

# Comparison of Measured Versus Predicted Energy Requirements in Critically Ill Cancer Patients

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**BACKGROUND:** Accurate determination of caloric requirements is essential to avoid feeding-associated complications in critically ill patients. **METHODS:** In critically ill cancer patients we compared the measured and estimated resting energy expenditures. All patients admitted to the oncology intensive care unit between March 2004 and July 2005 were considered for inclusion. For those patients enrolled ( $n = 34$ ) we measured resting energy expenditure via indirect calorimetry, and estimated resting energy expenditure in 2 ways: clinically estimated resting energy expenditure; and the Harris-Benedict basal energy expenditure equation. **RESULTS:** Clinically estimated resting energy expenditure was associated with underfeeding, appropriate feeding, and overfeeding in approximately 15%, 15%, and 71% of the patients, respectively. The Harris-Benedict basal energy expenditure was associated with underfeeding, appropriate feeding, and overfeeding in approximately 29%, 41%, and 29% of the patients, respectively. The mean measured resting energy expenditure ( $1,623 \pm 384$  kcal/d) was similar to the mean Harris-Benedict basal energy expenditure without the addition of stress or activity factors ( $1,613 \pm 382$  kcal/d,  $P = .87$ ), and both were significantly lower than the mean clinically estimated resting energy expenditure ( $1,862 \pm 330$  kcal/d,  $P \leq .003$  for both). There was a significant correlation only between mean measured resting energy expenditure and mean Harris-Benedict basal energy expenditure ( $P < .001$ ), but the correlation coefficient between those values was low ( $r = 0.587$ ). **CONCLUSIONS:** Underfeeding and overfeeding were common in our critically ill cancer patients when resting energy expenditure was estimated rather than measured. Indirect calorimetry is the method of choice for determining caloric need in critically ill cancer patients, but if indirect calorimetry is not available or feasible, the Harris-Benedict equation without added stress and activity factors is more accurate than the clinically estimated resting energy expenditure. *Key words:* indirect calorimetry, nutrition, cancer, critically ill. [Respir Care 2009;54(4):487–494. © 2009 Daedalus Enterprises]

## Introduction

Malnutrition is a common problem among patients in the intensive care unit (ICU).<sup>1</sup> Proper nutrition support benefits ICU patient outcomes (eg, fewer complications, shorter stay, and lower costs),<sup>2-6</sup> so adequate nutrition is an integral component of supportive care in critically ill pa-

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tients.<sup>3</sup> Malignancy-associated nutritional adverse effects are a serious problem among critically ill cancer patients, in whom protein-calorie malnutrition has been reported in up to 80% of patients.<sup>7</sup> Direct and indirect tumor effects,

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as well as the effects of surgery, radiation therapy, chemotherapy, and psychological problems are frequently associated with malnutrition at ICU admission and/or may exaggerate the effects of critical-illness-induced hypermetabolism and protein depletion.<sup>8</sup>

Accurate determination of caloric requirements is an essential component of nutrition support in ICU patients. Underestimation of caloric requirement can result in underfeeding, which may adversely affect tissue function and repair, and the immune system.<sup>8</sup> Severe malnutrition is associated with increased risk of postoperative complications and duration of hospitalization.<sup>9,10</sup> Overestimation of caloric need, and associated overfeeding are no less deleterious. Prolonged mechanical ventilation, hyperglycemia, hepatic dysfunction, hyperosmolar state, azotemia, and immune dysfunction are some of the known complications of overfeeding in the ICU.<sup>11-14</sup>

Several methods have been described for estimating and measuring the caloric requirements of critically ill patients, but the estimation methods are imprecise, and the measurement method (indirect calorimetry) is not feasible in all ICU settings, so none of the methods has achieved universal acceptance. In our literature review for this study we found no reports that focused on the determination of the caloric requirements in mechanically ventilated critically ill cancer patients.

### Methods

After obtaining institutional review board approval, we conducted this study at the University of Texas MD Anderson Cancer Center's medical and surgical oncology ICU, a 53-bed ICU devoted exclusively to critically ill surgical and medical patients with cancer.

We used indirect calorimetry to measure the caloric requirements of mechanically ventilated critically ill cancer patients, and we evaluated the agreement between those measurements and the estimates we obtained with 2 commonly used methods: clinical estimation, and the Harris-Benedict equation.

All adult patients who were admitted to the ICU between March 2004 and July 2005 and who had an indirect calorimetry as part of their nutritional assessment were included in this retrospective study. Indirect calorimetry was considered only in patients who were mechanically ventilated for > 7 days and met our indirect calorimetry protocol criteria.

### Indirect Calorimetry Protocol

All indirect calorimetry (Vmax Spectra V29n, Sensor-Medics/Viasys Healthcare, Yorba Linda, California) was performed by specially trained critical care respiratory therapists, according to our institutional procedure and the

guidelines for indirect calorimetry in mechanically ventilated ICU patients. That same protocol also identifies which patients could benefit from indirect calorimetry. Each patient was studied for at least 30 min, in the supine position, or until steady state was achieved. Steady state was defined as a variability of < 10% in the measurements of oxygen consumption and carbon dioxide production, and < 5% in the respiratory quotient from minute to minute, for at least two 5-min periods of continuous data collection. All patients were receiving sedation according to our institutional protocol and the sedation guidelines, and the Ramsay sedation scale target score was 2 throughout mechanical ventilation. The calorimeter was calibrated before each use. Calorimetry was not performed if there were any of the following: hemodynamic instability (eg, cardiac arrhythmia, mean arterial pressure < 65 mm Hg, need for vasoactive drug support); fraction of inspired oxygen > 0.60; positive end-expiratory pressure > 10 cm H<sub>2</sub>O; maximum airway pressure > 60 cm H<sub>2</sub>O; agitation; neuromuscular blockers; air leak in the ventilator circuit, around the endotracheal tube cuff, or from a bronchopleural fistula; or a change or interruption in feeding regimen in the 24 hours before the measurement. With patients who required renal replacement therapy, dialysis was stopped at least 3 hours prior to the indirect calorimetry and was not resumed during the measurement. Measured resting energy expenditure is reported in kcal/d. The indirect calorimetry measurement was considered invalid if a steady state was not achieved or maintained. The calorimeter's instrumental precision was  $\pm 1\%$ .

### Nutritional Assessment

All the patients had a nutritional assessment by a dietitian within 72 hours of ICU admission. The nutrition-assessment form was developed by our clinical nutrition department. The nutrition assessment includes measurement of weight and height, and calculation of body mass index, ideal body weight (with the Hamwi method<sup>15</sup>), and daily energy expenditure. The clinically estimated resting energy expenditure was defined as the energy expenditure when the patient is lying in bed, awake, and aware of his or her surroundings. For those with anasarca or ascites at admission, we obtained a dry weight from the patient or medical record, for determining the clinically estimated resting energy expenditure. Daily caloric need was based on total calories for all calculations (enteral, parenteral, or oral). The clinically estimated resting energy expenditure and nutrition route were based on the American Society for Parenteral and Enteral Nutrition's 2002 "Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients"<sup>16</sup> and 2004 "Safe Practices for Parenteral Nutrition."<sup>17</sup> Calculation of caloric need in overweight patients (body mass index > 27 and/or > 125% of ideal body weight) were based on reported hypocaloric reg-

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Table 1. Harris-Benedict Equations and Clinical Estimation Methods for Resting Energy Expenditure

	Resting Energy Expenditure
Harris-Benedict equation <sup>20</sup>	
Male	$66.47 + (13.75 \times \text{weight}) + (5.003 \text{ height}) - (6.775 \text{ age in years})$
Female	$655.09 + (9.563 \times \text{weight}) + (1.85 \text{ height}) - (4.676 \text{ age in years})$
Clinically estimated <sup>16,17</sup>	
Mild or moderate illness (kcal/kg/d)	20–25
Sepsis or major surgery (kcal/kg/d)	25–30
If weight < 70% of ideal body weight (kcal/kg/d)	30–35
If weight > 125% of ideal body weight and/or body mass index > 30 kg/m <sup>2</sup> (kcal/kg ideal body weight/d)	20–25

imens.<sup>18,19</sup> Nutrition support goals were adjusted for each patient, based on follow-up nutritional (prealbumin) and clinical (eg, development of fistulae, wound healing) markers.

We calculated basal energy expenditure with the Harris-Benedict equation (Table 1),<sup>20</sup> which we selected because: it is the oldest formula still in use; it is the most extensively validated equation; it has the most extensive body of literature; and it is one of the most common equations used by practitioners to calculate caloric requirements. We did not add stress and activity factors to the Harris-Benedict equation.

Underfeeding was defined as a clinically estimated resting energy expenditure or Harris-Benedict basal energy expenditure < 90% of the measured resting energy expenditure. Appropriate feeding was defined as a clinically estimated resting energy expenditure or Harris-Benedict basal energy expenditure within 10% of the measured resting energy expenditure. Overfeeding was defined as a clinically estimated resting energy expenditure or Harris-Benedict basal energy expenditure > 110% of the measured resting energy expenditure. Other recorded data included demographics, diagnosis, reason for ICU admission, Acute Physiology and Chronic Health Evaluation (APACHE II) score, duration of mechanical ventilation before the indirect calorimetry, feeding route (enteral, parenteral, or both enteral and parenteral), serum albumin, serum prealbumin, 24-hour urinary urea nitrogen, and nitrogen balance. Nitrogen balance (in g/d), calculated as:

$$\begin{aligned} & (\text{Protein or amino-acid intake}/6.25) \\ & - (\text{urinary urea nitrogen} + 4) \end{aligned}$$

### Statistical Analysis

We used statistics software (SPSS 12.0, SPSS, Chicago, Illinois) and the results are presented as mean  $\pm$  SD. We used the paired-sample *t* test to compare the measured, clinically estimated, and Harris-Benedict basal energy expenditure values. We calculated Pearson correlation coefficients to assess the relationships between the measured,

clinically estimated, and Harris-Benedict basal energy expenditure. We used Bland-Altman analysis to evaluate agreement between the methods. Differences were considered statistically significant when  $P < .05$ .

### Results

During the study period, 3,708 patients were admitted to our ICU, 1,476 underwent mechanical ventilation, and 219 were ventilated for > 7 days. Among those 219 patients, 56 (25%) underwent indirect calorimetry, and 34 met the criteria to be included in the analyses (Table 2). Twenty-six (76%) of the 34 included patients were postoperative. Twenty-seven (80%) were admitted to the ICU for respiratory failure. Nineteen (56%) were overweight or obese. Twenty (59%) were fed enterally, 13 (38%) were fed parenterally, and one (3%) was fed both enterally and parenterally.

The mean measured and Harris-Benedict basal energy expenditure values (Table 3) were not significantly different ( $P = .87$  for kcal/d, and  $P = .58$  for kcal/kg/d). However, both the measured and the Harris-Benedict values were significantly lower than the clinically estimated resting energy expenditure ( $P \leq .003$  for both). Both the Harris-Benedict and clinically estimated methods were associated with high occurrences of either underfeeding (29% and 15%, respectively) or overfeeding (29% with the Harris-Benedict equation, and 71% with the clinical estimation method). The Pearson correlation coefficient revealed a significant ( $P < .001$ ) correlation between the measured resting energy expenditure and the Harris-Benedict basal energy expenditure ( $r = 0.587$ , Fig. 1). There was no significant correlation between the measured and the clinically estimated resting energy expenditure ( $r = 0.241$ ,  $P = .17$ ) (Fig. 2), nor between the measured resting energy expenditure and the APACHE II score ( $r = 0.378$ ,  $P = .161$ ). Mean protein administration at the time of the study was  $103 \pm 37$  g/d ( $1.5 \pm 0.1$  g/kg/d).

The overall mean respiratory quotient was  $0.85 \pm 0.10$ . The mean respiratory quotient for underfeeding, appropriate feeding, and overfeeding associated with the clinically

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Table 2. Patient Demographics, Diagnoses, and ICU Data (n = 34)

Age (mean ± SD y)	60.9 ± 14.9
Sex (M/F)	26/8
Weight (mean ± SD kg)	82.6 ± 27.1
BMI (mean ± SD kg/m <sup>2</sup> )	28.7 ± 8.7
Weight category (n, %)	
Underweight (BMI < 18.9 kg/m <sup>2</sup> )	2 (6)
Normal (BMI 18.5–24.9 kg/m <sup>2</sup> )	13 (38)
Overweight (BMI 25.0–29.9 kg/m <sup>2</sup> )	5 (15)
Obese (BMI > 30.0 kg/m <sup>2</sup> )	14 (41)
Primary diagnosis (n, %)	
Lung cancer	10 (29)
Gastrointestinal cancer	6 (18)
Leukemia	5 (15)
Squamous cell carcinoma of the oral cavity	3 (9)
Central nervous system tumor	2 (6)
Sarcoma	2 (6)
Miscellaneous*	6 (18)
Postoperative	
Yes (n, %)	26 (76)
No (n, %)	8 (24)
Reason for ICU admission (n, %) <sup>†</sup>	
Respiratory failure	27 (80)
Sepsis	4 (12)
Hypotension	2 (6)
Acute renal failure	1 (3)
APACHE II score on study day (mean ± SD)	19.1 ± 6.6
Mechanical ventilation variables (mean ± SD)	
F <sub>IO<sub>2</sub></sub>	0.37 ± 0.07
PEEP (cm H <sub>2</sub> O)	6.7 ± 1.8
Maximum airway pressure (cm H <sub>2</sub> O)	23.2 ± 6.4
Duration of mechanical ventilation before the study (d)	15.6 ± 13.9
Feeding route (n, %)	
Enteral	20 (59)
Parenteral	13 (38)
Enteral and parenteral	1 (3)

\* Miscellaneous: 1 each of hepatocellular carcinoma, laryngeal carcinoma, mesothelioma, neuroendocrine tumor, renal cell carcinoma, and transitional cell carcinoma of the bladder.

<sup>†</sup> Percent values do not sum to 100 because of rounding.

ICU = intensive care unit

BMI = body mass index

APACHE = Acute Physiology and Chronic Health Evaluation

F<sub>IO<sub>2</sub></sub> = fraction of inspired oxygen

PEEP = positive end-expiratory pressure

estimated resting energy expenditure were  $0.79 \pm 0.02$ ,  $0.82 \pm 0.10$ , and  $0.86 \pm 0.11$ , respectively. The mean respiratory quotient values for underfeeding, appropriate feeding, and overfeeding associated with the Harris-Benedict basal energy expenditure were  $0.82 \pm 0.08$ ,  $0.85 \pm 0.13$ , and  $0.87 \pm 0.08$ , respectively.

Figures 3 and 4 show the Bland-Altman plots. The mean bias between the measured and the clinically estimated resting energy expenditure was  $-240 \pm 442$  kcal/d, and the 95% limits of agreement (mean bias ± 2 SD) between the measured and the clinically estimated values

ranged from  $-1,124$  kcal/d to  $645$  kcal/d. The mean bias between the measured and Harris-Benedict values was  $10 \pm 348.3$  kcal/d.

At the time of the indirect calorimetry, 24-hour urinary-urea-nitrogen and nitrogen-balance were measured in 21 (62%) of the 34 included patients. Of the 13 patients who did not have a urinary-urea-nitrogen measurement, 9 were receiving dialysis for acute renal failure, and 4 had incomplete urine collections. The mean 24-hour urinary-urea-nitrogen and nitrogen-balance values were  $15.1 \pm 5.1$  g/d and  $-0.8 \pm 5.2$  g/d, respectively. The mean serum albumin and prealbumin values were  $2.2 \pm 0.5$  g/dL and  $13.2 \pm 6.4$  mg/dL, respectively.

### Discussion

When resting energy expenditure was clinically estimated or calculated with the Harris-Benedict basal energy expenditure equation, underfeeding and overfeeding occurred in > 70% of the patients in the study. The Harris-Benedict equation without added stress and activity factors was more accurate (ie, correlated better with the measured value) than the clinically estimated value.

To avoid underfeeding and overfeeding and to optimize the benefits of nutrition support in ICU patients, precise measurement or calculation of caloric need is crucial. Indirect calorimetry is the accepted reference method for measuring caloric expenditure in mechanically ventilated ICU patients,<sup>1,8</sup> and it is convenient and available in many institutions,<sup>21</sup> but is still not widely used, because it requires expensive equipment and specially trained personnel. Thus, equations, such as the Harris-Benedict equation,<sup>20</sup> the Ireton-Jones equation,<sup>22</sup> the American College of Chest Physicians recommendation for applied nutrition in ICU patients,<sup>1</sup> and American Society for Parenteral and Enteral Nutrition guidelines,<sup>16,17</sup> are still the most commonly used methods for estimating resting energy expenditure in daily practice.

The mean measured resting energy expenditure and mean Harris-Benedict basal energy expenditure were similar ( $1,623 \pm 384$  and  $1,613 \pm 382$ , respectively,  $P = .87$ ), and they both were significantly lower than the clinically estimated resting energy expenditure ( $P \leq .003$  for both). Only the Harris-Benedict equation without the addition of stress and activity factors significantly correlated with the measured resting energy expenditure ( $P < .001$ ), but that correlation was modest ( $r = 0.587$ ). Thus, although the mean Harris-Benedict basal energy expenditure gave an excellent estimate of the mean measured resting energy expenditure for the entire group, the Harris-Benedict equation was less predictive for individuals.

Several studies have found the Harris-Benedict basal energy expenditure an acceptable substitute for indirect calorimetry,<sup>23-27</sup> whereas others have reported a poor cor-

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Table 3. Measured Versus Estimated Resting Energy Expenditure, and Frequency of Underfeeding, Appropriate Feeding, and Overfeeding

	Clinically Estimated	Harris-Benedict Equation	Measured
Resting energy expenditure (kcal/d)	1,862 ± 330*	1,613 ± 382	1,623 ± 384
Resting energy expenditure (kcal/kg/d)	27.6 ± 6.2†	23.4 ± 3.6	23.8 ± 5.7
Underfeeding (n, %) <sup>‡</sup>	5 (15)	10 (29)	NA
Appropriate feeding (n, %)	5 (15)	14 (41)	NA
Overfeeding (n, %)	24 (71) <sup>§</sup>	10 (29)	NA

\*  $P = .002$  for clinically estimated resting energy expenditure versus resting energy expenditure calculated with the Harris-Benedict equation.  $P = .003$  for clinically estimated resting energy expenditure versus measured resting energy expenditure.

†  $P < .001$  for clinically estimated resting energy expenditure versus resting energy expenditure calculated with the Harris-Benedict equation, and for clinically estimated resting energy expenditure versus measured resting energy expenditure.

‡ Appropriate feeding means the patient received 90–110% of the measured resting energy expenditure.

§ Percent values do not sum to 100 because of rounding.

NA = not applicable, because the measured value was taken as the indicator of the actual calorie need.

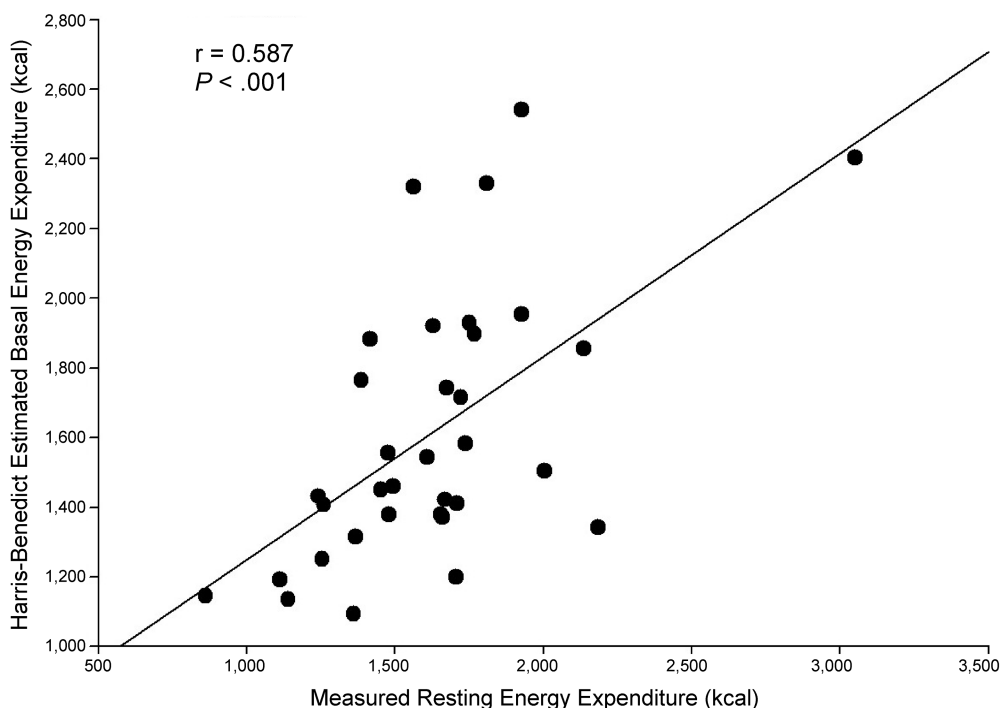


Fig. 1. Pearson correlation of measured resting energy expenditure and resting energy expenditure calculated with the Harris-Benedict estimated basal energy expenditure equation.

relation between measured and calculated resting energy expenditure, and concluded that indirect calorimetry is the only reliable tool.<sup>28-36</sup> We believe that, although both the clinical estimation and Harris-Benedict estimation are far from perfect, the current literature and our findings indicate that the Harris-Benedict equation without activity and stress factors is superior to the clinical estimation method in critically ill cancer patients.

Though several studies have investigated the agreement between the measured and calculated resting energy expenditure in various ICU settings,<sup>22,23,25-28,30-35,37-40</sup> to the best of our knowledge this is the first study to compare measured to calculated resting energy expenditure values

from critically ill cancer patients. We did not include stress or activity factors in the Harris-Benedict equation, because our preliminary observations revealed high rates of overfeeding when we included an activity or stress factor.

We did not use the Ireton-Jones equation because it was originally developed for patients with burns, and a recent study found that equation biased in mechanically ventilated critically ill patients who did not have burns.<sup>23</sup>

Both the Harris-Benedict equation and clinically estimated resting energy expenditure were associated with underfeeding and overfeeding (59% and 85%, respectively) in our critically ill cancer patients. That finding is consistent with previous studies, which found underfeeding and



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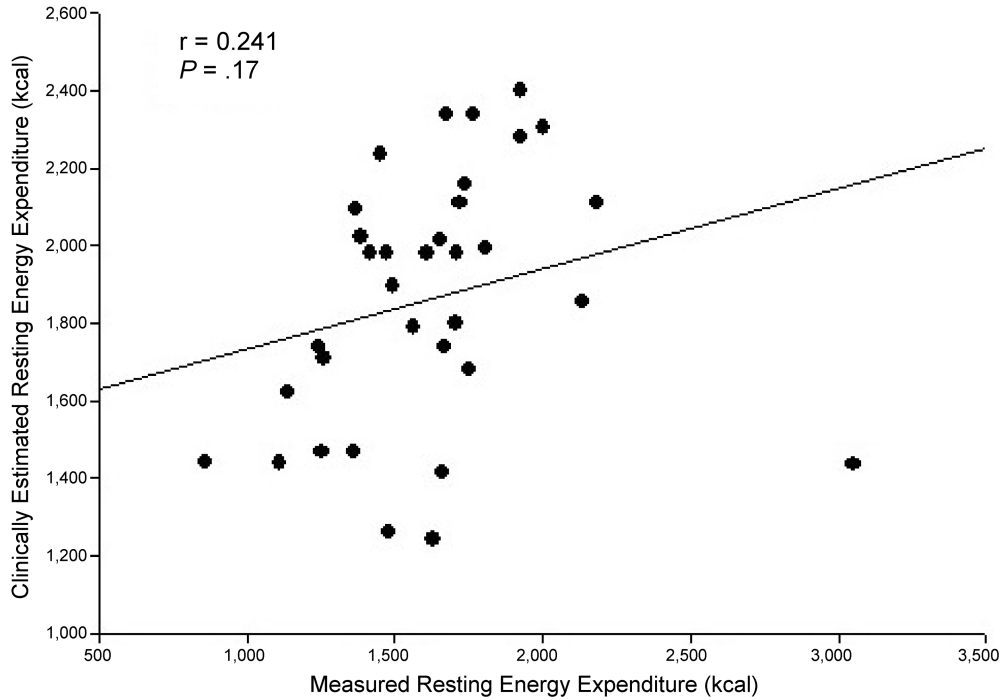


Fig. 2. Pearson correlation of measured versus clinically estimated resting energy expenditure.

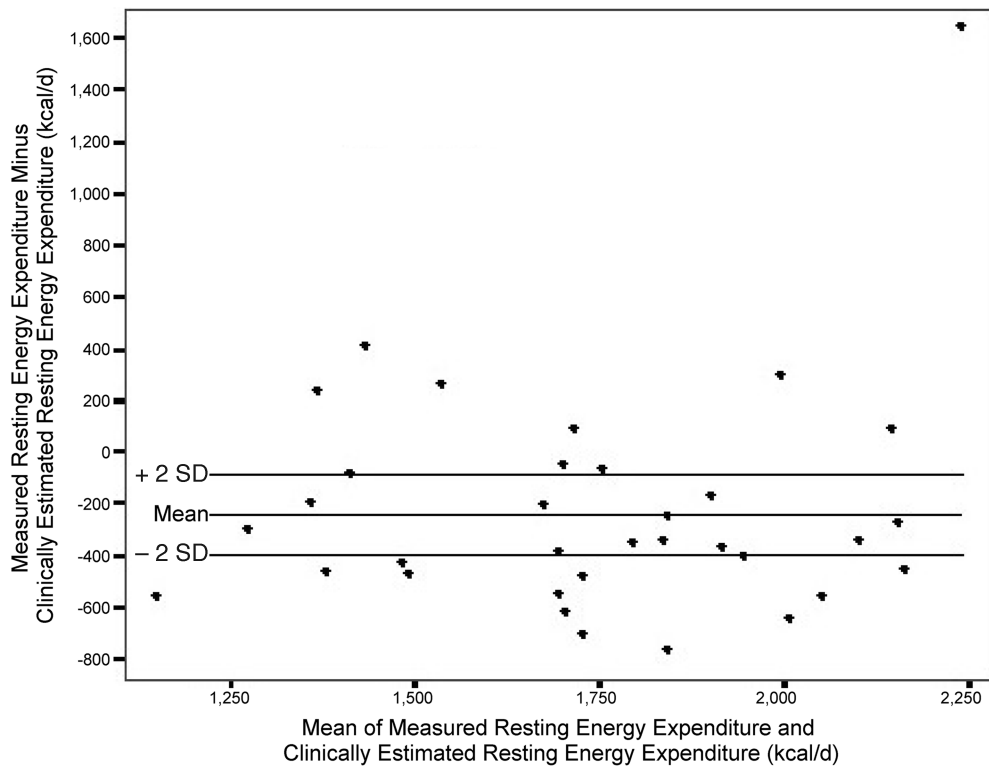


Fig. 3. Bland-Altman plot of measured versus clinically estimated resting energy expenditure.

overfeeding common in ICU patients when resting energy expenditure was estimated instead of measured.<sup>28-34,41</sup> In 263 ICU patients, McClave et al<sup>41</sup> found overfeeding and

underfeeding in 42% and 34%, respectively. Seventy-one percent of our patients were overfed with clinically estimated resting energy expenditure. Krishnan et al,<sup>42</sup> as-

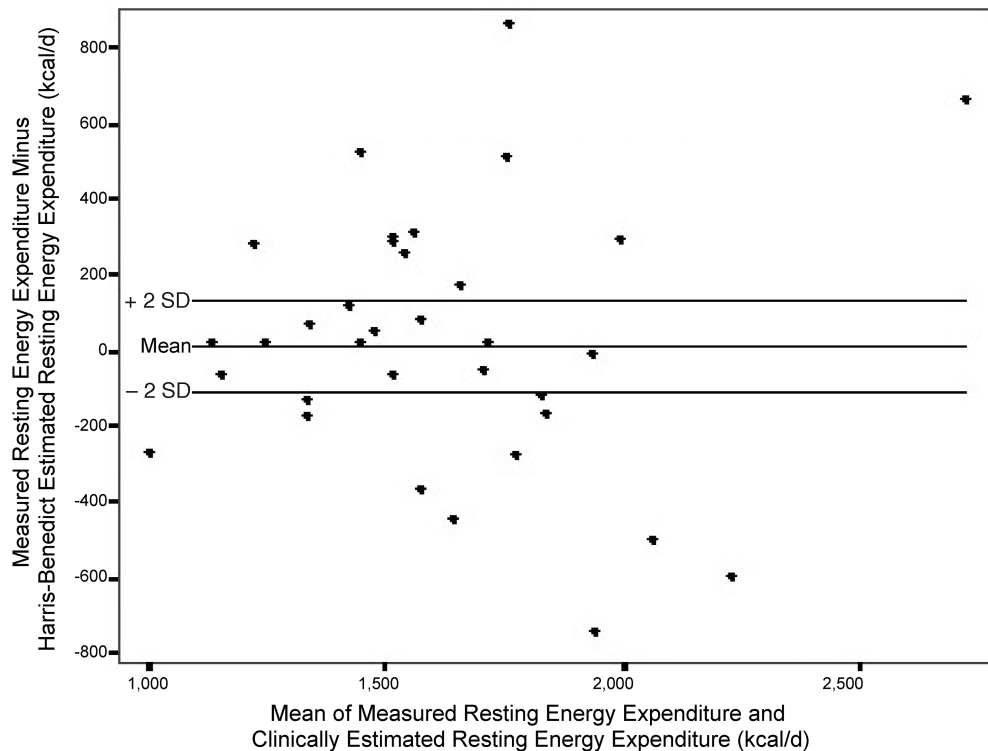


Fig. 4. Bland-Altman plot of measured versus Harris-Benedict estimated basal energy expenditure.

essed caloric intake per the American College of Chest Physicians recommendations<sup>1</sup> in 187 ICU patients, and concluded that, although those patients were underfed according to the American College of Chest Physicians target, that target may overestimate caloric need, because moderate caloric intake was associated with better outcomes than was higher caloric intake.

One limitation to this study is that it was retrospective. A prospective study with a larger number of patients would provide further information. The number of patients in this study was adequate to perform Pearson correlation analyses ( $\beta$  value of 0.15 for  $r = 0.587$ ), but more patients would be needed to perform a regression analysis to find an equation to estimate the resting energy expenditure more precisely than the Harris-Benedict equation.

Another problem is that our categorization of underfeeding, overfeeding, and appropriate feeding were based on calculated caloric requirements instead of the number of calories the patients were actually receiving at the time. There is a big discrepancy between the calculated and actually delivered calories in ICU patients,<sup>42,43</sup> so a patient who was considered overfed based on calculated resting energy expenditure might actually have been appropriately fed or underfed because of delivery logistics. Regardless of the number of calories actually delivered, the objective is always to deliver the number of calories and nutrients that are calculated for the patient; therefore, the caloric requirement calculation should always be as accurate as possible.

## Conclusions

Underfeeding and overfeeding are common in critically ill cancer patients when resting energy expenditure is estimated rather than measured, so indirect calorimetry is the preferred method for determining caloric need, but if indirect calorimetry is not feasible, the Harris-Benedict basal energy expenditure equation without added stress and activity factors correlates better with measured resting energy expenditure than does the clinically estimated resting energy expenditure.

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