INTRODUCTION

Critically ill patients comprise a non-homogeneous sample of individuals who, due to different acute conditions, require complex care and constant monitoring. Therefore, these patients generally require hospitalization in an intensive care unit (ICU).1

The nutritional status of hospitalized patients has a significant impact on their clinical outcome.2 According to Logan and Hildebrandt,3 protein-energy malnutrition is a prevalent problem and affects 30 to 60% of hospitalized patients. Many of these patients lose weight during the hospitalization, and such phenomena have multifactorial origins (e.g., the severity of the illness and the lack of adequate nutritional support).4

ABSTRACT

Objective: Given the inaccessibility of indirect calorimetry, intensive care units generally use predictive equations or recommendations that are established by international societies to determine energy expenditure. The aim of the present study was to compare the energy expenditure of critically ill patients, as determined using indirect calorimetry, to the values obtained using the Harris-Benedict equation.

Methods: A retrospective observational study was conducted at the Intensive Care Unit 1 of the Centro Hospitalar do Porto. The energy requirements of hospitalized critically ill patients as determined using indirect calorimetry were assessed between January 2003 and April 2012. The accuracy (± 10% difference between the measured and estimated values), the mean differences and the limits of agreement were determined for the studied equations.

Results: Eighty-five patients were assessed using 288 indirect calorimetry measurements. The following energy requirement values were obtained for the different methods: 1,753.98±391.13 kcal/day (24.48 ± 5.95 kcal/kg/day) for indirect calorimetry and 1,504.11 ± 266.99 kcal/day (20.72±2.43 kcal/kg/day) for the Harris-Benedict equation. The equation had a precision of 31.76% with a mean difference of -259.86 kcal/day and limits of agreement between -858.84 and 339.12 kcal/day. Sex (p=0.023), temperature (p=0.009) and body mass index (p<0.001) were found to significantly affect energy expenditure.

Conclusion: The Harris-Benedict equation is inaccurate and tends to underestimate energy expenditure. In addition, the Harris-Benedict equation is associated with significant differences between the predicted and true energy expenditure at an individual level.

Keywords: Indirect calorimetry; Diet therapy; Nutritional therapy; Energy metabolism; Respiration, artificial; Intensive care units
This problem is even more prominent in critically ill patients given that they are in a state of clinical hypermetabolism and hypercatabolism,\(^\text{5,6}\) exhibit hemodynamic instability and, occasionally, lack an available enteral route. These states ultimately prevent early nutritional support. Moreover, the problem of nutritional support for these patients is aggravated by the fact that energy expenditure (EE) is conditioned by certain medical and pharmacological procedures, thus promoting a reduction in the metabolic response.\(^\text{7}\)

In this scenario, which can easily lead to malnutrition, an estimation of EE is recommended, and this estimation should be as accurate as possible. The early institution of nutritional support (NS) is also recommended. Guidelines from different societies for enteral and parenteral nutrition recommend NS for all critically ill patients who have no prospect of ingesting a complete oral diet within the first 3 days of admission to the ICU. Ideally, this NS should be initiated within the first 24 to 48 hours following hospitalization.\(^\text{8}\)

Therefore, the accurate determination of EE in these patients is mandatory to guarantee that their energy requirements are met and to avoid the multiple deleterious consequences that are associated with hyperalimentation or caloric restriction.\(^\text{9-14}\)

Many methods have been described to assess EE in critically ill patients; however, all these methods have limitations. Indirect calorimetry (IC) is a noninvasive method that determines energy requirements and substrate utilization rates based on oxygen consumption (VO\(_2\)) and carbon dioxide production (VCO\(_2\)). These values are obtained through the analysis of the inspired and expired air from the lungs.\(^\text{15}\) This method is currently considered to be the gold standard for determining total EE\(^\text{16}\) despite its well-known technical limitations, such as the requirement for trained personnel, the requirement for an inspired oxygen fraction that is lower than 0.6 and the high cost of the necessary equipment.\(^\text{15}\)

In addition to the use of equations, other methods with easier applicability have been more commonly used to estimate EE to optimize nutritional support, including the clinical recommendations of the American Society for Parenteral and Enteral Nutrition (ASPEN) and the European Society for Clinical Nutrition and Metabolism (ESPEN).\(^\text{10}\) Over 200 equations have been documented for predicting EE,\(^\text{17}\) although the most widely examined and used in clinical practice\(^\text{18}\) is the Harris-Benedict (HB) equation.\(^\text{19}\) However, these predictive methods are often considered to be inaccurate,\(^\text{6,20-22}\) and thus no method has gained universal acceptance.

The primary aim of the present study was to evaluate the EEs of critically ill patients as measured using IC, comparing these measurements (i) to values that were calculated using the HB predictive equation and (ii) to ESPEN’s recommendations for nutritional support. Moreover, an attempt was made to identify the parameters that could influence energy intake.

**METHODS**

**Study design**

A retrospective observational analytical study was conducted at the Intensive Care Unit 1 of the Centro Hospitalar do Porto - CHP. All the critically ill patients with a minimum of 3 days of hospitalization, who were subjected to IC, whose anthropometric data were recorded and who were hospitalized between January 2003 and April 2012 were included in the study.

The exclusion criteria included the absence of data that would allow for the use of the HB equation for estimating EE (i.e., weight, height and age) and individuals who were younger than 18 years of age. IC measurements that revealed respiratory quotients (RQs) <0.6 or >1.25 or an inspired oxygen fraction >0.6 were considered to be low-quality measurements and thus were excluded.\(^\text{23}\) No admitting diagnoses were excluded.

The study was approved by the CHP’s Health Ethics Committee, with no requirement for informed consent forms. The demographic data, the type of admission (e.g., neurosurgical pathology, medical, transplants, urgent surgery and scheduled surgery), the Sequential Organ Failure Assessment (SOFA) severity index, the albumin levels, the serum prealbumin levels, the C-reactive protein (CRP) levels, the total leucocyte count (TLC) and the 24-hour urea and creatinine clearance were recorded.

Weight and height data were obtained on admission by asking the patient or the closest family member (preadmission weight) or by consulting the patient’s recent primary care medical records. The patients’ body mass indices (BMIs) were grouped into five classes based on the World Health Organization (WHO) classification system:\(^\text{24}\) <18.5 (malnutrition), 18.5 to 24.99 (euthrophia), 25 to 29.99 (overweight), 30 to 34.99 (class I obesity) and ≥35 (classes II and III obesity). Given that BMI alone does not reflect the nutritional diagnosis of critically ill patients, the WHO’s definitions were adapted to the following limits: <18.5 (underweight), 18.5 to 24.99 (normal weight), 25 to 29.99 (overweight), 30 to 34.99 (class I obesity) and ≥35 (classes II and III obesity).

The patients’ true EEs were measured using respiratory
IC. All the measurements were performed by a single individual from the institution. This individual had experience using the technique, thereby limiting operator-dependent errors. The data were collected from all the measurements that were made beginning on the second day of hospitalization onwards, respecting the criteria for inclusion in the study.

All the patients were continually assessed for a minimum of 25 minutes during mechanical ventilation while lying in bed in supine position. The patients made minimal movements and were maintained in a thermoneutral environment. Only one measurement was performed per day, and a specific time was not established for this purpose.

The RQ, VO₂ and VCO₂ values, as well as catecholamine administration, the patient’s temperature and the presence or absence of sedation were recorded for each IC measurement. The metabolic monitor Deltatract™ II (Datex-Ohmeda, Finland) was used for the IC measurements. This device was calibrated (gas and pressure) prior to each measurement according to the manufacturer’s recommendations. The EE values are given in kcal/day and kcal/kg/day. The measurements were obtained while maintaining continuous nutrition once NS was established.

The albumin levels, the leucocyte counts and the CRP and SOFA scores were also obtained for each patient on the day of the first IC measurement. The prealbumin levels and the 24-hour urea and creatinine clearance were obtained on subsequent days as close as possible to the first IC measurement.

The baseline EE (kcal/day) was calculated using the HB predictive equation for males \[66.47 + (13.75 \times \text{weight}) + (5.003 \times \text{height}) - (6.775 \times \text{age})\] and for females \[655.09 + (9.563 \times \text{weight}) + (1.85 \times \text{height}) - (4.676 \times \text{age})\], where weight was expressed in kilograms, height in centimeters and age in years. Stress/activity factors were not applied to the equation, as these factors are believed to introduce an empirical character to the estimates.

**Statistical analysis**

The Statistical Package for the Social Sciences (SPSS) program, version 17, was used for the analysis and treatment of statistical data; statistical significance was considered to be p<0.05 for all the tests. The results are given as the mean ± standard deviation (SD).

The mean IC readings for each patient were used for statistical comparisons with the values that were obtained using the HB equation. Pearson’s correlation coefficient was calculated to assess the relationship between the EEs that were obtained using the HB equation and those that were obtained using IC. The correlation measured the strength and the direction of the relationship; this value (r) ranges from 0 (no correlation) to 1 (perfect correlation). Bland & Altman’s method allows for the description of the agreement between the two quantitative measurements that measure the same characteristic on the same scale. This method was used to assess the agreement between the values that were obtained by the two methods. There is no probative value to describe the agreement, which is based on the concept that the difference between the two measurements is compared to the average of the two measurements. It is recommended that 95% of the data included is within ±1.96 SD of the mean difference and that the bias is close to 0.

The degree of precision of the HB equation was calculated and expressed by the percentage of the results that fell within ±10% of the values that were obtained using IC. When the estimated values were outside this range, they were considered to be inaccurate. HB equation-derived values that were <90% of the values that were measured using IC were classified as caloric restriction, and values that were >110% of the IC values were classified as hyperalimentation.

The mean difference of the EE that was obtained using the HB equation, and IC was also calculated for all the measurements and grouped according to BMI. The results were expressed as kcal/day and as 95% confidence intervals of the mean difference. The HB equation was considered to coincide with IC if this confidence interval included the value 0.

The relationships between the true EE per kilogram of body weight and the following parameters were assessed: sex, age, sedation, the administration of amines, patient temperature, type of admission and SOFA score.

Regression models were used to compare the continuous variables. Student’s t-test and an analysis of variance (ANOVA) were used to compare the continuous and categorical variables and the dichotomous and polychotomous variables, respectively.

**RESULTS**

Of the 136 patients who were subjected to IC, 85 patients met the inclusion criteria. The sample was 71.76% (n=61) male and had a mean age of 60.08±17.05 years, a mean BMI of 25.84±5.13 and a mortality rate of 23.8%. The reasons for admission included the following: neurosurgical (50.6%), medical (16.5%), transplants (7.1%), urgent surgery (15.3%) and scheduled surgery (10.6%). The mean hospital stay duration was 13.42±13.86 days, with a minimum of 3 days and maximum of 76 days.
The average RQ that was obtained for each IC measurement was 0.77±0.16. Of the total sample, 30.4% of the patients underwent therapy with catecholamines, 65.9% were under sedation and 34.8% had temperatures ≥38°C. With respect to the biochemical data, the following means were highlighted: CRP of 112.60±106.82 mg/L, SOFA score of 5.46±3.02, prealbumin levels of 141.83±72.05 mg/L, 24-hour urea clearance of 25.53±14.19 g per day and 24-hour creatinine clearance of 1,139.08±536.99 mg per day.

The examined patients had an average BMI of 25.84±5.13. This metric was distributed as follows: 5.9% (n=5) had a BMI < 18.5 (underweight), 38.8% (n=33) had a BMI between 18.5 and 24.99 (normal weight), 36.5% (n=31) had a BMI between 25 and 29.99 (overweight), 15.3% (n=13) had a BMI between 30 and 34.99 (class I obesity) and 3.5% (n=3) had a BMI ≥ 35 (classes II and III obesity).

Two hundred and eighty-eight measurements were made using IC, with an average of 3.38±2.18 measurements per patient and a mean duration of 12.12±9.43 hours. The mean EE was 1,753.98±391.13 kcal/day.

The mean EE obtained by the HB equation was 1,504.11±266.99 kcal/day. With respect to the daily kcal per kilogram of body weight, the average IC-determined value was 24.48±5.95 and the HB estimated a value of 20.72±2.43, as opposed to the 25-kcal daily recommendation that is made by ESPEN (2009).[8] Therefore, the HB equation indicated an EE that corresponded to an average of 85.75% of that measured using IC. The HB equation predicted adequate energy supply in only 31.8% of the patients (n=58). The HB equation predicted caloric restriction (predicted value <90% of measured value) in 60% (n=27) of the patients and hyperalimentation (value >110%) in 8.24% (n=7) of the patients.

Pearson’s correlation coefficient revealed a significant (p<0.001; n=85) but moderate (r=0.627) correlation between the EE that was obtained by the HB equation and the EE that measured using IC (Figure 1).

Figure 2 shows the representation of the Bland–Altman method. It should be noted that 6/85 (7.06%) points are beyond the ± 1.96 SD cutoffs. The mean difference between the two methods was -259.86±305.60 kcal/day and the limits of agreement ranged from -858.84 (mean -1.96 SD) to 339.12 (mean +1.96 SD).

The HB equation did not coincide with IC values when considering the total measurements (95% confidence interval: -315.78 to -183.95) but only coincided in the patients with class II or III obesity (Table 1). The HB equation underestimated the true EE for the majority of the measurements and for all BMI classes. The mean difference was higher for normal-weight individuals (-356.08 kcal/day) and lower for patients with class II or III obesity (-78.03 kcal per day). The accuracy of the equation was observed to be lower in patients with low body weights (20%) and increased in patients with class II or III obesity (66.67%). The mean correction factor of the HB equation to IC (i.e., the value that should be multiplied by the HB-derived value to predict the IC-derived value) was 1.17.

The statistical relationships between the different variables and EE were sought. It was noted that the EE was significantly greater in males (p=0.023), with mean values of 24.66±6.38 kcal/kg/day versus 21.17±6.01 kcal/kg/day for females.
Individuals with body temperature ≥38°C had a significantly greater EE (26.29±7.23 kcal/kg/day; p=0.009) when compared to those with lower body temperature (23.68±6.69 kcal/kg/day). Reduced energy requirements were observed (ANOVA, p<0.001) in classes with higher BMIs, with the true EEs ranging from 30.54±9.31 kcal/kg/day for individuals with BMI <18.5 to 16.72±1.86 kcal/kg/day for individuals with BMI ≥35 (Figure 3). No significant differences were detected in EE with the administration of amines (p=0.167) or sedation (p=0.328), nor were differences observed with respect to the SOFA severity index (p=0.778). Moreover, we noted a decrease in EE with age (linear regression, p<0.001, r=0.371).

Despite the absence of significant mean differences (p=0.402) in true EE between the different types of admissions, it was noted that the highest value corresponded to transplant patients, who exhibited an average EE of 26.84±4.30 kcal/kg/day. The lowest EE value was observed for patients who underwent urgent surgery, who exhibited a value of 20.90±4.57 kcal/kg/day (Figure 4). The comparison between the type of admission and the BMI is given in table 2.
DISCUSSION

The HB equation was observed to be inaccurate (31.76% accuracy), biased and to have wide limits of agreement, ranging from -858.84 to 339.12 kcal/day. According to Frankenfield et al.,(28) accuracy values < 50% do not appear to be adequate from a clinical perspective. Therefore, the practical usefulness of the HB equation is limited. Our results indicate inadequately estimated nutritional support in 68.24% of the patients, which is consistent with the literature. Kross et al.(20) observed an inaccuracy rate of 68.7% (inadequate nutrition) when using the HB equation in 927 critically ill patients. Pirat et al.(6) reported that this equation resulted in a 58% rate of inadequate nutrition (29% for both caloric restriction and hyperalimentation) in 34 critically ill patients with cancer. Boullata et al.(22) observed a 57% rate of ineffective predictions in 395 patients.

The present study demonstrated a significant correlation of only 62.7% between the EE that was obtained by the HB equation (1,504.11 kcal/day) and the value that was measured using IC (1,753.98 kcal/day; p<0.001). Therefore, this equation induces caloric restriction (the equation predicted, on average, only 85.75% of the nutritional support required). The methods exhibited a mean difference of -259.86 kcal/day, corresponding to a caloric restriction requirement (the HB equation tends to underestimate the true nutritional requirements). However, the results of other authors indicate that the HB equation in an acceptable substitute for IC.(9,32)

The latest ESPEN guidelines(8) recommend that, in the absence of IC, the critically ill patient should receive 25 kcal/kg per day and that this value should reached over 2 to 3 days after the beginning of NS. By verifying the average energy requirements of 24.48 kcal/kg/day, our results indicated that overall, the value that is recommended by the European society is suitable for the overall requirement of patients in this ICU, although a slight hyperalimentation may occur, particularly in obese individuals. This result is even more relevant given the recent recommendations(35) that suggest the adoption of a hypocaloric (11 to 14 kcal/kg per day of current weight) and a high protein diet for obese patients who have no contraindications. Stucky et al.(34) even recommend the use of hypocaloric diets for all patients who are admitted to the ICU.

Long et al.(35) introduced the use of activity/stress factors as correction values to the estimates that are made by the HB equation. These factors were introduced for specific metabolic conditions of critically ill patients, ranging from 0.7 if the patient is hungry to 2.1 if the patient is a burn victim. These factors are now considered to be unreliable in practical terms given that several parameters, some of which are undetermined, contribute to the total EE and vary according to the universality of these parameters in an ICU. We therefore only present the correction value of HB to IC (i.e., 1.17), as we believe that without a concrete understanding of all of the variables that justify a correction value, it is only possible to determine such a factor retrospectively and to provide only a description of the overall state of metabolic stress.

The type of admission did not affect the EE measured, although it should be noted that 50.6% of individuals belonged to a single class (neurosurgical). Although it has been described that sedation reduces the true EE, whereas Reid’s study(18) and suggest that the HB equation (with no correction factors) is a good predictor of EE in individuals with BMI ≥ 35 (100% accuracy).

The presence of a correlation between the HB equation and IC is consistent with the results that were reported by Boullata et al.;(22) however, once again, this correlation was not reflected in the accuracy of the equation or in the lack of acceptable differences, which are more clinically useful than the strength of correlation. In summary, the present study corroborates several results that have been previously published in the literature that indicate (i) the ineffectiveness of predictive equations(20,22,28,29) and (ii) that the HB equation tends to underestimate the true nutritional requirements. However, the results of other authors indicate that the HB equation in an acceptable substitute for IC.(9,32)
As vasoactive amines increase the EE, this association was not observed in the present study. However, no sedation scale was used to quantify the level of sedation in these patients.

Furthermore, the present study demonstrated no relationship between the true EE and the disease severity as assessed using the SOFA score. However, the true EE was significantly greater in individuals with body temperature ≥38°C. These findings support the conclusions that were made by Bruder et al., where body temperature was the greatest determinant of EE in sedated subjects.

We must not neglect to mention the study’s limitations, including the fact that the study was retrospective and was conducted on a nonrandom sample of patients. Thus, our conclusions may not be generalizable to all critically ill patients. Another limitation is the fact that only the necessary energy requirements were considered and not those that were effectively administered; therefore, a considerable discrepancy is possible.

Given that IC is recognized as a reference method for measuring EE in critically ill patients under mechanical ventilation, its accompanying limitations have encouraged the use of equations, such as the HB equation, and recommendations from nutrition societies. These methods are among the more commonly used techniques to estimate the EE in clinical practice. Despite the limitations of these methods, our results confirm the requirement to develop or improve the most commonly used methods for predicting EE and to support the maintenance of IC as the most reliable method for its determination.

CONCLUSION

The HB equation is inaccurate and tends to underestimate EE, resulting in significant differences between the predicted and true EEs at an individual level.

REFERENCES


RESUMO

Objetivo: As unidades de terapia intensiva recorrem às equações preditivas, para determinar o gasto energético, ou às recomendações estabelecidas por sociedades internacionais, devido à inacessibilidade da calorimetria indireta. O objetivo deste trabalho foi comparar o gasto energético de pacientes críticos, por calorimetria indireta, aos calculados por meio da equação de Harris-Benedict.

Métodos: Estudo retrospectivo observacional realizado no Serviço de Cuidados Intensivos 1 do Centro Hospitalar do Porto. Foram avaliadas as necessidades energéticas, desde janeiro de 2003 até abril de 2012, dos pacientes críticos internados em que foi realizada calorimetria indireta. Procedeu-se ao cálculo da precisão (intervalo de ±10% entre os valores medidos e estimados), da diferença média e dos limites de concordância e da equação estudada.

Resultados: Foram avaliados 85 pacientes, em que se efetuaram 288 medições por calorimetria indireta. Valores obtidos para necessidades energéticas em diferentes métodos: calorimetria indireta 1.753,98±391,13 kcal ao dia (24,48±5,95 kcal/kg ao dia), equação de Harris-Benedict 1.504,11±266,99 kcal ao dia (20,72±4,43 kcal/kg ao dia). A precisão da equação foi de 31,76%, a diferença média de -259,86 kcal ao dia, com limites de concordância entre -858,84 a 339,12 kcal ao dia. O gênero (p=0,023), a temperatura (p=0,009) e o índice de massa corporal (p<0,001) revelaram-se fatores com impacto significativo no gasto energético.

Conclusão: A equação de Harris-Benedict não é precisa na determinação do gasto energético, subestimando-o e apresentando diferenças significativas para predizer, a nível individual, o gasto energético real.

Descritores: Calorimetria indireta; Dietoterapia; Terapia nutricional; Metabolismo energético; Respiração artificial; Unidades de terapia intensiva


