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Energy expenditure of patients on ECMO: A prospective pilot study

Elisabeth De Waele[1,2] | Joop Jonckheer[1] | Joeri J. Pen[2,3] | Joy Demol[1,2] | Kurt Staessens[4] | Luc Puis[4] | Mark La Meir[4] | Patrick M. Honoré[5] | Manu L. N. G. Malbrain[1,6] | Herbert D. Spapen[1,6]

[1]Intensive Care Unit, UZ Brussel, Vrije Universiteit Brussel (VUB), Brussels, Belgium

[2]Department of Nutrition, UZ Brussel, Vrije Universiteit Brussel (VUB), Brussels, Belgium

[3]Diabetes Clinic, Department of Internal Medicine, UZ Brussel, Vrije Universiteit Brussel (VUB), Brussels, Belgium

[4]Department of cardiac surgery, UZ Brussel, Vrije Universiteit Brussel (VUB), Brussels, Belgium

[5]Intensive Care Unit CHU Brugmann, Brussels, Belgium

[6]Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel (VUB), Brussels, Belgium

Correspondence
Elisabeth De Waele, Intensive Care Unit, UZ Brussel, Vrije Universiteit Brussel (VUB), Brussels, Belgium.
Email: Elisabeth.DeWaele@uzbrussel.be

Background: An optimal nutritional approach sustained by convenient monitoring of metabolic status and reliable assessment of energy expenditure (EE) may improve the outcome of critically ill patients on extracorporeal membrane oxygenation (ECMO). We previously demonstrated the feasibility of indirect calorimetry (IC)—the standard of care technique to determine caloric targets—in patients undergoing ECMO. This study aims to compare measured with calculated EE during ECMO treatment. We additionally provide median EE values for use in settings where IC is not available.

Methods: IC was performed in seven stable ECMO patients. Gas exchange was analyzed at the ventilator, and ECMO side and values were introduced in a modified Weir formula to calculate resting EE. Results were compared with EE calculated with the Harris-Benedict equation and with the 25 kcal/kg/day ESPEN recommendation.

Results: Total median oxygen consumption rate was 196 (Q1-Q3 158-331) mL/min, and total median carbon dioxide production was 150 (Q1-Q3 104-203) mL/min. Clinically relevant differences between calculated and measured EE were observed in all patients. The median EE was 1334 (Q1-Q3 1134-2119) kcal/24 hours or 18 (Q1-Q3 15-27) kcal/kg/day.

Conclusion: Compared with measured EE, calculation of EE both over- and underestimated caloric needs during ECMO treatment. Despite a median EE of 21 kcal/kg/day, large variability in metabolic rate was found and demands further investigation.

KEYWORDS

extracorporeal membrane oxygenation, ICU, indirect calorimetry, nutrition, resting energy expenditure

1 | INTRODUCTION

Nutrition therapy is recognized as an important component in the treatment of critically ill patients. Correct dosing of calories and proteins is vital in a general intensive care unit (ICU) population because under- and overfeeding are associated with significant morbidity and mortality.[1] There is a significant correlation with improved outcome in ICU patients in whom a caloric intake of 70% of measured energy expenditure (EE) and high protein intake is guaranteed.[2]

Indirect calorimetry (IC) is the gold standard for measuring EE.[3] European and American guidelines advocate the use of indirect calorimetry to determine EE and optimize nutritional therapy in ICU patients.[4,5] Nevertheless, many ICU clinicians still apply formulas to calculate EE when IC is not available. Various formulas have been proposed, all showing poor correlation or very wide limits of agreement with measured values.[6] Old-generation metabolic carts were costly and complex, but the evolution in technology and recent launch of a user-friendly and inexpensive IC device could substantially boost metabolic monitoring.[3]

There is no consensus on determining nutritional needs of patients on extracorporeal membrane oxygenation (ECMO). Pediatric patients on ECMO who received nutrition close to targeted energy intake had improved survival to hospital discharge.[7] Early low-volume enteral feeding could be achieved, but supplemental parenteral nutrition was essential to prevent cumulative energy and protein deficits during the first week of ECMO.[8] Yet, caloric goals were calculated and not measured because of the technical restraints withholding IC use in ECMO patients.

The current study aims to measure resting EE (REE) according to our previously developed concept and technical setup for using IC in ECMO patients.[9] The calorimeter was first connected to the ventilator and oxygen consumption (VO_2) and carbon dioxide transport (VCO_2) were measured until steady state was reached. Subsequently, we connected the calorimeter to the membrane oxygenator and performed a similar gas analysis. VO_2 and VCO_2 values at the native and artificial lung were summed and incorporated in a modified Weir equation to obtain a resting EE composite. Measured and calculated EE were compared. Finally, we provide a median measured EE of critically ill patients on ECMO to enable near optimal caloric loading in a setting without metabolic monitoring.

2 | METHODS

The study was approved by the Institutional Review Board of the University Hospital Brussel (UZ Brussel, Ethic Vote BUN 143201524713) and performed in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent of the patients' next of kin was obtained. Patients were included when following criteria were met: aged 18 years or older, undergoing venovenous or veno-arterial ECMO, stable condition (ie, no ECMO or ventilator adaptations during and within 60 minutes preceding measurements), and no contraindications for IC. The ECMO device (Eurosets, Medolla, Italy) was operated by a perfusionist under permanent supervision of the attending ICU physician and the senior researcher. The ECMO oxygenator was equipped with a long-term, nonporous 1.81 m^2 polymethylpentene membrane and a phosphorylcholine-coated antithrombotic tubing set. ECMO settings were decided by the in-house ECMO team and not influenced by the research setting. Measurements of gas exchange were performed according to a standard institutional ICU protocol. Briefly, a 30-minute metabolic evaluation was performed at the ventilator side. Gas sampling and flow measurements were obtained with a metabolic cart (VIASYS Healthcare Inc, Yorba Linda, CA, USA) following the American Association for Respiratory Care (AARC) guidelines.[10] The metabolic cart was subsequently installed at the ECMO side. Data were collected minute-to-minute for at least 30 minutes using breath-by-breath technology[9] and then inserted in a modified Weir formula software program.[9]

Data are presented as median with percentiles (IQR) or as indicated in the legend.

Editorial Comment

Knowledge of energy expenditure is necessary when making decisions on energy intake needs for patients, energy expenditure may be measured by indirect calorimetry, which is easy for patients on mechanical ventilation. Also, for patients on extracorporeal membrane oxygenation, these findings show that energy expenditure can be measured with a modified indirect calorimetry.

3 | RESULTS

Seven (five male and two female) patients were included. Patient characteristics are given in Table 1. Median age was 64 (60-77) years, median weight was 78 (68-90) kg, and median height was 175 (168-185) cm. ECMO settings, VO_2, and VCO_2 are depicted in Table 2. One thousand and sixty-six gas samples were analyzed at the ventilator level and 945 at the ECMO oxygenator level. Mean sampling time per patient took 65 min. Six of seven patients had the metabolic evaluation done on a median of 2.5 days after the start of ECMO, patient 7 had the measurement on day 7 of the ECMO treatment, which lasted for 11 days. The patients' average measured resting EE was 1841 kcal/24 hours, with a median of 1334 kcal/day. Resting EE of each individual patient is shown in Figure 1. Gas exchange predominantly took place at the ECMO level. In two patients, with lower ECMO gas flow settings, the lungs had a greater functionality (Figures 2 and 3). EE expressed per kg body weight varied between 12 and 33 kcal/kg/day (Figure 4). Figure 5 compares for each individual patient the measured resting EE, the EE calculated by the original and stress-adjusted Harris-Benedict formula, and the 25 kcal/kg actual body weight/day ESPEN recommendation. The median EE of a patient on ECMO was 21 kcal/kg/day.

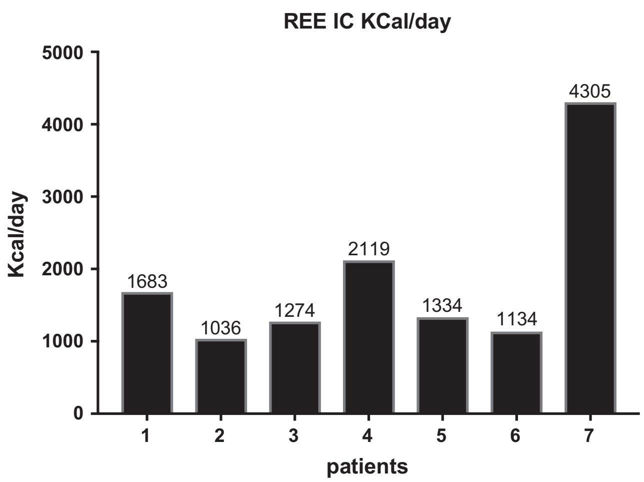

FIGURE 1 Measured Resting Energy Expenditure of each individual patient, in kcal/day

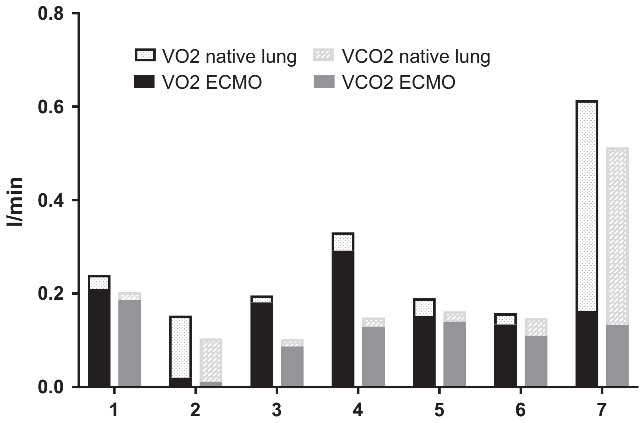

FIGURE 2 Gas exchange at the level of the lungs and at the level of the ECMO, in L/min, of seven patients

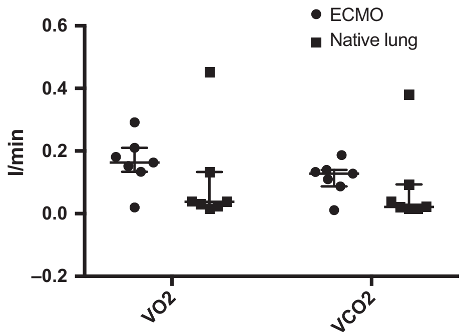

FIGURE 3 Gas exchange at the level of the lungs and at the level of the ECMO, in L/min, in median with interquartile ranges

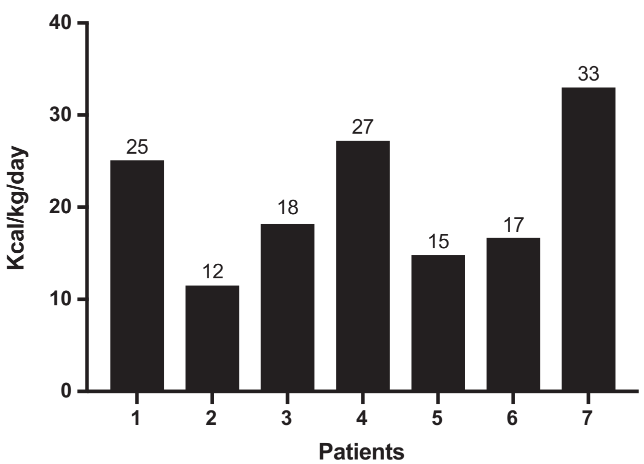

FIGURE 4 Resting Energy Expenditure expressed per kg of body weight

4 | DISCUSSION

Energy expenditure showed large interpatient variability. Although the small sample size does not allow to detect correlations with ongoing inflammation or underlying disease, we hypothesize that the metabolic state of our patients was determined by their

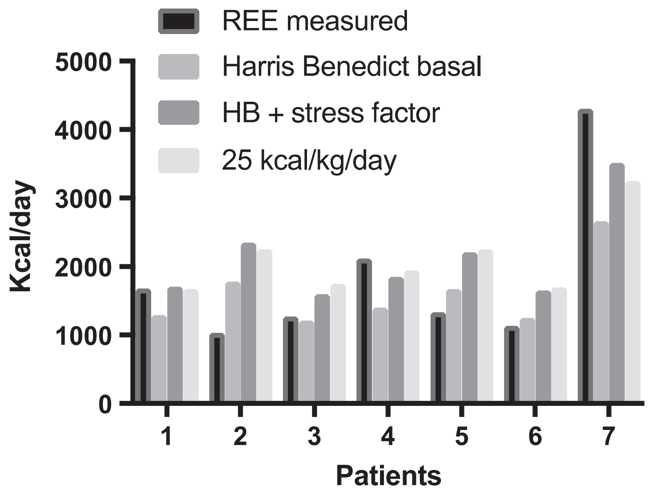

FIGURE 5 Resting energy expenditure (REE) as measured by IC, calculated by Harris-Benedict formula, this formula adjusted for stress situations, and 25 kcal/kg/day ESPEN recommendation for each patient

characteristics rather than by the ECMO setting. This is in line with data on metabolic rate in pediatric patients[11] and in patients on continuous renal replacement therapy.[12]

We found a median EE of 21 kcal/kg/day in our patient cohort. This is lower than currently proposed in the literature and much below the 25 kcal/kg/day recommended by ESPEN.[4] Formula-dependent EE overestimated and underestimated EE in four and three patients, respectively. Hereby the previously described lack of correlation between measured and calculated EE in a general ICU population is confirmed.[6] Wollersheim et al also recently reported large variations in EE and poor correlation between measured and calculated resting EE values between ECMO-treated and ECMO-naive acute respiratory distress syndrome (ARDS) patients.[13] We found a much lower average EE than in the Wollersheim study. This is in line with the fact that calculations usually overestimate EE and may also be explained by the difference in patient population, as Wollersheim et al only studied “hypermetabolic” ARDS patients.

In the Wollersheim setup, conventional IC is performed and extended by calculating O_2 uptake and CO_2 elimination through the difference in gas content before and after the filter and the extracorporeal life support (ECLS) blood flow. While easier to perform, this technique relies on ideal circumstances for the calculation part, which is not always the case in ECMO patients: blood flow can vary, patients' plasma can vary in acidity, lung function may alter… which are not represented in a snapshot analysis. Nevertheless, due to lower complexity, this approach could be advocated as a baseline measurement.

Overall, EE measured by IC was lower than EE calculated by formulas. Formulas use parameters that relate to healthy humans or have a sparse relationship with gas exchange. Depending on the type of ECMO, heart and lung function is partially taken over which may result in a lower resting EE as compared with “normal” physiological conditions.

Repeated or continuous metabolic monitoring may be the next promising step to gather metabolic information in this particularly vulnerable patient population.

Incorrect estimation of EE predisposes ICU patients to "iatrogenic" malnutrition due to frank over- or underfeeding and may result in worse outcome.[2] Our study underscores that IC offers an individualized EE approach. However, IC is not available in every ICU, and the demanding setup during ECMO (skilled healthcare practitioners to handle IC, permanent supervision of patient and interventions, time-consuming data collection and analysis) render routine use difficult to advocate. Nonetheless, ECMO is performed in expert centers and an optimal nutritional therapy should be part of this expertise. We therefore look forward to a higher readiness level of this approach.

The importance of the optimal and combined provision of energy and protein to improve clinical outcome has repeatedly been highlighted[14,15] and a correlation was recently objectified between a caloric intake of 70%-80% of measured EE and a protein intake of at least 1.5 g/kg/day and mortality.[2] Evidence is available to prove that IC can guide nutritional therapy and beneficially influence the outcome of critically ill patients.[16] However, the superiority of a nutritional therapy based on measured EE has not been proven in randomized controlled studies. Delivery of 100% of the measured energy target from day 4 to 8 significantly reduced nosocomial infection rate in ICU patients.[17] In contrast, IC-based covering of 100% of energy requirements from the first day of ICU stay in mechanically ventilated ICU patients did not affect the physical quality of life at 6 months or other important outcomes as compared to standard nutrition care.[18] Such discrepancy in outcome is difficult to explain but may rely on a difference in timing of caloric provision and inherently large variations in the metabolic and physiological response to acute disease.

The variation in metabolic reactions and physiological responses to acute disease in patients could partially explain the nonuniformity of the energy expenditure of the studied patients. Most of the patients in this study had the metabolic evaluation done in the early phase of treatment (first half or half of the ECMO run). The only patient with IC performed in the second half of treatment had the highest metabolic rate of the entire study population. Nevertheless, the cohort is too small to make any suggestions in this field, but with growing experience, patterns could become visible. Common sense suggests that the presence of an ECMO could not be appointed to as creating a hypermetabolic state in a patient, just as the presence of other extracorporeal modalities such as continuous venovenous hemofiltration can no longer be considered as pro-inflammatory. The evolution in technical modalities may explain the possible lower impact of these treatment modalities on our patients, making the metabolic state primarily determined by the original disease.

In conclusion, our study suggests that calculated EE offers inappropriate metabolic information in patients on ECMO. IC remains the gold standard and may become feasible in an adequately equipped center of expertise. An EE of 21 kcal/kg actual body weight/day was objectified, but the large variation in metabolic rate between patients should be subject of further investigation.

TABLE 1 Patient characteristics

Gender (f/m)	2/5
Age in years, median [25th/75th percentile]	64 [60/77]
Height in cm, median [25th/75th percentile]	175 [68/185]
Body weight in kg, median [25th/75th percentile]	78 [68/90]
BMI, median [25th/75th percentile]	26 [25/27]
Medical/surgical, n	5/2
Renal impairment yes/no, n	1/6
APACHE II score median [25th/75th percentile]	19 [13/23]

TABLE 2 ECMO and ventilator settings

ECMO: VV/VA	3/4
Gas flow L/min median [25th/75th percentile]	3.5 [2/6]
Blood flow L/min median [25th/75th percentile]	3.4 [3.1/4.4]
FiO2 ECMO % median [25th/75th percentile]	100 [65/100]
Fi02 ventilator % median [25th/75th percentile]	35 [30/41]
PEEP cm H20 median [25th/75th percentile]	10 [6/13]

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None.

CONFLICT OF INTEREST

The authors declare no conflict of interest in relation to the contents of this paper.

ORCID

Elisabeth De Waele http://orcid.org/0000-0002-5126-3500

REFERENCES

1. Preiser J-C, van Zanten A, Berger MM, et al. Metabolic and nutritional support of critically ill patients: consensus and controversies. *Crit Care*. 2015;19:35. https://doi.org/10.1186/s13054-015-0737-8.
2. Zusman O, Theilla M, Cohen J, Kagan I, Bendavid I, Singer P. Resting energy expenditure, calorie and protein consumption in critically ill patients: a retrospective cohort study. *Crit Care*. 2016;20:367. https://doi.org/10.1186/s13054-016-1538-4.
3. Oshima T, Berger MM, DeWaele E, et al. Indirect calorimetry in nutritional therapy. A position paper by the ICALIC study group. *Clin Nutr*. 2017;36:651–662.
4. Singer P, Berger MM, Van den Berghe G, et al. ESPEN Guidelines on Parenteral Nutrition: intensive care. *Clin Nutr*. 2009;28:387–400. https://doi.org/10.1016/j.clnu.2009.04.024.
5. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically Ill Patient. *J Parenter Enter Nutr*. 2016;40(2):159–211.

6. De Waele E, Opsomer T, Honoré PM, et al. Measured versus calculated resting energy expenditure in critically ill adult patients. Do mathematics match the gold standard? *Minerva Anestesiol*. 2015;81:272–282.
7. Greathouse KC, Sakellaris KT, Tumin D, et al. Impact of early initiation of enteral nutrition on survival during pediatric extracorporeal membrane oxygenation. *JPEN J Parenter Enteral Nutr*. 2018;42:205–211. https://doi.org/10.1002/jpen.1032.
8. Armstrong LB, Ariagno K, Smallwood CD, Hong C, Arbuthnot M, Mehta NM. Nutrition delivery during pediatric extracorporeal membrane oxygenation therapy. *JPEN J Parenter Enteral Nutr*. 2018;42(7):1133–1138. https://doi.org/10.1002/jpen.1154.
9. De Waele E, van Zwam K, Mattens S, et al. Measuring resting energy expenditure during extracorporeal membrane oxygenation: preliminary clinical experience with a proposed theoretical model. *Acta Anaesthesiol Scand*. 2015;59:1296–1302. https://doi.org/10.1111/aas.12564.
10. AARC_Guideline. AARC Clinical Practice Guideline Metabolic Measurement Using Indirect Calorimetry During Mechanical Ventilation — 2004 Revision & Update. *Respir Care*. 2004;49:1073–1079.
11. Dechert R, Wesley J, Schafer L, et al. Comparison of oxygen consumption, carbon dioxide production, and resting energy expenditure in premature and full-term infants. *J Pediatr Surg*. 1985;20:792–798.
12. Wu C, Wang X, Yu W, et al. Short-term consequences of continuous renal replacement therapy on body composition and metabolic status in sepsis. *Asia Pac J Clin Nutr*. 2016;25(2):300–307. https://doi.org/10.6133/apjcn.2016.25.2.29. PMID: 27222413.
13. Wollersheim T, Frank S, Müller MC, et al. Measuring energy expenditure in extracorporeal lung support patients (MEEP) - protocol, feasibility and pilot trial. *Clin Nutr*. 2018;37:301–307. https://doi.org/10.1016/j.clnu.2017.01.001.
14. Oshima T, Deutz NE, Doig G, Wischmeyer PE, Pichard C. Protein-energy nutrition in the ICU is the power couple: A hypothesis forming analysis. *Clin Nutr*. 2016;35:968–974. https://doi.org/10.1016/j.clnu.2015.10.016.
15. Strack van Schijndel R, Weijs P, Sauerwein HP, deGroot S, Beishuizen A, Girbes A. An algorithm for balanced protein/energy provision in critically ill mechanically ventilated patients. *E-SPEN*. 2007;2:69–74.
16. De Waele E, Honoré PM, Malbrain M. Does the use of indirect calorimetry change outcome in the ICU? Yes it does. *Curr Opin Clin Nutr Metab Care*. 2018;21:126–129. https://doi.org/10.1097/MCO.0000000000000452.
17. Heidegger CP, Berger MM, Graf S, et al. Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: a randomised controlled clinical trial. *Lancet*. 2013;381:385–393. https://doi.org/10.1016/S0140-6736(12)61351-8.
18. Allingstrup MJ, Kondrup J, Wiis J, et al. Early goal-directed nutrition in ICU patients (EAT-ICU): protocol for a randomised trial. *Dan Med J*. 2016;63:A5271.

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