Can 2-hour Indirect Calorimetry Measurement Accurately Predict 24-hour Energy Expenditure in Critically Ill Surgical Patients?

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Abstract

Background

Measuring energy expenditure (EE) by indirect calorimetry (IC) has become the gold standard tool for critically ill patients in order to define energy targets and tailor nutrition. Debate remains as to the optimal duration of measurements, or the optimal time of day in which to perform IC.

Methods

In this retrospective observational study, we analyzed results of daily continuous IC in 270 mechanically ventilated, critically ill patients, admitted to the surgical intensive care unit (SICU) in a tertiary medical center, and compared measurements performed at different hours of the day.

Results

A total of 51,448 IC hours was recorded, with an average 24-hour EE of 1523 ± 443 kcal/day. Night shift (00:00–8:00) was found to have a significantly lower EE measurements (mean 1498 kcal/day, 95% CI 1445–1551), than afternoon (16:00–00:00, mean 1526 kcal/day 95% CI 1473–1577) and morning (8:00–16:00, mean 1539 kcal/day, 95% CI 1483–1594) measurements (p < 0.001 for all). The bihourly time frame which most closely resembled the daily mean was 18:00–19:59, with a mean of 1523 ± 434 kcal/day. Daily EE measurements of the continuous IC at days 3–7 of admission showed a trend towards a daily increase in 24-hour EE, but the difference was not statistically significant (p = 0.077).

Conclusions

Periodic measurements of EE can differ slightly when performed in various hours of the day, but the error range is small and may not necessarily have a clinical impact. When continuous IC is not available, a 2-hour EE measurement between 18:00–19:59 can serve as a reasonable alternative.

Introduction

Providing nutrition to critically ill patients is a therapeutic intervention of significant impact (1–3). Predictive equations that estimate energy expenditure are the most available and commonly used method but are often inaccurate due to various factors (4–6). Indirect calorimetry (IC) measures oxygen consumption (VO₂) and carbon dioxide production (VCO₂) to calculate energy expenditure (EE) and the respiratory quotient (RQ) (7) and has become the gold standard measurement tool for ventilated patients (8). Current guidelines by the European and American Societies of Clinical Nutrition (ESPEN and ASPEN, respectively) recommend the use of IC, whenever available, to determine energy requirements, in lieu of predictive weight-based equations (9–10). A recent meta-analysis demonstrated that IC-guided energy delivery significantly reduced short-term
mortality without prolonging length of mechanical ventilation or hospitalization (11), however debate remains on whether the use of EE measurement-guided nutrition has a significant positive effect on long term clinical outcomes (6, 12). The optimal duration of measurement or the time of day in which to perform IC is unclear since EE may vary at different times of day and with different activity levels. Previous studies examined the ability of a short duration IC to accurately predict 24-hour EE in a limited number of critically ill medical patients (13–14).

In this retrospective study, we analyzed results of continuous IC in ventilated critically ill patients admitted to the surgical intensive care unit (SICU) in a tertiary medical center and compared measurements performed at different hours of the day to the daily mean measurements.

Materials And Methods

This was a retrospective observational study. Study data was routinely collected for clinical use in intubated patients admitted to the surgical intensive care unit (SICU) in the Tel Aviv Medical Center following general surgery operations, complication of surgeries, trauma and GI bleeding. Indirect calorimetry (M-COVX, Datex-Ohmeda, Helsinki, Finland) was measured continuously for patients starting at a time when enteral feeding adjustment was needed. Measurements were made every one minute, for a minimum of 24 hours. Twenty-four-hour EE was calculated using the modified Weir equation: 24-hour EE (kcal per day) = 1440 (3.9 VO2 + 1.1 VCO2). The data was recorded in the SICU database (MetaVision, IMDsoft) as part of routine clinical practice, and retrospective collection and analysis of this data was approved by the ethics committee of the Tel Aviv Medical Center (Institutional Review Board No. 0726-21-TLV).

Minute to minute data was reduced to hourly, bi-hourly, shift and daily calorimetry averages. The total hours of EE collected per patient ranged widely from 22 to 1211 hours. We therefore aimed our analysis to represent all the patients evenly, and avoid the overrepresentation of patients with very prolonged ICU stays. To this end, if a patient had continuous measurements of more than 24 hours, daily or bi-hourly EE was calculated as the daily and bi-hourly average of that patient during the EE measurement period.

The mean daily measurement was compared to the mean measurements obtained during the 3 daily shifts (8:00 to 16:00, 16:00 to 24:00 and 00:00 to 8:00) and the mean measurements of bi-hourly time frames to explore the accuracy of the mean daily results.

Statistical Analysis

All continuous variables are displayed as means (SD) for normally distributed variables or medians (interquartile range [IQR]) for non-normally distributed variables. Categorical variables are displayed as numbers (%) of participants within each group. Comparison of EE during different time points was performed using the repeated measures ANOVA test. Sphericity was assessed using the Mauchly method. Logistic regression was performed to assess the association of different variables on EE. Participants with missing data were excluded from all analyses. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 27 (IBM Corp., Armonk, N.Y., USA)
Results

During the years 2014–2022, 3,532 patients were admitted in our surgical intensive care unit, of them 1,291 patients had an ICU stay of 4 days or more. Continuous calorimetry was obtained for 305 intubated patients. Of these patients, 270 patients had continuous calorimetry recordings of more than 23 hours and were included in this analysis. Two patients had a missing hourly time period and were excluded from shift and bi-hourly analyses. Calorimetry measurements were started 6.2 ± 5.8 days after admission. The mean calorimetry duration recorded for each patient in this study was 191 ± 185 hours (range 23-1211 hours) with a total of 51,448 recorded hours.

The mean age was 66 ± 17.3 years with a range of 17–100 years, and 158 (58%) were male. The most common indication for admission was post-operative management n = 179 (66%). The mean Sequential Organ Failure Assessment (SOFA) score at the time of admission was 5.7 ± 3.4. Patient’s characteristics are summarized in table 1. The mean 24-hour EE, as per indirect calorimetry, was 1523 ± 443 kcal/day per patient, and 20.61 ± 5.6 kcal/kg/day per patient.

The EE average measures (n = 268) during 3 shifts were calculated: Morning – 8:00–16:00, (mean of 1539 kcal/day, 95% CI 1483–1594), afternoon – 16:00–00:00- (mean of 1526 kcal/day 95% CI 1473–1577) and night – 00:00–8:00 (mean of 1498 kcal/day, 95% CI 1445–1551). Repeated measures ANOVA with Huynh-Feldt correction showed a statistically significant difference between EE during shifts with p < 0.001. Pairwise comparisons yielded small but statistically significant increase in EE during morning shift compared with night shift (p < 0.001) but not compared to the afternoon shift (p = 0.253). The night shift mean was significantly lower than the afternoon shift (p < 0.001). Repeated measures ANOVA with Greenhouse-Geisser correction on twelve bi-hourly daily periods, showed a statistically significant difference with p < 0.001 (table 2 and Fig. 1). The bihourly time frame which most closely resembled the daily mean was 18:00–19:59 with mean of 1523 ± 434 kcal/day, similar to the daily mean. When comparing this period to each of the other 11 periods using a repeated measures ANOVA with Bonferroni adjustment, no difference was noted (p = 0.076). The bihourly time frame with the highest calorimetry was 10:00–11:59 with mean of 1548 ± 462 kcal/day. The bihourly time frame with the lowest calorimetry was 02:00–3:59 with mean of 1496 ± 436 kcal/day. The difference between the highest and lowest periods was statistically significant with p < 0.001 after Bonferroni adjustment.

In order to check the day-by-day variability of EE, the daily mean EE was compared among 44 patients for whom data was available for 5 consecutive days, on days 3–7 from admission: day 3 – mean of 1507 ± 462 kcal/day; day 4 - mean of 1468 ± 418 kcal/day; day 5 – mean of 1527 ± 420 kcal/day; day 6 - mean of 1557 ± 450 kcal/day; day 7 - mean of 1580 ± 451 kcal/day. Despite a trend towards an increase in 24-hour EE from day 3 to day 7, repeated measures ANOVA with Greenhouse-Geisser correction did not reach statistical significance (p = 0.077). The daily mean EE is shown in table 3 and Fig. 2. In this group of patients, subgroup analysis of daily variability by admission cause, also did not reach statistical significance between patients undergoing elective surgeries (n = 9, p = 0.234) or urgent surgeries (n = 20, p = 0.30).
To assess the effect of baseline covariates on time-of-day EE, a multivariable linear logistic regression was performed. After adjusting for age, sex, weight, SOFA score and admission diagnosis, time-of-day remained a statistically significant factor affecting bi-hourly EE ($p < 0.001$ for all). These variables were found to predict EE results with $R^2 = .251$, $p < 0.001$.

**Discussion**

Measuring continuous indirect calorimetry at the bedside for critically ill patients can shed light on their metabolic needs and help tailor their nutrition during different stages of illness, potentially improving outcomes (1). Performing IC requires equipment and compatible monitors and can be challenging in resource-limited centers or during surge capacity. In this study we investigated whether a short-term IC measurement of 2-hours, or during one shift, can serve as a credible surrogate for the 24-hour EE. To the best of our knowledge, this is the largest database of continuous IC measurements in critically ill surgical patients.

The main results of our study indicate that: 1) there are statistically significant differences in EE measurements throughout the day, with morning time being higher than night time; 2) the highest EE measurement of the day is 10:00–11:59, and the lowest is 2:00–3:59; 3) EE measured between 18:00 and 19:59 is the closest to the average 24-hour EE; 4) there appears to be a trend towards increase in EE between days 3 and 7, however this did not reach statistical significance.

The observed variability in calorimetry measurements throughout the day most probably represents different activities that take place in our unit's daily routine. Procedures, mobility and physiotherapy mostly take place in the morning and noon hours, while during the night hours the conditions in the unit are adjusted to promote rest and natural sleep for patients. Despite being statistically significant, the differences in measurements are small, reaching a maximum of 48kcal between the lowest EE measured at night and the highest measured at day, which is presumed to have minimal impact on clinical outcomes.

Very small studies in the past investigated the ability of shorter duration of IC to predict 24-hour EE. In 1997, Smyrnios et al. compared 30-minute measurements with 24-hour measurements in 8 medical ICU patients and found that 30-minute studies were within 20% of 24-hour measurements for 89% of intervals, with the largest error range between 15:00–23:00 (13). In 2007, Zijlstra et al. compared 1-hour with 24-hour measurements in 12 critically ill patients and found that EE during the day fluctuated by 234 kcal in the most constant patient to 1190 kcal in the least constant patient, with a mean fluctuation of 521 kcal (14). Our study demonstrates smaller variability, on a much bigger sample size.

Latest ESPEN guidelines recommend that early full enteral nutrition shall not be used in critically ill patients but shall be prescribed within three to seven days. (Grade of recommendation A, 100% consensus) (9). Surgical patients have not been evaluated as far as their energy needs are concerned. Given the unique characteristics of critically ill surgical patients, most of them undergoing major abdominal surgeries, EN was usually initiated in days 3–7, therefore IC measurements were begun relatively late over the course of hospitalization. Continuous EE measurements did not significantly differ throughout this five-day course, in
alignment with the hypothesis that the metabolic needs of patients in this late period of the acute phase are gradually stabilizing, following successful resuscitation and establishment of hemodynamic stability with restoration of oxygen delivery (15–18).

Several limitations should be noted in our study. First, this is a single center retrospective observational study, among surgical ICU patients, therefore results are subject to possible unmeasured confounders and may not be generalizable to other patient populations. Second the EE measurements were obtained using the COVX module, a first generation of continuous REE measurements. This device has been shown to be less accurate than other devices and a more recent and accurate device has been developed since (19). However, a more recent comparison between COVX and a new generation of calorimeters did not reveal a significant difference (20). Third, results may have been affected by the use of continuous renal replacement therapy (CRRT) in 45 of 270 patients (16.66%), with unknown overlap between calorimetry measurement and CRRT times. IC may be less accurate when performed during CRRT (21). This is attributed to several mechanisms such as the conversion of bicarbonate infusion to CO2, uncompensated heat loss, and the small contribution of citrate to the caloric intake. However, all of these are considered very mild, altering measurements by up to 3% (22–23). Fourth, IC is less reliable when the fraction of inspired oxygen is above 0.6, however in this study we compared different periods of measurements during the same day, and during different days, therefore the ratio is likely to remain unaffected. The strength of this study includes the size and heterogeneity of the study population, the prolonged periods of IC measurements for each patient, and the width of baseline data available for each patient, allowing for adjustment to multiple covariates. To our knowledge, this is the largest study to include only ICU surgical patients being continuously monitored by indirect calorimetry.

In conclusion, periodic measurements of EE using indirect calorimetry can differ slightly when performed in various hours of the day and do not accurately represent 24-hour EE, however the error range is small and therefore may not necessarily have a clinical impact. The time period of 18:00–19:59 was found to correlate best with 24-h EE, and can be a reasonable alternative when continuous IC is not available.

**Declarations**

**Data Availability Statement**

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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**Author Contributions Statements**

YL: Conceived and designed the work that led to the submission, played an important role in interpreting the results, drafted and revised the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
OS: Designed the work that led to the submission, acquired data, revised the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

YA: Designed the work that led to the submission, played an important role in interpreting the results, revised the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

EN: Designed the work that led to the submission, acquired data, revised the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

FG: Designed the work that led to the submission, acquired data, revised the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

AGO: Designed the work that led to the submission, played an important role in interpreting the results, revised the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DS: Designed the work that led to the submission, played an important role in interpreting the results, revised the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

AN: Designed the work that led to the submission, acquired data, revised the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

PS: Designed the work that led to the submission, played an important role in interpreting the results, revised the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

NG: Conceived and designed the work that led to the submission, acquired data and played an important role in interpreting the results, drafted and revised the manuscript, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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**Ethical Approval:** The ethics committee of the Tel Aviv Medical Center approved the study, Institutional Review Board No. 0726-21-TLV.

**Competing Interests:** All authors declare no competing interests.

**References**


Tables

Tables 1-3 is available in the Supplementary Files section.

Figures
Figure 1

Two-hours calorimetry averages during different times of day, with 95% confidence intervals, analyzed by repeated measures ANOVA. The analysis is statistically significant difference with p<0.001
24-hour calorimetry averages during 5 consecutive days, with 95% confidence intervals, analyzed by repeated measures ANOVA. The analysis did not reach statistically significant difference with $p=0.077$.

**Supplementary Files**

This is a list of supplementary files associated with this preprint. Click to download.

- Table12022EJCN0972Lichteretal.xlsx
- Table22022EJCN0972Lichteretal.xlsx
- Table32022EJCN0972Lichteretal.xlsx