Continuous Calorimetry in Critically Ill Patients

Kontinuálna kalorimetria u kriticky chorých pacientov

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Abstract
Objectives: The aim of the study was to assess the energy expenditure changes in critically ill patients using continuous indirect calorimetry and compare it with current theoretical models.
Material and Methods: 20 patients consecutively admitted to the intensive care unit of the Martin University Hospital. Energy expenditure has been monitored continuously during the stay in the unit using indirect calorimetry analysis of every breath by E-sCOVX module in connection with mechanical ventilator GE S 860. Subsequently, patients were divided into two phases: the first phase were patients during the time of full sedation and mechanical ventilation and the second phase were patients during the weaning period until extubation. The monitoring has been continuous with an analysis performed four times a day (24 hours were divided into foru 6 hours intervals, analysis was done in each interval during steady state). Standard requirements for indirect calorimetry were used.
Results: Energy expenditure during sedation and ventilation has been 1700 – 2000 kcal/kg/day, mean 1824 kcal/day (16 – 21 kcal/kg/day, mean 18 kcal/kg/day) without significant changes. There were no diurnal variations. In weaning, there was steady increase in energy expenditure since day 3 after cessation of sedation up to more than 5000 kcal/day.
Conclusions: It seems, that the course of energy expenditure in critically ill should be modified itno to phases: the initial metabolic supression lasting during the period of sedation and mechanical ventilation and the subsequent transition into hypermetabolism during weaning after cessation of sedation.

Keywords: Indirect calorimetry. Critical illness. Energy expenditure.

Abstrakt
Ciele: Kontinuálne sledovanie dynamiky zmien energetického výdaja kriticky chorých pacientov.
Materiál a metodika: Súbor tvorilo 20 kriticky chorých pacientov prijatých na Kliniku anestéziológie a intenzívnej medicíny Univerzitnej nemocnice v Martine. Energetický výdaj sa monitoroval kontinuálne počas celej doby hospitalizácie použitím nepriamej kalorimetrie technikou analýzy každého dychu u pacientov na umelej pľúcnej ventilácii. Technicky bol použitý ventilátor General Electric S 860 v spojení metabolickým modulom E-sCOVX. Pre analýzu boli pacienti rozdelení do dvoch fáz: prvú fázu tvorili pacienti počas plnej sedácie a umelej pľúcnej ventilácie, druhú fázu pacienti počas odpájania od ventilátora. Meranie sa robilo kontinuálne s analýzou 4-krát za deň (24 hodín bolo rozdelených do 6-hodinových intervalov, pričom v každom intervale sa robila jedna analýza počas ustáleného stavu) za dodržania štandardných podmienok pre nepriamu kalorimetriu.
Výsledky: Počas obdobia sedácie a ventilácie (fáza 1) sa nameraný energetický výdaj pohyboval medzi 1 700 a 200 kcal/deň, priemer 1 824 kcal/deň (16 až 21 kcal/kg/deň, priemer 18 kcal/kg/deň), bez štatisticky významných zmien. Nezistili sme ani významnú diurnálnu variáciu. Počas odpájania došlo k zvýšeniu energetického výdaja od tretieho dňa po zastavení sedácie až na hodnoty presahujúce 5 000 kcal/deň.
Záver: Zdá sa, že krivku priebehu EE u kriticky chorých pacientov je vhodné modifikovať na dve fázy. Iniciálna supresia metabolizmu, ktorá trvá počas celej fázy sedácie a ventilácie a následný prechod do hypermetabolizmu vo fáze odpájania od ventilátora a extubácie.

Kľúčové slová: Nepriama kalorimetria. Kritické ochorenie. Energetický výdaj.

Introduction

Critical illness is defined as organ failure that, without treatment, leads to death or significant organ damage, while being potentially curable [1]. According to the traditional theories, critical illness alters a patient's energy metabolism. The concept of metabolic response to stress was introduced by David Cuthbertson in 1942 [2,3]. According to the theory, the response consists of the initial „ebb" phase, characterized by metabolic suppression during the fight for survival. If the patient survives, a flow phase follows, marked by an increased metabolic rate and hypermetabolism during regeneration and recovery. The period was later divided into catabolic and anabolic flow. In the recent nutritional guidelines, these phases have been renamed as the acute and late phase [4,5,6].

Despite frequent citations of this concept in the literature, to our knowledge, continuous measurement of the metabolic rate has never been conducted in critical illness. Therefore, there is no clear evidence when these phases begin and end or the extent of changes in metabolic rate. This is an important information in intensive care, particularly regarding nutritional adjustment. Current indirect calorimetry methods allow fast intermittent or continuous measurements of patient energy expenditure (7,8).

In this study, E-sCOVX indirect calorimetry was used to continuously measure total energy expenditure (EE) in critically ill patients to evaluate dynamic metabolic changes during intensive care unit (ICU) hospitalization. We hypothesized that these changes would correspond to the current understanding of metabolic responses in critical illness.

Methods

The study was approved by Institutional Ethical Committee of the Jessenius Faculty of Medicine, Comenius University in Martin, Slovakia. Informed consent was not required, as the study involved only standard intensive care monitoring a therapeutic intervention and no personal patient data were included in the results. The study group consisted of patients hospitalized in the ICU of Martin University Hospital, Martin, Slovakia between October 15, 2022 and February 28, 2023. Inclusion criteria were age ≥ 19 years and presence of single or multiple organ failure requiring mechanical ventilation. The severity of illness was assessed using the sequential organ failure assessment score (SOFA). Patients were enrolled consecutively depending on the availability of one of two metabolic modules. Initially, the following data were collected: age, sex, height, weight, body mass index (BMI) and ideal body weight (IBW). BMI was calculated as weight in kilograms divided by height in meters squared (m^2). IBW was determined by using following formula for males: IBW = 50 kg + 2.3 kg for each inch over 5 feet, and for females: IBW = 45.5 kg + 2.3 kg for each inch over 5 feet. During calorimetric measurements body temperature, heart rate, blood pressure, Glasgow Coma Scale (GCS), as well as dosing and types of sedation and circulatory support medications were recorded. Daily records included SOFA, C-reactive protein, procalcitonin, nutritional support and energy intake. Intensive care was provided according to the standard protocols of the institution and decisions of the managing physician: sedation for comfort (midazolam, sufentanil, propofol, dexmedetomidine) without muscle relaxation, mechanical ventilation to achieve normoxemia and normocapnia, circulatory support to achieve normotension (noradrenaline, vasopressin). Parenteral and enteral nutrition were initiated according to the tolerance on the second or third day with the goal of 25 kcal/kg/day on the fifth to seventh day. No extracorporeal renal, lung or heart support was used. The measurement period was divided into two distinct phases. The first phase was the period of full sedation and mechanical ventilation. The second phase began following the cessation of sedation and initiation of weaning from mechanical ventilation, continuing until extubation, discharge form the ICU or death.

Indirect calorimetry with breath-by-breath analysis was used in patients on mechanical ventilation. In this study we used General Electric S 860 ventilator with E-sCOVX metabolic module and sampling T-piece inserted in ventilatory circuit. Continuously measured parameters included concentration of oxygen and carbon dioxide and expiratory tidal volumes. Carbon dioxide was measured by side-stream infrared spectrum absorption technique and oxygen by paramagnetic susceptibility. Tidal volume (Vt) was measured by pressure difference using General Electric D-lite module. The E-sCOVX modules were calibrated by authorized service personnel in accordance with the manufacturer‘s guidelines. Criteria for measurements were oxygen fraction (FiO2) less than 0.7, stable inspired O_2 concentration (variability less than 10 %), no significant air leaks (inspiratory/expiratory Vt difference <10 %). Measurements were done during metabolic steady state defined as oxygen consumption (VO_2) and carbon dioxide production (VCO_2) variability less than 10 % during a period of 20 minutes. Recorded parameters were: VO_2 (ml/kg), VCO_2 (ml/kg), respiratory quotient (RQ), total energy expenditure (EE, kcal/day), EE per body weight, EE per BSA. Measurement was continuous with 4 daily analyses during the steady state performed every 6 hours.

The results are presented as a mean values and standard deviation (SD). Mann-Whitney test and descriptive statistics were used for data analysis.

Table 1 *Patient group characteristics*

	Males	Females
Number:	10	10
Average age:	54,5	61,8
Average height (cm)	179,4	168,7
Average weight (kg)	99,5	94,8
Average BSA (m^2)	2,32	2,07
Average IBW	75,7	59,9
Average BMI	31,01	33,33
Average admission SOFA	11,25	10,9
Average admission GCS	4	3,66

BSA – body surface area, IBW – ideal body weight, BMI – body mass index, SOFA – sequential organ failure assessment, GCS – Glasgow Coma Scale

Results

The total of 20 patients were included – 10 males and 10 females in the age between 37 and 79 years (Table 1). Admission diagnoses are presented in Table 2. The maximal duration of both first and second phase was 7 days. The first phase involved all 20 patients, while the second phase included 8 patients. Patients were subsequently extubated, discharged from the ICU (still on ventilatory support) or died. Calorimetry began immediately after initiation of mechanical ventilation and the first analysis was performed within 4 hours after admission to the ICU.

Table 2 *Admission diagnosis*

	Diagnosis
1	Subarachnoid hemorrhage, a. basilaris aneurysmal rupture
2	Hemorragic shock, st.p. sleeve gastric resection
3	Hemorragic shock, esophageal varices
4	Facial trauma, fall of bicycle
5	CPR with ROSC, STEMI, st. p. PCI
6	Spontaneous intracranial bleeding
7	Acute hepatic failure
8	Hemorrhagic shock, abdominal aneurysm resection
9	Myocardial infarction, st. p. PCI
10	Subarachnoid hemorrhage, MCA aneurysmal rupture
11	Pneumonia, COPD exacerbation
12	CPR with ROSC, STEMI, st. p. PCI
13	Subarachnoid hemorrhage
14	Aspiration pneumonia
15	Pneumonia
16	Traumatic brain injury, brain edema
17	CPR with ROSC
18	Subarachnoid hemorrhage, traumatic
19	Pneumonia
20	Septic shock, coxitis l. sin, st. p. TEP

CPR – cardiopulmonary resuscitation, STEMI – ST segment elevation myocardial infarction, PCI – percutaneous coronary intervention, COPD – chronic obstructive pulmonary disease, TEP – total endoprothesis, ROSC – return of spontaneous circulation

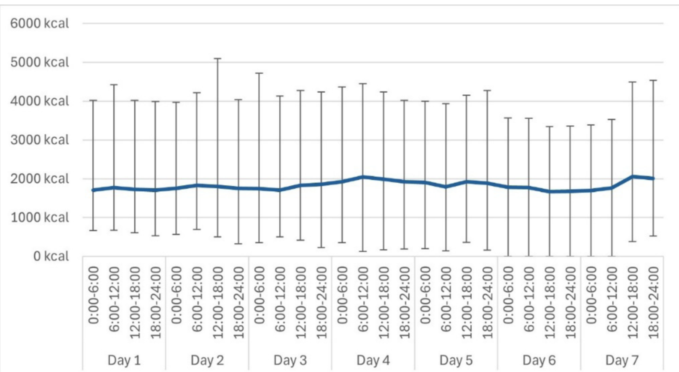
During the period of sedation and ventilation (phase 1), the energy expenditure ranged between 1700 and 2000 kcal/day, mean 1824 kcal/day (16 – 21 kcal/kg/day, mean 18 kcal/kg/day) with no statistically significant changes (Graph 1,2). No significant diurnal variability was observed. During the second phase continuous increase in EE was observed starting around day 3 post-sedation, reaching values above 5000 kcal/day (Graph 3, 4). Changes in SOFA and GCS are displayed in Figure 5.

Discussion

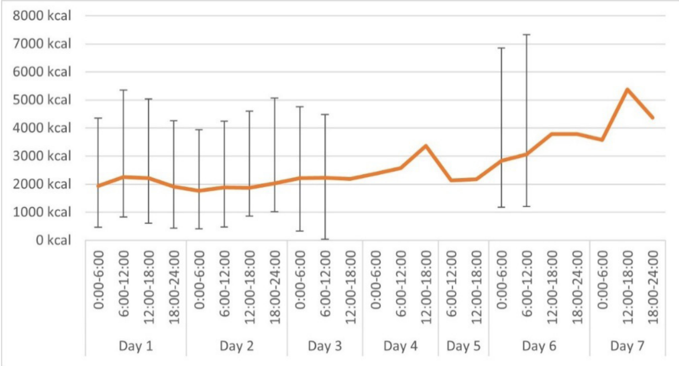
This study represents the first continuous measurement of energy expenditure in critically ill patients over the entire duration of their ICU stay. Our results diverge from the generally accepted metabolic model. The observed EE dynamics suggest the existence of two phases. An initial phase, marked by a decrease in EE to approximately 18 kcal/kg/day, lasting during the whole period of sedation and mechanical ventilation without significant changes. The second phase was characterized by a progressive increase of EE, reaching up to 30 kcal/kg/day during the process of weaning and extubation. Previous studies relied on intermittent measurements taken over in intervals of several days or weeks, potentially missing dynamic metabolic changes occurring between the measurements. There are three studies with similar design as ours.

The first prospective study measured energy expenditure in patients with COVID-19 over a 7-week hospitalization period using Q-NRG technology. Measurements were performed three times a week, however, no clear data indicate the length of sedation, ventilation, or weaning from the ventilator. The authors observed an initial mean EE of 21.3 kcal/kg/day (15 – 20 kcal/kg/day), followed by subsequent increase to 28.1 kcal/kg/day after the third week. While the initial results are in accordance with our results, the observed increase occurred later. Prolonged sedation, ventilation, and weaning, typically required in patients with COVID-19, might be the cause the delayed increase in EE [10].

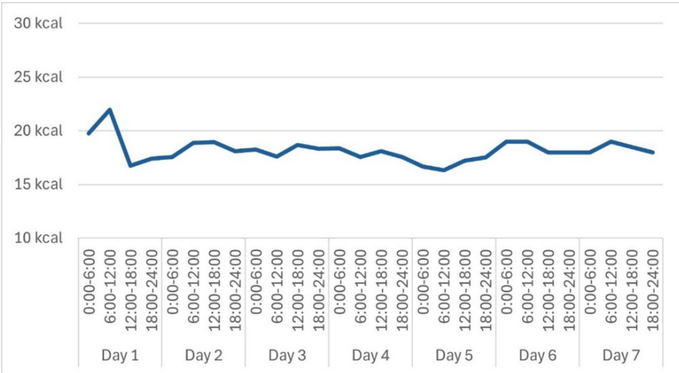
Moonen et. al. [2023] conducted another prospective observational study involved measurements using Q-NRG technology every 3 days in patients in the ICU, followed by canopy-based measurements after extubation during the regular ward stay. During the intensive phase the EE ranged from 1608 to 2110 kcal/day (18 – 23 kcal/kg/day). The authors describe an increase in EE after day four to 110 % of predicted EE, but without statistical significance. As in the previous study, the duration of sedation and ventilation has not been specified. Significant increase in EE was noted after exubation and discharge to regular ward [11].



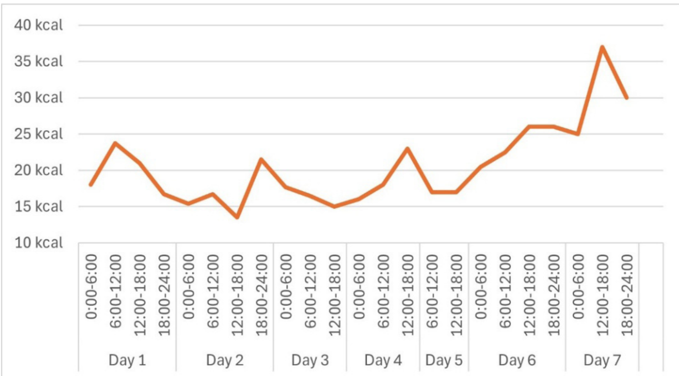
***Graph 1** Total energy expenditure in phase 1*



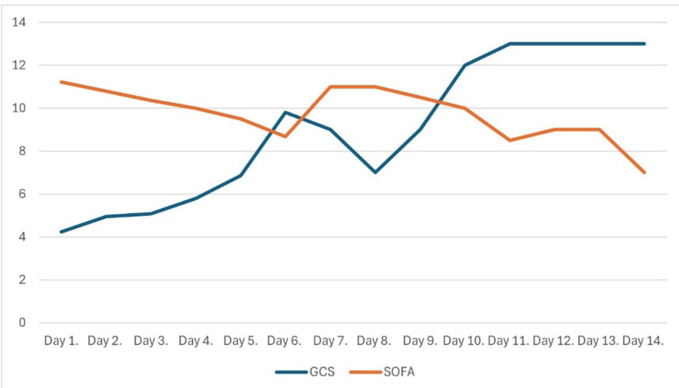
***Graph 2** Total energy expenditure in phase 2*



***Graph 3** Energy expenditure per kg body weight in phase 1*



***Graph 4** Energy expenditure per kg body weight in phase 2*



***Graph 5** Time course of SOFA and GCS in the whole group*

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An American prospective study included 22 patients with COVID-19 in whom the EE was measured using Q-NRG technology with measurements taken every 3 days during the first 3 weeks of illness. The reported average EE values were as follows: during the first week 1 568 kcal/day (1 175 - 2 215 kcal), what represents 19 kcal/kg/day (13.7 – 28.5 kcal/kg/day), during the second week 1 830 kcal/day (1 465 - 2 467 kcal), 26 kcal/kg/day (22 - 42 kcal/kg/day) and the third week 2 789 kcal/day (1 776 - 3 262 kcal), 30,4 kcal/kg/day (27 – 35.8 kcal/kg/day). However, the exact length of sedation and ventilation has not been described, the findings confirm the initial low EE during the first week with its subsequent increase [12].

Among the studies relevant to our research is TICACOS study, which primarily observed the relationship between nutrition and EE measured by Deltatrac. However, the study lacked clearly defined measurement intervals and durations. The average EE values during hospitalization were 1 838 kcal/day (1 370 - 2 306 kcal/day), 17 - 29 kcal/kg/day [13].

A retrospective study from Israel observed the relationship between nutrition, EE and prognosis of critically ill patients. Included 1 171 ventilated patients with average EE of 1 944.1 kcal/day (1 449 - 2 439 kcal/day), 18 - 30 kcal/kg/day. Measurements were obtained by Deltatrac, again without detailed information regarding the timing and duration of assessment [14]. Based on the methodology of these two studies, it may be reasonable to infer that the lower levels of EE have been in the initial phase of hospitalization, what is in accordance with our findings.

A prospective study from Asia focused on 16 patients in septic shock and EE measurements during the first three days following the initiation of mechanical ventilation. The average EE was 1 448 kcal/day, 1 449 kcal/day a 1 560 kcal/day, representing 26.7 kcal/kg/day (21.4 – 32 kcal/kg/day). The absolute values may be influenced by different anthropometric values in Asian population. Nevertheless, the study supports the presence of initial decreased and stable EE during sedation and ventilation of patients in critical illness [15].

In our study, we recorded all parameters known to influence EE [16]. However, analyzing the individual contributions of these factors to EE variation was not the aim of the study and would require more extensive analysis. On the other hand, it is worth noting, that the decrease in the SOFA score alongside a concurrent increase in GCS – reflecting reduced disease severity, weaning of sedation and return of mental and physical activity – was associated with a corresponding increase in EE.

The study has several limitations. First limitation is the validation of the methodology. Several studies comparing E-sCOVX to Deltatrac reported around 10% overestimation, while Deltatrac has traditionally been considered the gold standard for indirect calorimetry [17,18]. However, when comparing our results with those obtained by Q-NRG, no significant differences were observed. Q-NRG has been validated against mass spectroscopy and is widely considered to be a valid method [4,19,20]. It remains debatable, whether it is correct to continue considering the 35-year-old Deltatrac technique to be the gold standard for modern technologies [21]. Another limitation is small sample size and relatively short ICU stay, which limited the ability to perform robust statistical analysis – especially in the second phase of the study – necessitating reliance only on descriptive methods. Finally, we did not analyze the influence of the factors known to contribute to EE changes. Such an analysis would be highly complex and would require a larger study.

Conclusions

It seems, that the EE curve in critically ill patients might be modified into two phases: the initial phase of metabolic suppression lasting during the whole period of sedation and mechanical ventilation and the subsequent phase of increased EE during weaning and extubation. It may change the current nutritional goals in these patients.

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