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ORIGINAL ARTICLE

A Comparison between Continuous Indirect Calorimetry and Single Weight-Based Formula in Estimating Resting Energy Expenditure in Nutritional Therapy: A Prospective Randomized Controlled Study in Critically Ill Patients

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ABSTRAK

Nutrisi yang optimum adalah penting dalam kalangan pesakit kritikal di unit rawatan rapi. Alatan kalorimetri tidak langsung kini merupakan penilaian yang piawai untuk mengukur keperluan tenaga ketika rehat pada pesakit kritikal. Untuk kajian ini, sebanyak 146 pesakit yang memerlukan alatan pernafasan di unit rawatan rapi diasingkan secara rawak kepada 2 kumpulan samada untuk menerima nutrisi berdasarkan pengukuran kalorimetri tidak langsung secara berterusan (kumpulan kajian, n=73) atau mengikut kiraan berat badan 25 kcal/kg/hari (kumpulan kawalan, n=73). Daripada keputusan kajian ini, kita mendapati bahawa tiada perbezaan dalam pemboleh ubah asas di antara kedua-dua kumpulan. Sementara itu, kita juga mendapati bahawa tenaga ketika rehat pada kumpulan kajian adalah lebih rendah berbanding dengan kumpulan kawalan (1668.1 ± 231.7 vs 1512.0 ± 177.1 kcal, p<0.001). Keseimbangan tenaga pesakit, samada harian (-148.8 ± 105.1 vs. -4.99 ± 44.0 kcal, p<0.001) atau kumulatif (-1165.3 ± 958.1 vs. 46.5 ± 369.5 kcal, p<0.001), adalah lebih seimbang dalam kumpulan kajian berbanding dengan kumpulan kawalan. Daripada kajian graf Kaplan-Meier, kita mendapati bahawa kematian di unit rawatan rapi adalah lebih rendah di dalam kumpulan kajian (log-rank test, p=0.03) tetapi tiada perbezaan dalam kalangan kumpulan kajian dan kumpulan kawalan dalam tempoh tinggal di unit rawatan rapi, tempoh keperluan alatan pernafasan dan kejadian intoleransi makanan. Kajian ini telah menyimpulkan bahawa terapi pemakanan yang dikawal secara ketat berdasarkan pengukuran kalorimetri tidak langsung dapat mencapai keseimbangan tenaga yang signifikan dan juga pengurangan kadar kematian di unit rawatan rapi.

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Kata kunci: *kalorimetri tidak langsung, nutrisi, unit rawatan rapi*

ABSTRACT

Optimal nutritional therapy is important to improve outcome in critically ill population in an intensive care unit (ICU). Although indirect calorimetry (IC) is currently a gold standard for resting energy expenditure (REE) measurement, yet it is still not routinely used in the ICU. A total of 146 mechanically ventilated patients were randomised to receive enteral nutrition (EN) with energy targeted based on continuous indirect calorimetry (IC) measurements (IC group, n=73) or according to 25 kcal/kg/day (SWB group, n=73). Patient characteristics were equally distributed and the IC group showed lower mean measured REE (1668.1 $\pm$ 231.7 vs 1512.0 $\pm$ 177.1 kcal, $p<0.001$). Results also showed a significant deficiency in the daily (-148.8 $\pm$ 105.1 vs. -4.99 $\pm$ 44.0 kcal, $p<0.001$) and total cumulative energy balances (-1165.3 $\pm$ 958.1 vs. 46.5 $\pm$ 369.5 kcal, $p<0.001$) in the SWB group as compared to the IC group. From the Kaplan-Meier survival analysis, we found that ICU mortality was significantly lower in the IC group with better survival probability compared to the SWB group (log-rank test, $p = 0.03$). However, both groups showed comparable results in terms of ICU length of stay, duration of mechanical ventilation and incidence of feeding intolerance. In conclusion, this study showed that tightly supervised nutritional therapy based on continuous IC measurement provides significantly less mean daily and cumulative energy deficits as well as significantly reduced ICU mortality rate.

Keywords: indirect calorimetry, intensive care unit, nutrition therapy

INTRODUCTION

The recognition of optimal energy requirement in the critically ill population is important to ensure nutrition being delivered is near to the caloric target (Oshima et al. 2016). Gross underfeeding is closely associated with risk of infections, prolonged mechanical ventilation (MV) and duration of intensive care unit (ICU) stay as well as overfeeding has also been associated with poor outcomes (Rattanachaiwong & Singer 2019; Tan et al. 2018).

Nevertheless, for accurate determination of energy requirement requires complicated measurement methods (Rattanachaiwong & Singer 2018). Predictive equations have been formulated and used widely in order to evaluate resting energy expenditure (REE). Harris-Benedict (Harris & Benedict 1918) and Mifflin (Mifflin et al. 1990) equations were originally intended as a mean to measure REE in healthy population. However, in the presence of diseases, many reports have revealed that simple predictive equations are less accurate (Oshima et al. 2016). The metabolic pattern is significantly influenced by illnesses and highly variable, depending on the severity of the disease (Faisy et al. 2003). To date, many guidelines recommended indirect calorimetry (IC) over predictive equations to determine caloric goal setting in nutrition therapy (De Waele et al. 2013). Therefore, IC is currently considered a gold standard in the assessment of REE in critically ill patients (Singer et al. 2011; McClave et al. 2016).

Indirect calorimetry provides an easy and reliable assessment of energy expenditure (Bursztein et al. 1989). It is measured by the Weir equation [($V0_2$ L/min x 3.94) + (VCO_2 L/min x 1.11) x 1440] (Weir 1949). Although it has been established as the gold standard to assess energy requirement across various group of patients including in the critically ill, this technique is still not routinely used in ICU (Heyland et al. 2011). Based on a large prospective study, it has been shown that small percentage of patients underwent IC assessment (Singer et al. 2019). This is largely due to the lack of skilled operators, unavailability of equipment as well as inexperience in interpretation and high cost of IC (Singer & Singer 2016). In our center, we are not routinely using IC monitoring for REE measurement due to the inaccessibility; instead we use the patients' weight. By using patients' weight for REE measurement, it is relatively more convenient than IC, yet patients' weight is a static measurement and does not vary with the dynamic metabolic changes among critically ill patients.

The European Society of Parenteral and Enteral Nutrition (ESPEN) guidelines used a single weight-based (SWB) formula 25-30 kcal/kg/day for energy delivery in the critically ill (Kreymann et al. 2006). Singer et al. (2011) has conducted a pilot study which showed that providing energy requirement based on repeated REE measurements within 48 hours after ICU admission was associated with lower hospital mortality (Singer et al. 2011). Therefore, we aimed to perform a study to explore the comparison between IC and the SWB formula in REE estimation and its consequent clinical implication in the critically ill.

MATERIALS AND METHODS

This prospective, randomised controlled study was conducted from December 2019 until September 2020 in the general ICU of the Universiti Kebangsaan Malaysia Medical Centre (UKMMC) after approval from the Research and Medical Ethics Committee of UKM (JEP-2019-650). Written informed consent was obtained either from the patient's next of kin or the patient his/herself. All mechanically ventilated patients aged over 18 years old and anticipated to stay more than 4 days in ICU were included into the study. The exclusion criteria were high inspired oxygen concentration (FiO_2) ≥0.6, air leaks through chest drain, continuous renal replacement therapy, severe liver disease (Child-Pugh score C), pregnancy and ICU readmission.

This was a single-blinded study. Recruited patients were randomly assigned using computer-generated program to the IC or SWB groups. The IC group received calories based on energy target measured by CARESCAPE™ R860 IC and metabolic feature (GE Healthcare, United States). The SWB group comprised subjects with energy target determined by single weight-based formula, 25 kcal/kg/day. Adjusted body weight was used for body mass index (BMI) below 18.5, actual body weight was used for BMI between 18.5 to 29.9 and ideal body weight was used for BMI above 30 (McClave et al. 2013).

The IC measurements were derived at steady state during which oxygen consumption and carbon dioxide production varied by approximately only 10% in 5 consecutive minutes, 6 times a day at 0000H, 0400H, 0800H, 1200H, 1600H and 2000H. In the IC group, energy was delivered according to the REE measurement on the daily basis, whereas in the SWB group, the patients' initial weight was taken upon admission and energy delivered was kept constant according to the initial weight-based assessment of the energy requirement. Both groups were monitored for up to 2 weeks. Nutritional therapies with enteral nutrition (EN) were targeted at 0.7 to 1.0 of measured energy expenditure (EE) in both groups. After 48 hours, supplemental parenteral nutrition (PN) was considered for inadequate EN delivery. The patient would be dropped out from the study if feeding was not established after 48 hours.

The EN formulae used in our centre were tailored to the patient's specific requirement; for example, Osmolite® (1.05 kcal/L, 44.3 g/L protein, Abbott Nutrition®); Glucerna® (1.0 kcal/L, 60 g/L protein, Abbott Nutrition®) and Novasource® (2 kcal/L, 91.1 g/L protein, Nestle HealthScience©). The PN formulae used were SmofKabiven® peripheral (1.0 kcal/L, 46 g/L protein, Fresenius Kabi Malaysia Sdn. Bhd©) and central, (1.5 kcal/L, Fresenius Kabi Malaysia Sdn. Bhd©). The choice of EN and PN formulae was decided by the clinician in charge. Intravenous insulin therapy was initiated once blood sugar level exceeds 10 mmol/L. When there was any feeding intolerance (gastric residual volume of more than 300 ml), prokinetic agents such as metochlorpramide or erythromycin would be initiated.

For the data collection, we included patients' age, gender, body weight, height, BMI and admission categories. On the day of admission, we also included patients' nutritional status and illness severity score, such as Nutrition Risk in Critically Ill (NUTRIC) score, Acute Physiology and Chronic Health Evaluation II (APACHE II) score and the Sequential Organ Failure Assessment (SOFA) score. Cumulative energy balance and protein intake were also calculated daily. Daily blood sugar level and daily insulin requirement were recorded. Incidence of gastrointestinal intolerance and prokinetic agents prescribed were also recorded. The endpoints of the study were the ICU mortality rate (defined as the death rate during patients' stay in ICU within the study period), the duration of MV, and ICU length of stay (LOS).

Statistical Test

For the statistical analysis, alpha value

Table 1: Demographic characteristics of study population (n = 146). Data were expressed as mean ± SD and number (%) as appropriate.

Variable	Group SWB (n = 73)	Group IC (n = 73)	p-value
Age (years)	57.0 ± 19.0	57.0 ± 17.0	0.94
Gender			
Male, n (%)	40 (55)	48 (66)	0.18
Female, n (%)	33 (45)	25 (34)	
Weight (kg)	66.9 ± 9.0	67.8 ± 15.9	0.70
BMI	24.7 ± 2.7	25.0 ± 5.2	0.73
SOFA score day 1	11.7 ± 1.5	11.9 ± 1.7	0.51
APACHE II score	22.2 ± 7.2	22.2 ± 7.0	0.99
NUTRIC score	6.0 ± 1.0	6.2 ± 1.0	0.30
Admission category			
Surgical, n (%)	39 (49)	32 (44)	0.33
Medical, n (%)	34 (51)	40 (55)	
Trauma, n (%)	0 (0)	1 (1)	

was set at 0.05 and 80% power of study. Sample size was calculated using Snedecor and Cochran formula based on previous study by Singer et al. (2011) with mean difference of 5.60 and pooled standard deviation of 11.94 in regards to length of ventilation comparing indirect calorimetry group and control group (Snedecor & Cochran 1989). For the study, we are using SPSS for Windows version 23.0 (IBM Corp, Armonk, NY, USA). Results were presented as mean standard deviation, median (interquartile range) and frequency (percentages) where appropriate. For between-group analysis, independent t test and Mann-Whitney U test were used for quantitative data while Chi square test and Fisher exact test were used for qualitative data. A p value <0.05 was considered as statistically significant.

RESULTS

In this study, a total of 146 patients were recruited into both IC and SWB groups, with both groups equally randomised.

Table 2: Summary of energy parameters for both groups (n=146). Data were expressed as mean ± SD and number (%) as appropriate.

Parameter	Group SWB (n = 73)	Group IC (n = 73)	p-value
Mean REE (kcal/day)	1668.1 ± 231.7	1512.0 ± 177.1	< 0.001*
Mean energy delivered/day (kcal/day)	1519.3 ± 200.9	1507.1 ± 172.7	0.69
Mean daily energy balance (kcal)	-148.8 ± 105.1	-4.99 ± 44.0	< 0.001*
Cumulative energy balance (kcal)	-1165.3 ± 958.1	46.5 ± 369.5	< 0.001*
Daily mean blood glucose (mmol/l)	8.0 (1.0)	7.6 (1.0)	0.01*
Daily mean insulin requirement (IU)	17.7 (16.3)	16.5 (36.5)	0.80
p<0.05 is considered significant*			

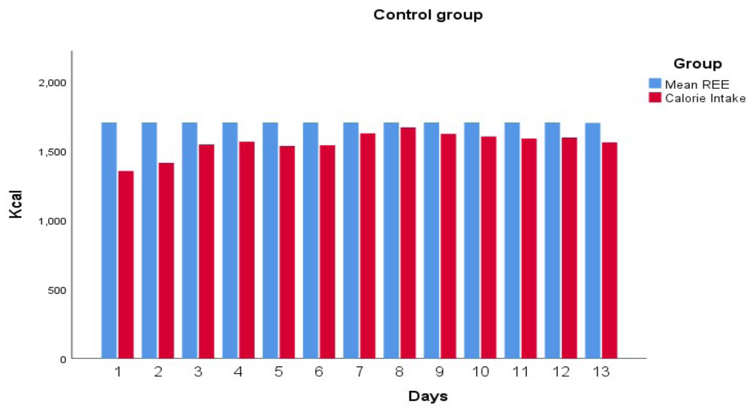

Figure 1: Mean daily energy targets compared to the daily energy intake for SWB group

Patient characteristics are shown in Table 1 and were normally distributed with no significant differences between the groups. One patient from the IC group received supplemental PN.

Table 2 showed mean energy values for the patients. There was no difference in mean daily calorie intake in both groups, but the average of measured REE was significantly lower in the IC group. There was a significant deficiency in the daily and total cumulative energy balances in the SWB group (Figure 1) in comparison to the IC group (Figure 2). Mean daily blood glucose level was significantly lower in the IC group, with no significant difference in insulin requirement in the two groups. For the secondary outcomes, the incidence of feeding intolerance, duration of MV and ICU LOS were not significantly different between the two groups (Table 3). A Kaplan Meier curve for ICU mortality demonstrated better survival probability in the IC group compared to the SWB group (Figure 3).

DISCUSSION

From our study, we found that lower mean REE were measured when using continuous IC as compared to SWB formula for ventilated ICU patients. However, both group of patients were able to achieve near targeted energy intake (0.7 to 1.0 of measured EE) without requiring significant supplemental nutrition.

For the mean daily energy and cumulative energy balances, there were greater energy deficits seen in

Table 3: Secondary outcomes. Data were expressed as mean ± SD and number (%) as appropriate

Variable	Group SWB (n = 73)	Group IC (n = 73)	p-value
Feeding intolerance (%)	6 (8.2)	10 (13.7)	0.29
Duration of mechanical ventilation (days)	8.3 ± 5.3	8.2 ± 7.9	0.95
Duration of ICU stay (days)	9.4 ± 5.6	9.7 ± 7.8	0.79

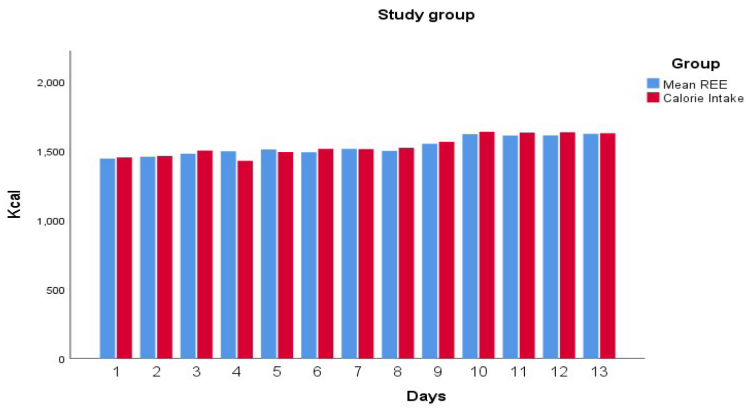

Figure 2: Mean daily energy targets compared to the daily energy intake for IC group. In the SWB group, energy intake was consistently lower than the calculated energy targets throughout the study period.

the SWB group as compared with IC group, mainly due to the periods of fasting before ICU related procedures, feeding intolerance and interruptions due to the need of transportation for imaging. These were actually comparable with those studies done by Singer et al. (2011) and Allingstrup et al. (2017) whereby patients receiving nutrition based on IC measurement on REE had significantly less deficit in mean daily energy and total cumulative energy compared to the SWB group. However, in both studies, patients in the IC group received significantly higher energy intake compared to the weight-based group (Singer et al. 2011, Allingstrup et al. 2017) as opposed to our study which the mean daily energy intake was comparable in both groups.

In this study, we observed that lower energy deficits in the IC group was associated with significantly lower mean daily blood glucose given the amount of insulin received were comparable in the two groups.

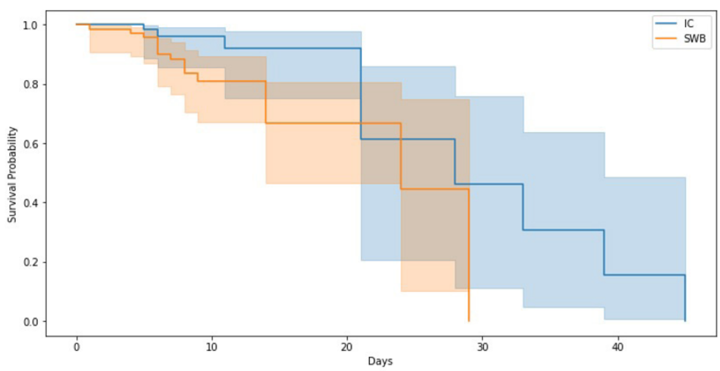

Figure 3: Kaplan-Meier curve for ICU mortality for both SWB and IC groups. The ICU mortality was significantly lower in the IC group with better survival probability compared to the SWB group (log rank test, $p = 0.03$).

There was no hyperglycemic or hypoglycemic events detected in both groups. Similarly, in Singer et al. (2011), the incidence of hyperglycemia was not reported given the higher energy intake in the IC group and the mean daily blood sugar levels were comparable between both groups. However, this was contradictory to the results showed by Allingstrup et al. (2017) where patients in the IC group that received higher energy intake (1877 kcal/day) had severe hyperglycemia with blood glucose above 15 mmol/l and received higher doses of insulin as compared to those in the weight-based group (1061 kcal/day).

Regarding the incidence of feeding intolerance, there was no significant difference between the IC and SWB groups in this study. A prospective study by Petros et al. (2014) showed a correlation between incidence of gastrointestinal intolerance and the amount of caloric intake measured with IC and observed that patients received lesser calorie had significantly less incidence of gastric regurgitation compared from the higher energy group. In the present study, the comparable amount of daily calorie intake in both groups may cause the incidence of feeding intolerance to be unremarkable.

In the present study, we observed less deficit in the daily and total cumulative energy balances in the IC group as compared with SWB group which was associated with a significant lower ICU mortality rate while no significant difference in terms of duration of MV and ICU LOS. This is partially in parallel with a study done by Singer et al. (2011) in which those patients who received EN with an energy target determined by repeated IC measurements had higher mean energy intake but showed an improvement in the hospital mortality yet no difference in the MV days and ICU LOS. A previous study done by Allingstrup et al. (2017) showed that early goal-directed nutrition group using IC measurement had significant less negative energy balance yet no significant differences in terms of ICU mortality rate, length of MV and duration of ICU stay.

Our study has limitations. For the SWB group, we didn't perform repeated body weight measurements throughout the study period, so the energy requirement was only based on the first initial weight. This was a single-centre trial with limited funding, therefore, bigger scale studies involving different centres are better in generalising the results for a heterogeneous population group.

CONCLUSION

In conclusion, this study has shown that tightly supervised nutritional therapy based on continuous REE measurement using IC was associated with lower ICU mortality rate. Despite significant energy deficit in SWB group, both groups were comparable in terms of the duration of MV, ICU LOS and feeding intolerance incidence.

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