9, 516.9, and 519.7 kcal/d for comparison of REE_{IC} with REE_{HB1}, REE_{HB2}, and REE_{HB3}, respectively.

The population was distributed into 5 subgroups with respect to BMI: 5.4% (n = 11) with BMI less than 18.5, 42.0% (n = 86) with a BMI of 18.5 to 24.9, 28.3% (n = 58) with a BMI of 25.0 to 29.9, 21.5% (n = 44) with a BMI of 30 to 39.9, and 2.9% (n = 6) with a BMI of 40 or greater. REE_{IC} and REE_{HB} agreed better in the subgroup with a BMI of 18.5 to 24.9 (eutrophic), with bias of -3.9 kcal/d for REE_{HB2}, -4.7 kcal/d for REE_{HB1}, and -4.9 kcal/d for REE_{HB3}). For the eutrophic patients, the positive limits of agreement were 561.8, 573.7, and 579.7 kcal/d and the negative limits of agreement were 570.9, 581.6, and 589.1 kcal/d for comparison of REE_{IC} with REE_{HB1}, REE_{HB2}, and REE_{HB3}, respectively. With regard to BMI, analysis of all the limits of agreement for the studied population evidenced overestimation of values within the range of +287.2 to +1138.8 kcal/d, and underestimation within the range of -75.7 to -909.5 kcal/d (Tables 2 and 3).

Discussion

A review of the literature clearly shows that most studies adopt indirect calorimetry , and not predictive equations, as the most accurate method for measuring REE.[21-24] Many researchers have stated that the difficulty in measuring REE accurately often culminates in inadequate nutritional intervention; that is, the daily calorie requirement is either underestimated or overestimated.[24,25] Provision of insufficient energy to critically ill patients can result in loss of muscle mass and significant elimination of nitrogen in the urine, which rapidly deteriorates the patient's health and nutritional status. On the other hand, the excessive provision can result in other situations, such as hypercapnia and infectious complications.

In 2013, McClave et al[26] published a review in which they compared REE_{IC} with REE calculated via predictive equations. Those authors verified that the equations were not very accurate, especially with respect to the variable BMI, and that the corresponding results were inadequate to calculate nutritional support in critically ill patients. In the present work, comparison between REE_{IC} and REE_{HB} calculated on the basis of different sources of body weight also revealed underestimated and overestimated REE in all the evaluated groups for the variables sex, age, and BMI.

Frankenfield et al[27] conducted a validation study to compare REE_{IC} with REE calculated by using predictive equations. That study involved 202 critically ill patients undergoing mechanical ventilation who had received a diagnosis of traumatic injury, had undergone surgery, or were clinical patients. The patients were subdivided into groups according to age (< 60 years and ≥ 60 years) and BMI (< 30 and ≥ 30). The authors evaluated 17 equations. The HB equation furnished accuracy of 34% for all the groups; the accuracy was 46% when the authors used the correction factor HB × 1.25. The Penn State equation afforded the best accuracy: 67% in all the groups and 77% in the elderly with BMI less than 30.

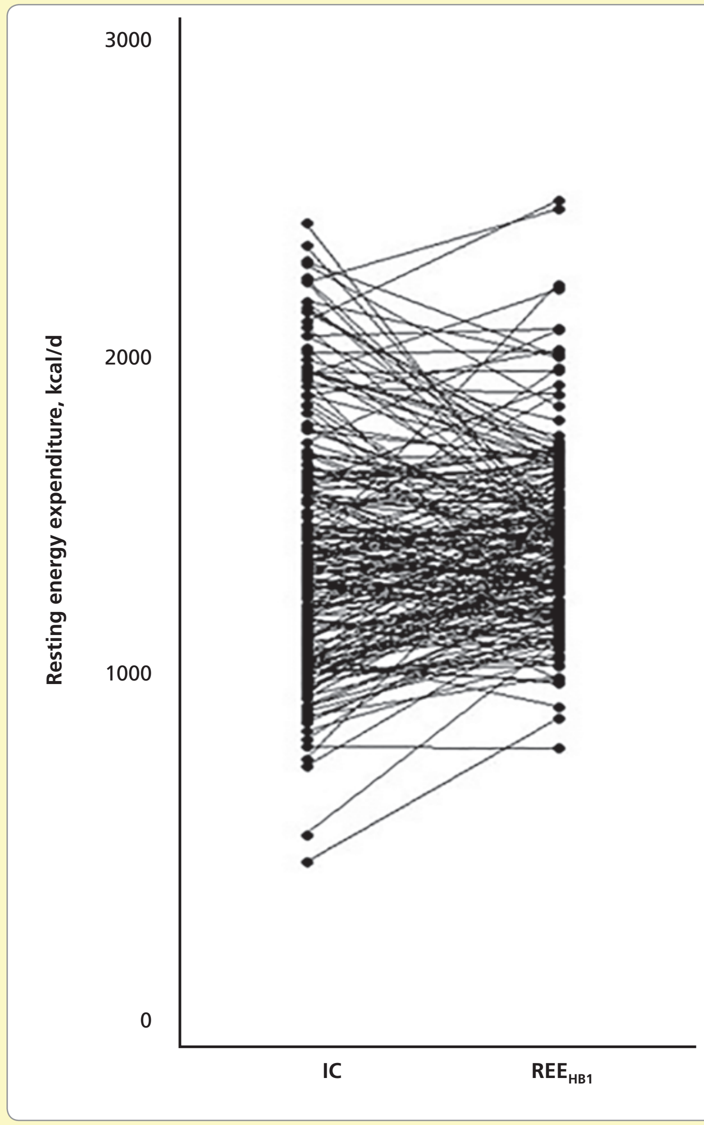

Figure 1 Comparison of resting energy expenditure measured by indirect calorimetry (IC) and resting energy expenditure calculated by using the Harris-Benedict equation with body weight determined by bed scale (REE_{HB1}) in 205 patients studied (P = .13, Wilcoxon test).

Compared with any other equation, the HB equation has been the most frequent object of validation studies. Since the original work of Harris and Benedict, approximately 138 formulas have been published by 40 different authors, all based on different sources of body weight.[11-14,28]

Although the HB equation is accurate for predicting the energy requirements within a healthy

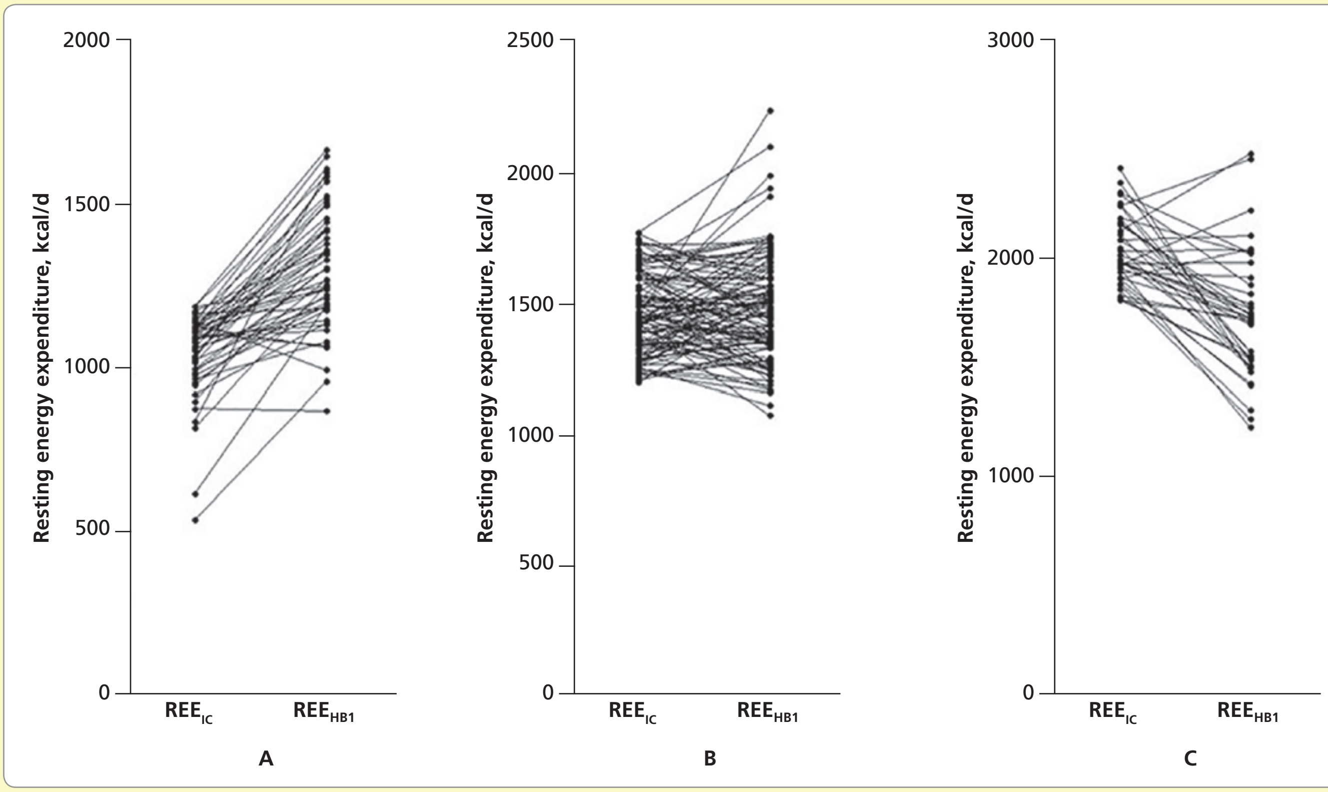

Figure 2 Comparison of resting energy expenditure (REE) measured by indirect calorimetry (IC) and REE calculated by using the Harris-Benedict equation with body weight determined by bed scale (REE$_{HB1}$) in (A) 53 patients with REE$_{IC}$ less than 1200 kcal/d (P<.001, Wilcoxon test), (B) 113 patients with REE$_{IC}$ between 1200 and 1800 kcal/d (P=.59, Wilcoxon test), and (C) 39 patients with REE$_{IC}$ greater than 1800 kcal/d (P<.001, Wilcoxon test).

population, it is not as reliable for critically ill patients.[14,25,29-32] In fact, REE$_{IC}$ and REE$_{HB}$ did not agree well in the population investigated herein. Application of the Wilcoxon test to compare REE$_{IC}$ with REE$_{HB1}$ did not reveal any significant differences for most of the population; however, it is worth noting that this test compares median values, which might constitute a limitation when one compares the extremes of a group. This limitation became evident when we divided the population into 3 groups according to REE$_{IC}$: the extreme REE$_{IC}$ values disagreed with REE$_{HB1}$ the most, with underestimated REE in the group with an REE$_{IC}$ less than 1200 kcal/d and overestimated REE in the group with REE$_{IC}$ greater than 1800 kcal/d. The difference persisted in the intermediate REE$_{IC}$ group (between 1200 and 1800 kcal/d), but it was smaller than in the other 2 groups.

Indirect calorimetry is better than other methods for estimating energy expenditure in critically ill patients.

In an effort to explain this discrepancy, another relevant aspect to consider is the fact that the HB equation does not take clinical variables that could also interfere in metabolism into account; for example, fever and use of vasoactive drugs or sedation, which could increase or decrease REE, respectively. Additionally, acute diseases, which were the main issue in our population, are known to elevate REE. Together, these aspects could explain why the HB equation does not reflect REE reliably.

Researchers in countless studies agree that indirect calorimetry is the reference standard method for measuring REE in critically ill patients. Nevertheless, most ICUs do not have this equipment, which is expensive and requires skilled staff for its operation. Certainly the cost to the patient when the actual caloric needs are not precisely calculated is high, translating into damage such as decreased immunity and its consequences, such as the occurrence of infectious diseases, worsening the prognosis and prolonging the hospital stay, also increasing the costs to the health system. Unfortunately, no cost-effectiveness studies have been done to compare indirect calorimetry with other methods, and such studies are essential to get an idea of the budget impact for patients, their families, and the hospital of using indirect calorimetry versus other methods to calculate energy demand in critically ill patients. Fortunately, technological advances have enabled the development of more compact and less costly calorimeters coupled

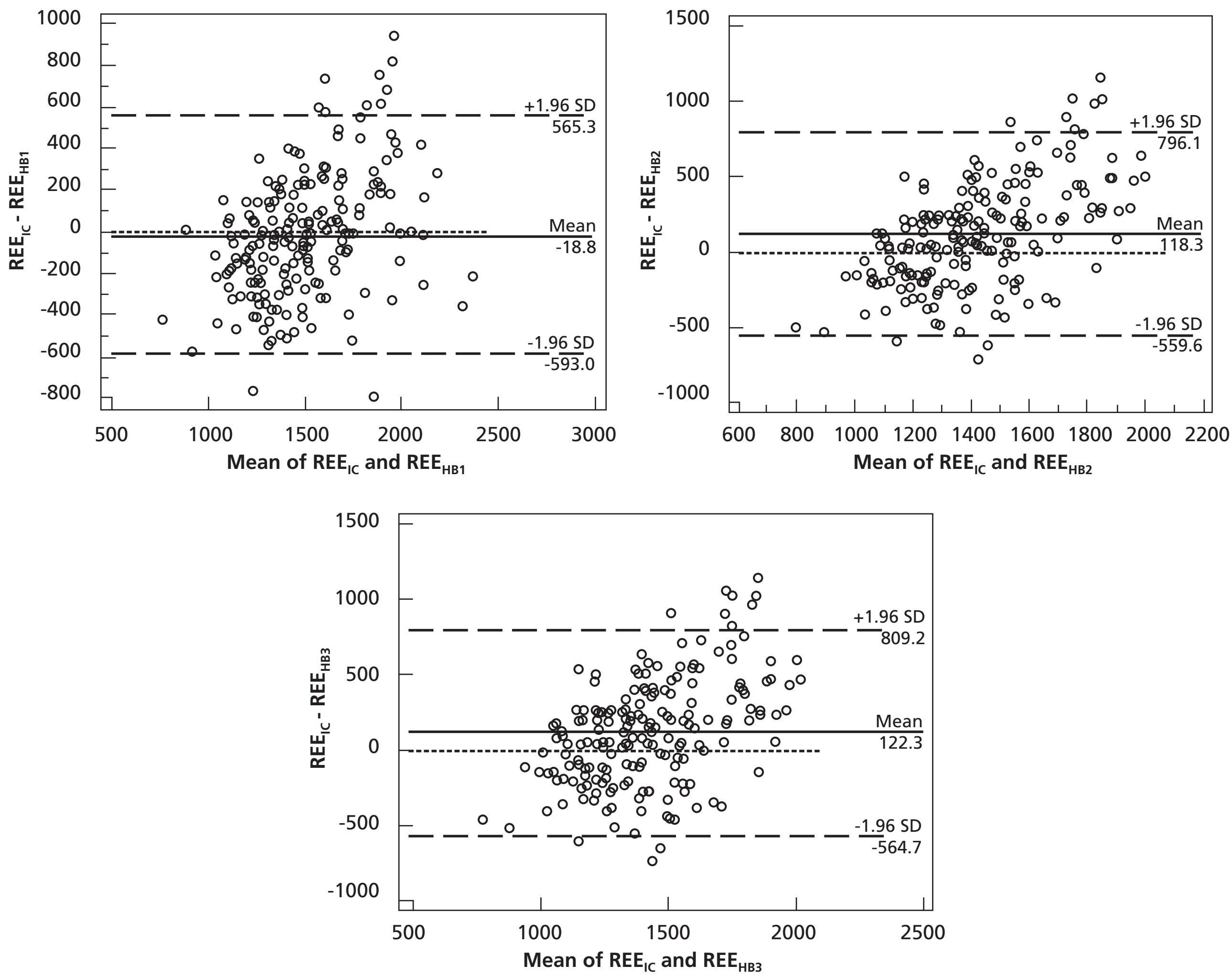

Figure 3 Comparison of resting energy expenditure (REE) measured by indirect calorimetry (IC) and REE calculated by using the Harris-Benedict equation with body weight determined by bed scale (REE$_{HB1}$), the ideal body weight (REE$_{HB2}$), and the predicted body weight (REE$_{HB3}$) in 205 patients studied.

to mechanical ventilators, which facilitates their routine use. This convenience may aid widespread use of this method among health professionals, especially those who work in ICUs.

The present study demonstrated the poor accuracy of the HB equation for calculating REE in our sample. Agreement between REE$_{IC}$ and REE$_{HB1}$ evidenced a bias of -18.8 kcal/d between the methods, with underestimation or overestimation in all the cases, as verified by Bland-Altman analysis. Even the subgroup with better statistical agreement did not furnish a clinically acceptable level of agreement. Therefore, the HB equation cannot substitute for indirect calorimetry for estimating REE in critically ill patients even if one uses the body weight measured with a bed scale.

This study had some limitations. To begin with, REE$_{IC}$ and REE$_{HB}$ measurement took place

Table 2
Positive limits of agreement obtained via Bland-Altman method according to body mass index

	Limit of agreement, kcal/d		
BMI	REE$_{HB1}$	REE$_{HB2}$	REE$_{HB3}$
< 18.5	422.2	287.2	317.5
18.5-24.9	561.8	573.7	579.7
25.0-29.9	552.2	766.4	774.3
30.0-39.9	584.6	946.0	959.4
≥ 40.0	517.8	1138.8	1134.4

Abbreviations: BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; REE$_{HB1}$, resting energy expenditure from Harris-Benedict equation using body weight determined by bed scale; REE$_{HB2}$, resting energy expenditure from Harris-Benedict equation using the ideal body weight; REE$_{HB3}$, resting energy expenditure from Harris-Benedict equation using the predicted body weight.

Table 3
Negative limits of agreement obtained via Bland-Altman method according to body mass index

BMI	Limit of agreement, kcal/d		
	REE_{HB1}	REE_{HB2}	REE_{HB3}
< 18.5	668.0	731.6	736.7
18.5-24.9	570.9	581.6	589.1
25.0-29.9	630.3	490.0	500.5
30.0-39.9	549.4	225.0	202.2
≥ 40.0	909.5	88.5	75.7

Abbreviations: BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; REE_{HB1}, resting energy expenditure from Harris-Benedict equation using body weight determined by bed scale; REE_{HB2}, resting energy expenditure from Harris-Benedict equation using the ideal body weight; REE_{HB3}, resting energy expenditure from Harris-Benedict equation using the predicted body weight.

within the first 48 hours of patient's admission to the ICU. Although energy metabolism undergoes dynamic changes in critically ill patients, this study did not assess such alterations. Second, evaluation of the factors that could affect REE_{IC} measurement, such as type of diet and administration route, did not occur on an individual basis, because the routine practice in the ICU involved prescription of a diet that ensured an adequate amount of calories to the patient. Besides, energy provision may not have interfered in our assessment because this was a paired study that compared 2 different methods for the same patient. Finally, the ventilation mode was not recorded at the time of assessment, because this parameter does not affect indirect calorimetry variables in critically ill patients.[33]

Conclusion

In conclusion, our findings corroborated published evidence that indirect calorimetry is better than other methods for measuring REE in critically ill patients undergoing mechanical ventilation. Using indirect calorimetry ensures that critically ill patients receive more accurate nutritional support. Moreover, the attempt to use different sources of body weight failed to improve the accuracy of the HB equation for predicting REE in critically ill patients.

Regarding REE measurement in critically ill patients undergoing mechanical ventilation, our results showed that the Harris-Benedict equation is not reliable as a substitute for indirect calorimetry, regardless of the source of body weight.

FINANCIAL DISCLOSURES
None reported.

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