Measured versus estimated energy requirement in hospitalized patients

Houmøller, Caroline P.; Hellerup, Sebastian H.; Nøhr, Niels K.; Winther, Gustav; Mikkelsen, Sabina; Geisler, Lea; Holst, Mette

Published in:
Clinical Nutrition ESPEN

DOI (link to publication from Publisher):
10.1016/j.clnesp.2023.12.011

Publication date:
2024

Document Version
Publisher's PDF, also known as Version of record

Clinical Nutrition ESPEN 59 (2024) 312–319

Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: http://www.clinicalnutritionespen.com

Original article

Measured versus estimated energy requirement in hospitalized patients

Caroline P. Houmøller [a], Sebastian H. Hellerup [a], Niels K. Nøhr [a], Gustav Winther [a], Sabina Mikkelsen [b], Lea Geisler [b], Mette Holst [c, *]

[a] Department of Health, Science and Technology, Aalborg University, Denmark
[b] Centre for Nutrition and Intestinal Failure, Aalborg University Hospital, Denmark
[c] Centre for Nutrition and Intestinal Failure, Department of Gastroenterology, Aalborg University Hospital and Department of Clinical Medicine, Aalborg University, Denmark

ARTICLE INFO

Article history:
Received 15 August 2023
Accepted 8 December 2023

Keywords:
Indirect calorimetry
Harris Benedict equation
Malnutrition
Dietician
Hospital

SUMMARY

Background & aim: Failure to identify a patient's energy requirement has a variety of consequences both physiological and economical. Previous studies have shown that predictive formulas, including the Harris Benedict equation (HB), both over- and underestimates energy requirement in severely ill patients and healthy younger adults, compared to the golden standard, indirect calorimetry (IC). The comparison between measured and estimated energy requirements in hospitalized patients in regular wards is underreported. The aim of this study was to assess the agreement between measured energy requirements and requirements estimated by HB in the individual hospitalized patients, and to investigate whether those findings were associated with other specific patient characteristics.

Methods: IC (n = 86) was used to measure resting energy expenditure (REE) and bioimpedance analysis (BIA) (n = 67) was used for body composition in patients admitted to Aalborg University Hospital. Furthermore, height, weight, body mass index, calf circumference, while information regarding hospital ward, vital values, dieticians estimated energy requirements and blood samples were collected in the patients' electronic medical records. Bland-Altman plots, multiple linear regression analysis, and Chi^2 tests were performed.

Results: On average a difference between IC compared with the HB (6.2%), dietitians' estimation (7.8%) and BIA (4.50%) was observed ($p < 0.05$). Association between REE and skeletal muscle mass (SMM) ($R^2 = 0.58$, $\beta = 149.0$ kJ), body fat mass (BFM) ($R^2 = 0.51$, $\beta = 59.1$ kJ), and weight ($R^2 = 0.62$, $\beta = 45.6$ kJ) were found ($p < 0.05$). A positive association between measured REE and HB were found in the following variables ($p < 0.05$): CRP, age, surgical patients, and respiratory rate.

Conclusion: This study found a general underestimation of estimated energy expenditure compared to measured REE. A positive correlation between measured REE and SMM, BRM and weight was found. Lastly, the study found a greater association between CRP, age, surgical patients, and respiratory rate and a general greater than ±10% difference between measured and estimation of energy requirements.

1. Introduction

Nutrition is vital for proper function of the human body. European Society for Clinical Nutrition and Metabolism (ESPEN) defines malnutrition as “a state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat-free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease” [1]. Research shows that up to 50% of hospitalized patients have variable degrees of malnutrition [2]. Early screening using the nutritional risk screening 2002 (NRS-2002), score >3, and proper intervention has shown to have a positive impact on the patients' clinical outcomes and quality of life [1,3], as well as provide large economic gains [1,3–5]. Studies show increased expenses of up to 308.9% and a prolonged stay of 6.6 ± 12.8 days due to malnutrition [4].

* Corresponding author. . Centre for Nutrition and Intestinal Failure, Department of Gastroenterology, Aalborg University Hospital and Department of Clinical Medicine, Aalborg University, Sdr. Skovvej 5, 1, DK-9000 Aalborg, Denmark

E-mail addresses: caroline.houmoeller@rn.dk (C.P. Houmøller), shelle20@student.aau.dk (S.H. Hellerup), nnahr20@student.aau.dk (N.K. Nøhr), gwinth20@student.aau.dk (G. Winther), sabina.mikkelsen@rn.dk (S. Mikkelsen), leageisler@hotmail.com (L. Geisler), mette.holst@rn.dk (M. Holst).

https://doi.org/10.1016/j.clnesp.2023.12.011
2405-4577/

Abbreviations

AF	Activity factor
BF%	Body fat percentage
BFM	Body fat mass
BIA	Bioelectrical impedance analysis
BMR	Basal metabolic rate
BP	Blood pressure
CV for VO_2	Coefficient of variation for inspired volume of O_2
EE	Energy expenditure
ESPEN	European Society for Clinical Nutrition and Metabolism
HB	Harris Benedict equation
HR	Heart rate
IC	Indirect calorimetry
NRS-2002	Nutritional risk screening 2002
REE	Resting Energy Expenditure
RR	Respiratory rate
RQ	Respiratory quotient
SD	Standard deviation
SMM	Skeletal muscle mass
TEE	Total Energy Expenditure
VO2	Oxygen consumption
VCO2	Carbon dioxide production
95% CI	95% Confidence interval

Metabolic rate in hospitalized patients is considerably higher compared to healthy individuals as critical illness induces hypermetabolism and hypercatabolism [6]. Furthermore, catabolism may increase the risk of mortality, rate of infections, multiple organ failure, and other complications [7].

Total energy expenditure (TEE) is divided into resting energy expenditure (REE) and activity-related energy expenditure. REE is subdivided into diet induced thermogenesis and basal metabolic rate (BMR) [8]. One study found that 26% of the total variance in BMR between individuals could not be explained by difference in age, sex or body composition [9]. Body composition may partly explain the variation in REE seen in the non-hospitalized population, as adipose tissue consumes 19 kJ/kg/day during rest, whereas skeletal muscles consume 55 kJ/kg/day [10]. Calf circumference has shown correlation with appendicular skeletal muscle mass (SMM) measured by DXA, which is known as the golden standard for measuring body composition [11,12] thus calf circumference may give an indication of the patient's nutritional status [12].

The Harris Benedict equation (HB) using weight, height, sex and age to calculate BMR is commonly used in patients [13]. The agreement between HB and IC has been explored, but often in critically ill patients and not in the general hospitalized population [14–18]. Previous studies have found predictive equations to generally over- or underestimate REE [14,16–18]. While overestimation has for instance been found in stable polio survivors [17], underestimation is often seen in patients with cancer [18].

Previous studies have found significant as well as indeterminate association with EE in the critically ill [19]. ESPEN guidelines make an estimate of appropriate nutrition, including daily calorie and protein intake, which is further based on the patient's level of stress metabolism, but recommend measurement in many cases [20]. Therefore, the aim of this study was to assess the agreement between measured and estimated energy requirements in hospitalized patients and to investigate whether those findings were associated with specific patient characteristics including disease activity and body composition.

2. Materials & methods

2.1. Study design and participants

The study design was a cross-sectional study as illustrated in Fig. 1. This study included patients admitted to a wide range of hospital wards at Aalborg University Hospital, Denmark. This includes pulmonology, gastroenterology, otorhinolaryngology, geriatrics, orthopedics, neurology, gynecology, infectiously, endocrinology, hematology, urology and nephrology.

2.1.1. Inclusion criteria

We included patients above 18 years of age, who had the ability to understand the provided oral and written information, The included patients had to comply with a list of set criteria in preparation for the test. The compliance to these criteria was checked the morning of the measurement and included no exercise <24 h prior, a fasting period of ≥8 h, including oral, enteral and parenteral feeding as well as fluids. Half a cup of water with medication was allowed to not interfere with the patients' treatment [22,23]. Written informed consent was obtained prior to inclusion.

2.1.2. Exclusion criteria

Patients who were not able to understand and sign informed consent were not included. Patients who did not comply with fasting regimen were excluded prior to measurement.

2.2. Data collection

The measurement of each patient took place over two days. The patient was included in the afternoon on day 0, where the patients signed the statement of informed consent prior to inclusion in the study. Thereafter, the patient's height, weight and calf circumference were measured. The patient's height was measured while standing with their feet together, heels touching the wall. Weight was measured on the calibrated weighing scale, used in the wards on an everyday basis. If a patient was unable to participate in these measurements, the most recent recorded height and weight (no later than three days old) were retrieved from their electronic medical records. Calf circumference was measured three times at the widest point of the calf. If there was a slight discrepancy between measurements, the mean value was used. On day 1 the bioelectrical impedance analysis (BIA) and indirect calorimetry (IC) were performed. For all measures the standard protocol used in the Nutrition Laboratory at the hospital was used. This is in accordance to the standard provided by InBody.

An activity factor (AF) was set for each of the patients, where 1.1 was given to a bedridden patient, 1.2 was given to a patient who was able to mobilize to a chair, and 1.3 was given to the patients able to walk around the ward, which are described in the guidelines on Danish institutional diet by the Danish Health Authority [21]. These were chosen based on their medical record or our observations during the inclusion.

2.2.1. Data from electronic medical system

The following data were collected from the patient's electronic medical record in “NordEPJ”: Sex, age, diagnosis, hospital ward, date of hospitalization, date of blood samples, energy requirement estimated by the medical record system and/or energy requirement

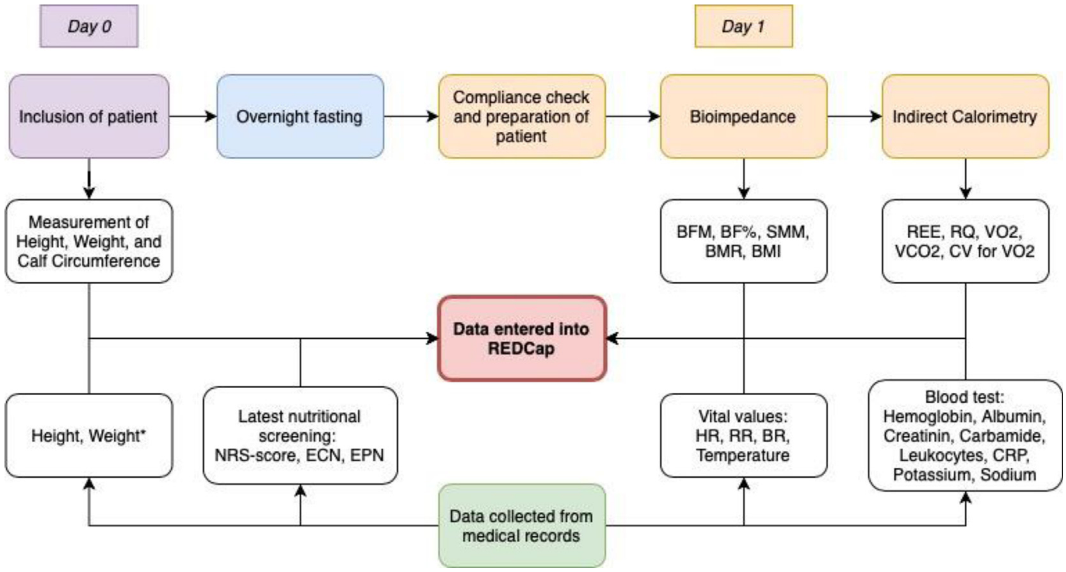

Fig. 1. The study design. NRS-score: Nutrition risk screening, ECN: Estimated caloric need, EPN: Estimated protein need, BFM: Body fat mass, BF%: Body fat percentage, SMM: Skeletal muscle mass, BMR: Basal metabolic rate, BMI: Body mass index, HR: Heart rate, RR: Respiratory rate, BP: Blood pressure, REE: Resting energy expenditure, RQ: Respiratory quotient, VO_2: Volume of inspired oxygen, VCO_2: Volume of expired carbon dioxide, CV for VO_2: Coefficient of variation for VO_2,. *if height and weight were not possible to measure.

estimated by the hospital associated dietitian and an assessment of nutritional risk based on NRS-2002. Furthermore, the latest vital values (heart rate (HR), temperature, respiratory rate (RR), and blood pressure (BP), and whether the patient had undergone surgery as well as the date of surgery were collected. The following values from the blood sample closest to the time of the IC and BIA measurements were collected from NordEPJ; CRP, albumin, hemoglobin, sodium, potassium, creatinine, and blood urea nitrogen.

2.2.2. Indirect calorimetry

IC is widely considered as the golden standard for measuring REE [22]. In this study the Q-NRG+ ® from COSMED was used. The measurement was performed by placing a canopy over the patient's head, while they were lying down and sealing a plastic veil around the canopy to prevent air from the outside environment from interfering with the measurement. The canopy was connected to the Q-NRG+ by a single-use anti-bacterial filter and a corrugated tube. Prior to usage the apparatus was calibrated in accordance with the COSMED guidelines.

For a precise measurement of energy expenditure, a series of conditions must be met [22]. The measurements were conducted in a quiet environment. Prior to the measurement the patient rested for at least 10–15 min. The BIA was conducted in the meantime. The IC measurement time was set at 15 min with the first 5 min discarded. The best 5-min steady state interval was then recorded. REE, oxygen consumption (VO_2), carbon dioxide production (VCO_2), respiratory quotient (RQ), and Coefficient of variation for inspired volume of O_2 (CV for VO_2) were obtained.

2.2.3. Bioimpedance

Assessment of the patients' body composition was performed using the InBody S10 (Inbody USA, Cerritos, CA) body water analyser. Weight, height age, sex and ethnicity were registered in the InBody S10 before the analysis. The BIA was conducted by placing two electrodes on each of the patient's hands and feet. The measurement took approximately 2 min and during the analysis the patient was positioned in a supine position, arms abducted at least 30°, and legs abducted at approximately 45°, not touching each other. Based on the resistance measurements, an algorithm then calculated body composition parameters such as BFM, body fat percentage (BF%), SMM, BMR, and BMI [24]. The individual patients ethnicity setting was chosen for all measurements.

To ensure the most accurate result and to reduce patient harm, several criteria were set: Firstly, no pacemaker-, dialysis-, or pregnant patients, and no patients with visible edema or ascites. Secondly, the patients must not exercise or drink alcohol for 8 h prior, as well as no food, drinks, and IV-fluids, except necessary antibiotics, for 4 h prior. Lastly, bladder must be emptied no longer than 30 min before the test, and the patients had to lie still for at least 10 min before the test. Additional precautions in the interpretations of the results must be taken if the patient has body implants or a BMI <16/>34.

2.3. Statistics

Data were stored in REDCap (version 13.1.26) and STATA (version 17.64). Descriptive statistics were described using n (%) for frequencies and mean (± standard deviation (SD)) for continuous variables. Potential differences between measured and estimated energy requirements were explored by Bland-Altman plots. The normality of the differences in measurements was tested using the Sharpiro-Wilk test. Paired t-tests were performed to check the significance of the difference ($\alpha = 0.05$) as well as the Wilcoxon signed rank test.

Multiple linear regression analysis was used to examine the relationships between measured energy requirements as the dependent variable and influencing factors (SMM, BFM, weight, calf circumference, patient temperature, CRP, albumin) as the independent variables. Each of the variables were adjusted for sex and age.

For comparing categorical variables in which the estimations were grouped as accurate, under-, or overestimated (±10%) [25], the Chi^2-test was used. The level for statistical significance was set to $p < 0.05$.

2.4. Ethical considerations

The study was approved by the North Jutland protection agency (2022-154). The project is exempt from the ethical committees (LBK no. 1083 of 15/09/2017) definition of a health science research project and must therefore not be approved by the committee, cf. section 14, subsection of the committee act. 1, cf. § 2, nos. 1–3.

Participation was voluntary and the patients signed the statement of informed consent and the study was compliant to the Helsinki declaration and patients were informed that they could withdraw from the study at any time, with no significance for their ongoing or further treatment. All participants were assigned a personal identification number to ensure that information could not be traced to the individual.

3. Results

This study included 121 patients as presented in Fig. 2. Afterwards a selection (n = 35) of patients were excluded for various reasons including not being able to complete the fast or not wanting to continue their participation. Among the included patients, 86 patients had an IC measurement performed. Of these, all 86 patients had HB calculated, 67 patients had a BIA performed, and 47 patients had an estimation of energy requirement made by a dietitian.

The mean age was 62.2 ± 16.1 years, mean BMI was 24.5 ± 6.1 kg/m^{2}and 53.5% were female. The wards with most patients included were gastroenterology (43.0%), hematology (9.3%), nephrology (8.1%) and otorhinolaryngology (8.1%). Only a small percentage of patients had undergone surgery (9.3%). Among the included patient, 53 were screened for nutritional risk with NRS-2002 (63.1%), of which 36 patients (65.5%) had been classified as being at nutritional risk. Alle participants were Caucasian. Table 1 summarizes patient baseline characteristics.

The variability of IC-measurements are presented in Table 2.

In this study the mean EE measured by REE × AF was 8391.8 ± 1843.2 kJ (1998.1 ± 438.9 kcal), the mean EE calculated by HB × AF was 7823.9 ± 1727.1 kJ (1862.8 ± 411.2 kcal), the mean EE estimated by BMR × AF was 7973.3 ± 1491.3 kJ (1898.4 ± 355.1 kcal), and the mean EE from the dietitian's estimations was 7826.2 ± 2000.1 kJ (1863.4 ± 476.2 kcal), which are illustrated in Table 3.

Additionally, 10.5% of patients had energy requirements which were overestimated by more than 10%, and 44.2% were underestimated by more than 10%, when comparing EE calculated by HB to the EE measured from IC. When comparing EE estimated by the dietitians to the EE measured from IC, 21.3% of patients were overestimated by more than 10%, and 38.3% were underestimated by more than 10%.

The Bland-Altman plots compared the measured REE by IC with the EE estimations from the HB (n = 86), the dietitians (where IC was multiplied with AF) (n = 47), and the BIA (n = 67). The Bland-Altmann plots showed an average difference of 452 kJ (107.6 kcal), 650 kJ (154.8 kcal), and 437 kJ (104.1 kcal) respectively (See Figs. 3A, B, and C). The mean IC measurements are 6554 kJ (1560.5 kcal) and 8391 kJ (1997.9 kcal) with AF, whereof the differences in energy requirements are 6.2%, 7.8%, and 4.5% respectively. Of the measurements 5.8%, 4.3%, and 6.0% fell outside the limits of agreement.

Furthermore, the differences between REE measured by IC and the EE estimations from the HB, the dietitians (where IC was multiplied with AF), and with BMR from the BIA were all statistically significantly different ($p < 0.05$).

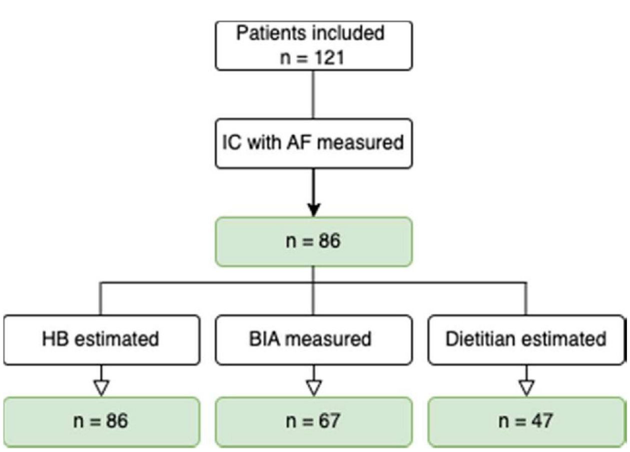

Fig. 2. Flow chart of estimations and measurements performed on the study sample.

Table 1
Descriptive statistics of patients with REE measured by indirect calorimetry.

Variable	All patients, n = 86
Gender, n (%)	
Female	46 (53.5)
Male	40 (46.5)
Age, years (mean ± SD)	62.2 ± 16.1
Age, n (%)	
Adult: 19-44	14 (16.3)
Middle aged: 45-64	29 (33.7)
Aged: 65-79	31 (36.1)
Aged 80 and over: ≥80	12 (14.0)
Hospital ward, n (%)	
Geriatrics	4 (4.7)
Endocrinology	6 (7.0)
Gastroenterology	37 (43.0)
Hematology	8 (9.3)
Physiatry	1 (1.2)
Acute admission unit	2 (2.3)
Nephrology	7 (8.1)
Pulmonology	5 (5.8)
Gynecology	2 (2.3)
Urology	4 (4.7)
Otorhinolaryngology	7 (8.1)
Neurology	3 (3.5)
Surgical patients, n (%)	8 (9.3)
*NRS-screened patients, n (%)	53 (63.1)
**Patients in nutritional risk, n (%)	36 (65.5)
Activity factor, n (%)	
1.1	2 (2.3)
1.2	12 (14.0)
1.3	72 (83.7)
***Temperature, °C (mean ± SD)	36.8 ± 0.5
***Temperature, n (%)	
Non-febrilia: <37°C	54 (72.0)
Sub-febrilia: 37–38°C	18 (24.0)
Febrilia: >38°C	3 (4.0)
BMI, kg/m^2 (mean ± SD)	25.0 ± 6.1
BMI, n (%)	
<18.5 kg/m^2	10 (11.6)
18.5 < 25 kg/m^2	39 (45.4)
≥25 kg/m^2	37 (43.0)
Height, cm (mean ± SD)	170.8 ± 10.1
Weight, kg (mean ± SD)	73.3 ± 20.5
*Admitted from, n (%)	
Home	70 (83.3)
Residential home	1 (1.2)
ICU	1 (1.2)
Other hospital wards	12 (14.3)

*n = 84, **n = 55, ***n = 75.
Presented with mean ± standard deviation or percentage.

Table 2
Statistics from the indirect calorimetry.

Variable		IC, (mean ± SD)
RQ	*n = 85*	0.8 ± 0.1
CV for VO2, %	*n = 57*	4.5 ± 2.7
Measurement time, min	*n = 85*	20.0 ± 6.3

RQ: Respiratory quotient, CV for VO_2: Coefficient of variation for VO_2. Presented with mean ± standard deviation.

Table 3
The mean energy expenditure by four different methods.

Variable		Energy expenditure, kJ (mean ± SD)
REE	*n* = 86	6553.8 ± 1380.1
REE × AF	*n* = 86	8391.8 ± 1843.2
HB × AF	*n* = 86	7823.9 ± 1727.1
BMR × AF	*n* = 67	7973.3 ± 1491.3
Dietitian's evaluation	*n* = 47	7826.2 ± 2000.1

REE × AF: The measured resting energy expenditure using IC multiplied with the patient's AF. HB × AF: The calculated energy expenditure using the HB multiplied by AF. BMR × AF: The basal metabolic rate calculated by the Inbody machine when conducting the BIA multiplied by AF. Dietitian's evaluation is an estimation by the hospital associated dietitians. Presented with mean ± standard deviation.

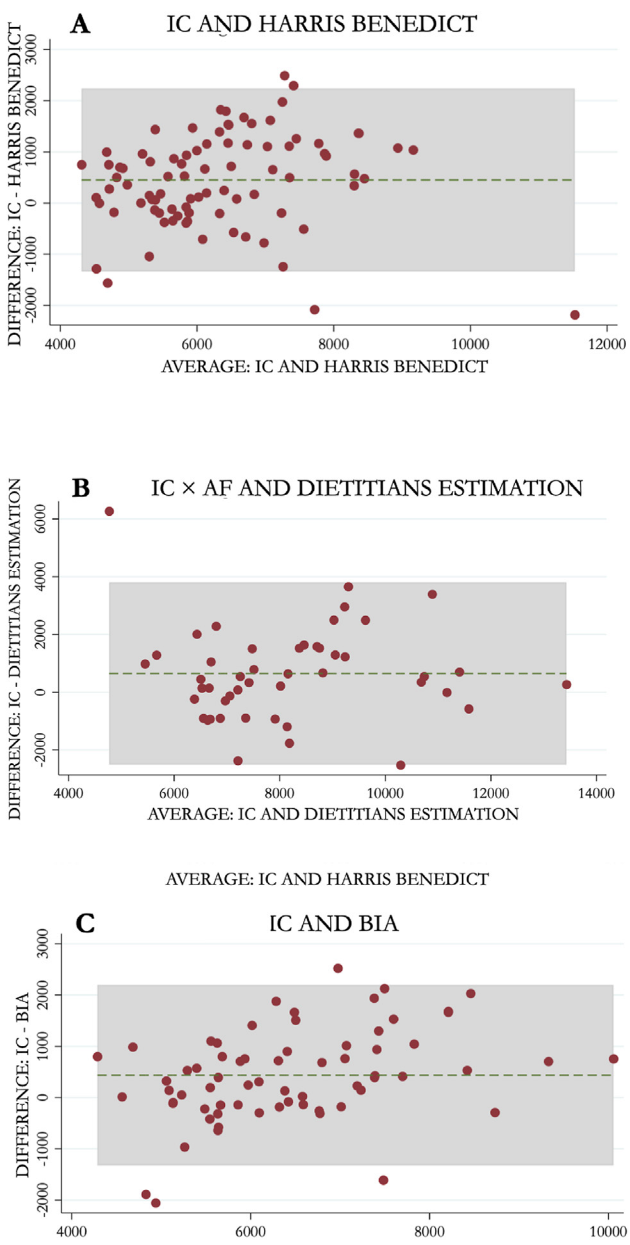

Fig. 3. Bland Altman plots of the agreement between different methods of estimations of energy requirement. Values in kJ. A: Comparison between REE measured with IC and EE calculated with the Harris Benedict equation. B: Comparison between REE measured with IC multiplied with an AF and EE estimation by hospital dietician. C: Comparison between REE measured with IC BMR measured with BIA.

The regression analyses showed a positive association between REE and FFM with a coefficient of 92.7 ($R^2 = 0.63$), SMM with a coefficient of 149.0 ($R^2 = 0.58$), BFM with a coefficient of 59.1 ($R^2 = 0.51$), and weight with a coefficient of 45.6 ($R^2 = 0.62$). No significant associations were found between REE and the patient's temperature with a coefficient of 376.2 ($R^2 = 0.25$), calf circumference with a coefficient of 8.9 ($R^2 = 0.11$), CRP with a coefficient of 4.2 ($R^2 = 0.22$) and albumin with a coefficient of −14.4 ($R^2 = 0.26$). These data are illustrated in Table 4.

Based on the analysis, significant associations were found between overestimation (+10%), and underestimation (−10%) of energy requirement when comparing measured REE and calculated EE by the HB and the variables CRP ($p = 0.040$), hospital ward ($p = 0.064$), sex ($p = 0.413$), temperature ($p = 0.207$), age ($p = 0.017$), surgical patients ($p = 0.030$), HR ($p = 0.117$), RR ($p = 0.004$), calf circumference ($p = 0.121$), height ($p = 0.549$), and albumin ($p = 0.687$). The results are illustrated in Table 5.

4. Discussion

This study investigated REE in hospitalized patients and the proportion of patients with estimated energy requirements deviating more than ±10% from measured energy requirements. A significant difference was found towards both the HB and the dietitians' estimations. The Bland-Altman plots showed an average underestimation equal to 6.9%, 7.8%, and 6.7% for IC compared with HB, dietitian's estimation, and BIA respectively. From these results there is a clear tendency that predictive equations and estimations underestimate the energy requirement of hospitalized patients. Furthermore, it was found that 44.2% of the patients were underestimated by more than 10% using HB and for the dietitian's this underestimation was seen in 38.3%.

4.1. Deviance in estimation of energy requirement

Studies comparing the HB estimated REE to the IC measured REE in various clinical settings have found a mean underestimation of 33.0% [18], an underestimation of more than 10% in 51% of patients [25], and an underestimation by 139 kcal (584 kJ) on average [27]. In addition to this present study, these studies show a clear tendency for HB to underestimate REE [18,26,27]. However, in the Bland-Altman plot overestimations are observed as well.

We found a limit of agreement for IC and HB estimated between −1336 kJ (−318 kcal) and 2240 kJ (533 kcal) meaning that in 95% of measurements the HB-estimate would differ from IC in this interval, but also that 5% would be more extreme deviations. Considering the average REE of 6554 kJ (1560 kcal) as presented in Table 3 and accepting this as the average REE of a hospitalized patient, it would indicate that the HB estimations would fall between −34.2% and 20.4% of the measured IC value in 95% of cases and therefore the range of estimations far exceeds the limits of ±10%. Furthermore, the most extreme cases in our study found an overestimation of 40% and an underestimation of 29%. These results highlight the potential risks of relying excessively on a formula to estimate REE. However even when including individual assessments by a dietitian, the results are similar with a limit of agreement −2507 kJ (−597 kcal) and 3808 kJ (907 kcal). Boulleta et al. set the clinical unacceptable boundary at a wrongful estimation of 250 kcal/day [27]. We observed 23 (26.7%) patients to be underestimated by more than this amount using the HB and 17 (36.2%) patients using dietitians estimations compared to measured IC.

Due to the general tendency to underestimate requirements, patient care and clinical outcome may benefit from more accurate estimation methods or widespread use of IC. At the very least, these

Table 4
The correlation between measured resting energy expenditure and skeletal muscle mass (SMM), body fat mass (BFM), calf circumference, weight, temperature, CRP, and albumin.

Variable	Unadjusted model			Adjusted model		
	Coefficient (B)	p-value	95% CI	Coefficient (B)	p-value	95% CI
Resting energy expenditure, kJ						
FFM, kg	91.5	<0.001[a]	75.2; 107.9	92.7	<0.001[a]	71.4; 114.0
SMM, kg	149.0	<0.001[a]	120.5; 177.4	149.0	<0.0001[a]	112.1; 185.9
BFM, kg	55.0	<0.001[a]	33.9; 76.2	59.1	<0.0001[a]	41.2; 77.0
[b]Calf circumference, cm	−5.1	0.929	−119.0; 108.8	8.9	0.879	−107.6; 125.3
CRP, mg/L	6.1	0.069	−0.5; 12.6	4.2	0.164	−1.8; 10.3
Albumin, g/L	0.7	0.976	−46.8; 48.3	−14.4	0.504	−57.1; 28.3
Weight, kg	51.0	<0.001[a]	41.4; 60.5	45.6	<0.0001[a]	36.0; 55.2
Temperature, °C	436.8	0.149	−159.8; 1033.4	376.2	0.156	−146.8; 899.1

95% Confidence interval.
Multiple linear regression with adjusted variables: sex and age.
[a] p<0.05.
[b] The calf circumference is adjusted for BMI as defined by Gonzalez et al. [9].

results suggest motivation for further exploration of this issue, since we find the limit of agreement too wide for a sufficient clinical practice.

4.2. Factors associated with energy requirement

Strong correlations were found for weight, SMM, and BFM with R^2-values of respectively 0.62, 0.58, and 0.51. This indicates that these variables explain at least >51% of the variance in the measured REE. Regarding muscle and fat, SMM increased REE the most, with a coefficient of 149.0 kJ (35.5 kcal) compared to the 59.1 kJ (14.1 kcal) of BFM, thereby specifying larger energy requirements for SMM per kg juxtaposed with BFM per kg. Of the variables, weight had the largest correlation. Weight could explain 62% of the variance in the measured REE and increasing body weight by 1 kg would increase the REE with 45.6 kJ (10.9 kcal). This is in line with a study, that show a 1 kg change in weight would increase the daily EE by 44.5 kJ (10.6 kcal) [28]. As weight may explain up to 62% of the variance, this leaves almost 40% unexplained. It is unlikely to be FFM, SMM or BFM since these are not truly independent of weight. The magnitude of this unexplained variation is likely to be the major basis for prediction error and hence potential clinical consequences. This must be further investigated. On the other hand, no significant correlation between REE, measured by IC, and calf circumference, temperature, CRP and albumin were found.

A systematic review found a moderately correlation between daily EE and temperature in critically ill patients ($R = 0.46$ translating to $R^2 = 0.21$) [19], where we found $R^2 = 0.25$. This suggests that it could be beneficial to not only use age, height and weight as in HB but also consider the patient's body composition and temperature.

4.3. Factors associated with inaccurate energy estimation

In the present study, we found a significant association between CRP, age, surgical patients, and RR and a greater than ±10% difference in estimation of energy requirement. In addition, we found no association between hospital ward, sex, temperature, HR, calf circumference, height, and albumin and a greater than ±10% difference in estimation of energy requirement. Age evidently influences the estimation of energy expenditure [28], as it is considered when estimating EE with HB [29], but interestingly we found that age was associated with inaccurate estimations.

4.4. Strengths and limitations

A limitation of BIA is that it relies on predictive algorithms and assumptions based on population means, which might not apply to all patients [30,31]. Even though BIA is not a golden standard for estimating body composition, it is a less invasive method and can be used in less mobile patients compared to using the golden standard DXA-scan [32].

The quality and accuracy of the IC measurements relied on the criteria; however, these were challenging to maintain. Noise and disturbances during measurements were difficult to eradicate. Furthermore, verifying the compliance of the fasting relied on the patients' account. As presented in Table 2 the mean CV for VO_2 was 4.5 ± 2.7% and the range of the measurements was 1%–12%. The standard protocol for IC made by the Academy of Nutrition and Dietetics recommends that the CV for VO_2 should be ≤ 10% to ensure the quality of the measurement [33,34]. Two (3.6%) of the registered measurements were above this threshold.

Since the body weight of the patients were not measured in a fasting state, but rather on the day of inclusion, this might have led to the registered body weight being higher than during the IC and BIA. Since IC does not need weight and height for measuring REE, and HB does, this might explain some of the inaccuracies presented in the estimations by HB, BIA, and dietitians. When measuring height, some patients were unable to stand up straight, which might therefore have led to inaccurate estimations.

The RQ when metabolizing only carbohydrates is 1, whereas it will be 0.70 when metabolizing only fat [35]. Fatty acids are typically mobilized after 12 h of fasting [36], where the fasting for our measurement was set at >8 h. Since the mean RQ was 0.76 ± 0.06 the average patient may burn fat to a higher degree than carbohydrates, indicating compliance with the fasting criteria.

4.5. Discussion of methods used

As 43% of the study sample were found at the gastroenterology ward the hospital representativeness can be discussed. The sickest patients might lack the energy to participate, and those dependent on oxygen supply were not included. Our findings might therefore only apply on the most well proportion of the hospitalized population.

In an attempt to minimize interpretation bias, the best 5 min interval of the IC measurement was chosen by the Q-

Table 5
The association between the accuracy of estimation of energy requirement using Harris Benedict equation (HB) compared to Indirect calorimetry (IC) and a selection of variables.

Variable	IC vs HB		p-value
	Underestimated (−10%)	Overestimated (+10%)	
	n (%)	n (%)	
Age, years			*0.017*[a]
18–44	3 (3.5%)	5 (5.8%)	
45–64	11 (12.8%)	2 (2.3%)	
65–79	12 (20.9%)	1 (1.2%)	
≥80	7 (8.1%)	1 (1.2%)	
CRP, mg/L			*0.040*[a]
≤10	12 (16.4%)	0 (0.0%)	
>10	21 (28.8%)	6 (8.2%)	
Sex			*0.413*
Female	21 (24.4%)	3 (3.5%)	
Male	18 (20.9%)	6 (7.0%)	
Hospital ward			*0.064*
Pulmonology	2 (2.3%)	1 (1.2%)	
Gastroenterology	14 (16.3%)	3 (3.5%)	
Otorhinolaryngology	1 (1.2%)	3 (3.5%)	
Geriatrics	4 (4.7%)	0 (0.0%)	
Neurology	3 (3.5%)	0 (0.0%)	
Gynecology	1 (1.2%)	0 (0.0%)	
Endocrinology	2 (2.3%)	0 (0.0%)	
Hematology	5 (5.8%)	0 (0.0%)	
Physiatry	0 (0.0%)	0 (0.0%)	
Urology	4 (4.7%)	0 (0.0%)	
Nephrology	2 (2.3%)	1 (1.2%)	
Acute admission unit	1 (1.2%)	1 (1.2%)	
[b]**Albumin**			*0.687*
Below normal	17 (27.4%)	5 (8.1%)	
Normal	9 (14.5)	1 (1.6%)	
Above normal	0 (0.0%)	0 (0.0%)	
Temperature, °C			*0.207*
<37	24 (27.9%)	4 (4.7%)	
≥37	11 (12.8%)	3 (3.5%)	
≥38	4 (4.7%)	2 (2.3%)	
Surgical patient			*0.030*[a]
No	36 (41.9%)	6 (7.0%)	
Yes	3 (3.5%)	3 (3.5%)	
Heart rate, beats per minute			*0.117*
<60	2 (2.7%)	2 (2.7%)	
≥60	34 (46.6%)	5 (6.8%)	
≥100	1 (1.4%)	0 (0.0%)	
Respiratory Rate, breaths/min			*0.004*[a]
<12	0 (0.0%)	1 (1.4%)	
≥12	26 (35.1%)	6 (8.1%)	
>18	11 (14.9%)	0 (0.0%)	
[c]**Calf circumference, cm**			*0.121*
Below normal	20 (40.8%)	2 (4.1%)	
Normal (females ≥33 and males ≥34)	7 (14.3%)	2 (4.1%)	
Height			*0.549*
Below mean (−3%)	20 (23.3%)	3 (3.5%)	
Mean (±3%)	15 (17.4%)	4 (4.7%)	
Above mean (3%)	4 (4.7%)	2 (2.3%)	
BMI			*0.211*
<18.5	3 (3.5%)	1 (1.2%)	
18.5–24.9	17 (19.8%)	2 (2.3%)	
25–29.9	10 (11.6%)	3 (3.5%)	
≥30	9 (10.5%)	3 (3.5%)	

[a] $p<0.05$.
[b] The grouping of the variable was inspired from the following sources [26].
[c] The calf circumference adjusted for BMI as defined by Gonzalez et al. as well as the grouping of the variable [9].

NRG+ machine itself. The metabolic monitor used has a stated accuracy of ±3% or 36 kcal (151 kJ) [37], which may explain some of the differences between the IC and estimations.

As a Chi^2 test is produced on categorical values, the observations had to be placed in groups, which may have influenced the results, as an association or lack thereof may have been found if the groups were defined differently.

5. Conclusion

In a general sample of hospitalized patients, this study found an underestimation of 6.2% (n = 86), 7.8% (n = 47), and 4.5% (n = 67) when comparing estimated EE by HB, dietitians, and BIA respectively, to measured REE by IC. Correlation between measured REE by IC and weight, FFM, SMM, and BFM was found. However, variables such as CRP, albumin, patient temperature, and calf circumference were found to be non-correlated to REE. The study found a significant association between CRP, age, surgical patients, and RR and a greater than ±10% difference in estimation between IC and HB. Lastly, the study found no association between hospital ward, sex, temperature, HR, calf circumference, height, and albumin, and a greater than ±10% difference in estimation. The wide limit of agreement between individuals has potential clinical implications.

Author contribution

CPH: Investigation, Formal analysis, Validation, Writing - Original Draft, Writing - Review & Editing. SHH: Investigation, Formal analysis, Validation, Writing - Original Draft, Writing - Review & Editing. NKN: Investigation, Formal analysis, Validation, Writing - Original Draft, Writing - Review & Editing. GW: Investigation, Formal analysis, Validation, Writing - Original Draft, Writing - Review & Editing. SM: Conceptualization, Methodology, Resources, Validation, Writing - Review & Editing, Supervision. LG: Data collection- Review & Editing. MH: Conceptualization, Methodology, Resources, Validation, Writing - Review & Editing, Supervision.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

There is no conflict of interest to declare.

Acknowledgement

The included patients must be thanked for participating in this study. In addition, the staff nurses at the 14 units should also be thanked for the help and positive attitude during the data collection. Furthermore, the authors want to thank two data collectors for helping with the data collection: Marianne Køhler and Trine Friedrich and to Professor Henrik Højgaard Rasmussen for contribution to medical content discussions and providing internal funding for the IC.

References

[1] Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr 2017 Feb;36(1):49–64.
[2] Pichard C, Kyle UG, Morabia A, Perrier A, Vermeulen B, Unger P. Nutritional assessment: lean body mass depletion at hospital admission is associated with an increased length of stay. Am J Clin Nutr 2004 Apr;79(4):613–8.
[3] Schuetz P, Fehr R, Baechli V, Geiser M, Deiss M, Gomes F, et al. Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial. Lancet 2019 Jun 8;393(10188):2312–21.
[4] Isabel T D Correia M, Waitzberg DL. The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. Clin Nutr 2003;22(3):235–9.
[5] Kondrup J, Rasmussen HH, Hamberg O, Stanga Z. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. Clin Nutr 2003 Jun;22(3):321–36. https://doi.org/10.1016/s0261-5614(02)00214-5.
[6] Ratzlaff R, Nowak D, Gordillo D, Cresci GA, Faulhaber K, Mascha EJ, et al. Mechanically ventilated, cardiothoracic surgical patients have significantly different energy requirements comparing indirect calorimetry and the Penn state equations. JPEN - J Parenter Enter Nutr 2016 Sep;40(7):959–65.
[7] Thibault R, Pichard C. Nutrition and clinical outcome in intensive care patients. Curr Opin Clin Nutr Metab Care 2010;13(2):177–83. https://doi.org/10.1097/MCO.0b013e32833574b9.
[8] Clapham JC. Central control of thermogenesis. Neuropharmacology 2012;63(1):111–23.
[9] Johnstone AM, Murison SD, Duncan JS, Rance KA, Speakman JR. Factors influencing variation in basal metabolic rate include fat-free mass, fat mass, age, and circulating thyroxine but not sex, circulating leptin, or triiodothyronine2. Am J Clin Nutr 2005;82(5):941–8.
[10] Illner K, Brinkmann G, Heller M, Bosy-Westphal A, Müller MJ. Metabolically active components of fat free mass and resting energy expenditure in non-obese adults. Am J Physiol 2000 Feb;278(2). https://doi.org/10.1152/ajpendo.2000.278.2.E308.
[11] Gonzalez MC, Mehrnezhad A, Razaviarab N, Barbosa-Silva TG, Heymsfield SB. Calf circumference: cutoff values from the NHANES 1999-2006. Am J Clin Nutr 2021 Jun 1;113(6):1679–87.
[12] Sun Y, Kao T, Chang Y, Fang W, Wang C, Wu L, et al. Calf circumference as a novel tool for risk of disability of the elderly population. Sci Rep 2017 Nov 27;7(1):16359-9.
[13] Harris JA, Benedict FG. A biometric study of human basal metabolism. Proc Natl Acad Sci USA 1918;4(12):370–3. https://doi.org/10.1073/pnas.4.12.370.
[14] Taboni A, Vinetti G, Piva S, Gorghelli G, Ferretti G, Fagoni N. Comparison of resting energy expenditure measured with metabolic cart and calculated with predictive formulas in critically ill patients on mechanical ventilation. Respir Physiol Neurobiol 2023;311:104025.
[15] Gupta RD, Ramachandran R, Venkatesan P, Anoop S, Joseph M, Thomas N. Indirect calorimetry: from bench to bedside. Indian J Endocrinol Metab 2017;21(4):594–9. https://doi.org/10.4103/ijem.IJEM_484_16.
[16] Melo AF, Carvalho RB, Eleutério MJ, Costa H, Sousa I. Determination of energy expenditure in ventilated critically ill patients indirect calorimetry vs predictive formulas. Clinical Nutrition ESPEN 2021;46:S649–50.
[17] Genêt F, Salga M, De Brier G, Jouvion A, Genêt G, Lofaso F, et al. Accuracy of resting energy expenditure estimation equations in polio survivors. Arch Phys Med Rehabil 2023;104(3):418–24.
[18] Barcellos PS, Borges N, Torres DPM. Resting energy expenditure in cancer patients: agreement between predictive equations and indirect calorimetry. Clinical Nutrition ESPEN 2021 Jan 10:42.
[19] Mtaweh H, Soto Aguero MJ, Campbell M, Allard JP, Pencharz P, Pullenayegum E, et al. Systematic review of factors associated with energy expenditure in the critically ill. Clinical Nutrition ESPEN 2019;33:111–24.
[20] Kondrup J, Allison SP, Elia M, Vellas B, Plauth M. ESPEN guidelines for nutrition screening 2002. Clin Nutr 2003;22(4):415–21.
[21] Pedersen AN, Beck AM, Borre M, Martinsen A, Ovesen L, Rasmussen HH, et al., editors. Anbefalinger for den danske institutionskost. Fødevarestyrelsen, Sundhedsstyrelsen og DTU Fødevareinstituttet; 2015.
[22] Haugen HA, Chan L, Li F. Indirect calorimetry: a practical guide for clinicians. Nutr Clin Pract 2007 Aug;22(4):377–88.
[23] Boschmann M, Steiniger J, Hille U, Tank J, Adams F, Sharma AM, et al. Water-induced thermogenesis. J Clin Endocrinol Metab 2003;88(12):6015–9.
[24] InBody U. InBody S10 body water analyzer. https://inbodyusa.com/products/inbodys10/. [Accessed 6 March 2023].
[25] Kruizenga HM, Hofsteenge GH, Weijs PJM. Predicting resting energy expenditure in underweight, normal weight, overweight, and obese adult hospital patients. Nutr Metab 2016 Nov 24;13:85-3. eCollection 2016.
[26] Axelsen LK. Referenceintervaller. 2022. Available at: https://www.gentoftehospital.dk/afdelinger-og-klinikker/klinisk-biokemisk-afdeling/til-sundhedsfaglige/Documents/Referenceintervaller%2014-11-2022_For%20fagfolk.pdf. [Accessed 30 March 2023].
[27] Boullata J, Williams J, Cottrell F, Hudson L, Compher C. Accurate determination of energy needs in hospitalized patients. J Am Diet Assoc 2007;107(3):393–401.
[28] Widmer A, Mercante MG, Silver HJ. TG/HDL ratio is an independent predictor for estimating resting energy expenditure in adults with normal weight, overweight, and obesity. Nutrients 2022 Dec 1;14(23):5106. https://doi.org/10.3390/nu14235106.
[29] Silva JE. Thermogenic mechanisms and their hormonal regulation. Physiol Rev 2006;86(2):435–64.
[30] Ward LC. Bioelectrical impedance analysis for body composition assessment: reflections on accuracy, clinical utility, and standardisation. Eur J Clin Nutr 2019;73(2):194–9.
[31] Mulasi U, Kuchnia AJ, Cole AJ, Earthman CP. Bioimpedance at the bedside: current applications, limitations, and opportunities. Nutr Clin Pract 2015;30(2):180–93.
[32] Larsen MN, Krustrup P, Araújo Póvoas SC, Castagna C. Accuracy and reliability of the InBody 270 multi-frequency body composition analyser in 10-12-year-old children. PLoS One 2021 Mar 26;16(3):e0247362.
[33] Popp CJ, Butler M, Curran M, Illiano P, Sevick MA, St-Jules DE. Evaluating steady-state resting energy expenditure using indirect calorimetry in adults with overweight and obesity. Clin Nutr 2020;39(7):2220–6.
[34] Achamrah N, Delsoglio M, De Waele E, Berger MM, Pichard C. Indirect calorimetry: the 6 main issues. Clin Nutr 2021;40(1):4–14.
[35] Patel H, Kerndt CC, Bhardwaj A. Physiology, respiratory quotient. StatPearls treasure Island (FL). StatPearls Publishing LLC; 2023.
[36] Anton SD, Moehl K, Donahoo WT, Marosi K, Lee SA, Mainous AG3, et al. Flipping the metabolic switch: understanding and applying the health benefits of fasting. Obesity 2018 Feb;26(2):254–68.
[37] COSMED Srl. Q-NRG TM+ metabolic monitor technical specifications. https://www.cosmed.com/hires/Q-NRG+_Technical_Specs_A4_C04672-22-80_EN_print.pdf. [Accessed 29 March 2023].