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A Comparative Analysis of Equations to Estimate Patient Energy Requirements Following Cardiopulmonary Bypass for Correction of Congenital Heart Disease

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Abstract

Background: No consensus exists on the optimal method to estimate resting energy expenditure (REE) in critically ill children following cardiopulmonary bypass (CPB). This study assesses the accuracy of REE estimation equations in children with congenital heart disease following CPB and tests the feasibility of using allometric scaling as an alternative energy prediction equation. *Methods:* A retrospective analysis of a pediatric cohort following CPB (n = 107; median age 5.2 months, median weight 5.65 kg) who underwent serial measures (median 5 measurements) of REE using indirect calorimetry for 72 hours following CPB. We estimated REE using common estimation methods (Dietary Reference Intake, Harris Benedict, Schofield, World Health Organization [WHO]) as well as novel allometric equations. We compared estimated with measured REE to determine accuracy of each equation using overall discrepancy, calculated as a time-weighted average of the absolute deviation. *Results:* All equations incorrectly estimated REE at all time points following CPB, with overestimation error predominating. WHO had the lowest discrepancy at 10.7 ± 8.4 kcal/kg/d. The allometric equation was inferior, with an overall discrepancy of 16.9 ± 10.4. There is a strong nonlinear relationship between body surface area and measured REE in this cohort, which is a key source of estimation error using linear equations. *Conclusion:* In a cohort of pediatric patients with congenital heart disease following CPB, no currently utilized clinical estimation equation reliably estimated REE. Allometric scaling proved inferior in estimating REE in children following CPB. Indirect calorimetry remains the ideal method of determining REE after CPB until nonlinear methods can be derived due to overestimation using linear equations. (*JPEN J Parenter Enteral Nutr.* 2020;44:444–453)

Keywords

calorimetry; cardiopulmonary bypass; congenital heart disease; energy; pediatric

Clinical Relevancy Statement

The ideal method to estimate energy needs in children following cardiopulmonary bypass (CPB) continues to be unknown. This novel use of allometric scaling to determine energy needs in critically ill pediatric patients appears inferior to typical equations in its current form. This demonstration of the nonlinear relationship between patient size

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and discrepancy in prediction equations illustrates the fundamental limitation with current methods in determining energy needs in post-CPB pediatric patients.

Introduction

Critical illness is associated with metabolic derangements that pose challenges for medical providers in estimating patient needs in order to provide appropriate fluid management and energy balance.[1] Providing energy and nutrition to minimize catabolism and promote growth and healing is a crucial pillar of supportive critical care medicine. Inaccurate fluid and caloric management is associated with preventable patient morbidity, with studies showing that underfeeding is associated with decreased wound healing and delayed return of immune function.[2] Conversely, overfeeding during recovery is common and contributes to difficulty liberating patients from mechanical ventilation and the potential development of a hypermetabolic inflammatory state.[3]

Resting energy expenditure (REE) measured via indirect calorimetry is the clinical gold standard used to guide nutrition management. The majority of children in a pediatric intensive care unit (PICU) meet the American Society for Parenteral and Enteral Nutrition recommendation to use indirect calorimetry to determine nutrition needs.[4,5] Despite this endorsement, many PICUs lack the required technology or patients are unable to have accurate measurements obtained due to modifiers like high oxygen requirements, high positive end-expiratory pressure (PEEP) requirements or the presence of chest tubes.[4] As a result, surrogate methods to estimate patient REE have been used, including the Harris-Benedict (HB),[5] the World Health Organization (WHO),[6] Schofield,[7] and the Dietary Reference Intake (DRI)[8] formulas. Recently published consensus guidelines suggest use of Schofield or WHO as the primary estimation method used for these patients; however, numerous studies have demonstrated poor concordance between equations as well as inaccuracy in estimating true REE, and the guidelines acknowledge these shortcomings. [4-6,11] The clinical imperative and these accumulated observations about the inadequacy of current methods support the need for improved methods of energy estimation.

Repair of congenital heart disease requiring cardiopulmonary bypass (CPB) alters energy requirements.[9] Extracorporeal support with a CPB circuit is proinflammatory as a result of the interaction between the formed elements of blood and circuit components.[10] Perioperative steroid administration and other anesthetic practices aim to counteract these effects by attenuating the stress response. Subsequent medical management with interventions like temperature control, ventilator support, and neuromuscular blockade further alter REE, but the cumulative magnitude of interventions on REE can be difficult to predict.[9,11] Due to this complex milieu, there is no consensus on the ideal equation for estimating REE in pediatric patients following CPB. Existing studies have shown poor performance of these estimates overall.[12]

In this study, the utility of a novel method of estimating REE is assessed compared with gold standard indirect calorimetry in a cohort of critically ill children following CPB. An additional objective of this study was to perform a comparative analysis of the accuracy of this novel methodology relative to other currently used clinical equations with reference to indirect calorimetry measurement. Finally, subgroup analyses were done to ascertain whether specific patient characteristics modified the accuracy of estimation of REE in this patient population.

Objectives

1) Determine whether equations based upon principles of allometric scaling can be adapted and used accurately to estimate REE in a critically ill patient population.
2) Compare REE estimates generated using the allometric method to gold standard measurement of REE via indirect calorimetry as well as the relative accuracy of these estimates to commonly used clinical equations (WHO and Schofield)
3) Assess whether specific patient characteristics (age, weight, single-ventricle heart disease, CPB strategy, or neuromuscular blockade) significantly affect the accuracy of equations used to estimate REE. The goal of this aim is to determine whether there are subpopulations at particular risk of inaccurate REE estimation.

Methods

Study Design

This is a secondary analysis of a prospective cohort trial of pediatric patients after CPB examining postoperative glucose metabolism and systemic inflammation.[9] A data-sharing agreement and institutional review board waiver was obtained for this study from both the Toronto Hospital for Sick Children and Ann & Robert H. Lurie Children's Hospital of Chicago. Consecutive patients undergoing CPB were recruited and included if they were born at term (>36 completed weeks gestation), intubated at PICU admission, and had indwelling arterial and central venous lines for blood sampling. Those who weighed under 2.5 kg, had a diagnosis of diabetes or metabolic disease, preoperative renal and/or liver dysfunction, undergoing heart transplantation, or had >10% leak around the endotracheal tube were excluded.

Respiratory mass spectrometry (AMIS 2000, Innovision A/S, Odense, Denmark) was connected in line with the

patient ventilator to continuously measure volumetric oxygen consumed (VO_2) and volumetric carbon dioxide produced (VCO_2). REE was then calculated using the modified Weir equation at predetermined intervals: PICU admission and every 6 hours following CPB.

The methodology for estimation of REE introduced in this study has never been assessed for clinical utility in critically ill patient populations. It is based on principles of allometric scaling and describes a proportionate scaling relationship of metabolic processes to body surface area (BSA) in exothermic organisms (like mammals) that takes into consideration the fractal network of vessels and body cellular mass rather than simply total mass, in kilograms, of the organism. To predict REE and other metabolic processes, the allometric framework is operationalized by mass-based constants (k) and Brody's number, B (mass, *kg,* to the three-fourths power). Equations derived using this methodology have already been successfully applied and validated in healthy pediatric patients undergoing closed circuit anesthesia. This method accurately estimates VO_2, VCO_2, and then REE, using the modified Weir equation:[13]

$$\mathrm{REE} = [\mathrm{VO_2}\,(3.941) + \mathrm{VCO_2}\,(1.11)] \times 1.44$$

This equation has never been applied to the estimation of energy requirements in critically ill children.[14,15]

Predictive Equations for REE

Estimated REE was calculated using the allometric scaling framework in which predetermined weight-based constants (k_1–k_4) are multiplied by Brody's number, defined as $B = x^{3/4}$, where x = mass in kilograms, to determine dependent variables VCO_2, VO_2, free water need, and cardiac output. The modified Weir Equation is then completed to determine REE prediction. This supplementary material was removed on the second review by recommendation of the reviewers. The calculations were completed using a typical respiratory quotient (RQ) of 0.8 and then also calculated using an RQ of 0.89, which has been shown in the literature to be a better assumed RQ in critically ill populations.[16-19] Estimated REE was also determined according to the DRI, Schofield, WHO, and then more rarely used Harris-Benedict equations for each time point. Each method of estimation was calculated for each patient in a Microsoft Excel operator based on age, sex, weight, and height. Stress factors (1.2 x REE, based on institutional dietitian practice) were added to the final values of the estimations as would typically have been utilized by the clinical nutritionists in our unit for the average patient. Additional demographic factors were collected, including but not limited to age, sex, weight, height, single or biventricular heart disease, and comorbid diseases.

Outcomes

The goal of this analysis was assessment of the accuracy of a novel equation relative to other commonly used equations to estimate REE when compared with gold standard indirect calorimetry measurement. The clinical effects of inaccuracy in estimation of REE on patient course and outcome were not analyzed. There was a median of 5 measurements of energy expenditure obtained for each subject. To account for the variation in measurements from 1 patient to another, the outcome considered in the analysis was the overall discrepancy calculated as a time-weighted average of the absolute deviations between measured and estimated REE across serial measurements.

Statistical Analysis

Clinical characteristics were summarized in medians and interquartile range (IQR) for continuous variables and frequencies and proportions for binary and polytomous variables. Next, for each REE estimation method, absolute differences were used to assess deviation of estimating REE equations from the indirect calorimetry–measured REE at each time point. The equations were then ranked by comparing the discrepancy of each estimated REE, overall and by hour. The results of this comparison were summarized graphically.

Univariable analysis was conducted comparing overall discrepancy in the following predetermined subgroups: age (neonate, infant, toddler vs child), weight (2.5–5 kg vs >5 kg), use of CPB and deep hypothermic circulatory arrest (DHCA), use of postoperative pharmacological paralytic agents, and ventricular physiology (biventricular or univentricular). The results of the comparisons were summarized in tables. Between-group differences were assessed using either *t*-tests for two groups (eg, CPB vs DHCA) or *F*-tests for >2 groups (ie, age groups). In addition, we explored the association of BSA and CPB duration with the overall discrepancies using parametric linear regression and nonparametric locally estimated scatterplot smoothing (LOESS) methods.

Multivariable linear regression was applied to assess the association between clinical characteristics and the discrepancies between measured and calculated REE equations; the log-transformed time-weighted difference was used as the outcome measure in the regression model. Independent variables included age group, sex, ventricle type, BSA, weight, CPB minutes, DHCA use, and if the patient was ever exposed to neuromuscular blockade. Restricted cubic splines were applied for continuous independent variables to quantify the nonlinear association with the outcome. The results of the model were summarized in terms of regression-adjusted coefficients with their corresponding 95% confidence intervals and *P*-values, which were evaulated

Table 1. Patient Population.

Clinical characteristics of study participants	N	Statistic
Age (months)	107	5.2 (0.8–10.7)
Age group	107	
Neonate (<28 days)		28 (26%)
Infant (29 d–12 months)		56 (52%)
Toddler (1–5 years)		14 (13%)
Child (>5 years)		9 (8%)
Male	107	59 (55%)
Ventricle type	107	
Biventricular		94 (88%)
Single ventricle		13 (12%)
Weight (kg)	107	5.65 (3.92–7.70)
Height (cm)	107	70.01 (58.14–81.26)
Body surface area (m^2)	107	0.41 ± 0.30
Inotrope score post-operatively	105	0.5 ± 2.0
Inotrope score pre-operatively	105	0.0 (0.0–0.0)
Cardiopulmonary bypass time (min)	107	134 ± 61
Deep hypothermic circulatory arrest	107	19 (18%)
Length of intubation (days)	107	1 (1–5)
Days in ICU	107	4 (2–9)
Cardiac output at respiratory quotient 0.8 (L/min/kg)	107	3.33 ± 0.30

cm, centimeter; ICU, intensive care unit; kg, kilogram; m, meter.

using *t*-statistics based on the robust estimates of standard errors.

All statistical analyses were assumed with the significance level of 5% and performed using R v3.4.1.

Results

A total of 107 patients were studied, of whom 55% were male (N = 59) with a median (IQR) age of 5.2 (0.8–10.7) months (Table 1). The median number of indirect calorimetry measurements per patient was five. Patients in this study had a median REE on the lower end of previously reported values for patients following CBP surgery at 46.5 kcal/kg/d.[20,21] Measured REE trends lower over the first 24 hours and then remained relatively stable from hour 24 to 72 (Figure 1). REE was highest at 6 hours following separation from CPB.

Comparison of Typical Estimation Equations

Table 2 provides the overall absolute discrepancy from the measured values for each estimation method. All equations overestimated REE when compared to the gold standard measurement at all time points. Among the estimation methods, the WHO equation, the Schofield equation, and the allometric scaling methodology with an assumed RQ of 0.8 have the least discrepancy from measured REE overall. Given the significant overestimation found when comparing DRI and HB methods and recent guidelines cautioning against their use in pediatric ICU patients, these methods were excluded from further study.

Subgroup Analysis

The univariate analysis of subgroups is described in Table 3. The largest discrepancies between estimated and measured REE occurred in neonatal patients, and the smallest discrepancies were observed in children (ie, age of 5 years or older). Similarly, all estimation methods except for WHO had larger absolute discrepancies in patients with weight ≤5 kg than those >5 kg. The WHO equation had the lowest discrepancy in the patients ≤5 kg. However, in patients >5 kg, Schofield and the allometric equation with RQ = 0.8 performed best. No significant difference was seen in the magnitude of discrepancy between estimated REE vs measured REE in patients with biventricular and univentricular heart disease. Greater absolute discrepancies between estimates of REE and measured values were seen in patients exposed to DHCA when compared with standard CPB alone. Patients exposed to paralytic medication were found to have a significantly larger discrepancy with allometric methods but not with Schofield or WHO.

Graphical representation of univariate analysis of BSA vs overall discrepancy using both parametric linear regression and nonparametric LOESS methods are shown in Figure 2. The results showed a strong nonlinear association of BSA with overall discrepancy. Figure 2 also demonstrates the effect of increasing duration of CPB on the accuracy of estimated REE in the postoperative period using both parametric linear regression and the nonparametric LOESS method. The results showed a strong nonlinear association of CPB time with measurement accuracy, with the greatest discrepancy measured around a CPB time of 160 minutes.

Results of the multivariable regression model of log-transformed overall discrepancy for allometric methods are displayed in Table 4. The overall discrepancies after adjustment for covariates for both allometric at RQ 0.8 and 0.89 increased with age (overall $P = 0.089$ [allometric at RQ 0.8] and 0.011 [allometric at RQ 0.89]). The regression-adjusted nonlinear association of BSA was statistically significant ($P < 0.001$) for both metrics. As can be seen in Figure 3, the overall discrepancy decreased as BSA increased, and the reduction was most rapid when BSA increased from 0.25 to 0.6. The regression-adjusted nonlinear association of CPB time was significant (overall $P = 0.003$ [allometric at RQ 0.8] and 0.019 [allometric at RQ 0.89]). The inverted U shape of the nonlinear association suggests that the overall discrepancies peaked when CPB was between 120 and 160 minutes.

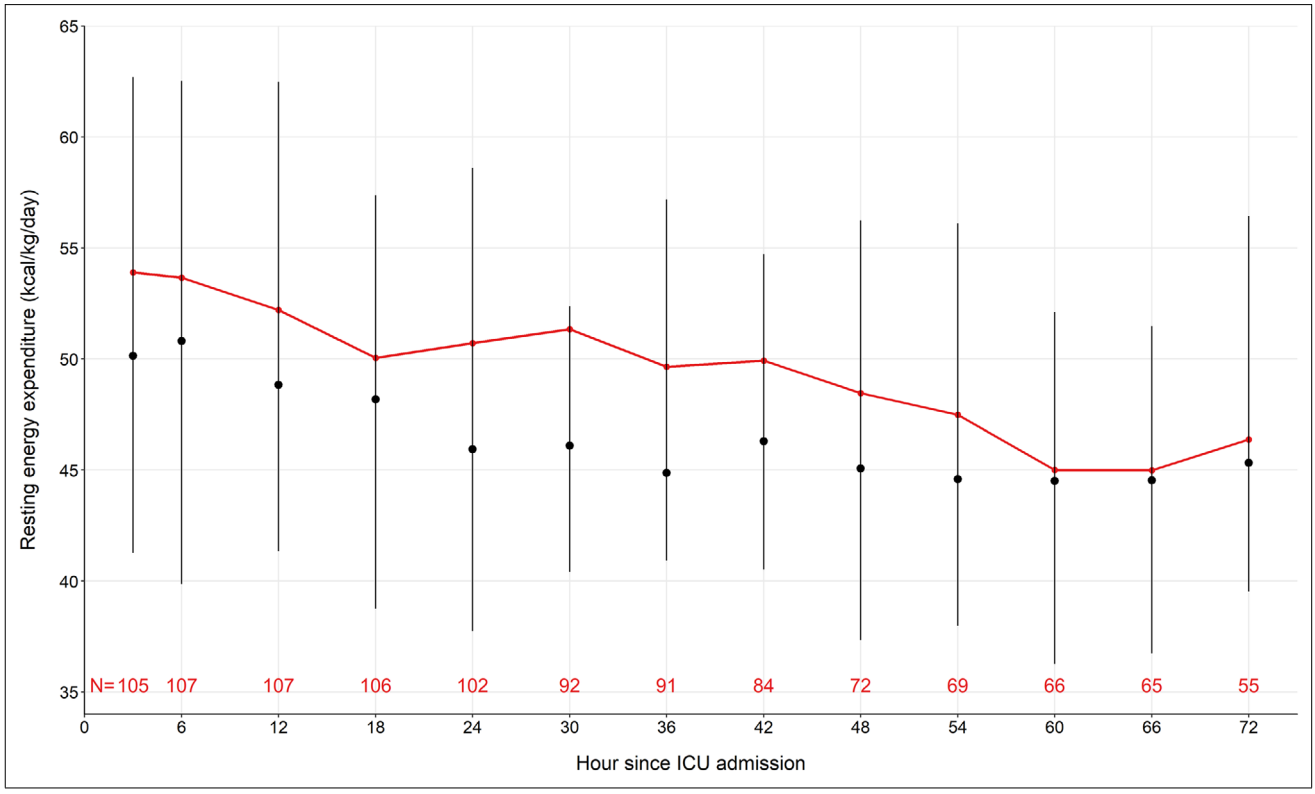

Figure 1. Measured patient REE over the first 72 hours in the pediatric ICU. Red shows the mean of REE, and black shows median REE at each time point. The error bars represent the interquartile range of the REE. ICU, intensive care unit; REE, resting energy expenditure.

Table 2. The Overall Discrepancy (kcal/kg/d) of Each Estimation Method Was Summarized Without Stress Factors and With Stress Factors Included in Calculations.

Standardized absolute discrepancy without stress factors		
	N	kcal/kg/d
Allometric at respiratory quotient 0.8	107	16.9 ± 10.4
Allometric at respiratory quotient 0.89	107	20.3 ± 13.4
Schofield	107	11.3 ± 7.4
WHO	107	10.7 ± 8.4
Harris-Benedict	107	64.9 ± 57.0
Standardized absolute discrepancy with stress factors		
Schofield	107	18.5 ± 9.5
WHO	107	16.7 ± 8.5
DRI	107	55.2 ± 28.4

DRI, dietary reference intake; WHO, World Health Organization.

Discussion

The methodology based upon allometric scaling principles proved inferior to the best performing equations currently being used to guide practice. The assumption was tested that adapting the allometric equation to assume an RQ of 0.89 would provide greater precision in this population, as this has previously been shown to be a more accurate RQ when directly measured in critically ill children.[9] However, the allometric equations using a typically assumed RQ = 0.8 proved to be more accurate. The paradoxical finding of a lack of improved precision with biologically plausible modification of the allometric scaling methodology suggests that this equation in its current form is not the solution to improved energy estimation in critically ill patients. In this study, although not an equation frequently used in the cardiac population, the WHO equation performed best overall and best in the subgroup of patients weighing <5 kg. The absolute discrepancies associated with each method evaluated do not support the use of DRI, Harris-Benedict or stress factors in this patient population, as these methods overestimated REE to such a degree that we removed them from subsequent analysis.

The key finding of this study is the nonlinear relationship between BSA and measured REE. All of the available equations used to estimate REE assume a linear relationship between BSA, or its covariates of weight and height, and this is a fundamental barrier to consistent and accurate performance of the available equations in this patient cohort.

Table 3. The Absolute Discrepancy (kcal/kg/d) of Each Estimation Method Was Summarized for the Univariate Analysis.

	N	Allometric at RQ 0.8	Allometric at RQ 0.89	Schofield	WHO
Weight					
≤5 kg	47	24.6 ± 8.9	31.3 ± 10.6	11.9 ± 6.9	10.3 ± 8.7
>5 kg	60	10.8 ± 7.0	11.7 ± 8.1	10.8 ± 7.7	11.0 ± 8.3
P-value		<0.001	<0.001	0.44	0.65
Age cohort					
Neonate	28	26.8 ± 8.5	33.9 ± 9.9	12.1 ± 6.8	10.3 ± 8.5
Infant	56	14.6 ± 8.5	17.8 ± 11.5	11.1 ± 6.9	10.8 ± 8.0
Toddler	14	10.9 ± 9.5	10.5 ± 7.6	12.7 ± 9.7	12.9 ± 10.2
Child	9	9.2 ± 6.8	9.0 ± 6.1	7.7 ± 7.9	7.7 ± 7.9
P-value		<0.001	<0.001	0.50	0.59
Heart Disease					
Single	13	19.1 ± 13.9	21.7 ± 17.7	15.2 ± 8.3	14.9 ± 10.1
Biventricle	94	16.6 ± 9.9	20.1 ± 12.8	10.7 ± 7.1	10.1 ± 8.1
P-value		0.54	0.76	0.082	0.125
Bypass					
Standard	88	15.2 ± 9.8	18.2 ± 12.7	10.5 ± 7.2	10.0 ± 8.2
DHCA	19	24.5 ± 10.2	30.2 ± 12.6	15.0 ± 7.1	13.7 ± 9.2
P-value		0.001	<0.001	0.018	0.125
Paralysis					
Never	61	14.9 ± 10.3	17.3 ± 12.9	11.1 ± 7.7	10.9 ± 8.4
Ever	46	19.5 ± 10.1	24.4 ± 13.1	11. 5 ± 6.9	10.4 ± 8.5
P-value		0.024	0.006	0.82	0.74

DHCA, deep hypothermic circulatory arrest; RQ, respiratory quotient; WHO, World Health Organization.

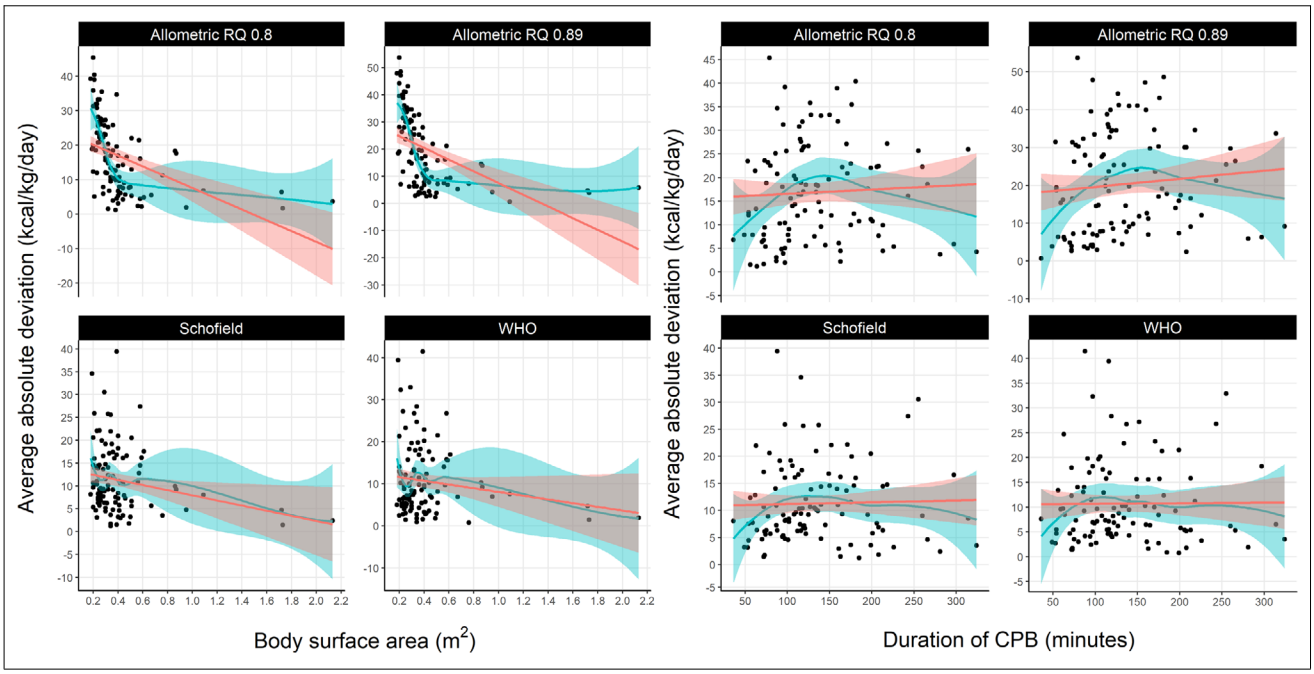

Figure 2. The univariate/crude association between the standardized absolute discrepancies and body surface area were assessed using both parametric linear regression and nonparametric LOESS methods. The effect of increasing duration of cardiopulmonary bypass on the accuracy of estimated resting energy expenditure in the postoperative period is examined using both parametric linear regression and the nonparametric LOESS method. CPB, cardiopulmonary bypass; LOESS, locally estimated scatterplot smoothing; RQ, respiratory quotient; WHO, World Health Organization.

Table 4. The Results of Multiple Regression Model on the Log-Transformed Standardized Absolute Deviations for the Allometric Equations Were Summarized.

	Allometric at RQ 0.8		Allometric at RQ 0.89	
Variable	Coefficient [95% CI]	*P*-value	Coefficient [95% CI]	*P*-value
Age [ref: neonate]		0.089		0.011
Infant	−0.105 [−0.403, 0.194]	0.49	−0.025 [−0.319, 0.270]	0.87
Toddler	0.642 [−0.082, 1.365]	0.082	0.850 [0.160, 1.540]	0.016
Child	1.012 [0.004, 2.019]	0.049	1.417 [0.487, 2.348]	0.003
Male vs female	0.116 [-0.107, 0.339]	0.30	0.069 [−0.144, 0.281]	0.52
BSA, linear	0.853 [−7.617, 9.324]	0.84	1.055 [−7.439, 9.549]	0.81
Nonlinear		<0.001		<0.001
CPB time, linear	−0.001 [−0.022, 0.019]	0.89	0.010 [−0.011, 0.031]	0.33
Nonlinear		0.003		0.019
DHCA vs standard CPB	0.204 [−0.086, 0.495]	0.166	0.132 [−0.179, 0.443]	0.40
Biventricle vs single ventricle	0.128 [−0.323, 0.579]	0.57	0.162 [−0.217, 0.541]	0.40
Ever paralyzed	−0.117 [−0.338, 0.104]	0.30	−0.132 [−0.387, 0.123]	0.31

BSA, body surface area; CI, confidence interval; CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest.

The importance of this observation is not limited by the fact that this was not uniformly identified as a statistically significant source of error for all estimation equations in this particular retrospective analysis.

This study shows that at all time points following CPB, all currently utilized estimation equations overestimate REE when compared with gold standard measurement with an important degree of error. The largest estimation errors are made in the smallest patients, in both size and age. Because of the decrease in measured energy expenditure in the first 24 hours following CPB and the static nature of the estimate equations, the estimation error of all equations increases over time in this cohort. This is an important observation because the most error occurs when the patient's REE is at its plateau and it is likely that the 30% of patients who are still intubated at 72 hours represent a particularly fragile subgroup at greatest risk of difficulty being liberated from the ventilator in addition to other morbidity and mortality. Importantly, most programs are beginning to advance nutrition toward calculated goals at this time when typically utilized equation's estimates are the most incorrect.[22]

Equation performance is reported using standardized absolute discrepancy as a measure of comparison of the gold standard to estimation equations. Previous literature has used inaccuracies within 10% of the measured REE as the margin of acceptable error.[19,23,24] However, there is no evidence that supports this margin of error as the level that effects clinical outcomes or morbidity. Therefore, utilizing standardized absolute discrepancies avoids making any judgements of when the margin of error becomes significant. Given the variability of each patient's measured REE over time, we can expect that the clinical course of critically ill patients will vary and that each patient's tolerance for error will depend greatly on their individual clinical condition. This study initially compared our institutional practice of equation use with stress factors to gold standard measured values. The addition of stress factors to estimation equations in critically ill patients varies between institutions and guidelines recommend against inclusion, as they have been shown to overestimate energy requirements in mechanically ventilated patients.[25] This analysis further confirms that this is an important source of additional imprecision in estimating energy requirements. Because of this additional imprecision and guideline recommendations against this practice, we chose to include comparisons of equations without stress factors and ultimately not include HB and DRI in our final analysis.

In addition to assessing accuracy of estimation for the entire cohort, the subgroup analysis focused on clinical characteristics believed to potentially modify patient REE and affect accuracy of estimations. The finding that the greatest errors in estimation occur in the smallest patients (<5 kg) is important as this is already an at-risk population as a result of their small size, critical congenital heart disease, and organ system immaturity.[26] Imprecision in estimation of requirements for this population of patients likely contributes to preventable morbidity.

CBP is an injurious stimulus that causes metabolic disruption and derangement of background energy utilization. Standard CPB could be assumed to have with less injury than DHCA, in which patients are exposed to a greater degree of hypothermia and organs and tissues experience circulatory arrest. In this cohort, a patient's exposure to DHCA was found to have a significant effect on the discrepancy of energy estimation in all equations except for HB.

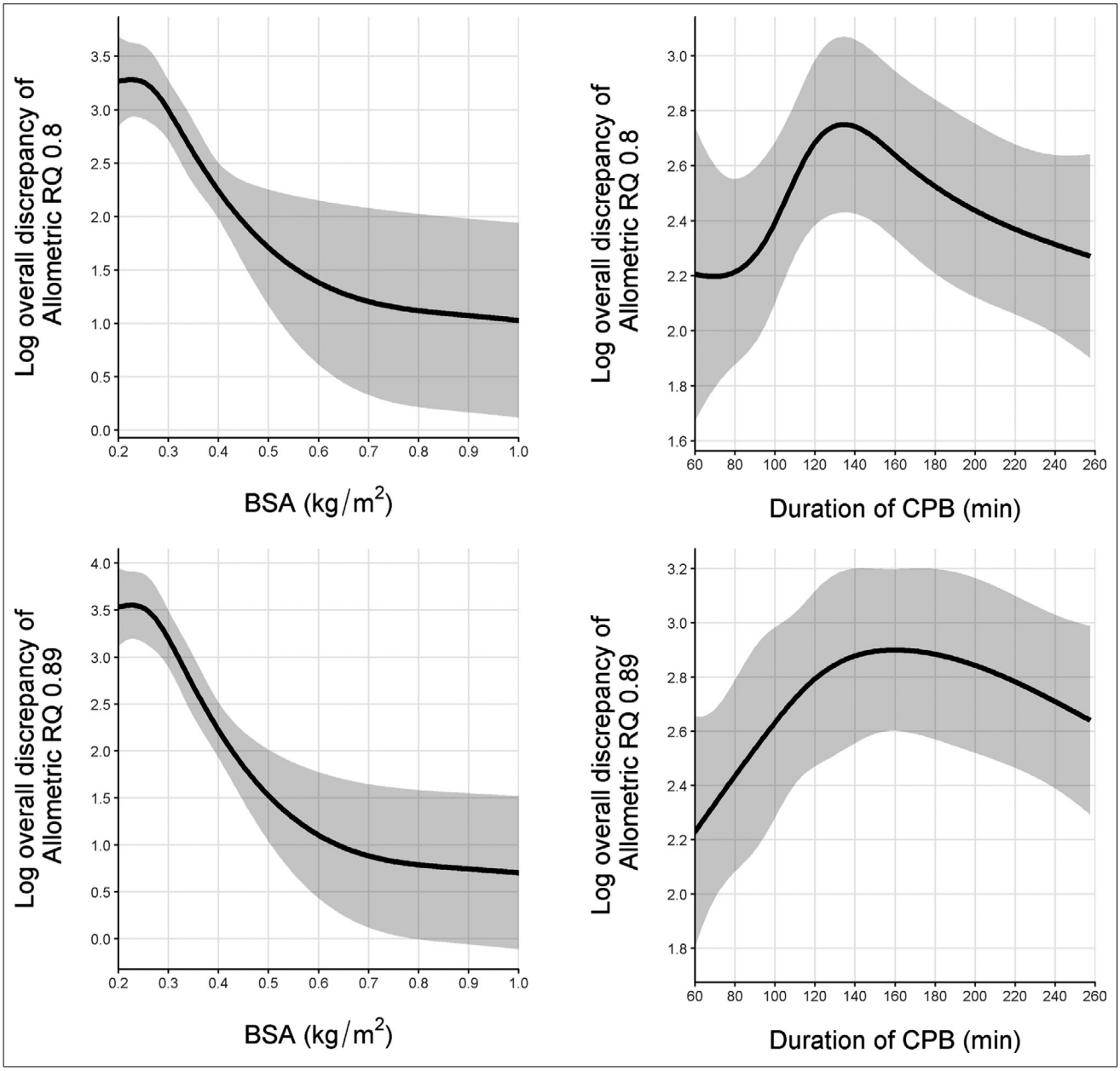

Figure 3. The results of multiple regression model on the log-transformed standardized absolute deviations for allometric at RQ 0.8 and 0.89 were summarized. BSA, body surface area; CPB, cardiopulmonary bypass; RQ, respiratory quotient.

Use of neuromuscular blockade (NMB) following bypass modifies basal energy expenditure by limiting voluntary movement and respiratory effort and thereby decreasing REE. The discrepancy difference between populations that had NMB at any time point following CPB was found to be significant only for allometric methods of estimation, with greater errors of estimation seen in the group of patients exposed to NMB. This suggests that the observation that use of NMB is an important variable to consider when estimating energy requirements in critically ill populations.

Univentricular congenital heart disease surgeries are technically demanding, with long CPB times and exposure to DHCA. Postoperative energy requirements in this group of patients are unpredictable as a result of being partially dependent on the presence of residual lesions and their physiological consequences (such as tachypnea in patients with generous postoperative pulmonary blood flow). In this analysis, there was not a significant difference in estimation error between patients with biventricular and univentricular heart disease; however, the small number of univentricular

patients in this cohort may have limited our ability to identify an effect.

In the multiple regression model, after controlling for covariates, the only statistically significant relationship found in all estimation equations was the nonlinear relationship between BSA and absolute discrepancy in which higher BSA was associated with lower absolute discrepancy for all methods. The association between CPT time and the absolute discrepancies were nonlinear, where the CPT time around 160 minutes was associated with greater discrepancies. It is not possible to speculate on the reasons for the observed nonlinear relationship between CPB time and estimation error with the data elements available as part of this retrospective database. The finding that estimation error is greatest at a CPB time of 160 minutes may indicate a subpopulation of patients at increased risk for morbidity as a result of their underlying characteristics or a particular exposure and would require additional operative and patient characteristics to define.

It is not clear to what extent the observations made in this study can be generalized to other critically ill patient populations. Although CPB represents a compelling and well-defined injurious stimulus, there are numerous potential metabolic modifiers that patients exposed to CPB experience that are not present in other inflammatory or injurious stimuli. Perioperative practices like steroid administration and the ability of effective anesthetic management to attenuate the stress response have potentially complex and variable effects on REE postoperatively. These variables likely limit the effect to which these observations could be generalized to patients experiencing a systemic inflammatory response syndrome due to other triggers, like infection.

The results of this study continue to build the case that a more personalized and dynamic nonlinear method to estimate REE following CPB, and in critical illness as a whole, is needed. Accurate estimation in this patient population remains a challenge, as previous authors have demonstrated that REE is very dynamic both within cohorts of critically ill patients and within individual patients at different points in their timecourse.[19]

Limitations

There are important limitations in the approach described above. This is a retrospective dataset that does not include data about a variety of important clinical variables (such as patient temperature) that may have an effect on REE and as a result, the accuracy of estimation. An ideal approach would have allowed adjustment where possible for these variables with correction of estimates at each time point before comparison with measured REE. Because this method of indirect calorimetry necessitates that a patient be intubated, this study may select a patient population with a greater degree of critical illness than the general population of all patients following CPB.

Conclusion

All current equations to estimate REE inaccurately predict postoperative energy requirement in pediatric patients undergoing CPB. Adaptation of allometric scaling methodology is an inferior method to currently available equations in critically ill patient populations. All current equations are limited as a result of being linear methodologies attempting to estimate a nonlinear biological process. In this patient population, indirect calorimetry remains the gold standard and ideally should be applied wherever possible to measure the dynamic energy requirement of this cohort. Populations that deserve particular attention are those <5kg and patients following CPB that require protracted mechanical ventilation, as the magnitude of estimation error is greatest in this group. A better understanding of both how critical illness disrupts metabolism and how clinical interventions modify these changes is required to formulate more accurate means of estimation. Additional innovation in estimating REE using more dynamic and nonlinear methods is required to minimize preventable patient harm associated with imprecise fluid and nutrition management.

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Statement of Authorship

N. Roebuck and M. L. Mazwi equally contributed to the conception and design of the research; A. Floh and Z. L. Harris contributed to the design of the research; C. S. Fan, N. Roebuck, M. L. Mazwi, and A. Floh contributed to the acquisition and analysis of the data; C. S. Fan, N. Roebuck, and M. L. Mazwi contributed to the interpretation of the data; and N. Roebuck and M. L. Mazwi drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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