

# Comparison of indirect calorimetry, the Fick method, and prediction equations in estimating the energy requirements of critically ill patients<sup>1,2</sup>

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## ABSTRACT

**Background:** Accurate measurement of resting energy expenditure (REE) is helpful in determining the energy needs of critically ill patients requiring nutritional support. Currently, the most accurate clinical tool used to measure REE is indirect calorimetry, which is expensive, requires trained personnel, and has significant error at higher inspired oxygen concentrations.

**Objective:** The purpose of this study was to compare REE measured by indirect calorimetry with REE calculated by using the Fick method and prediction equations by Harris-Benedict, Ireton-Jones, Fusco, and Frankenfield.

**Design:** REEs of 36 patients [12 men and 24 women, mean age  $58 \pm 22$  y and mean Acute Physiology and Chronic Health Evaluation II score  $22 \pm 8$ ] in a hospital intensive care unit and receiving mechanical ventilation and total parenteral nutrition (TPN) were measured for  $\geq 15$  min by using indirect calorimetry and compared with REEs calculated from a mean of 2 sets of hemodynamic measurements taken during the metabolic testing period with an oximetric pulmonary artery catheter.

**Results:** Mean REE by indirect calorimetry was  $8381 \pm 1940$  kJ/d and correlated poorly with the other methods tested ( $r^2 = 0.057-0.154$ ). This correlation did not improve after adjusting for changes in respiratory quotient ( $r^2 = 0.28$ ).

**Conclusions:** These data do not support previous findings showing a strong correlation between REE determined by the Fick method and other prediction equations and indirect calorimetry. In critically ill patients receiving TPN, indirect calorimetry, if available, remains the most appropriate clinical tool for accurate measurement of REE. *Am J Clin Nutr* 1999;69:461-6.

## KEY WORDS

Energy expenditure, critical illness, indirect calorimetry, Fick equation, Harris-Benedict equation, Ireton-Jones equation, Frankenfield equation, total parenteral nutrition

## INTRODUCTION

Critical illness and its treatment can profoundly alter metabolism and significantly increase or decrease energy expenditure (1-6). For these reasons, accurate determination of resting energy expenditure (REE) is necessary in patients receiving nutritional support to ensure that their energy needs are met and avoid the complications associated with over- or underfeeding

(5-11). Overfeeding, usually caused by excessive administration of carbohydrate or fat, can result in fatty infiltration of the liver and pulmonary compromise; underfeeding can lead to poor wound healing and immunologic compromise (5-11). Many methods are available for measurement or estimation of REE, but they all have limitations. At one end of the spectrum is measurement of REE by indirect calorimetry, generally considered the gold standard. This method, although accurate, is technically demanding, time consuming, involves the use of expensive, specialized equipment that is not universally available, and requires trained personnel to perform it (12-14). In addition, indirect calorimetry can be inaccurate under a variety of circumstances that commonly affect critically ill patients (12-15). At the other end of the spectrum is the use of standardized equations, such as the Harris-Benedict equation, modified by various stress and activity factors to account for the clinical state of the patient (16). These equations, although easy to use, inexpensive, and universally available, have been shown to be inaccurate in a variety of clinical settings and vary considerably from measured values (17-20). Because of these problems, attempts to devise alternative methods for measuring or estimating REE that are accurate, cheap, easy to perform, and readily available have persisted.

One such new method is based on the Fick equation, which uses hemodynamic data (specifically cardiac output), hemoglobin concentration, and arterial and mixed venous oxygen concentrations (obtained from a pulmonary artery catheter) to calculate REE (21-28). Several studies that used this method showed high correlations with indirect calorimetry measurements (21-27), other studies, however, did not find the correlations to be as good (28). Several other investigators have devised formulas to estimate energy expenditure based on analysis of empirical data (29-31). The durability of these latter equations in this population has not been adequately documented as yet.

The purpose of this study was to compare REE as measured by indirect calorimetry with estimated REE as determined by the Fick method and 4 predictive equations—Harris-Benedict (16),

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Ireton-Jones (29), Frankenfield (30), and Fusco (31)—to ascertain their clinical reliability.

## SUBJECTS AND METHODS

The study protocol was approved by the Biomedical Sciences Human Subjects Review Committee of the Ohio State University, and voluntary informed consent was obtained from each subject before entry. No patient charges were generated as a result of any of the tests used for the purposes of the study.

### Subjects

Thirty-six patients (12 men and 24 women) admitted to the surgical intensive care unit of The Ohio State University Hospitals participated in the study. All patients were mechanically ventilated, were receiving total parenteral nutrition, and already had an oximetric pulmonary artery catheter in place for the purpose of enhancing clinical care at the time of evaluation. Patient care was not interrupted during testing.

### Indirect calorimetry

Indirect calorimetry measurements were obtained on all patients (MedGraphics Critical Care Monitor; MedGraphics Corp, St Paul). Subjects were measured for  $\geq 15$  min. All attempts were made to avoid concomitant invasive and evaluative procedures. If the patient did not achieve respiratory equilibrium by 5 min into the test (defined as a  $<10\%$  change in average oxygen consumption and carbon dioxide production per minute), the test was discontinued. The device was calibrated before each use. No patients had an inspired oxygen concentration  $\geq 0.5$ . The open circuit, breath-by-breath method of indirect calorimetry was used. The gas sample line was connected to the patients' breathing circuits near the endotracheal tube. Inspired and expired gases were measured separately and the respiratory quotient (RQ) and REE were calculated using concentrations of oxygen and carbon dioxide.

### Fick method

Simultaneous measurements of cardiac output and arterial and mixed venous oxygen saturations were performed at the beginning and end of the indirect calorimetry assessment for determination of energy expenditure by the Fick method. Measurements were made by using the thermodilution technique with a venous oxygen saturation–cardiac output computer (Abbott Critical Care Systems, Inc, Chicago). Rapid injections of iced 5% dextrose in water solution were used to determine cardiac output. Cardiac output values were compared with the thermodilution curve to ensure proper measurement. Three values were obtained and averaged to use as the result if they were within 10% of each other. Mixed venous oxygen saturation was obtained spectrophotometrically from the oximetric pulmonary artery catheter containing a fiberoptic bundle (Abbott Critical Care Systems, Inc). Arterial oxygen saturation was determined by using a continuous pulse oximeter (Nellcore; Puritan Bennett, Inc, Pleasanton, CA). Blood samples for hemoglobin determination were obtained at the time of cardiac output measurement. The REE was calculated using the following equation:

$$\text{REE} = \text{CO} \times \text{Hb}(\text{SaO}_2 - \text{SvO}_2)95.18 \quad (1)$$

where REE is in resting energy expenditure in kcal/d, CO is cardiac output (in L/min), Hb is hemoglobin concentration (in

mg/L),  $\text{SaO}_2$  is the oxygen saturation of arterial blood, and  $\text{SvO}_2$  is the oxygen saturation of mixed venous blood.

### Equations for determining estimated energy expenditure

Results from indirect calorimetry and from the Fick thermodilution method were compared with 4 equations that have also been devised and recommended for use in determining energy requirements (in kcal/d):

Harris-Benedict (16):

$$\text{EEE (males)} = 66 + 13.7(\text{wt in kg}) + 5(\text{ht in cm}) - 6.8(\text{age in y}) \quad (2)$$

$$\text{EEE (females)} = 665 + 9.6(\text{wt in kg}) + 1.8(\text{ht in cm}) - 4.7(\text{age in y}) \quad (3)$$

where EEE is estimated energy expenditure, wt is weight, and ht is height.

Ireton-Jones equation for ventilated patients (29):

$$\text{EEE} = 1925 - 10(\text{age in y}) + 5(\text{wt in kg}) + 281 \text{ sex} + 292 \text{ trauma} + 851 \text{ burn} \quad (4)$$

where sex is 0 for females and 1 for males, trauma is 1 for yes and 0 for no, and burn is 1 for yes and 0 for no.

Frankenfield et al (30):

$$\text{EEE} = -1000 + 100(\dot{V}_E) + 1.3(\text{Hb}) + 300 \text{ (sepsis)} \quad (5)$$

where  $\dot{V}_E$  is expired minute ventilation and sepsis is 1 for yes and 0 for no.

Fusco et al (31):

$$\text{EEE} = -983 - 4(\text{age in y}) + 32(\text{ht in in}) + 11 \text{ (wt in kg)} \quad (6)$$

REE and EEE (in kcal/d) calculated with each of the above formulas was converted to kJ/d by using a conversion factor of 1 kcal = 4.18 kJ. Only 19 patients had the raw data for  $\dot{V}_E$  available and were eligible for analysis according to Frankenfield et al (30).

### Statistical analysis

Data were first analyzed by repeated-measures analysis of variance based on the null hypothesis. Differences between measures were evaluated by determining 95% CIs for the difference in means between the methods and the standard (indirect calorimetry) using standard paired *t* tests and the Bonferroni inequality (32). The relative ordering of the methods was determined by calculating correlation coefficients and the mean absolute differences were determined.

## RESULTS

Characteristics of the subject population are shown in **Table 1**. There were 12 men and 24 women, with a mean ( $\pm$  SD) age of  $59 \pm 22$  y. The average height and weight for men was 178 cm (70 in) and 88.6 kg (195 lb), respectively, conforming with national averages. Women in the sample tended to be heavier than average, averaging 160 cm (63 in) in height and 81.8 kg (180 lb) in weight. Overall, the severity of illness was moderate to severe, with mean Acute Physiology and Chronic Health

TABLE 1

Characteristics of study subjects

Patient no	Height <i>cm</i>	Weight <i>kg</i>	APACHE II		Sex	Diagnosis	Surgical procedure
			score <sup>1</sup>	Age <i>y</i>			
1	168	92	17	37	M	Small-bowel perforation	Bowel resection
2	178	79	41	64	M	Postoperative pancreatitis	Gastrectomy
3	170	67	13	21	M	Epilepsy	Corpus callosotomy
4	155	83	25	70	F	Intraabdominal abscess	Drainage
5	160	62	22	98	F	Bowel obstruction	Exploratory laparotomy
6	167	88	20	46	F	Sepsis	None
7	185	117	28	39	M	End-stage renal disease	Kidney transplant
8	188	109	23	50	M	End-stage renal disease	Kidney transplant
9	162	111	32	73	F	Diverticulitis	Colectomy and splenectomy
10	155	66	7	45	F	Acute embolism	Bilateral femoral embolectomy
11	165	109	11	74	F	Ovarian cancer	Exploratory laparotomy
12	152	60	17	29	F	End-stage renal disease and diabetes mellitus	Pancreas and kidney transplant
13	173	93	20	29	M	Peritonitis	Exploratory laparotomy
14	163	74	22	70	F	Cholelithiasis	Cholecystectomy
15	127	76	35	86	F	Colon cancer	Sigmoid resection
16	178	68	22	17	M	Gunshot wound to head	None
17	155	107	24	64	F	Postoperative sepsis	Hernia repair
18	178	63	22	15	M	Gunshot wound to head	None
19	163	84	23	61	F	Necrotizing pancreatitis	Pancreatectomy
20	188	106	21	35	M	Motor vehicle accident	None
21	163	85	13	77	F	Colon cancer	Colon resection
22	150	77	16	61	F	Peripheral vascular disease	Aortobifemoral bypass
23	170	88	8	45	F	Motor vehicle accident	None
24	165	86	11	38	F	Ovarian cancer	Radical hysterectomy and omentectomy
25	165	81	19	44	M	Upper gastrointestinal hemorrhage	None
26	152	85	20	83	F	Intestinal angina	Mesenteric revascularization
27	168	102	21	76	F	Ischemic bowel	Small-bowel resection
28	180	87	36	86	M	Abdominal aortic aneurysm	Elective repair
29	170	68	23	69	F	Abdominal aortic aneurysm	Elective repair
30	152	50	17	65	F	Peripheral vascular disease	Aortic biiliac graft
31	163	65	24	75	F	Respiratory arrest	Gastrostomy tube placement
32	152	55	22	65	F	Peripheral vascular disease	Aortic biiliac graft
33	163	118	26	73	F	Thoracoabdominal aortic aneurysm	Thoracoabdominal aneurysmectomy
34	185	103	29	63	M	Abdominal aortic aneurysm	Elective repair
35	167	88	24	80	F	Peritonitis	Exploratory laparotomy
36	152	71	26	84	F	Peritonitis	Sigmoid colectomy

<sup>1</sup>Acute Physiology and Chronic Health Evaluation (33).

Evaluation (APACHE) II (33) score of 22, and the patients suffered from a wide array of diseases and surgical conditions.

The measured and calculated values for energy expenditure are shown in **Table 2**. All 5 measures of REE were normally distributed, with 2 minor exceptions. The Fick method had 1 extreme value of 15 587 kJ/d (3729 kcal/d) for subject 35, and the Ireton-Jones calculations had a ceiling of 11 286 kJ/d (2700 kcal/d), with the 6 highest values between 10 868 and 11 286 kJ/d (2600 and 2700 kcal/d). These minor deviations from normality had little effect on the results, which remained the same when the data were artificially altered to conform to normality assumptions. The data were also analyzed based on sex and age (> or <60 y old) and similar patterns were found.

Analysis of the data based on the null hypothesis, assuming that all 6 measurements of REE had a common mean, strongly rejected the assumption of equal means (repeated measures analysis of variance,  $F_{4,175} = 16.9$ ,  $P < 0.0001$ ). Mean differences in REE calculated by using 3 methods significantly underesti-

mated the average REE by indirect calorimetry (**Table 3**), ranging from 915 kJ/d (219 kcal/d) for the Fusco method to 2128 kJ/d (509 kcal/d) by the Fick method. Estimates using the Ireton-Jones and Frankenfield formulas were not significantly different from the mean REE by indirect calorimetry. Furthermore, recalibration of the formulas to adjust for the specific populations at hand was not feasible because there were serious disagreements between the measures as to which patients had high or low REE, as shown by correlation analysis (below).

Pearson correlation coefficients were calculated to determine the relative ordering of the methods compared with indirect calorimetry (**Table 4**). It is clear from the  $r$  values, ranging from 0.24 to 0.39, that none of the formulas account for >15% of the variability of indirect calorimetry among the patients. To estimate the overall agreement between the formulas and indirect calorimetry, the mean absolute differences between values and the percentage of values that underestimated the REE were calculated. The magnitude of typical differences based on the for-



**TABLE 2**  
Comparison of indirect calorimetry with other methods and formulas<sup>1</sup>

Method and reference	Energy expenditure
	<i>kJ/d (kcal/d)</i>
Indirect calorimetry (12–14) <sup>2</sup>	8381 ± 1940 (2005 + 464)
Fick (21–28) <sup>2</sup>	6253 ± 2466 (1496 + 590) <sup>3</sup>
Harris-Benedict (16) <sup>2</sup>	6429 ± 1329 (1538 + 318) <sup>3</sup>
Ireton-Jones (29) <sup>2</sup>	9012 ± 1388 (2156 + 332)
Fusco (31) <sup>2</sup>	7465 ± 1363 (1786 + 326) <sup>3</sup>
Frankenfield (30) <sup>4</sup>	9815 ± 2621 (2348 + 627)

<sup>1</sup> $\bar{x} \pm SD$ .

<sup>2</sup> $n = 36$ .

<sup>3</sup>Significantly different from indirect calorimetry,  $P < 0.05$  (paired  $t$  test).

<sup>4</sup> $n = 19$ .

mulas was in the range of 1672–2926 kJ/d (400–700 kcal/d), with >80% of the differences being underestimates of the REE using each of the formulas except the Frankenfield formula.

## DISCUSSION

In this study, none of the methods evaluated (Fick, Harris-Benedict, Ireton-Jones, Frankenfield, and Fusco) correlated with indirect calorimetry in estimating daily energy requirements for nutritional support. Although predicted energy expenditure using the Ireton-Jones and Frankenfield equations did not differ significantly from measured energy expenditure by indirect calorimetry, the correlation coefficients were low,  $r = 0.26$  and  $r = 0.39$ , respectively, indicating that in individual patients each was a poor predictor.

These result differ from those of several other studies (21–28) that found the Fick method to correlate strongly with the indirect calorimetry measurements, as high as  $r = 0.90$  in one case (21). The correlation between methods in the present study was poor ( $r = 0.24$ – $0.39$ ). It is possible that the patients' RQs were so widely varied that the assumed RQ of 0.85 in the Fick equation allowed for error. Nevertheless, when the equation was adjusted for the various RQs of each patient, the mean difference between the Fick method and indirect calorimetry was still high,  $1994 \pm 2671$  kJ/d ( $477 \pm 639$  kcal/d), and the correlation was only 0.31. Thus, adjusting for RQ in the equation did not improve the accuracy.

In all but 7 patients studied, energy expenditure determined by indirect calorimetry was higher than that calculated using the Fick equation. Others have reported similar findings. Cobean et al (25) found the Fick equation to underestimate REE by 367.8

**TABLE 3**  
Mean differences between calculated resting energy expenditure (REE) and REE measured by indirect calorimetry

Method and reference	Lower limit REE	Average difference	Upper limit REE
	<i>kJ (kcal)</i>		
Fick (21–28)	–2863(–685)	–2128(–509)	–974(–233)
Harris-Benedict (16)	–3281(–785)	–1952(–467)	1045(–250)
Ireton-Jones (29)	–280(–67)	627(150)	1538(368)
Fusco (31)	–1818(–435)	–915(–219)	–17(–4)
Frankenfield (30)	–3432(–821)	1154(276)	6759(1617)

**TABLE 4**  
Correlation, mean absolute difference (MAD), and percentage underestimation of calculated resting energy expenditure (REE) compared with REE measured by indirect calorimetry

Method and reference	Correlation	MAD	Underestimation
	<i>r</i>		%
Fick (21–28)	0.31	680	83
Harris-Benedict (16)	0.24	528	89
Ireton-Jones (29)	0.26	386	89
Fusco (31)	0.26	406	89
Frankenfield (30)	0.39	528	37

kJ/d (88 kcal), on average. Using a similar equation, Brandi et al (26) also found the indirect calorimetry measurement to be high, with mean measurements of REE by cart and by the Fick method of 4243 kJ/d (1015 kcal/d) and 4042 kJ/d (967 kcal/d), respectively. One possible explanation for this is that the Fick method cannot measure oxygen consumption in the lung, as indirect calorimetry can, thereby underestimating REE (24, 34). This difference can be further exaggerated in patients with compromised pulmonary function. Only 3 of the subjects in the present study had adult respiratory distress syndrome, therefore pulmonary effects on the variation were probably not significant.

Accurate measurement of hemodynamic variables to be used in determining REE depends on proper placement of the catheter and reliable, consistent samples. Obviously, a variation in any components of the Fick equation will introduce error in the calculation of REE. One hemodynamic variable that could cause fluctuation in REE values is SvO<sub>2</sub>. A normal value for SvO<sub>2</sub> is between 60% and 80% (35). When SvO<sub>2</sub> drops below 60%, it is indicative of an increase in oxygen consumption or a compromise of one of the variables of oxygen transport (36). This may be seen in conditions such as hypoxemia, hyperthermia, or seizures in the clinical setting. Five of the patients in the current study had SvO<sub>2</sub> values <60%, with a mean SvO<sub>2</sub> of 56%. Their values were, however, stable over the 2 measurement periods. SvO<sub>2</sub> values >80%, as seen in 3 patients in the present study, are related to an increase in oxygen delivery (36), a decrease in oxygen requirements, or compromised ability of tissues to extract oxygen, as occurs with sepsis or hyperoxia. These small errors can translate into a varied oxygen consumption and, therefore, an REE that is slightly off the true value.

Another potential explanation for the lack of correlation between indirect calorimetry and the Fick method is the altered relation between oxygen delivery and consumption that has been described in critically ill patients (37–41). “Flow-dependent” or “supply-dependent” oxygen consumption has been noted in patients with adult respiratory distress syndrome, sepsis, and hypermetabolism (36–40). The validity of this concept has been challenged because of its use of mathematical coupling (42), in which both cardiac output and hemoglobin concentration appear on both sides of the equation for calculating oxygen consumption, with only oxygen saturation differing. Other studies using both indirect calorimetry and the Fick method have shown that there is no supply- or flow-dependent relation between oxygen delivery and consumption in critically ill patients, and that these 2 functions remain independent of each other (43–46). However, these results are not universal (47). On the basis of these data, it is not surprising that our results did not show good correlations

among methods. Mathematically, in patients with higher SvO<sub>2</sub> in which the difference between arterial and venous oxygen contents would be a low number, a higher degree of correlation among methods could be expected. Conversely, in patients with normal or low SvO<sub>2</sub>, the difference between arterial and venous oxygen would be greater and the correlation among methods correspondingly lower. Indeed, when the data were analyzed in this fashion, this explanation was borne out.

Last, the lack of correlation may partly have been due to the differences between the patient population that we studied and the population from which the formulas were originally derived. For example, the Harris-Benedict equation was devised to estimate REE in healthy individuals. The Ireton-Jones formula (29) was developed in and for trauma and burn victims, whereas the Frankenfield formula (30) was developed for patients with severe trauma, sepsis, or both. Finally, the population targeted by Fusco (31) is not well defined. Although burn, trauma, and critically ill patients share many of the metabolic and physiologic responses to stress, it may be that these formulas, developed based on empirical data, are indeed disease specific and not readily applicable to a broader, more diverse population in an intensive care unit, such as studied here.

The patients in the present study were metabolically stressed with a mean REE of 8381 ± 1940 kJ/d (2005 ± 464 kcal/d). Their average score with the APACHE II scoring system, which was designed to measure disease severity and correlates highly with mortality, was 22, indicating severe illness. This scoring system is also valuable in predicting energy expenditure (34). When studying the energy expenditures of critically ill patients, Swinamer et al (34) found good correlation between individual APACHE II scores and increases in measured REE above predicted REE. This suggests that the more severe the illness, the higher the energy expenditure. In the current study, several of the patients with high APACHE II scores also exhibited high metabolic rates; however, there was too much individual variability to attribute REE fluctuations to the severity of illness. An interesting finding was that in the patients with APACHE II scores > 20, there was a high average difference (27%) in indirect calorimetry and Fick method measurements. Individual patient measurements varied up to 50% between methods in some cases. Most other studies evaluating this method did not report APACHE II scores, so it is difficult to compare the severity of disease in the separate patient populations. This may account for some of the extreme variances in REEs in the present patient population. Also, although the men in this study had relatively normal weights for heights, most (two-thirds) of the patients were women, who tended to be overweight.

The goal of this study was to determine whether, in this critically ill patient population, REE obtained by the Fick equation or estimated by several formulas was significantly different from that obtained using indirect calorimetry. The results of this study do not support the findings of other studies in which indirect calorimetry was compared with the Fick equation and the pulmonary artery catheter method or with the findings of those who developed the other prediction formulas. Whereas it is possible that mechanical errors could have occurred in the measurement process, it is unlikely that the extreme variation between methods was due entirely to human error. It is more likely that a difference in patient populations, including disease states, contributed to the variation. Indirect calorimetry should remain an integral part of all nutrition support regimens, if available. It

remains the standard by which all other methods are tested and provides accurate, reliable measurements of REE. 

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