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## Energy balance in obese, mechanically ventilated intensive care unit patients

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### Abstract

**Objectives:** The aims of this study were, first, to compare the predicted (calculated) energy requirements based on standard equations with target energy requirement based on indirect calorimetry (IC) in critically ill, obese mechanically ventilated patients; and second, to compare actual energy intake to target energy requirements.

**Methods:** We conducted a prospective cohort study of mechanically ventilated critically ill patients with body mass index  $\geq 30.0$  kg/m<sup>2</sup> for whom enteral feeding was planned. Clinical and demographic data were prospectively collected. Resting energy expenditure was measured by open-circuit IC. American Society of Parenteral and Enteral Nutrition (ASPEN)/Society of Critical Care Medicine (SCCM) 2016 equations were used to determine predicted (calculated) energy requirements. Target energy requirements were set at 65% to 70% of measured resting energy expenditure as recommended by ASPEN/SCCM. Nitrogen balance was determined via simultaneous measurement of 24-h urinary nitrogen concentration and protein intake.

**Results:** Twenty-five patients (mean age:  $64.5 \pm 11.8$  y, mean body mass index:  $35.2 \pm 3.6$  kg/m<sup>2</sup>) underwent IC. The mean predicted energy requirement was 1227 kcal/d compared with mean measured target energy requirement of 1691 kcal/d. Predicted (calculated) energy

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Supplementary materials

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requirements derived from ASPEN/SCCM equations were less than the target energy requirements in most cases. Actual energy intake from enteral nutrition met 57% of target energy requirements. Protein intake met 25% of target protein requirement and the mean nitrogen balance was  $-2.3 \pm 5.1$  g/d.

**Conclusions:** Predictive equations underestimated target energy needs in this population. Further, we found that feeding to goal was often delayed resulting in failure to meet both protein and energy intake goals.

### Keywords

Obesity; Intensive care unit; Nutrition; Energy expenditure; Indirect calorimetry; Mechanical ventilation

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## Introduction

Overfeeding critically ill patients has been associated with poor outcomes [1–3]. More than 25% of critical ill patients in the United States are obese [4,5]. Obesity presents a challenge beyond normal weight in intensive care unit (ICU) patients because of the comorbidities and metabolic anomalies associated with obesity [6–8]. This makes determining an appropriate dose of enteral nutrition and concerns about potential harms from overfeeding even greater in the obese critically ill population than in the normal weight population.

Improved outcomes such as decreased length of stay have been associated with hypocaloric feeding of obese critically ill patients [8] but an association between negative energy balance and increased infections has also been reported [9]. It is also widely recognized that obese patients can be malnourished [10]. So, although a degree of underfeeding may be beneficial, provision of adequate nutrient intake to prevent malnutrition and loss of lean body mass is also important [11,12]. Guidelines from the American Society of Enteral and Parenteral Nutrition/Society of Critical Care Medicine (ASPEN/SCCM) published in 2016 strike a balance on these issues by recommending provision of nutrition to obese ICU patients within 24–48 h of admission but also recommending that feeding be hypocaloric [13]. To establish energy intake goals, it is recommended that, when possible, these patients undergo indirect calorimetry (IC) and that enteral nutrition for obese critically ill patients not exceed 65% to 70% of energy expenditure measured by IC [13]. In contrast, the recently published European Society of Parenteral and Enteral Nutrition guidelines recommend an isocaloric rather than hypocaloric diet based on IC [14]. When IC is not available, they recommend use of adjusted body weight in formulas to determine caloric needs [14].

For many patients, IC cannot be accurately measured or interpreted, such as for those patients on high fractions (>60%) of inspired oxygen. For many other patients, logistical or institutional barriers make IC impractical. Indeed, a feasibility study on the use of IC in critically ill patients reported that IC was only possible on 39% of those with an indication for its use [15]. For these patients, ASPEN/SCCM 2016 guidelines recommend using weight based empirical equations to estimate energy requirements. These equations were validated in a retrospective pilot study of 31 obese patients who underwent IC as part of usual clinical care [16]. The findings from this study were the basis for the ASPEN/SCCM 2016

recommendations [13]. Briefly, the equations were found to perform adequately for estimating 65% of measured resting energy expenditure (REE). However, given the small sample size, clinicians might still be concerned about inadvertently overfeeding patients when IC is not available.

Therefore we sought to compare the predicted (calculated) energy requirements based on ASPEN/SCCM 2016 equations [13], the target energy requirement based on IC [13], and the actual energy intake of patients to determine the prevalence of under or overfeeding. We then evaluated nitrogen balance because inadvertently delivering low protein is a risk of hypocaloric feeding.

## Methods

We conducted a prospective observational cohort study of adult (> 18 y of age), obese (body mass index [BMI]  $\geq 30$  kg/m<sup>2</sup>), mechanically ventilated men and women admitted to the medical, cardiac, or neurologic ICUs between January 1, 2015 and February 28, 2016. Patients who were pregnant or for whom the medical team was not planning standard enteral tube feedings were excluded from the study. Patient characteristics (age, sex, ethnicity, height, weight), collected as part of medical care, were extracted from the medical chart. Patients were followed until extubation, death, or until the latter of either completion of IC or completion of 4 d follow-up. This study was approved by our Institutional Review Board by Expedited Review per 45 Combined Federal Regulation 46.110(f) (2) (b) (3) (4) (5) (Internal Christiana Care number: 34155).

### Energy balance measures

REE was measured by open-circuit IC using a computerized metabolic cart (MedGraphics CCM Express, St Paul, MN, USA) for a minimum of 35 min. The first 5 min of every test were discarded, and of the remaining minutes, steady state was defined as the period where the coefficient of variation for oxygen consumption and carbon dioxide production was  $\leq 10\%$  for at least 25 min. Total energy intake (calories from enteral feedings including protein supplements, if used, and propofol if used for sedation) was determined from daily input and output records; energy and protein intake from enteral feedings alone was also calculated.

### Target and predicted energy requirements

The target energy requirement was determined using ASPEN/SCCM 2016 guidelines [13], which state that, for all classes of obesity, energy intake should not exceed 65% to 70% of energy requirements as measured by IC. Predicted energy requirements were determined using ASPEN/SCCM 2016 equations [13], which call for 11 to 14 kcal/kg actual body weight per day for patients with a BMI in the range of 30 to 50 [13]. For patients with a BMI  $>50$  kg/m<sup>2</sup>, 22 to 25 kcal/kg ideal body weight is recommended [13]. Because of a small sample size ( $n = 3$  patients with BMI  $>50$  kg/m<sup>2</sup>), we could not draw conclusions about the equation recommended for patients with a BMI  $>50$  and excluded these patients from the analysis. The typical practice in the Christiana Care Healthcare System is to initiate enteral

feeding within 24 to 48 h of ICU admission at a rate of 20 mL/h and advance to goal by adding 20 mL to the rate every 8 h.

### Nitrogen balance

Nitrogen balance was determined by collecting a 24-h urine sample with simultaneous measurement of protein intake during the same 24-h period. Urinary nitrogen concentration was assessed via spectrophotometry at the Christiana Care Healthcare System laboratory. Nitrogen balance was calculated using the following equation: Protein intake (g)/6.25 – urine nitrogen excreted (g) – 4 [17].

### Severity of illness and nutritional risk

Three different methods were used to assess illness severity: the Sequential Organ Failure Assessment (SOFA) [18], the Acute Physiology and Chronic Health Evaluation Scores (APACHE II) [19], and the Nutrition Risk in the Critically Ill (NUTRIC) score [20].

### Statistics

Descriptive statistics were used to summarize patient population characteristics. Per ASPEN guidelines [13], target energy intake for critically ill obese patients should not exceed 65% to 70% of energy expenditure measured by indirect calorimetry. As such, measured REE for each patient was multiplied by the low, average, and high (0.65, 0.675, and 0.70) range of the guideline for target energy requirements [13]. The predicted (calculated) energy requirement recommended for obese, critically ill patients with a BMI between 30 and 50 kg/m<sup>2</sup> is 11 to 14 kcal/kg actual bodyweight [13]. The predicted (calculated) energy requirement for each patient was determined based on the low end of the range (ASPEN\_Low; 11 kcal/kg), the average of the range (ASPEN\_Average; 12.5 kcal/kg), and the high end of the range (ASPEN\_High; 14 kcal/kg). For each patient, we also calculated the ratio of actual energy and protein intake over the target energy and protein intake. Next, the group mean from each ASPEN equation was compared with the ASPEN target energy requirement group mean. Finally, we calculated the correlation coefficient between the calculated energy requirement from the ASPEN equations and the ASPEN target energy requirement from the measured REE. A  $P < 0.05$  was considered significant. Statistical analysis was performed using STATA Version 13.1 (College Station, TX, USA).

### Results

A total of 55 patients were enrolled in the study; however, REE could not be measured for 27 patients (Fig. 1). Three patients had BMI >50 kg/m<sup>2</sup> and were excluded. As shown in Table 1, a total of 25 patients with a BMI between 30 to 50 kg/m<sup>2</sup> had a successful REE measurement. These patients were critically ill based on APACHE II and SOFA scores. Based on the mean NUTRIC score, our participants were at low nutritional risk. Three patients (12.0%) died during their hospital stay, and 6 patients (24.0%) were discharged to hospice. The reasons for ICU admission were pneumonia ( $n = 5$ ), sepsis ( $n = 3$ ), respiratory failure ( $n = 3$ ), altered mental status ( $n = 4$ ), stroke ( $n = 4$ ), cardiac arrest ( $n = 3$ ), pulmonary embolism ( $n = 1$ ), seizures ( $n = 1$ ), and overdose ( $n = 1$ ).

As recommended by ASPEN/SCCM, the target energy requirement for critically ill obese patients is 65% to 70% of the measured REE; taking the average of this range (67.5% measured REE), this equated to a mean target energy requirement of  $1691 \pm 505$  kcal/d for our participants (Table 2). Overall, only four patients (Fig. 2) had a calculated energy goal between 65% and 70% of measured REE. For the ASPEN\_Low predictive equation (11 kcal/kg), one patient's calculation (4%) was within the target range (65%–70% of the measured REE) and no patients' calculations (0%) exceeded 70% of the measured REE. For the ASPEN\_Average predictive equation (12.5 kcal/kg), two patients' calculation (8%) were within the target range and two patients' calculations exceeded 70% of the measured REE. For the ASPEN\_High predictive equation (14 kcal/kg), three patients' calculations (12%) were within the target range, and three patients (12%) had calculations that exceed 70% of the measured REE. All the remaining calculations were less than the target range. Appendix 1 shows the measured and calculated energy ranges for all 25 patients.

The mean actual total energy intake (enteral feeding + propofol); and energy intake from enteral feeding alone was 57% and 52% of the target energy requirement (67.5% measured REE), respectively. A total of nine patients received propofol in addition to enteral feedings. Only one of 25 patients' actual total energy intakes exceeded the target energy requirement (70% of REE measured by IC), with the remaining 24 failing to achieve the target measured energy requirement. Enteral feeding products included a high-protein polymeric formula, Replete (Nestle Health Science, Bridgewater Township, NJ, USA;  $n = 20$ ); a volume-restricted polymeric formula, Nutren 1.5 (Nestle Health Science;  $n = 2$ ); and a volume-restricted renal formula, Nova Source Renal (Nestle Health Science;  $n = 1$ ). One patient received both Isosource and Replete, and one patient received both Nova Source and Replete. Only two patients received protein supplements (ProSource, Medtrition, Lancaster, PA, USA). We obtained 24-h urine collections on 19 patients. The mean nitrogen balance was  $-2.3 \pm 5.1$  g/d. The mean change in body weight during the study period was  $+2.2 \pm 5.4$  kg.

The correlation between the calculated energy requirement from the ASPEN equations and the ASPEN target energy requirement from the measured REE was low with an  $r = 0.64$  and  $P$  value  $< 0.001$ .

## Discussion

We found that the 2016 ASPEN/SCCM equations for predicting (calculating) energy requirements of obese mechanically ventilated ICU patients underestimated energy needs compared with 65% to 70% of the goal (IC measure) for the majority of patients. Further, despite initiation of energy feedings within 24 to 48 h of ICU admission, actual energy and protein intake during the study period was lower than calculated energy and protein requirements. We focused only on obese patients, which is a population where estimation of energy expenditure is known to be particularly problematic.

Hypocaloric feeding has been suggested as a way of improving outcomes in obese patients [21–23]. This is reflected in the ASPEN guideline recommendation to provide no more than 70% of energy needs to obese patients [13]. Moreover, it has recently been suggested that

feeding to goal may be dangerous, especially early in the course of critical illness [24]. Enteral nutrition's impact on autophagy has been suggested as a possible mechanism for this harm. Autophagy is a cellular repair process that plays a role in both homeostasis and disease recovery [24,25]. Autophagy is inhibited by increased insulin, glucose, and nutrients, so disruption of autophagy by enteral nutrition could be a mechanism of harm [24,25].

Therefore it is reasonable for clinicians to be concerned about the potential for overfeeding obese patients. Because 24 of the 25 patients in our study did not actually achieve the target energy intake during the study period, our data indicate that overfeeding may not be a major concern at least in the early phase of critical illness. However, the patients in our study received only 52% to 57% of goal energy and 25% of goal protein needs.

Our data are consistent with a large observational cohort study of 167 intensive care units that reported overall critically ill patients received 59.2% of calories and 56% of protein prescribed [12]. Lower mortality was associated with higher protein and caloric feeding at extremes of BMI (>35 and <25) [12]. Providing protein in a dose between 2.0 and 2.5 g/kg per day is recommended by ASPEN guidelines for patients with BMI >40 based on data suggesting negative nitrogen balance with lower protein doses [12,13]. Some authors have suggested that for critically ill patients the provision of adequate protein may be more important than providing energy through feeding [26,27]. If this proves to be true, then perhaps earlier use of protein supplements would be beneficial.

Our study is consistent with prior studies that report poor agreement between measured resting energy expenditure and energy expenditure estimated by predictive equations [28–31]. For example, one study found that the correlation between a predictive equation and measured REE was similar ( $r = 0.59$ ) [32]. However, most prior studies have not used the predictive formulas recommended in the ASPEN/SCCM 2016 guidelines or focused on critically ill obese patients. Because of our focus on this population with a recommended goal of hypocaloric feeding, our methods of comparing predictive equations to a percent of REE is different than many prior studies that compared predictive equations to total REE. Our study design differs from that of the validation study [16] of ASPEN equations in that we conducted a prospective study of mechanical ventilated ICU patients, excluding surgical patients, whereas their study was a retrospective study of medical and surgical ICU patients and included spontaneously breathing patients. In addition, we were able to capture data on severity of illness and nutritional risk, which they were not able to obtain retrospectively. Our results differ in that we found predictive equations underestimated the energy needs of obese patients, which was not reported in the validation study.

The mortality risk estimated by average SOFA scores [33,34] in our population is around 20%. In addition, on average, our population was at low nutritional risk based on the NUTRIC score [20]. It is possible that the performance of predictive equations might be influenced by the severity of illness of the patients. Therefore it is possible that recommended equations would perform better or worse in sicker or healthier populations. Future studies with a larger sample would allow for analysis that is stratified by severity of illness and nutritional risk.



Although our results are reassuring in terms of avoiding harms from overfeeding, our finding that the recommended equations resulted in target energy requirements that were less than 65% to 70% of the IC measure is concerning, especially because we were only able to obtain metabolic cart measurements on 50% of our enrolled patients, which is, however, higher than the 39% of patients with an indication for IC reported in a feasibility of IC [15]. Although the development of more accurate predictive equations for obese patients would be welcomed by clinicians, additional research is needed in larger populations to understand the patient factors that contribute to actual energy requirements that are higher than the predicted energy requirement. Moreover, practical methods for measuring energy expenditure with less disruption in routine nursing care and in patients currently ineligible for metabolic cart measurement for technical reasons, such as high fraction of inspired oxygen, are also needed.

This study had limitations. Although our success in obtaining REE by IC was similar to the reported literature [15], this limited our sample size. Further, because IC requires a low inspired oxygen, our population was limited to those with a relatively low severity of illness. In addition, our population had low nutritional risk and our results may not be generalizable to a sicker population with higher nutritional risk scores. Because of the small sample size we cannot draw conclusion about the possibility of the equations performing differently in different racial and ethnic groups. Finally, we do not have data related to why enteral feedings were held or not advanced in specific patients. In our practice, enteral tube feedings are normally advanced by 20 mL every 8 h, and as such most patients would have reached goal feeding in 24 to 48 h. However, at our institution, checking residual volumes and holding feeds for residuals greater than a specified amount (selected by the physician ordering the tube feed) is standard practice and this likely contributed to not reaching goal. In addition, some patients received vasopressors, and this may have contributed both to feeding intolerance and clinician discomfort with advancing feedings to goal. Holding feedings for procedures such as drains in interventional radiology could also have contributed. Finally, several recent high-profile trials comparing trophic to full feeding that failed to identify mortality benefits to full-dose feeding may have influenced clinician willingness to advance feeds to meet energy goals [35,36].

## Conclusions

We did not find evidence of overfeeding. In fact, we found that ASPEN guideline recommended equations underestimate the actual energy needs of obese patients as determined by REE/IC. Further, we found that, in our population, feeding to goal was often delayed and as such energy and protein needs were not met. This combination of underestimating needs and failing to deliver even what is estimated as needed could contribute to the unintentional development of energy deficits in this patient population.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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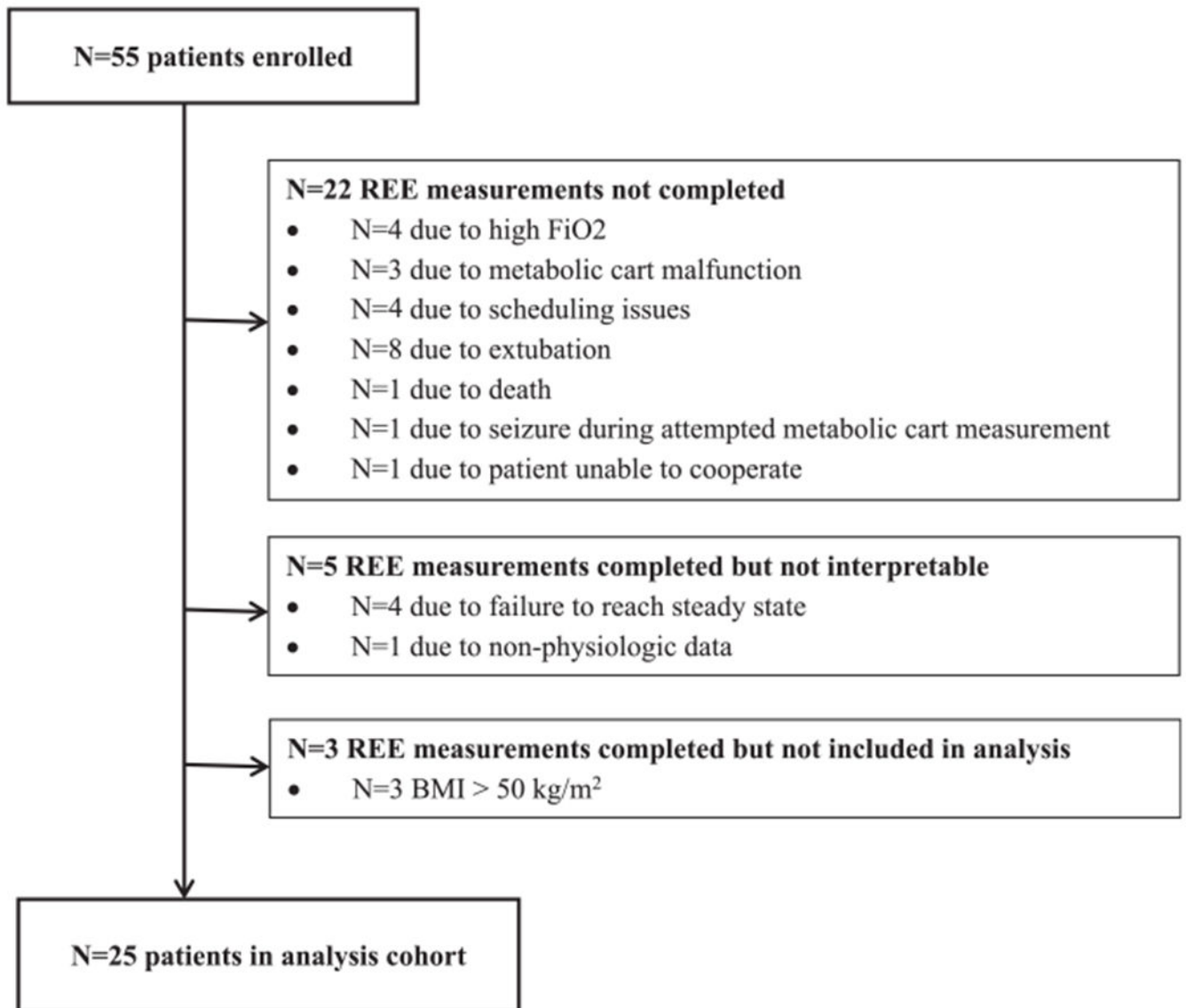
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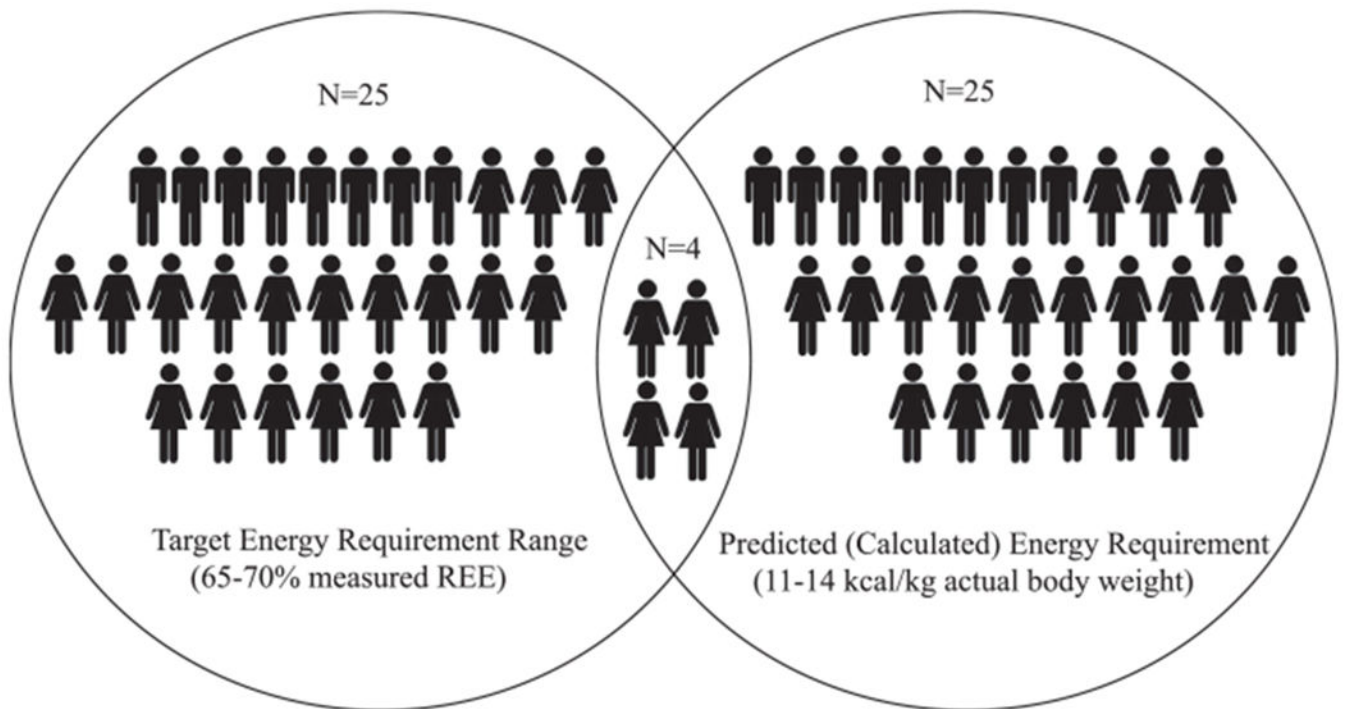
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**Fig. 1.** Flow diagram showing enrolled patients and construction of analytical data set. BMI, body mass index; REE, resting energy expenditure.



**Fig. 2.** Venn diagram showing degree of overlap between target energy requirement range based on measured resting energy expenditure (REE) and predicted (calculated) energy requirement.

**Table 1**

Characteristics of obese mechanically ventilated patients in the ICU

<b>Characteristic</b>	<b>Participants (<i>n</i> = 25)</b>
<b>Sex</b>	<i>n</i> (%)
Male	8 (32.0)
<b>Race</b>	
African American	1 (4.0)
Caucasian	24 (96.0)
<b>Ethnicity</b>	
Latin/Hispanic	0 (0)
Non-Latin/Hispanic	25 (100)
<b>Admitting diagnosis</b>	
Neurologic problem	9 (36%)
Sepsis and pneumonia	8 (32%)
Respiratory failure and PE	4 (16%)
Other	4 (16%)
<b>Receiving vasopressor on enrollment</b>	8 (32%)
	<b>Mean (SD)</b>
<b>Age, y</b>	64.5 (11.8)
<b>Height, cm</b>	166.5 (10.1)
<b>Weight, kg</b>	98.2 (18.2)
<b>BMI, kg/m<sup>2</sup></b>	35.2 (3.6)
<b>Hospital length of stay, d</b>	19.6 (11.7)
<b>Time in study, d</b>	4.2 (1.3)
<b>Enteral feeding, d</b>	3.8 (1.4)
<b>SOFA score</b>	8.0 (2.2)
<b>APACHE II score</b>	21.8 (5.6)
<b>NUTRIC score</b>	4.0 (1.1)

APACHE II, Acute Physiology and Chronic Health Evaluation II; BMI, body mass index; ICU, intensive care unit; PE, pulmonary embolism; NUTRIC score, Nutrition Risk in Critically Ill; SOFA, Sequential Organ Failure Assessment

**Table 2**

Energy and protein requirements and comparison with goals in obese, mechanically ventilated ICU patients

Calculation or measurement	Mean (SD)	Range (min–max)
<b>Energy and protein requirements</b>		
Measured REE, kcal/d	2506 (749)	1469–4105
Target energy requirements (65% measured REE <sup>*</sup> ), kcal/d	1629 (487)	954–2668
Target energy requirements (67.5% measured REE <sup>*</sup> ), kcal/d	1691 (505)	991–2770
Target energy requirements (70% measured REE <sup>*</sup> ), kcal/d	1754 (524)	1028–2873
Goal protein requirements, <sup>*</sup> g/kg/d	2.0	–
<b>Actual energy and protein intake</b>		
Total energy intake, <sup>†</sup> kcal/d	998 (465)	0–1916
Enteral nutrition energy intake, <sup>‡</sup> kcal/d	882 (429)	0–1916
Enteral nutrition protein intake, <sup>‡</sup> g/kg/d	0.57 (0.28)	0.0–1.9
<b>Nitrogen balance</b>		
Nitrogen balance, <sup>§</sup> g/d	–2.3 (5.1)	–11.6–7.9
<b>Predicted energy requirements (ASPEN equations)</b>		
Calculated energy requirement (ASPEN_Low), <sup>*</sup> kcal/d	1080 (200)	849–1663
Calculated energy requirement (ASPEN_Average), <sup>*</sup> kcal/d	1227 (227)	965–1890
Calculated energy requirement (ASPEN_High), <sup>*</sup> kcal/d	1375 (254)	1080–2116

ASPEN, American Society for Parenteral and Enteral Nutrition; ASPEN\_Low, minimum of recommended range; ASPEN\_High, maximum of recommended range; BMI, body mass index; ICU, intensive care unit; max, maximum; min, minimum; REE, resting energy expenditure

<sup>\*</sup> Per ASPEN guidelines [13] for obesity, the goal of the enteral nutrition regimen should not exceed 65% to 70% of energy requirements as measured by indirect calorimetry; if REE is not measured by IC, 11 to 14 kcal/kg actual body weight per day for patients with BMI in the range of 30 to 50 should be provided. The predicted (calculated) energy requirement for each patient was determined based on the low end of the range (ASPEN\_Low; 11 kcal/kg), the average of the range (ASPEN\_Average; 12.5 kcal/kg), and the high end of the range (ASPEN\_High; 14 kcal/kg).

<sup>†</sup> Enteral nutrition and propofol ( $n = 25$ ).

<sup>‡</sup> Enteral nutrition only ( $n = 25$ ).

<sup>§</sup> Calculated: Protein intake (g) / 6.25 – urine nitrogen excreted (g) – 4 [17] ( $n = 19$ ).