ORIGINAL ARTICLES

Analysis of Energy Expenditure in Adults With Cystic Fibrosis: Comparison of Indirect Calorimetry and Prediction Equations

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OBJECTIVE: Undernutrition, which implies an imbalance between energy intake and energy requirements, is common in patients with cystic fibrosis. The aim of this study was to compare resting energy expenditure determined by indirect calorimetry with that obtained with commonly used predictive equations in adults with cystic fibrosis and to assess the influence of clinical variables on the values obtained.

PATIENTS AND METHODS: We studied 21 patients with clinically stable cystic fibrosis, obtaining data on anthropometric variables, hand grip dynamometry, electrical bioimpedance, and resting energy expenditure by indirect calorimetry. We used the intraclass correlation coefficient (ICC) and the Bland–Altman method to assess agreement between the values obtained for resting energy expenditure measured by indirect calorimetry and those obtained with the World Health Organization (WHO) and Harris–Benedict prediction equations.

RESULTS: The prediction equations underestimated resting energy expenditure in more than 90% of cases. The agreement between the value obtained by indirect calorimetry and that calculated with the prediction equations was poor (ICC for comparisons with the WHO and Harris–Benedict equations, – 0.47 and 0.41, respectively). Bland–Altman analysis revealed a variable bias between the results of indirect calorimetry and those obtained with prediction equations, irrespective of the resting energy expenditure. The difference between the values measured by indirect calorimetry and those obtained with the WHO equation was significantly larger in patients homozygous for the ΔF508 mutation and in those with exocrine pancreatic insufficiency.

CONCLUSIONS: The WHO and Harris–Benedict prediction equations underestimate resting energy expenditure in adults with cystic fibrosis. There is poor agreement between the values for resting energy expenditure determined by indirect calorimetry and those estimated with prediction equations. Underestimation was greater in patients with exocrine pancreatic insufficiency and patients who were homozygous for ΔF508.

Key words: *Cystic fibrosis. Energy expenditure. Indirect calorimetry. Nutrition.*

Estudio del gasto energético en adultos con fibrosis quística: concordancia entre la calorimetría indirecta y diversas fórmulas estimativas

OBJETIVO: La desnutrición es frecuente en pacientes con fibrosis quística (FQ) e implica un desequilibrio entre la ingesta y los requerimientos. Nuestro objetivo ha sido calcular el gasto energético en reposo (GER) mediante calorimetría indirecta en adultos con FQ, compararlo con las fórmulas estimativas habitualmente empleadas y valorar la influencia de parámetros clínicos sobre el GER.

PACIENTES Y MÉTODOS: Estudiamos a 21 pacientes con FQ que se encontraban estables clínicamente. Se efectuaron medidas de parámetros antropométricos, dinamometría de mano, impedanciometría bioeléctrica y del GER medido por calorimetría indirecta (CI). Estudiamos la concordancia entre los valores del GER medidos y estimados por las fórmulas de la Organización Mundial de la Salud (OMS) y de Harris-Benedict (HB) mediante el coeficiente de correlación intraclase y el método de Bland-Altman.

RESULTADOS: Las ecuaciones infraestimaron el GER en más del 90% de los casos. La concordancia entre la CI y la estimada por las fórmulas fue escasa (para OMS, 0,47, y para HB, 0,41). Mediante el método de Bland-Altman observamos un sesgo variable entre la CI y las fórmulas, independiente de los valores del GER. La diferencia entre la CI respecto de la estimada por la fórmula de la OMS fue significativamente mayor en homocigóticos ΔF508 y en los pacientes con insuficiencia pancreática exocrina frente al resto.

CONCLUSIONES: En adultos con FQ, las fórmulas de la OMS y de HB infraestiman el GER. Hay una baja concordancia entre los valores del GER medidos y estimados. La infraestimación fue mayor en pacientes con insuficiencia pancreática exocrina y en homocigóticos ΔF508.

Palabras clave: *Fibrosis quística. Gasto energético. Calorimetría indirecta. Nutrición.*

Introduction

In recent years, there has been a notable increase in the survival of individuals with cystic fibrosis (CF). This is due to both improvements in diagnosis in the pediatric and adult population and to the use of integrated approaches in CF treatment units, where noteworthy recent advances include improved antibiotic therapy (oral, inhaled, and intravenous),

the incorporation of acid-resistant pancreatic enzymes in the 1980s, and effective monitoring of nutrition.[1-4]

Undernutrition in adults behaves as a risk factor for morbidity and mortality, although it is difficult to separate its effects from the severity of the lung disease.[5] However, in recent studies malnutrition has been found to act as a predictor of mortality independently of lung function.[6] The prevalence of malnutrition is high in patients with CF, although the exact figures are quite variable.[7] In a previous study by our group in a sample of 37 adults with CF, the prevalence of a body mass index (BMI) less than 18.5 was 19%.[8] Undernutrition is the result of an imbalance between energy intake and caloric expenditure and is determined by 3 factors: increased energy requirement, reduced intake, and increased losses.[9]

Since individuals with CF are at significant risk of undernutrition, they are advised to follow a diet that provides between 120% and 150% of the recommended calories for healthy individuals of the same age, sex, and body composition.[2,3] Consequently, it is of particular interest in clinical practice to estimate the energy requirements of patients with CF in order to provide individualized nutritional treatment. The ideal technique for measuring basal energy expenditure in CF patients is indirect calorimetry.[9] However, the technique is not available in many hospitals because of its complexity and cost. As a result, a variety of predictive equations are commonly used to measure basal or resting energy expenditure, with the application of correction factors for physical activity and disease severity. Nevertheless, although they are simple, their validity is limited.[10] These equations tend to underestimate energy expenditure in patients with CF,[2,11] although most studies have been performed in the pediatric and adolescent population.[11-14]

The aims of this study were to calculate resting energy expenditure using indirect calorimetry in adolescents and adults with CF, compare the results with those obtained with commonly used predictive equations, and assess the influence of various clinical variables on the values obtained.

Patients and Methods

A cross-sectional study was performed following approval by the ethics committee of the hospital. Patients attending the CF clinic who met the inclusion criteria and provided informed consent were consecutively enrolled over a period of 6 months. They were asked to attend the clinic during the same week for calorimetry to be performed.

Inclusion criteria were as follows: *a)* that the patients met diagnostic criteria for CF according to the 1998 consensus statement of the Cystic Fibrosis Foundation[15]; *b)* that they undertook periodic follow-up in the adult CF clinic of Complejo Hospitalario Carlos Haya, Malaga, Spain; *c)* that they were older than 16 years of age; *d)* that they had completed puberty; *e)* that they had remained clinically stable for the 3 months prior to the study (no hospital admissions or respiratory exacerbations); *f)* that their weight had not varied by more than 3% in the last 3 months; and *g)* that they understood the aims of the study and provided signed informed consent. Patients attending the CF clinic who did not meet any of these criteria were excluded.

An assessment of nutritional state was performed in the 21 patients who met the inclusion criteria to include the following elements:

1. Weight, height, and BMI. Weight was measured using clinical scales with a sensitivity of 0.25 kg in patients without their shoes on and height was measured with a stadiometer. Patients were classified according to BMI [weight in kg/(height in m)^2] according to the criteria of the Spanish Society for the Study of Obesity (SEEDO).[16]

2. Measurement of skinfolds (tricipital, abdominal, bicipital, and subscapular) using Holtain calipers.

3. Arm circumference, measured using a nonstretchable metric tape, and estimation of arm muscle circumference using the equation developed by Jelliffe.[17] The anthropometric measurements were performed in triplicate in the dominant limb by the same trained investigator and the mean value was determined. In all cases the results were compared with reference values for the Spanish population.[18]

4. Hand-grip dynamometry (Collin-type adult dynamometer; AS Medizintechnik, Tuttlingen, Germany). Three measurements were obtained with the dominant limb and the mean value calculated.

5. Bioelectric impedance analysis with a multifrequency impedance meter (Bioscan Multifrecuencia, Tecnología Médica SL, Barcelona, Spain) under resting conditions. The equations recommended by Pencharz and Azwe[19] and by Segal et al[20] were used to estimate body fat and lean body mass.

Resting energy expenditure was calculated by open-circuit indirect calorimetry using the metabolic breath-by-breath measurement system (Cardiopulmonary Exercise Testing [CPX], MedGraphics, Jacksonville, Florida, USA) over a 30-minute period and by gas analysis, oxygen consumption, carbon dioxide elimination, and minute volume. Prior to indirect calorimetry, the patients, who were fasting and had not undertaken intensive physical exercise the day before, remained resting for 20 minutes. Basal energy expenditure was also estimated using the Harris–Benedict equation[21] and resting energy expenditure using the equations of the World Health Organization (WHO).[22] In practice, we will use the terms resting energy expenditure and basal energy expenditure interchangeably, since their variation in the resting population is very small.

Forced spirometry was performed in the patients according to Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) guidelines.[23] Forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV$_1$) were recorded. The values were expressed in absolute terms (mL) and as a percentage of the theoretical value for individuals of the same age, weight, and height in the Spanish reference population.[24]

To assess the severity of the disease, the score on the Bhalla scale[25] was also assessed based on computed tomography of the chest along with the score on the modified National Institutes of Health (NIH) scale.[26]

CFTR genotypes were classified according to the published phenotypic effects of the mutations and the principal mechanism of the defective *CFTR*.[27,28] Thus, the genotypes were classified into 2 groups: severe and mild. The following mutations were included in the severe group: ΔF508, N1303K, G542X, 17/17-8 G→A, Q890X, P2055, 1811+1.6kbA→G, 2869insG, and P2055. The presence of 2 severe mutations was considered a severe genotype, and the coexistence of 2 mild mutations, a severe and a mild mutation, or only 1 identified mutation, were considered mild genotypes (Table 1).

Patients attended follow-up appointments in the CF unit every 2 or 3 months and a detailed clinical history was obtained from the time of diagnosis to the beginning of the study. The following aspects were included in routine clinical follow-up: sputum culture, complete blood count, automated biochemical workup, determination of albumin concentration, glucose loading test, and 72-hour feces for determination of fat content and nitrogen by spectrophotometry (FENIR 8820, Alerbio, Madrid, Spain).[29] Exocrine pancreatic insufficiency was defined as a history of the use of pancreatic

TABLE 1
Genotypes of the Patients

Patient	Gene A	Gene B	Classification*
1	F508	F508	Severe
2	F508	(712-16)>T	Mild
3	F508	F508	Severe
4	N1303K	F508	Severe
5	F508	Q890X	Severe
6	F508	F508	Severe
7	P2055	1811+GKGA→G	Severe
8	2183AA→G	2869insG	Mild
9	G542X	G542X	Severe
10	R334W	R334W	Mild
11	F508	5T V470/ M470	Mild
12	F508	D443Y	Mild
13	N1303k	V232D	Mild
14	F508	3272-26A→G	Mild
15	F508	F508	Severe
16	F508	F508	Severe
17	F508	17/17-8 G→A	Severe
18	R334W	F508	Mild
19	G542X	G542X	Severe
20	F508	R334W	Mild
21	Y1014C	5T-12TG-V470	Mild

*Patients without 2 genotyped mutations for cystic fibrosis met the diagnostic inclusion criteria if they had a positive sweat test.

enzymes with elastase concentrations of less than 50 μg/g in the feces. We analyzed initial colonization by microorganisms commonly observed in CF, considering the first appearance of the microorganism in the sputum (at least 3 positive sputum samples), independently of persistence at the time of the study.

Statistical Analysis

The statistical software package SPSS version 11.0 for Windows (SPSS, Inc, Illinois, USA) was used to analyze the data, which was stored in a specifically designed database. Quantitative variables were expressed as means (SD) and qualitative data as percentages. The nonparametric Mann–Whitney U test was used for between-group comparisons of quantitative variables. The Spearman test was used to analyze the correlation between 2 variables. The Wilcoxon test was used to compare the resting energy expenditure obtained by indirect calorimetry with that obtained using the prediction equations in paired comparisons. The Friedman test was used for comparisons of 3 related variables and analysis of variance (ANOVA) was used for unrelated variables. We used the intraclass correlation coefficient (ICC) and the Bland-Altman method to assess the extent of agreement between the values obtained for resting energy expenditure measured by indirect calorimetry and those obtained using prediction equations. Differences were considered statistically significant when 2-tailed P values were less than .05.

## Results

Patient Characteristics

Of the 21 patients included in the study, 12 (57%) were women. The main symptoms at the time of diagnosis were respiratory in 10 patients (47.6%) and digestive in another 10 (47.6%). Of the patients with predominantly digestive symptoms, 2 had meconium ileus. The remaining patient was diagnosed through the presence of obstructive azoospermia. Five patients (23.8%) were homozygous for

ΔF508 and 12 (57%) had 2 mutations classified as severe (Table 1). The mean (SD) age was 25.1 (13.8) years and the mean age at diagnosis was 12.9 (18) years. Fourteen patients (66%) had an FEV_1 greater than 50% of predicted. Colonization by *Haemophilus influenzae* was present in 66.7% of patients, by *Pseudomonas aeruginosa* in 66.7%, and by *Staphylococcus aureus* in 66.7%. Exocrine pancreatic insufficiency was found to be present in 61.9% of patients, who were treated with pancreatic enzymes and vitamin supplements at doses that were individualized according to the plasma concentrations. Five patients (23.8%) presented abnormal carbohydrate metabolism: 2 had diabetes without fasting hyperglycemia, 1 had diabetes with fasting hyperglycemia that was treated with insulin, and the remaining 2 patients had carbohydrate intolerance.[30] Table 2 shows the main clinical characteristics of the study group.

TABLE 2
Clinical, Anthropometric, and Analytical Characteristics of the Patients With Cystic Fibrosis (n=21)*

Patients diagnosed at age >16 years	7 (33%)
Men	9 (42.9%)
Women	12 (57.1%)
Genotype	
Severe	12 (57%)
Mild	9 (43%)
Homozygous ΔF508	5 (23.8%)
Abnormal carbohydrate metabolism	5 (23.8%)
Pancreatic insufficiency	13 (61.9%)
Age, y	25.1 (13.8)
Age at diagnosis, y	12.9 (17.9)
FEV_1, mL	2468 (1334)
FEV_1, % predicted	68 (29)
FVC, mL	3220 (1445)
FVC, % predicted	73 (22)
Score on modified NIH scale	77.7 (16.5)
Score on Bhalla scale	16.2 (4.0)
Weight, kg	58.3 (11.9)
Height, cm	162.2 (8)
BMI, kg/m²	22.1 (4)
Tricipital skinfold, percentile	28.6 (30.0)
Bicipital skinfold, percentile	33.4 (27.6)
Subscapular skinfold, percentile	24.6 (20.4)
Abdominal skinfold, percentile	13.3 (8.9)
Arm circumference, percentile	36.3 (28.5)
Arm circumference, cm	25.1 (3.9)
Arm muscle circumference, percentile	49.9 (31.7)
Arm muscle circumference, cm	20.4 (3.6)
Lean body weight, kg†	44.1 (9.5)
Lean body weight, %†	74.6 (10.3)
Body fat, kg†	15.4 (7.9)
Body fat, %†	25.3 (10.3)
Fat absorption in stool, %	91.3 (7.3)
Dynamometry, kg	19.6 (9.2)
Dynamometry per kg body weight	0.34 (0.12)
Glucose, mg/dL	100.4 (27.9)
Cholesterol, mg/dL	137.8 (41.1)
HDL-C, mg/dL	46.7 (13.2)
LDL-C, mg/dL	71.5 (32.9)
Triglycerides, mg/dL	97.1 (30.1)
Albumin, g/L	3.9 (0.4)

*Data are shown as number of patients (%) or means (SD).
HDL-C indicates high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; BMI, body mass index; NIH, National Institutes of Health.
†Estimated by bioelectric impedance analysis.
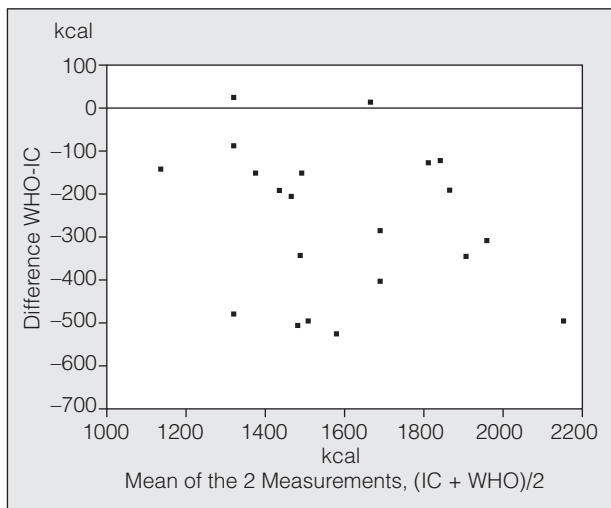
Figure 1. Bland–Altman analysis to assess the extent of agreement between resting energy expenditure measured by indirect calorimetry (IC) and that estimated with the World Health Organization (WHO) predictive equation. The horizontal axis shows the mean of the 2 measurements ([IC+WHO]/2) and the vertical axis shows the difference between the resting energy expenditure estimated with the WHO equation and that measured by IC.
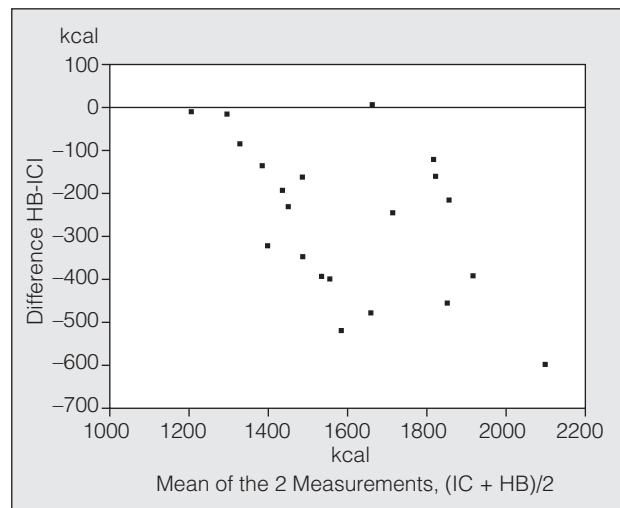
Figure 2. Bland–Altman analysis to assess the extent of agreement between resting energy expenditure measured by indirect calorimetry (IC) and that estimated with the Harris–Benedict (HB) equation. The horizontal axis shows the mean of the 2 measurements ([IC+HB]/2) and the vertical axis shows the difference between the resting energy expenditure estimated with the HB equation and that measured by IC.

Analysis of Energy Expenditure

As shown in Table 3, the values for energy expenditure estimated by indirect calorimetry were higher than those estimated by the WHO and Harris–Benedict prediction equations, and those differences were statistically significant in both cases.

The agreement between the resting energy expenditure measured by indirect calorimetry and that estimated with prediction equations was poor, as shown by the ICC (0.47 for comparison with WHO equations and 0.41 with the Harris–Benedict equation). The ICC between the 3 methods was 0.60. Bland–Altman analysis revealed a variable bias between the results of indirect calorimetry and those obtained with prediction equations, irrespective of the resting energy expenditure (Figures 1 and 2).

Normally nourished patients had a resting energy expenditure per kilogram of body weight (kcal/kg body weight measured by indirect calorimetry) of 29.47 (4.45) kcal/kg, the malnourished patients, 35.01 (3.99) kcal/kg, and the obese patients, 24.31 (8.04) kcal/kg ($P<.02$ between the 3 groups by ANOVA). However, the resting energy expenditure per kilogram lean body weight was similar and no statistically significant differences were observed

between the 3 groups: 38.4 (5.1) kcal/kg, 43.8 (3.3) kcal/kg, and 42.4 (0.04) kcal/kg, respectively.

Correlations Between Energy Expenditure and Clinical Variables (Table 4)

We observed significant positive correlations between basal energy expenditure measured by indirect calorimetry and weight (kg), height (cm), arm circumference (cm and percentage), arm muscle circumference (cm), lean body weight (kg), dynamometry results, FEV_1 and FVC (in mL and percentage of predicted), modified NIH score, and grams of fat in the feces.

The basal energy expenditure (measured by indirect calorimetry) corrected for lean body weight displayed a significant negative correlation with weight (kg), height (cm), arm circumference (cm), arm muscle circumference (cm), lean body weight (kg), dynamometry results, FEV_1 (mL and percentage), and FVC (mL).

Underestimation of Energy Expenditure

The WHO and Harris–Benedict equations underestimated energy expenditure in 90.4% and 95% of cases, respectively,

TABLE 3
Resting Energy Expenditure Analyzed by Different Methods*

	Indirect Calorimetry (n=21)	WHO Equation (n=21)	Harris–Benedict Equation (n=21)
REE	1727.3 (288.31)†	1466.05 (250.49)‡	1468.84 (201.89)§
REE/kg body weight	30.30 (5.38)†	25.46 (2.84)‡	25.7 (3.31)§
REE/kg lean body weight ‖	40.02 (4.96)†	33.8 (3.21)‡	34.16 (3.39)§

*Data are shown as mean (SD).
WHO indicates World Health Organization; REE, resting energy expenditure.
†$P<.0001$ (Friedman test between the 3 methods). ‡$P<.0001$ (Wilcoxon test between indirect calorimetry and WHO equation). §$P<.0001$ (Wilcoxon test between indirect calorimetry and Harris–Benedict equation). Wilcoxon test between the WHO and Harris–Benedict equations revealed no significant differences. ‖ Estimated by bioelectric impedance analysis.
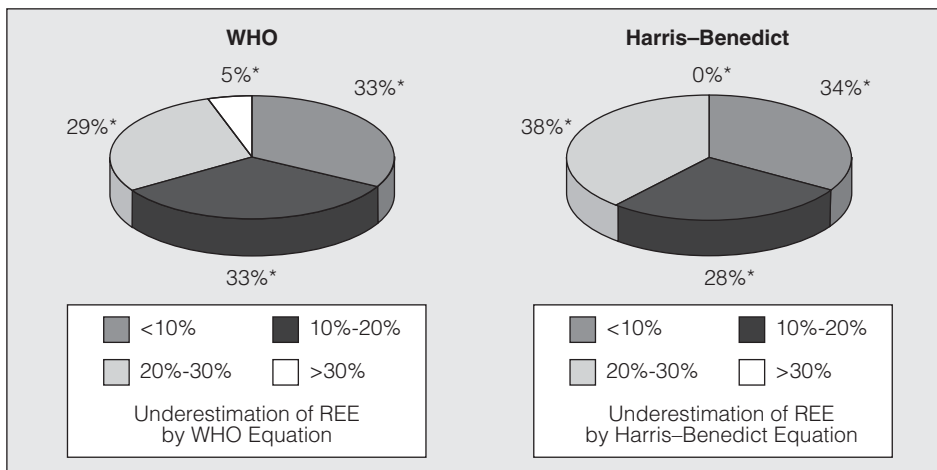
Figure 3. Underestimation of resting energy expenditure (REE) by the World Health Organization (WHO) and Harris–Benedict equations. *Percentage of patients classified according to the degree of underestimation with the equations (expressed as a percentage of the resting energy expenditure measured by indirect calorimetry).

if indirect calorimetry was taken as the gold standard. With the WHO equation the mean underestimation was 14.67% (9.37%) and with the Harris–Benedict equation it was 14.14% (8.8%). Figure 3 shows the percentages of patients

TABLE 4
Spearman Correlation Coefficients Between Resting Energy Expenditure by Indirect Calorimetry and Clinical, Anthropometric, and Laboratory Variables*

REE	REE/kg Lean Body Weight†			
	r	P	r	P
Age, y	−0.26	.25	−0.23	.32
Age at diagnosis, y	−0.28	.21	−15	.51
Score on modified NIH scale	0.53	.014	0.40	.09
Score on Bhalla scale	0.23	.29	−0.31	.19
FEV_1, mL	0.66	.001	−0.53	.019
FEV_1, %	0.49	.022	−0.44	.05
FVC, mL	0.76	.001	−0.54	.017
FVC, %	0.56	.008	−0.41	.079
Weight, kg	0.52	.014	−0.56	.01
Height, cm	0.57	.007	−0.65	.003
BMI, kg/m^2	0.34	.121	−0.25	.29
Tricipital skinfold, %	0.25	.26	−0.02	.9
Bicipital skinfold, %	0.24	.29	0.15	.52
Subscapular skinfold, %	0.20	.37	0.25	.29
Abdominal skinfold, %	0.25	.28	−0.31	.2
Arm circumference, cm	0.61	.003	−0.39	.01
Arm circumference, %	0.48	.025	−0.11	.64
Arm muscle circumference, cm	0.79	.000	−0.59	.007
Arm muscle circumference, %	0.39	.07	−0.23	.34
Lean body weight, kg	0.83	.000	−0.65	.002
Lean body weight, %	0.38	.10	−0.01	.94
Body fat, kg	0.01	.95	−0.18	.45
Body fat, %	−0.38	.10	0.01	.94
Dynamometry	0.73	.000	−0.49	.03
Fat in feces, g	0.46	.03	−0.007	.97
Glucose, mg/dL	−0.04	.83	0.03	.9
Cholesterol	−0.39	.07	−0.08	.74
HDL-C, mg/dL	−0.23	.30	0.47	.03
LDL-C, mg/dL	−0.34	.12	−0.16	.50
Triglycerides, mg/dL	0.23	.31	−0.22	.34
Albumin, mg/dL	0.21	.35	−0.27	.25

*HDL-C indicates high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; BMI, body mass index; NIH, National Institutes of Health. †Estimated by bioelectric impedance analysis.

according to the degree of underestimation of resting energy expenditure.

The difference between the values measured by indirect calorimetry and those obtained with the WHO equation was significantly larger in patients with exocrine pancreatic insufficiency and in those homozygous for the ΔF508 mutation. A nonsignificant trend was also observed toward greater underestimation in women and in patients who were undernourished, displayed abnormal carbohydrate metabolism, or were colonized by *P aeruginosa*. The difference between the resting energy expenditure measured by indirect calorimetry and that estimated with the Harris–Benedict equation displayed a nonsignificant tendency to be larger in patients homozygous for the ΔF508 mutation, those with abnormal carbohydrate metabolism, and those colonized by *P aeruginosa* (Table 5).

Discussion

In the majority of our adult CF patients, the prediction equations normally used in clinical practice (such as the WHO and Harris–Benedict equations) underestimated resting energy expenditure. These findings are similar to the results described by other authors.[2,11,12]

The values for energy expenditure measured by indirect calorimetry were higher than those estimated by the WHO and Harris–Benedict prediction equations, and those differences were statistically significant in both cases. Also, the extent of agreement between resting energy expenditure measured by indirect calorimetry and that estimated by the prediction equations was poor. With both equations, resting energy expenditure was found to be underestimated in more than 90% of cases. These equations were conceived for the healthy population with certain characteristics of body composition that may differ from those of patients with CF.[10] Recent studies in other conditions involving malnutrition, such as anorexia nervosa[31] and Crohn disease,[32] also found poor agreement between resting energy expenditure measured by indirect calorimetry and that estimated by different predictive equations. In our study, Bland–Altman analysis confirmed that there was a variable bias between the indirect calorimetry measurements and the prediction equations, but that was independent of the values of resting energy expenditure. This differs from the

TABLE 5
Underestimation of Energy Expenditure and Clinical Characteristics*

Clinical Characteristics	Difference Between the WHO Equation and Indirect Calorimetry, kcal	Difference Between the Harris–Benedict Equation and Indirect Calorimetry, kcal	Underestimation With the WHO Equation, %†	Underestimation With the Harris–Benedict Equation, %†
Sex				
Men (n=9)	–250.84 (158.16)	–293.35 (197.69)	12.27 (7.32)	14.27 (8.95)
Women (n=12)	–269.03 (189.34)	–232.00 (164.54	16.47 (10.59)	14.04 (9.09)
ΔF508				
Homozygotes (n=5)	–365.68 (162.34)‡	–366.43 (142.97)	22.10 (8.92)§	20.21 (7.18)
Others (n=16)	–219.22 (158.05)‡	–224.69 (177.27)	12.34 (8.46)§	12.24 (8.57)
BMI				
>18.5 kg/m² (n=16)	–234.71 (157.20)	–256.77 (171.74)	12.63 (8.03)	13.70 (8.05)
<18.5 kg/m² (n=5)	–346.10 (212.59)	–263.80 (216.25)	21.19 (11.26)	15.54 (11.88)
Exocrine pancreatic insufficiency				
No (n=8)	–180.46 (173.52)	–212.12 (194.62)	9.52 (8.47)‡	11.29 (8.94)
Yes (n=13)	–310.94 (159.07)	–286.94 (167.53)	17.84 (8.70)‡	15.89 (8.59)
Abnormal carbohydrate metabolism				
No (n=16)	–244.13 (163.15)	–250.07 (183.91)	13.66 (8.16)	13.59 (8.93)
Yes (n=5)	–315.98 (211.99)	–285.23 (171.45)	17.89 (13.11)	15.89 (9.11)
Pseudomonas aeruginosa colonization				
No (n=7)	–208.42 (179.64)	–215.30 (164.84)	11.51 (10.10)	11.90 (8.81)
Yes (n=14)	–287.64 (170.02)	–280.01 (185.45)	16.25 (8.93)	15.26 (8.91)
FEV₁				
>50% of predicted (n=14)	–269.95 (163.13)	–272.19 (181.32)	14.54 (8.44)	14.17 (8.58)
<50% of predicted (n=7)	–243.81 (203.95)	–230.94 (179.95)	14.93 (11.74)	14.08 (9.94)

*FEV_1 indicates forced expiratory volume in 1 second; BMI, body mass index; WHO, World Health Organization.
†Underestimation expressed as a percentage of resting energy expenditure measured by indirect calorimetry. ‡$P<.05$. §$P=.06$ (nonparametric Mann–Whitney test).

findings of Cuerda et al[31] in their study of patients with anorexia, where there was a clinically acceptable agreement for intermediate values of resting energy expenditure (approximately 1200 kcal/d) but overestimation of low values and underestimation of higher values.

In our study, the underestimation appears to be related to genotype (greater underestimation in patients who were homozygous for ΔF508) and the presence of exocrine pancreatic insufficiency. Various experimental studies, both in vitro and in vivo, have indicated that genotype would have a direct effect leading to increased basal energy expenditure,[12,33,34] which would be greater in patients homozygous for ΔF508. However, other authors have not observed this relationship following correction for lung function.[35-37] While we did not observe that worse lung function was associated with greater underestimation, we did find that underestimation was greater in those patients with other characteristics indicative of severity: there was a trend towards greater underestimation in individuals with a more severe phenotype (patients with exocrine pancreatic insufficiency, abnormal carbohydrate metabolism, or *P aeruginosa* colonization),as well as in women.

Therefore, as indicated in other published studies,[2,9,12,13,33,37-41] baseline energy expenditure appears to be increased in adults with CF compared with healthy individuals. There is little agreement regarding the causes of this increase. Pulmonary disease, along with secondary infections[41,42] and increased work of breathing, could increase basal energy expenditure.[9,35,38,39] It appears that patients with moderate lung disease may have very slightly increased resting energy expenditure, while their total energy expenditure increases drastically during exercise. However, in patients with severe pulmonary disease, resting energy expenditure would also be increased at rest, due to the lack of respiratory reserve.[13]

Thus, some authors have found negative correlations between lung function (spirometry) and resting energy expenditure,[12,33,39,43] while others found no such correlations.[36,37,44] This discrepancy may be explained by differences in the severity of the disease in the patients studied. In our study, with a sample of patients in whom respiratory disease was only moderate, resting energy expenditure displayed a significant negative correlation with spirometry variables only after correction for lean body weight.

Nutritional state as a factor that alters resting energy expenditure is also a topic of discussion. In our study, the undernourished patients had greater values for energy expenditure per kilogram body weight than those who were normally nourished or obese. However, after correcting calorimetry results for lean body weight, the results were similar between the 3 groups (independently of nutritional status), indicating that this parameter is the main determinant of resting energy expenditure. In addition, we observed significant correlations for resting energy expenditure (positive correlations) and resting energy expenditure corrected for lean body weight (negative correlations) with a number of variables indicative of lean body weight, such as weight, height, arm circumference, arm muscle circumference, lean weight in kilograms, and dynamometry results. Other authors have also observed positive correlations between basal energy expenditure and lean body weight,[14,43,44] indicating it to be one of the main determinants of energy expenditure in patients with CF.

Given that indirect calorimetry is not available in most hospitals and in all situations, we propose the following simple equation based on our results for the rapid estimation of resting energy expenditure:

$$\text{resting energy expenditure} = \text{weight (kg)} \times 30$$

In terms of nutritional status, in normally nourished individuals, resting energy expenditure = weight (kg) × 30; in undernourished patients (BMI<18.5 kg/m^2), resting energy expenditure = weight (kg) × 35; and in obese individuals (BMI>30 kg/m^2), resting energy expenditure = weight (kg) × 25.

In conclusion, the equations normally used to estimate resting energy expenditure in adults with CF systematically underestimate it, irrespective of the value for resting energy expenditure; the difference with respect to the measured resting energy expenditure is greater in patients with more severe disease (especially patients who are homozygous for ΔF508 and those with exocrine pancreatic insufficiency).

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