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Accuracy of predictive methods to estimate resting energy expenditure of thermally-injured patients

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Abstract

Background

The purpose of this study was to evaluate the bias and precision of 46 methods published from 1953 to 2000 for estimating resting energy expenditure (REE) of thermally injured patients.

Methods

Twenty-four adult patients with ≥20% body surface area burn admitted to a burn center who required specialized nutrition support and who had their REE measured via indirect calorimetry (IC) were evaluated. Patients with morbid obesity, human immunovirus, malignancy, pregnancy, hepatic or renal failure, neuromuscular paralysis, or those requiring a FiO2 >50% or positive end expiratory pressure (PEEP) ≥10 cm H2O were excluded. One steady-state measured REE measurement (MEE) was obtained per patient. The methods of Sheiner and Beal were used to assess bias and precision of these methods. The formulas were considered unbiased if the 95% confidence interval (CI) for the error (kilocalories per day) intersected 0 and were considered precise if the 95% CI for the absolute error (%) was within 15% of MEE.

Results

MEE was 2780 ± 567 kcal/d or 158% ± 34% of the Harris Benedict equations. None of the methods was precise (≤15% CI error). Over one-half (57%) of the 46 methods had a 95% confidence interval error >30% of the MEE. Forty-eight percent of the methods were unbiased, 33% were biased toward overpredicting MEE, and 19% consistently underpredicted MEE. The pre-1980s methods more frequently overpredicted MEE compared with the 1990 to 2000 ($p < .01$) and 1980 to 1989 ($p < .05$) published methods, respectively. The most precise unbiased methods for estimating MEE were those of Milner (1994) at a mean error of 16% (CI of 10% to 22%), Zawacki (1970) with a mean error of 16% (CI of 9% to 23%), and Xie (1993) at a mean error of 18% (CI of 12% to 24%). The "conventional 1.5 times the Harris Benedict equations" was also unbiased and had a mean error of 19% (CI of 9% to 29%).

Conclusions

Thermally injured patients are variably hypermetabolic and energy expenditure cannot be precisely predicted. If IC is not available, the most precise, unbiased methods were those of Milner (1994), Zawacki (1970), and Xie (1993).

Thermal injury is among the most hypermetabolic of all conditions encountered in clinical practice. As a result, research regarding the pathogenesis and nature of the observed hypermetabolism after thermal injury has been extensively conducted.[1-3] It is accepted that nutrition support may improve morbidity and mortality after severe thermal injury.[4] However, it is also known that excessive caloric intake cannot overcome the catabolic response to critical illness,[5,6] and the detrimental effects of overfeeding are well established.[7-10] Success of the nutrition management of the thermally injured patient may depend on how well this burn-related change in energy expenditure can be estimated and then matched by an appropriate level and mixture of macronutrients.[2] As a result, attempts have been made to improve methods for estimating energy requirements in thermally injured patients. Unfortunately, the abundance of predictive methods used for estimating energy expenditure and requirements in thermally injured patients may have led the clinician to further confusion rather than clarity. The purpose of this investigation was to evaluate the bias and precision of known methods for estimating energy expenditure in thermally injured adults and to identify the most precise, unbiased methods for use in clinical practice.

Clinical Relevancy Statement

This article evaluates the bias and precision of 46 methods for estimating resting energy expenditure (REE) in 24 thermally injured patients requiring specialized nutrition support. These data indicate that thermally injured patients are variably hypermetabolic and that energy expenditure cannot be precisely predicted. In the event indirect calorimetry is not available, the most precise unbiased methods for estimating REE were identified.

Materials and Methods

Adult patients, 18 to 59 years of age, admitted to the Firefighters Burn Center of the Regional Medical Center at Memphis with ≥20% body surface area burn (BSAB) who required specialized nutrition support and had their REE measured were identified for potential inclusion into the study. Measurement of REE, laboratory, and nutrition assessment measurements were conducted as part of the routine clinical care of these patients. Patients excluded from the study were those with morbid obesity (pre-resuscitation weight >150% ideal body weight), malignancy, human immunovirus (HIV) infection, pregnancy, or those undergoing neuromuscular paralysis. Laboratory tests were ordered by the patient's primary service or the Nutrition Support Service and performed by the hospital laboratory as part of the patient's routine clinical care. The study was approved and conducted in accordance with the guidelines established by the University of Tennessee Investigational Review Board. Because the REE was performed as part of the routine metabolic evaluation of the patient, informed consent was waived.

A single steady-state indirect calorimetry (IC) measurement was determined per patient. The indirect calorimetry techniques as outlined by the University of Pennsylvania group for obtaining an accurate resting measured energy expenditure were employed.[11] Measurements were performed at least 2 days postsurgery for wound excision and grafting and within the first 3 weeks postinjury. Patients undergoing hyperbaric oxygen or hydrotherapy were measured before leaving the intensive care unit for those procedures. Most gas exchange measurements were performed between 10:00 AM and 12:00 PM or 2:00 PM and 4:00 PM, with all measurements conducted at least 2 hours postprandial for any patient with intermittent *ad libitum* oral intake. All patients were lying in a bed or recliner chair at rest for at least 30 minutes and in a thermoneutral environment. The patient's nursing medication profile was examined to insure that any intermittent sedative or narcotic was not administered before the measurement. Nonventilator-dependent patients receiving supplemental oxygen by nasal cannula had the oxygen discontinued for 10 minutes before the measurement. A canopy system was used in these patients, and blood oxygen saturation was constantly monitored by a pulse oxymeter during the period off supplemental oxygen. The indirect calorimetry techniques as outlined by the University of Pennsylvania group for obtaining an accurate resting measured energy expenditure were employed.[11]

The MetaScope Metabolic Cart II (Sensormedics, Yorba Linda, CA) was used for the indirect calorimetry measurements. The MetaScope Metabolic Cart II has a differential paramagnetic oxygen analyzer accurate to 0.01% on a scale of 1% to 100% for measured inspired and expired oxygen concentrations, infrared carbon dioxide analyzer, Fleish pneumotachometer, and a baffled 3-L mixing chamber. The IC measurements were performed in 20-minute intervals up to a maximum of 3 intervals per patient until steady-state measurements were achieved. Inspired oxygen and carbon dioxide fractions were performed during the initial and final 2 minutes of the interval. Expired oxygen and carbon dioxide fractions were measured during the middle 16 minutes of the interval. Initial and terminal inspiratory gas fraction values were averaged and used as the mean FiO_2 and $FiCO_2$ values for the interval. This process provides adjustments for the effects of small variations in FiO_2 and $FiCO_2$, barometric pressure, and minor analyzer drifts.[12] Gas analyzers were calibrated immediately before each measurement using 95% oxygen/5% carbon dioxide and 100% nitrogen reference gases. FiO_2 stability was documented immediately before each patient measurement, and a mean oxygen consumption sensitivity error of ≤5% was achieved before proceeding to the patient care measurement.[13] Daily pneumotachometer calibration was conducted using a 3-L syringe: 3 consecutive determinations with <1% error from expected was accepted for successful calibration. Barometric pressure was calibrated using the institutional reference barometric pressure from the pulmonary function laboratory of the Regional Medical Center at Memphis, Tennessee. Temperature calibration was conducted using a thermometer accurate to 0.1°C at ambient temperature.

Steady-state gas exchange measurements were used to determine oxygen consumption and carbon dioxide production rates, which were then applied to the abbreviated Weir formula to calculate measured REE (MEE).[14] The abbreviated Weir formula was used since simultaneous urine collection for nitrogen was not conducted at the time of the indirect calorimetry measurement. Use of the abbreviated Weir formula in critically ill patients with high urinary nitrogen excretion can result in a 3% to 5% overestimation of actual measured resting energy expenditure. MEE was expressed as kilocalories per day and as a percent of the basal energy expenditure (BEE) based on the Harris-Benedict equations.[15] Steady state was defined as 5 consecutive 1-minute sampling intervals with a variation of ≤5% for oxygen consumption and carbon dioxide production rates, minute ventilation, and respiratory quotient measurements as previously described.[16-20] IC measurements were not performed in patients requiring ventilator support with an inspired oxygen concentration (FiO_2) > 0.50 or a positive end expiratory pressure > 10 cm H_2O. When using similar techniques, 95% of 72 normal adults had a REE within ±15% of predicted values by the Harris-Benedict equations.[21] Additionally, use of these techniques resulted in a mean difference between measurements that are performed on the same patient at various times throughout the day of <10%.[22] BEE was calculated based on current body weight using the Harris-Benedict equations.15 Despite their limitations,[23,24] the Harris-Benedict equations were used as the points of reference because of their wide acceptance and use.[16-19,21,22] Ideal body weight was estimated from the method of Devine,[25] and body surface area was calculated from DuBois and DuBois.[26] Basal metabolic rate was extracted from Aub and DuBois.[27] Patients were provided with a continuous infusion of either enteral or parenteral nutrition support with minimal (<500 kcal/d) or no *ad libitum* oral intake present at the time of the measurement. Calories were generally provided as a mixture of carbohydrate or dextrose, lipid, and protein. Initial energy goals were either 1.2 times the Toronto formula[28] or 35 to 40 kcal/kg per day until the REE was measured, and the regimen was readjusted to provide approximately 1 to 1.2 times the MEE. A protein intake of 2 to 2.5 g/kg per day was targeted for most patients. Patients were started on enteral nutrition support with a 1 kcal/mL, fiber-containing, high-protein formulation via nasoenteric feeding tube within several hours of admission to the burn center.

All of the patients were treated in a uniform fashion with regard to excisional and grafting therapy. Patients were taken to the operating room as soon as possible after hospitalization where wide excisional surgery was performed to remove all burned tissue for preparation of grafting using a combination of autografting, homografting, or artificial skin for initial wound coverage. Grafted wounds were dressed and the extremities were immobilized. After a period of immobilization, dressing changes and hydrotherapy were initiated. Patients returned to the operating room at periodic intervals for further autograft harvesting until the wounds were entirely closed.

The Tobiasen Abbreviated Burn Severity Index (BSI) was calculated based on gender, age, percent body surface area burn, presence of inhalation injury, and full thickness burn.[29] Patients with sepsis met the guidelines of the American College of Chest Physicians.[30] Pneumonia was evident by clinical signs and symptoms and confirmed by bronchoalveolar lavage with the presence of 105 or more colony-forming units/mL. The presence of inhalation injury was confirmed by bronchoscopy.

A PubMed (U.S. National Library of Medicine, Bethesda, MD) literature search was initially conducted to find citations that examined REE and caloric requirements in thermally-injured patients. These references were closely reviewed to find other citations that were not found in the PubMed search. Only studies that actually measured energy expenditure in the development of the predictive method were collated for this analysis. Exceptions included certain methods commonly used in clinical practice such as the Curreri formulas and its variations, the methods outlined in the burn dietitian practice survey, 2 times the Harris-Benedict equations, 35 kcal/kg per day, and 40 kcal/kg per day.[31-33] Only studies involving adult patients were included in the analysis. Additionally, the studies were examined to insure that the patients had significant thermal injury (>20% BSAB), measurements were conducted within the first few weeks postinjury, and the patients were stable, but critically ill, patients. The various methods found in the literature search were calculated for each patient and compared with actual MEE.

Bias and precision of the predictive formulas were determined according to the methods of Sheiner and Beal.[34] Root mean squared prediction error (a measure of precision) was calculated and normalized to MEE by the following formula:

$$\% \text{ error} = \frac{\text{SQRT } [(\text{PEE - MEE})^2]}{\text{MEE}} \times 100$$

Where SQRT is square root, PEE is predicted energy expenditure of the particular formula, and MEE is measured resting energy expenditure. Precision may be thought of in terms of accuracy of a prediction method. A formula was considered precise if the 95% CI for root mean squared prediction error was within 15% of the MEE. Bias was determined by examining the 95% CI for the mean error between predicted and MEE. The respective method was considered unbiased if the 95% CI for the error included 0. Continuous data were expressed as either mean ± SD and as (low, high) values of the 95% CI. All statistical analyses were conducted using SPSS for Windows, version 6.1 (SPSS, Inc, Chicago, IL). Nominal data were evaluated by either the x^2 or Fisher's exact test. Goodness of fit of the linear model between 2 variables was assessed from the coefficient of determination (r^2), which was derived from linear correlation using the Pearson product moment correlation coefficient. In addition to bias and precision, comparisons between the PEE by the respective methods and MEE were analyzed using the Wilcoxon matched pairs signed ranks test. The Mann-Whitney U test was used for comparisons of 2 independent samples. A $p \leq .05$ was established as statistically significant.

Results

Twenty-four thermally injured patients referred to the Nutrition Support Service for specialized nutrition support who had their REE measured were studied. Twenty-one patients were receiving enteral tube feeding; 1 patient was being given parenteral nutrition; and 2 patients had transitional feeding with combined parenteral and enteral nutrition therapy at the time of the indirect calorimetry study. The majority of the population was men, and most of patients were well-nourished before their injury. Demographic, laboratory, and nutrition assessment information are given in Table I. The extent of total body surface area burned of the population ranged from 20% to 80% with about two-thirds of the population ranging from 20% to 40% (Table II). The majority of the patients' thermal injury was a full thickness (third-degree) burn,

Table 1. Patient characteristics, laboratory, and nutritional assessment

Variable	Results
N	24
Gender: Male/Female (n/n)	19/5
Age (years)	36 ± 12
Weight (kg)	78 ± 14
Weight (% IBW)	113 ± 23
Height (cm)	174 ± 10
Body surface area (m^2)	1.96 ± 0.22
BEE (Harris Benedict equations, kcals/day)[15]	1793 ± 349
BMR (Aub-DuBois, kcal/m^2 per hour)[27]	38.5 ± 1.5
BMR (Fleisch, kcals/m^2 per hour)[63]	36.2 ± 1.3
Prealbumin (mg/dL)	10.7 ± 4.2
WBC (cells/m^3)	9.9 ± 5.5
Serum glucose (mg/dL)	157 ± 46
Serum creatnine (mg/dL)	0.91 ± 0.24

BMR, basal metabolic rate; IBW, ideal body weight; WBC, white blood cell count; BEE, basal energy expenditure. Continuous data are given as mean ± SD.

and less than one-half of the patients required ventilator support. The mean Tobiasen Burn Severity Index[29] of the study population was 7.3 and ranged from 5 to 12. About two-thirds of the population had pneumonia or sepsis at the time of the IC study. Details regarding the severity of the thermal injury and associated morbidity are given in Table II.

The results of the IC measurements are given in Table III. The mean MEE was 2780 kcal/d (range, 1571 to 3914 kcal/d), which was 158% (range, 67% to 207%) of the BEE (based on the Harris-Benedict equations). The distribution of the patients' MEE (normalized to BEE) is illustrated in Figure 1. Only 1 patient was hypometabolic (<90% of the BEE) and none of the patients was normometabolic (90% to 110% of the BEE). The remaining patients were hypermetabolic. The majority (approximately 80%) of the patients had a measured REE (MEE) of equal to or greater than 140% of the BEE (Fig. 1). Nine patients (38% of the population) had a MEE above 3000 kcal/d. The respiratory quotient (RQ) for the population ranged from 0.72 to 1.09. The single RQ above 1.0 in this study, reflective of net fat synthesis, was in a 33-year-old ventilator-dependent woman with a 23% body surface area burn without inhalational injury who had the lowest MEE of the entire population at 1571 kcal/d. Her total caloric intake was 1.45 × MEE at the time of the measurement. Other potential determinants of REE, including body and ambient temperatures and nutritional intake at the time of the measurement, are given in Table IV.

To ascertain whether severity of thermal injury might influence energy expenditure, MEE was compared with percent BSAB (Fig. 2) and the Tobiasen burn severity index (Fig. 3). No statistically or clinically significant correlations were observed between MEE and these indicators of severity of illness. In addition, the population was subgrouped according to various perturbations in disease states that might potentially influence energy expenditure such as the presence and absence of inhalation injury, ventilator dependency, wound excision and skin graft, large body surface area burn (eg, >40% BSAB), or pneumonia/sepsis. Although trends toward an

Table 2. Severity of thermal injury and associated morbidity

Variable	Results
% total body surface area burn	37 ± 15
Number of patients with:	
20-40% BSAB (% of total population)	17 (70%)
41-60% BSAB (% of total population)	4 (17%)
61-80% BSAB (% of total population)	3 (13%)
% of body as:	
Second-degree burn	16 ± 13%
Third-degree (full thickness) burn	20 ± 18%
Burn Severity Index[29]	7.3 ± 2.0
Inhalation Injury (*n*)	5
Ventilator dependent (*n*)	10
Wound excised and grafted at time of measurement (*n*)	11
Pneumonia or sepsis at time of measurement (*n*)	17

Continuous data are given as mean ± SD.
BSAB, body surface area burn.

Table 3. Indirect calorimetry measurements

Variable	Results
VO_2 (mL/min)	400 ± 82
VCO_2 (mL/min)	337 ± 71
RQ	0.85 ± 0.08
V_E (L/min)*	14.2 ± 3.3
Frequency (breaths/minute)*	20.9 ± 4.7
V_T (mL)*	702 ± 190
REE (kcal/d)	2780 ± 575
REE (% of BEE)	158 ± 34

*Data cannot be obtained during canopy measurements, and these data were derived from ventilator-dependent patients (n = 10).
BEE, basal energy expenditure as estimated by the Harris-Benedict equations; RQ, respiratory quotient (VCO_2/VO_2); VCO_2, carbon dioxide production; V_E, minute ventilation; VO_2, oxygen consumption; V_T, tidal volume.
Continuous data are given as mean ± SD.

increased MEE were observed for those with inhalation injury, ventilator dependency, and large body surface area burns, these differences were not statistically significant due to the variability in the data and limited number of subjects (Table V). To ascertain whether postinjury time influenced measured energy expenditure, the relationship between MEE (%BEE) to days post-thermal injury was examined. These data indicate the presence of sustained hypermetabolism throughout the 18-day observation period (Fig. 4) with no statistically or clinically significant correlation between MEE (%BEE) and days post-thermal injury.

Data compiled from various studies published from 1953 to 2000 regarding energy expenditure in thermally injured patients that may be used by various clinicians to estimate REE are given in Table VI. There were a total of 46 methods identified for evaluation of bias and precision. Forty-

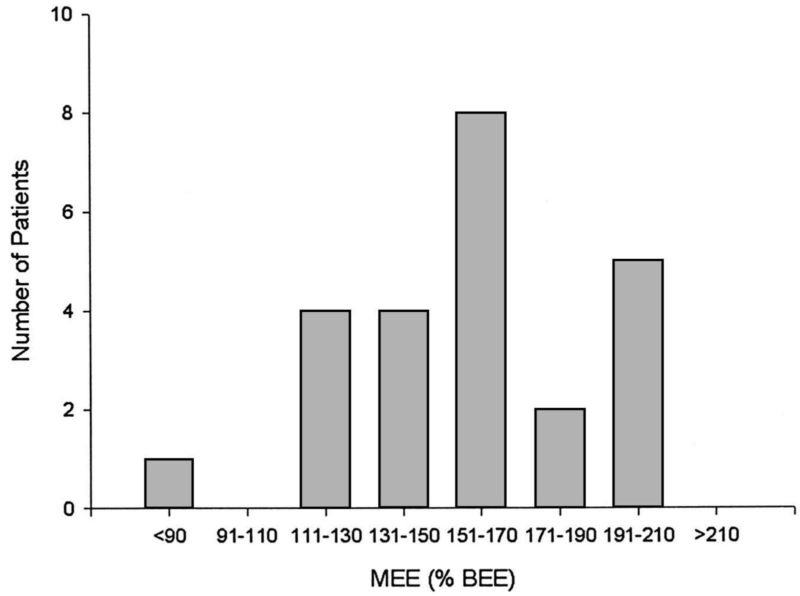

Figure 1. Distribution of MEE (% of BEE) of patients with thermal injury. One patient was less than ±10% of the expected values calculated by the Harris-Benedict equations using current body weight. None of the patients was within ±10% of the expected values. Eighty-three percent (20) of the 24 thermally injured patients were ≥140% of expected energy expenditure by the Harris Benedict equations. In contrast, 92% of normal adults in the study of Boothby and Sandiford[83] were within 10% of the expected energy expenditure.

Table IV. Other potential determinants of resting energy expenditure*

Variable	Results
Body temperature (°C)	37.8 ± 0.7
Ambient temperature (°C)	23.3 ± 2.8
Caloric intake (% of measured REE)	65 ± 43
Caloric intake (kcal/day)	1786 ± 1163
Protein intake (g/kg per day)	1.7 ± 1.1
Protein (g/day)	129 ± 89
Heart rate (beats/min)	117 ± 19
Day post burn	7.7 ± 4.8

*At the time of the indirect calorimetry measurement.
Continuous data are given as mean ± SD.

three methods were derived from the primary literature; an additional 3 methods used in clinical practice (2 × BEE, 35 kcal/kg per day, and 40 kcal/kg per day) were included and classified as "common practice" because a specific primary literature citation could not be identified for their source. The analysis led to a total of 1053 formula-patient case matches. The bias and precision for all methods are given in Table VII. Fifty-one methods (77% of all methods) predicted significantly different ($p < .05$) results than actual MEE (Table VII) and an additional 3 methods tended toward significantly different results ($p \leq .09$) for a total of 82% of the methods. Thirty-three percent of all of the methods were biased toward over-predicting MEE; 19% consistently underpredicted MEE; and 48% were unbiased (Fig. 5). Because innovations in the management of thermal injury have evolved over time that may influence REE, the formulas were further

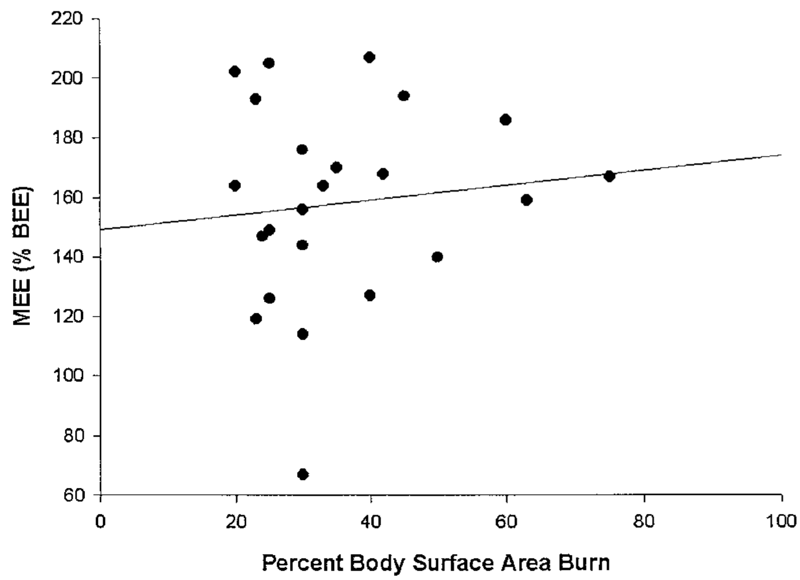

Figure 2. MEE (% of BEE via the Harris-Benedict equations) versus body surface area burn (%). No significant correlation between MEE (%BEE) and BSAB was observed ($y = 0.25 \times +149$, $r^2 = .014$, p = NS).

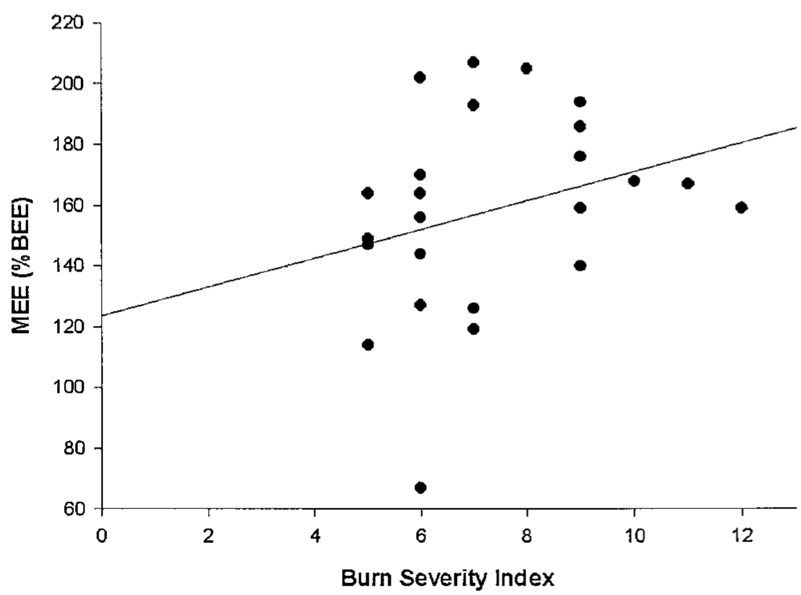

Figure 3. Relationship between MEE (% of BEE via the Harris-Benedict equations) versus the Tobiasen Burn Severity Index (BSI). No significant correlation between MEE (%BEE) and BSI was observed ($y = 4.78 \times +123$, $r^2 = .083$, p = NS).

stratified according to years before 1980, 1980 to 1989, and 1990 to 2000. Fifteen, 17, and 11 primary literature citations were obtained for each time range group, respectively, and 3 methods were added to the total as "common practice" and not allocated to any time range group. The pre-1980s publications had methods that were more frequently biased toward overpredicting MEE compared with the 1990 to 2000 ($p < .01$) and 1980 to 1989 ($p < .05$) publications, respectively (Fig. 5). None of the methods was precise as defined by a 95% CI for error within 15% of MEE.

Table 5. Perturbations in measured resting energy expenditure (% BEE)

Condition	Absent	Present*	$p <$
Inhalation injury	155 ± 35 (n = 19)	173 ± 19 (n = 5)	NS
Ventilator dependency	151 ± 37 (n = 14)	169 ± 25 (n = 10)	NS
>40% BSAB	155 ± 27 (n = 17)	168 ± 18 (n = 7)	NS
Sepsis/pneumonia	163 ± 32 (n = 7)	156 ± 34 (n = 17)	NS
Skin graft	156 ± 40 (n = 13)	161 ± 24 (n = 11)	NS

Continuous data are given as mean ± SD.
*Lack of significance for these perturbations may be due to variability in the data and limited number of subjects.
NS = not significant
See Table II for abbreviations

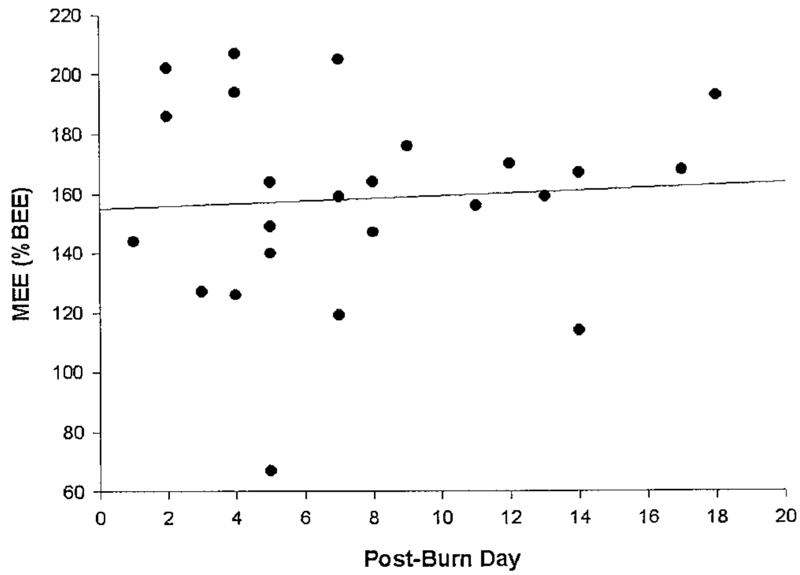

Figure 4. MEE (% of BEE via the Harris-Benedict equations) versus postburn days. No significant correlation MEE (%BEE) and postburn days was observed ($y = 0.44 \times +155$, $r^2 = .004$, p = NS). Sustained hypermetabolism was evident throughout the 18-day observation period.

Table 6. Methods used to estimate resting energy expenditure in thermally injured patients

Investigator, year	N	%BSAB mean ± SD, range	DPB mean ± SD, range	Predictive method
		Methods Based on Body Size as Body Surface Area		
Arturson, 1977[64]	16	43 ± 17 (13-66)	Serial (1-40)	1080 kcal/m^2/day
Belcher, 1989[65]	12	21 (15-45)	— (6-10)	1250 kcal/m^2/day
Gump, 1970[66]	8	43 ± 15 (25-65)	14 ± 7 (6-26)	1250 kcal/m^2/day (VO_2: 173 mL/m^2/min)
Zawacki, 1970[37]	12	41 ± 14 (17-68)	13 ± 5 (3-20)	1440 kcal/m^2/day
Aulick, 1979[67]	20	44 ± 22 (10-86)	12 ± 5 (7-18)	1536 kcal/m^2/day

Table 6. (continued)

Investigator, year	*N*	%BSAB mean ± SD, range	DPB mean ± SD, range	Predictive method
Wilmore, 1974[1]	20	45 ± 21 (7-84)	11 ± 6 (6-33)	1600 kcal/m^2/day
Epstein, 1963[68]	28	— (4-90)	— (1-5)	1630 kcal/m^2/day (VO_2: 225 mL/m^2/min)
Liljedahl, 1982[69]	16	56 ± 20 (30-90)	Serial (2-8)	1680 kcal/m^2/day
Bartlett, 1977*[47]	15	— (20-70)	Serial (1-55)	2160 kcal/m^2/day
Methods Based on Body Surface Area and Thermal Injury Descriptors				
Cunningham, 1989[39]	87	64 ± 18 (30-98)	38 (0-149)	BSAB > 30%: 1750 kcal/m^2/day
Neely, 1974[70]	7	46 ± 13 (36-75)	Serial —	Covered: 1680 kcal/m^2/day Open: 2520 kcal/m^2/day
Rutan, 1986[55]	7 6	67 ± 15 55 ± 7	Serial (4-30)	Early Excisional Tx: 1300 kcal/m^2/day Conservative Tx: 1600 kcal/m^2/day
Serog, 1983[40]	24	40 ± 15 (25-70)	2,3,6,9,12	$(1200 + (9.3 \times BSAB)) \times BSA\ (m^2)$
Xie, 1993[36]	75	— (5-98)	1,2,3,7,14,21,28	$(1000\ ) + (25 \times BSAB)$
Methods Based on the Harris-Benedict Equations (BEE)				
Barton, 1997[71]	14	26 ± 12 (7-48)	— (?-14)	Vent depend: 1 × BEE
Wolfe, 1987[72]*	18	74 ± 11 (60-95)	20 ± 19 (9-48)	1.23 × BEE
Schane, 1987[73]	21	31 ± 10 (21-81)	12 ± 7 (2-26)	1.4 × BEE
Garrel, 1993[50]	19	40 ± 16 (20-83)	17 ± 14 (4-59)	1.5 × BEE
Gore, 2000[74]	6	72 ± 11 —	8 ± 0 (8)	1.5 × BEE
Ireton, 1986[75]	17	43 ± 15 (26-79)	7 ± ? (2-26)	1.5 × BEE
Kelemen, 1996[52]	44	44 ± 19 (20-97)	11 ± 4 (6-21)	1.5 × BEE (at ambient temperatures of 32 to 35°C)
Turner, 1985[76]	35	34 ± 18 (10-75)	15 ± 15 (1-64)	1.73 × BEE - 886
Barr, 1969[46]	14	42 ± 22 (20-95)	Serial (1-21)	1.7 × BEE
Birke, 1959[77]	8	— (20-85)	— (1-10)	1.5 - 2 × BEE (used 1.75 × BEE for analysis)
Noordenbos, 2000[45]	24	44 ± ? (18-90)	Daily (1-42)	1.85 × BEE
"Common Practice"	—	—	—	2 × BEE
Long, 1979[78,79]	—	—	—	2.1 × BEE
Methods Based on the Harris-Benedict Equations (BEE) and Thermal Injury Descriptors				
Cunningham, 1989[39]	87	64 ± 18 (30-98)	38 ± 31 (0-149)	BSAB > 30% 2 × BEE

Table 6. (continued)

Investigator, year	*N*	%BSAB mean ± SD, range	DPB mean ± SD, range	Predictive method
Matsuda, 1987[41]	28	29 ± ? (8-58)	Serial —	11-30% BSAB: 1.35 × BEE 30-60% BSAB: 1.5 × BEE
Saffle, 1985[42]	29	35 ± ? (3-80)	10 ± ? (1-27)	BEE × (1.1 + 0.01 × BSAB)
Williamson, 1989[32]	—	—	—	BEE × Activity factor × Injury factor Activity factor: 1.2 = confined to bed 1.3 = out of bed Injury factor: 20-25% BSAB: 1.6 25-30% BSAB: 1.7 30-35% BSAB: 1.8 35-40% BSAB: 1.9 40-45% BSAB: 2.0 >45% BSAB: 2.1 (since this study examines formulas estimate REE, activity factors were not included in the analysis)
Yu, 1988[80]	12	36 ± 5 (10-60)	25 ± ? (8-50)	31 kcal/kg/d
"Common Practice"	—	—	—	35 kcal/kg/d
"Common Practice"	—	—	—	40 kcal/kg/d
		Methods Based on Weight and Thermal Injury Descriptors		
Curreri, 1974[31]	9	53 ± 5 (40-73)	25 ± ? (1-20)	(25 × WT) + (40 × BSAB)‡
		Multiple Variable Methods		
Allard, 1988[28]	23	39 ± 5 (7-90)	Serial Msmts	-4300 + 10.5 × BSAB + 0.23XEin + 0.84 × BEE - 11.4 Temp - 4.5 × DPB
Carlson[38]	62	45 ± 17 (12-91)	12 ± 3 (5-19)	BMR × (0.89142 + 0.01335 × BSAB) × BSA × 24
Cope, 1953[48]	11	— (20-68)	Serial (1-80)	1.2 - 1.8 × Aub-Dubois BMR[27] (used 1.5 × BMR for analysis)
Age/Gender adjusted	—	—	—	M: 25 kcal/kg × BMR factor + (40 × BSAB) F: 22 kcal/kg × BMR factor + (40 × BSAB) Where BMR factor = 20-40 years old: 1 40-50 years old: 0.95 50-60 years old: 0.90 75-100 years old: 0.80
Giatin, 1995[43]	23	35 ± 18 (10-75)	Weekly (?-21)	Fasting: -2358 + 1.45 × BEE + 18.48 × HR + 7.87 × BSAB Fed: -1013 + 0.95 × BEE + 10.35 × HR + 0.27 × caloric intake (kcal/d)
Harrison, 1964[81]	21	— (8-91)	— (1-10)	0-40% BSAB >40% BSAB male: 1150 kcal/m^2 per day 1625 kcal/m^2 per day female: 1100 kcal/m^2 per day 1550 kcal/m^2 per day

Investigator, year	*N*	%BSAB mean ± SD, range	DPB mean ± SD, range	Predictive method
Ireton-Jones, 1992†[82]	200	41 ± ? (3-84)	18 ± ? —	Vent dependent: 1925 - 10 × Age + 5 × WT + 281 × G + 292 × T + 851 × B Spont breathing: 629 × 11 × Age + 25 × WT - 609 × O
Milner, 1994[35]	20	47 ± 20 (21-88)	Serial (3-348)	(BMR × 24 × BSA) × (0.274 + 0.0079 × BSAB - 0.004 × DPB) + (BMR × 24 × BSA)
Wilmore, 1974[1]	20	45 ± 21 (7-84)	11 ± 6 (6-33)	(188.8 + (1.211 × BSAB) - (10.38 × AT) - (0.009274 × $BSAB^2$) + (0.1701 × AT^2)) × BSA × 24

*Included children with adults in the study.
†Included adolescents 14 years and older, trauma patients (23% of population), and other critically ill patients (44% in addition to thermally-injured patients (33%)
‡Energy expenditure not measured; recommended energy intake based on weight loss and clinical outcome
AT, ambient temperature °C; B, diagnosis of burn (1 = present; 0 = absent); BEE, basal energy expenditure as estimated by the Harris-Benedict equations[15]; BMR, basal metabolic rate (kcal/m^2 per hr) and can be calculated from the Fleisch formula for noninjured humans[63] or Aub and DuBois[27]; BSA, body surface area in m^2 [26]; BSAB, % body surface area burn; Ein, energy intake (kcal/day); G, gender (1 = male, 0 = female); HR, heart rate (beats per minute); Msmts, measurements; N, number of patients; O, Obesity above 130% of ideal body weight (1 = present; 0 = absent); PBD, post-burn days; T, diagnosis of trauma (1 = present, 0 = absent); Temp, body temperature (°C), Tx, therapy; VO_2, oxygen consumption and 5.04 kcal/L oxygen consumed; W, Watts (1 Watt = 0.83 kcal/hr); WT, weight (kg).

None of the methods had a 95% CI for error within 20% of MEE. Seven, or 15%, of the publications had a 95% CI error within a 20% to 25% of MEE whereas 54% of the publications (*n* = 25) had a method that resulted in a 95% CI for error that exceeded 30% of MEE (Fig. 6). Age of publication did not reveal any proportionate differences in precision between time groups (Fig. 6).

Of the most commonly used methods, the Curreri formula and its variations[31,32] markedly overestimated MEE (Table VII). Other common methods that significantly overpredicted measured REE included: 2 × the Harris-Benedict equations, 1600 kcal/m^2 per day, and 40 kcal/kg per day (Table VII). The Toronto formula[28] significantly underestimated measured REE. The most precise, unbiased methods for estimating REE in our population included the methods of Milner et al[35] at 10% to 22% for the 95% CI for error, Xie et al[36] at 12% to 24% for the 95% CI for error, and 1440 kcal/m^2 per day37 at 9% to 23% for the 95% CI for error. The “traditional 1.5 × the Harris Benedict equations” was unbiased and had a 95% CI for error ranging from 9% to 29%.

Table 7. Bias and precision of methods used to estimate resting energy expenditure in thermally injured patients

Method	Bias kcals/day 95% confidence interval	Precision (error) kcals/day mean ± SD	Precision (error) % of MEE mean ± SD (95% confidence interval)	p ≤ *
		Methods Based on Body Size as Surface Area		
1080 kcals/m^2/day[64]	-883 to -449	742 ± 427	25 ± 11 (21 to 30)	.001
1250 kcals/m^2/day[65,66]	-552 to -114	517 ± 369	18 ± 13 (13 to 24)	.01
1440 kcals/m^2/day[37]	-184 to 261	413 ± 366	16 ± 19 (9 to 23)	NS
1536 kcals/m^2/day[67]	2 to 451	434 ± 415	18 ± 22 (9 to 27)	.07
1600 kcals/m^2/day[1]	126 to 578	481 ± 455	20 ± 24 (11 to 30)	.01
1630 kcals/m^2/day[68]	241 to 697	550 ± 488	23 ± 26 (13 to 34)	.001
1680 kcals/m^2/day[69]	280 to 737	576 ± 500	24 ± 27 (14 to 35)	.001
2160 kcals/m^2/day†[47]	1202 to 1694	1448 ± 614	58 ± 36 (43 to 72)	.001
		Methods Based on Body Surface Area and Thermal Injury Descriptors		
BSAB > 30%: 1750 kcal/m^2/day[39]	-1176 to 254	716 ± 583	19 ± 28 (8 to 31)	.001
Covered: 1750 kcal/m^2/day Open: 2520 kcal/m^2/day[70]	-201 to 326	489 ± 434	19 ± 20 (11 to 27)	NS
Early Excis: 1300 kcal/m^2/day Conserv: 1600 kcal/m^2/day[55]	-265 to 233	457 ± 412	18 ± 20 (10 to 26)	NS
(1200 + (9.3 × BSAB)) × BSA[40]	7 to 472	489 ± 386	19 ± 19 (12 to 27)	.08
(1000 kcals/m^2/day) + (25 × BSAB)[36]	-145 to 335	488 ± 346	18 ± 15 (12 to 24)	NS
		Methods Based on the Harris-Benedict Equations (BEE)		
>30 BSAB: 2 × BEE[39]	-1283 to 647	925 ± 921	25 ± 42 (8 to 42)	.001
11-30% BSAB: 1.35 × BEE 30-60% BSAB: 1.5 × BEE[41]	-1032 to -124	870 ± 919	31 ± 33 (18 to 44)	.05
BEE × (1.1 + 0.01 × BSAB)[42]	-432 to 139	546 ± 471	20 ± 21 (12 to 28)	NS
20-25% BSAB: 1.6 × BEE 25-30% BSAB: 1.7 × BEE 30-35% BSAB: 1.8 × BEE 35-40% BSAB: 1.9 × BEE 40-45% BSAB: 2.0 × BEE >45% BSAB: 2.1 × BEE[32]	213 to 884	724 ± 686	29 ± 34 (15 to 42)	.01
		Methods based on Weight		
31 kcal/kg/day[80]	-572 to 93	626 ± 586	23 ± 29 (12 to 35)	.05
35 kcal/kg/day	-270 to 446	569 ± 686	23 ± 36 (8 to 37)	NS

40 kcal/kg/day	107 to 889	640 ± 888	27 ± 46 (9 to 45)	.01
Methods Based on Weight and Thermal Injury Descriptors				
(25 × WT) + (40 × BSAB)[31]	373 to 1098	899 ± 736	35 ± 35 (21 to 49)	.001
(25 × WT) + (40 × BSAB) (maximum limit of 50% BSAB for BSAB ≥ 5)[32]	302 to 966	863 ± 731	32 ± 34 (19 to 45)	.001
Multiple Variable Methods				
-4300 + 10.5 × BSAB + 0.23XEin 0.84 × BEE - 11.4 × Temp - 4.5 × DPB[28]	-876 to -273	726 ± 601	26 ± 21 (17 to 34)	.001
BMR × (0.89142 + 0.01335 × BSAB) × BSA × 24[38]	-179 to -661	554 ± 476	19 ± 15 (13 to 25)	.01
1.5 × Aub-Dubois BMR[48]	-290 to 168	435 ± 366	16 ± 17 (10 to 23)	NS
M: 25 kcal/kg × BMR factor + (40 × BSAB) F: 22 kcal/kg × BMR factor + (40 × BSAB) Where BMR factor = 20-40 years old: 1 40-50 years old: 0.95 50-60 years old: 0.90 75-100 years old: 0.80[32]	522 to 768	863 ± 731	33 ± 34 (29 to 38)	.01
Fasting: -2358 + 1.45 × BEE + 18.48 × HR + 7.87 × BSAB Fed: -1013 + 0.95 × BEE + 10.35 × HR + 0.27 × caloric intake (kcal/day)[43]	-60 to -640	688 ± 399	26 ± 18 (18 to 33)	.01
0-40% BSAB: male: 1150 kcals/m^2/day female: 1100 kcals/m^2/day >40% BSAB: male: 1625 kcals/m^2/day female: 1550 kcals/m^2/day[81]	241 to 697	550 ± 488	23 ± 26 (13 to 34)	.001
Vent dependent: 1925 - 10 × Age + 5 × WT + 281 × G + 292 × T + 851 × B[82]‡	-67 to 546	458 ± 356	20 ± 20 (12 to 28)	NS
Spont breathing: 629 - 11 × Age 25 × WT - 609 × O[82]‡	-804 to 346	823 ± 598	30 ± 29 (19 to 42)	NS
293 + 4.5 × BSAB + 1.3 × BEE - 10.5 × DPB[44]	-339 to 194	475 ± 464	18 ± 22 (9 to 27)	NS
(BMR-Fleisch × 24 × BSA) × (0.274 + 0.0079 × BSAB - 0.004 × DPB) + (BMR-Fleisch × 24 × BSA)[35]	-391 to 66	448 ± 379	16 ± 15 (10 to 22)	NS
(188.8 + (1.211 × BSAB) - (10.38 × AT) - (0.00974 × $BSAB^2$) + (0.1701 × AT^2)) × BSA × 24[1]	242 to 856	653 ± 417	27 ± 22 (18 to 36)	.001

*Significance between measured and predicted resting energy expenditure by respective method.
†Included children with adults in the study.
‡Included adolescents 14 years and older, trauma patients (23% of population) and other critically ill patients (44%) in addition to thermally injured patients (33%)

B, diagnosis of burn (1 = present; 0 = absent); BEE, basal energy expenditure as estimated by the Harris-Benedict equations[15]; BMR, basal metabolic rate (kcals/m^2/hr) and can be calculated from the Fleisch formula for noninjured humans[63] or Aub and DuBois[27]' BSA, body surface area in m^2 [26]; BSAB, % body surface area burn; Conserv, conservative (late excisional therapy); DPB, days post burn; Ein, energy intake (kcals/day); Excis, excisional therapy; G, gender (1 = male; 0 = female); HR, heart rate (beats per minute); Msmts, measurements; N, number of patients; O, Obesity above 130% of ideal body weight (1 = present; 0 = absent); PBD, post-burn days; T, diagnosis of trauma (1 = present; 0 = absent); Temp, body temperature (°C); Tx, therapy; VO_2, oxygen consumption and 5.04 kcals/L oxygen consumed; W, Watts (1 Watt = 0.83 kcal/hr); WT, weight (kg).

Discussion

Thermally injured patients are among the most hypermetabolic of all patients seen in clinical practice. As a result, extensive research regarding the pathogenesis and nature of the hypermetabolism has been conducted over the past few decades.[1-3] Unfortunately, the abundance of literature and predictive methods for estimating REE may have led to further confusion rather than clarity for clinicians involved in the management of these patients. The intent of this investigation was to evaluate predictive performance as assessed by bias and precision of various published and common methods used in clinical practice for estimating REE in thermally injured adults. As a result of this analysis, it was anticipated that the most accurate, unbiased methods for estimating REE could be identified for clinicians who do not have access to indirect calorimetry to use in their practice.

Although this study superficially seems redundant compared with the abundance of literature, it is novel in that we have evaluated the predictive performance of numerous methods published from 1953 to 2000 that may be used by some clinicians today to estimate REE in thermally injured patients. Many of the previous studies may have only compared the results of their study with a few common methods or reported their findings of MEE and associated determinants. In addition, some of these studies examining accuracy of published methods are erroneous as they simply examined the correlative relationship between the previously published methods and MEE.

Our data indicate that about one-third of the publications provide methods that are biased toward over-predicting MEE, whereas about one-fifth of the methods were biased toward under-predicting MEE. In addition, the older literature was biased toward over-predicting MEE; however, we are not the first to observe these differences.[38] None of the published methods was precise or accurate as defined by a 95% CI for error within 15% of MEE. None of the methods had a 95% CI for error within 20%. It must be noted that the intent of some of the publications summarized in Table VI might not have been to develop a predictive equation. Instead, it might have been the investigators' purpose to describe the mathematical relationship regarding various elements that potentially influenced MEE in their population. Since these mathematical relationships might be used by some clinicians to estimate energy requirements of thermally-injured patients, all articles found in the literature search describing MEE and relationships with potential determinants of MEE in adult patients were included in the analysis.

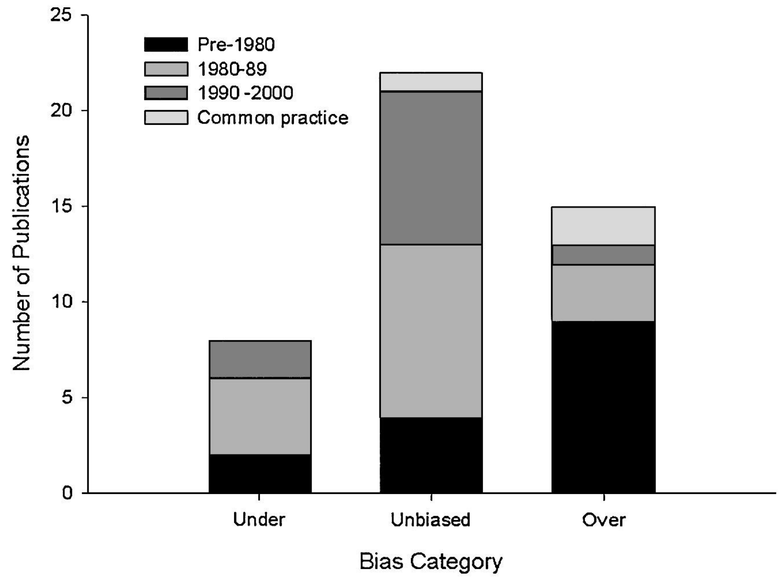

Figure 5. Bias of methods in estimating MEE. Thirty-three percent of the 46 publications had methods that were biased toward overpredicting MEE whereas 19% of the publications consistently underpredicted MEE. About one-half of the publications (48%) contained methods that were unbiased. The pre-1980s articles had proportionately more methods that were biased toward overpredicting MEE compared with the 1990 to 2000 publications ($p = .01$) and 1980 to 90 publications ($p = .05$).

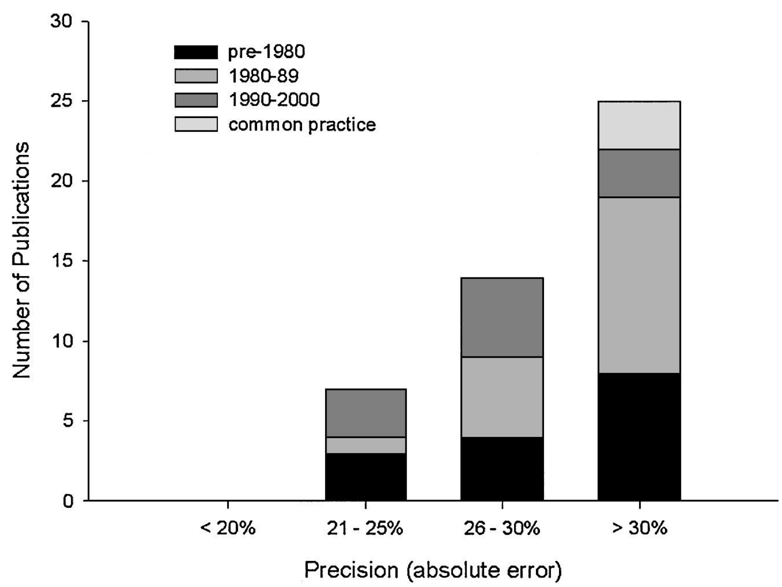

Figure 6. Accuracy of methods in estimating MEE. None of the papers contained methods that were found to be precise as defined by a 95% confidence interval (CI) within 15% of MEE. Seven (15%) publications had methods with a 95% CI that was within 20% to 25% of MEE. Over one-half (54%) of the publications' methods exceeded 30% error.

The exact mechanisms for the observed hypermetabolism associated with thermal injury are not entirely clear; however, there are numerous contributing factors, including extent of thermal injury, days postburn injury, thermogenesis of nutrients, ambient temperature, early wound excision and grafting, and implementation of early enteral nutrition support. The extent of thermal injury (%BSAB) has been suggested as a primary influencing factor by numerous investigators and, as a result, has been included in their predictive methods.[1,28,31,32,35,36,38-44] The more recent publications suggest a maximum MEE of about twice that of basal.[3,35,36,38] Our data corroborate these findings as none of the patients exceeded hypermetabolism beyond 207% of predicted by the Harris Benedict equations. In addition, our data confirm previous studies that illustrate ≥30% to 40% variability in MEE for any given level of BSAB (Fig. 2).[39,45] Days post-thermal injury may also be an important influencing factor.[28,35,42,44] Our data are in agreement with others in that patients with thermal injury demonstrate a sustained hypermetabolic plateau which may persist for 20 days or longer postburn (Fig. 4).[1,35,36,42,44,46-48]

The thermogenic effect of nutrient administration upon REE is another consideration in evaluating MEE. Our patients were measured during the continuous infusion of enteral tube feeding or parenteral nutrition but at least 2 hours postprandial in patients with limited *ad libitum* oral intake. The mean caloric intake from the continuous nutrient infusion at the time of the measurement was 65% of the MEE (Table IV). Continuous intragastric feeding in healthy subjects does not appreciably change MEE above fasting levels until the patients are overfed at over 2 × MEE and MEE increases only by about 10%.[49] Additionally, the thermogenic effect of continuous nutrient administration does not occur in thermally-injured patients who are already substantially hypermetabolic (MEE of ~150% of BEE or greater).[50] In contrast, the Toronto group found a significant thermogenic effect with an increase in REE by 34%.[28] However, the degree of hypermetabolism for their thermally-injured population was only 7% above the basal energy expenditure in the fasted state. Given that 80% of our population were hypermetabolic at ≥140% of the BEE and most fed less than their MEE at the time of the IC measurement (mean, 65% of MEE), it is unlikely that caloric intake substantially altered the MEE.

Ambient temperature may also be a contributing factor to REE post-thermal injury.[51,52] Patients in our study were kept at a mean ambient temperature of 23.3°C, which was similar to ambient temperatures reported by others.[39,47] Because the majority of the patients (n = 20, or 83% of the population) had 20% to 50% BSAB and their wounds were covered, it is unlikely that ambient temperature had a profound confounding effect on our measurements.

A major change in the management of thermally injured patients over the past couple of decades is the implementation of early burn wound excision and grafting. This management has resulted in reduced wound infection, decreased hospital stay, and may increase survival.[53] Our data (Table V) are in agreement with other clinical studies that suggest no effect from early burn wound excision and closure and that the hypermetabolism after burn injury is sustained.[45,54,55]

Early enteral nutrition support is another new advancement in the metabolic management of the thermally-injured patient. It has been reported in animal models that early enteral feeding can reduce postburn hypermetabolism and catabolism[56,57]; however, the data are conflicting.[58,59] Clinical data are lacking. We observed hypermetabolism in our patients despite early nutrition support, and these data are consistent with others.[45]

Improvements in analgesia may also play a role in ultimately reducing the hypermetabolic response[60,61] and could partially explain, along with the other advancements in the management of the thermally injured patient, the differences in current literature citations regarding energy expenditure compared with the older literature. Finally, differences in REE between our population and those described in the pre-1980s may also be partially attributable to improved techniques and technology in IC for acquiring a meaningful MEE.

In planning a nutritional regimen, estimation of total energy expenditure from MEE is necessary as the total caloric intake should meet total energy requirements. In critically ill, mechanically ventilated, non-thermally injured patients, total energy expenditure is no greater than 5% to 10% above REE.[62] However, thermally injured patients undergo activities and painful procedures, such as physiotherapy and dressing changes, which may alter their energy needs. Total energy expenditure averages 6% to 18% above the MEE; however, some studies measured their patients considerably later after thermal injury than when we measured our patients in this study.[4,60] As a result, their patients were less hypermetabolic and also exhibited the greatest difference between total energy expenditure and REE.[4,60]

In addition to bias and accuracy, practicality is another consideration in selecting a method for use in estimating energy requirements of a thermally injured patient. Of the 3 most accurate, unbiased methods identified in this study, the method of Milner et al[35] involves use of the Fleisch standards for calculation of basal metabolic rate. Given that this method for estimating basal metabolic rate is not common and since the Milner method additionally uses body surface area, body surface area burn, and days postburn in a regression equation, this difficulty in calculation detracts from its routine use in clinical practice. The method of Xie[36] entails use of only body surface area and body surface area burn, was derived from a reasonable sample size (75 patients), and seems particularly attractive for clinical practice. However, the equation was derived from Chinese adults who may differ in body size than their Western counterparts. The method of Zawacki (1440 kcal/m^2 per day), based on a fixed kilocalories per body surface area, was also among the few methods that performed better than the majority of the other methods. Finally, the "conventional 1.5 times the Harris Benedict equations" was also unbiased but should be used with caution as this method is associated with more error (mean 19%, CI from 9% to 29%) than the 3 other methods discussed. Given these choices, the methods of Xie et al36 and Zawacki et al[37]are the most accurate, unbiased, practical methods for estimating energy expenditure in our thermally-injured population.

This study may be limited in that our population may not exactly match the clinical characteristics with the populations of all of the published studies that were evaluated.

Comparison of our population with other study populations from which these formulas were derived might be difficult given the lack of descriptive information for some of the studies. Some studies may have had a different proportion of patients with infection, ventilator-dependency, presence of inhalation injury or enteral versus parenteral feeding, different timing of excision and grafting, and other factors that can potentially alter energy expenditure. Yet, our study population may share numerous attributes of other populations, including presence of critical illness (intensive care unit patients) and significant thermal injury, patient stability at the time of the measurement, the majority of the population being young to middle-age adults, and timing of the measurement postinjury. It is imperative that our patient population be reviewed to ascertain if our population is comparable with your respective institutions population before implementation of our recommendations.

Conclusion

Thermally injured patients are variably hypermetabolic and their energy requirements cannot be precisely predicted. It is recommended that REE be measured in thermally injured patients. In the event that indirect calorimetry is not available, the methods of Milner et al,[35] Xie et al,[36] and Zawacki et al (1440 kcal/m per day)[37] were the most accurate unbiased methods of those published in the literature. The latter 2 methods can be calculated with greater ease for the practicing clinician. Due to the lack of precision of these methods and our goal of providing optimal nutrition support without overfeeding, an adjustment factor for estimating the difference between REE and total energy expenditure is not recommended when using these estimation techniques.

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