Determining energy requirements in the ICU

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Abstract
Nutritionists, intensive care doctors, researchers, and innovators must collaborate to develop an indirect calorimeter to a reasonable cost (less than 10000 s) that is accurate and handy in the clinical setting. Since this instrument is not yet available, clinicians are left with good clinical practice and predictive formulas.

Reference

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Determining energy requirements in the ICU

Anne Berit Guttormsen a and Claude Pichard b

Purpose of review
Resting energy expenditure in critically ill patients is highly variable depending on the diagnoses, illness severity, nutritional status, and treatments. The main questions are the following: What is the optimal energy target in my critically ill patient in the ICU at a given time point of the ICU stay? Is measured energy expenditure equivalent with energy requirement?

Recent findings
There is uncertainty on the best way to feed the ICU patient; when to start, and what to give, especially concerning the amount of energy. Recent studies indicate that outcome is dependent on provision, components, and route. Indirect calorimetry is considered the gold standard to measure energy requirement and cannot be replaced by assumptions based on weight, height, sex, age, or minute ventilation. A main concern is that an indirect calorimeter with appropriate specifications to a reasonable cost is not available in the market. There are initiatives to solve this matter.

Summary
Nutritionists, intensive care doctors, researchers, and innovators must collaborate to develop an indirect calorimeter to a reasonable cost (less than 10 000 €) that is accurate and handy in the clinical setting. Since this instrument is not yet available, clinicians are left with good clinical practice and predictive formulas.

Keywords
critically ill, energy expenditure, hypermetabolism, hypometabolism, indirect calorimetry, intensive care

INTRODUCTION
Energy expenditure in critically ill patients is immensely variable depending on disease, illness severity, and nutritional status. The optimal energy target is not yet defined, and experts disagree on the best way (timing and amount) to feed these patients. Observation and intervention studies have shown that the amount of energy provided undoubtedly affects outcome. It is a common knowledge that predictive formulas developed to calculate resting energy expenditure (REE) in different categories of intensive care patients are clinically not relevant. Whizzes agree and urge intensive care physicians to measure REE with indirect calorimetry in order to optimize the prescription of nutritional support [1*]. This advice is in contrast to what is advocated in the Canadian guidelines of nutrition, claiming that there are insufficient data to prefer indirect calorimetry over predictive equations in the critically ill. It is added that this guidance is given as a result of lack of potent studies in the field. The foremost concern at the moment is that an indirect calorimeter with applicable specifications – easy to use and to a reasonable cost – is not available in the market [2**,3**]. In the ICU, REE is usually measured in the fed state, which also includes the thermogenesis of feeding.

THE EPANIC AND THE REDOXS STUDIES
These large multicenter studies comprising 4640 [4] and 1223 patients [5*], respectively, were recently published with exceedingly unexpected results. Among nutritionists, the studies were heavily criticized due to flaws in design, erroneous patient populations (either low-risk patients or too critically ill patients), and improper composition of the energy provided. It has been pointed out that the high dose of glucose (1200 kcal/24 h during the first 2 days) given to the parenteral nutrition group in the early versus late parenteral nutrition in critically ill patients significantly increased morbidity and mortality.

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ill adults (EPaNIC) study was harmful. An over-representation of cardiac and perioperative patients also reduced external validity. The concerns about the study design and the results were pinpointed in a recent commentary by McClave et al. [6]. In a recent post-hoc analysis of the data in the EPaNIC study, the lowest dose of macronutrients was associated with the fastest recovery. Any higher dose, administered parenteral or enteral, was associated with progressively more delayed recovery [7]. The conclusions from the EPaNIC study contradict results from observation studies showing that reduced intake of macronutrients and micronutrients is deleterious [8,9]. It should also be mentioned that malnourished patients (BMI <18.5 kg/m²) were not included in the EPaNIC trial. In the glutamine and antioxidants in critically ill patients (REDOXS) study [5**], very high doses of glutamine (total 65 g, 0.78 g/kg more than twice the recommended dose of 0.3 g/kg) were administered to critically ill patients with severe organ failure. Energy and protein provision were low, approximately 900 kcal and 45 g, respectively. In a commentary to the article, it was discussed that a supplement comprising 60% of needed dietary protein might cause imbalance in the protein pool and could be potentially toxic. In the REDOX study, long-time outcome (6 months) was inferior in the study groups receiving either glutamine or glutamine and selenium. Neither EPaNIC nor REDOX study used indirect calorimetry to guide provision of energy, leaving energy expenditure basically unknown.

**KEY POINTS**

- Estimation of energy requirement using equations or guideline recommendations is frequently inaccurate.
- An accurate, reasonably prized, and handy indirect calorimeter is obligatory to measure energy expenditure on a daily basis, and in research projects.
- Future studies about optimal energy provision should be multicenter with mixed endpoints, such as long-term survival, quality of life, and cost.

**HOW TO MAKE THE DECISION ON ENERGY SUPPLY OF THE INTENSIVE CARE PATIENT?**

This question is vital and has been heavily debated for ages. In the early seventies, intravenous hyper-alimentation (40–60 kcal/kg/24 h) was popular, complicated with high blood sugar and fatty liver. In the millennium, the pendulum has moved to deliver less energy, mostly provided through the gut [4,10,11]. Guidelines give divergent advice, leaving the clinician worryingly confused. There is an agreement among specialists that targeting energy delivery might be a good choice. A study aiming at comparing targeted energy provision as measured with indirect calorimetry, compared to standard of care has been performed [12]. One flaw in this study was a modest but systematic overfeeding since prescription of non-nutritional calories was not taken into account. Disappointingly, the intervention group stayed longer in the ICU and had fewer ventilator-free days. Post-ICU survival was higher in the targeted group, but one should keep in mind that the study was not powered to evaluate mortality. Studies have not investigated if the amount of energy measured is what should be provided to the critically ill patient. Since both observation and intervention studies indicate that less than targeted energy might be advantageous, this question should be investigated with a multicenter design. To gain reliable knowledge from such studies, an accurate indirect calorimeter has to be in place. Another imperative question is: What are the most meaningful endpoints in nutritional studies? – survival out of ICU, hospital survival, 1-year survival, quality of life, caloric deficit, infection, ventilator-free days and/or loss of muscle mass? The question remains open, but it is likely that a mix of long-term survival, quality of life, and cost will become the determining criteria. To achieve the needed discriminative power, collaboration across Europe is needed. The use of indirect calorimetry is currently time-consuming and costly, which discourages many clinicians to use it on a regular basis. In a recent feasibility study, 50% of the patients were applicable for indirect calorimetry, but it was only used in 20% of the patients [13*]. This means that most clinicians are left to use equations. This is a problem as energy demand changes over time, being initially low, and increasing toward the end of the ICU stay. The only method to scrutinize the variation in energy demand is indirect calorimetry. The Faisy equation is a dynamic formula since it includes tidal volume and temperature, but it is not proven better than other equations to estimate energy expenditure. The Toronto formula, used to calculate energy needs in the burn patient, takes fluctuation in energy demand into consideration, and is among burn specialists considered satisfactory to calculate energy pending indirect calorimetry.

**ESTIMATION OF THE ENERGY TARGET USING PREDICTIVE EQUATIONS**

Two patients with the same weight, age, and sex may differ considerably in energy expenditure.
Therefore, an estimate expressed by an equation or as kcal/kg does not correctly individualize the energy target. As already mentioned, the Toronto formula is applicable to estimate energy requirement in the intensive care burn patient. There are more than 200 suggested equations to estimate energy expenditure, and most of them are not applicable in the ICU setting [14]. Four equations used in ICU patients are given below:

1. **Harris-Benedict**

   \[
   \text{EE (men)} = 66.473 + 13.7516 \\
   \times \text{weight (kg)} + 5.003 \\
   \times \text{height (cm)} - 6.755 \\
   \times \text{age (year)}
   \]

   \[
   \text{EE (women)} = 655.0955 + 9.5634 \\
   \times \text{weight (kg)} + 1.8496 \\
   \times \text{height (cm)} - 4.6756 \\
   \times \text{age (year)}
   \]

2. **Faisy et al.’s**

   \[
   \text{EE (kcal/day)} = 8 \times \text{weight (kg)} + 14 \\
   \times \text{height (cm)} + 32 \\
   \times \text{minute ventilation (l/min)} \\
   + 94 \times \text{temperature (°C)} \\
   - 4834
   \]

3. **ESPEN**

   Acute or recovery phases: 20–25 or 25–30 kcal/kg body weight, respectively.

   In Burn Patients,

4. **Toronto**

   \[-4343 + (10.5 \times \% \text{burn surface area}) \\
   + (0.23 \times \text{caloric intake}) + (0.84) \\
   \times \text{Harris–Benedict equation} + (114) \\
   \times \text{body temperature} - (4.5) \\
   \times \text{postburn days} \]

**MEASUREMENT OF ENERGY EXPENDITURE**

The principles for direct and indirect calorimetry are shown in Fig. 1. Direct calorimetry requires the subject to be introduced into a sealed insulated chamber for a few hours to measure the energy losses by direct body thermic radiation. It is not applicable to patients and therefore is not discussed in this review.

**Indirect calorimetry**

Historically, the basics of energy metabolism were established by Lavoisier, Priestley, and Black some 200 years ago. They demonstrated that combustion consumed oxygen and produced CO\(_2\) and heat. Early in the 20th Century, Harris and Benedict, and Atwater revealed that heat production could be estimated by measuring gas exchange and computing corresponding heat production from the energy content of nutrients. When caloric values and equivalent gas volumes are known, equations combining oxidation of a substrate with O\(_2\) and CO\(_2\) production are constructed. To incorporate protein oxidation rate, an equation combining urea nitrogen production was also developed. On the basis of these data, J.D. de Weir developed the Weirs equation, used in indirect calorimetry algorithms for measurement of 24-h energy expenditure.

**Oxygen consumption (VO\(_2\))**

Under aerobic, but not under anaerobic, conditions, VO\(_2\) reflects cellular metabolic activity. The amount
of oxygen needed for production of 1 kcal from oxidation of carbohydrates (CHO), fat (F), and protein (P), respectively, is 207, 213, and 223 ml (Table 1). $\dot{V}O_2$ can also be measured as the product of cardiac output and the arterio-venous oxygen difference (Fick’s principle). Fick is an alternative technique whenever a Swan-Ganz catheter is available, but with accuracy limitations as it does not take into account the heart’s consumption of $O_2$.

**Carbon dioxide production ($VCO_2$)**

The only way to accurately measure $VCO_2$ is by indirect calorimetry, and in steady state, $VCO_2$ reflects the metabolic activity in the cells. Production of 1 kcal of heat from CHO, F, and P oxidation produces 207, 151, and 181 ml $CO_2$, respectively (Table 1).

**Respiratory quotient**

Respiratory quotient is the relation between produced $CO_2$ and used $O_2$ (respiratory quotient = $VO_2/VCO_2$). This relation usually differs between 0.65 and 1.2, dependent on which substrate is oxidized. Oxidation of CHO gives a respiratory quotient of 1.0. In relation to stress, the respiratory quotient decreases due to increased combustion of F. Intake of large amounts of CHO increases $VCO_2$ and the respiratory quotient.

**Calculation of substrates oxidation**

Oxidation rate of CHO, F, and P according to the values given in Table 1 is calculated as follows:

\[
\dot{V}_O_2 (l/min) = 0.829 \dot{V}_{O_2} + 2.019 \dot{V}_F + 6.04 \dot{U}_N \tag{1}
\]

\[
\dot{V}_C O_2 (l/min) = 0.829 \dot{V}_{O_2} + 1.427 \dot{V}_F + 4.89 \dot{U}_N \tag{2}
\]

where $\dot{U}_N$ = nitrogen.

By solving these equations oxidation rates of CHO, F, and P are:

\[
\dot{V}_{O_2} = 4.12 \dot{V}_{CO_2} - 2.91 \dot{V}_{O_2} - 2.54 \dot{U}_N \tag{3}
\]

\[
\dot{V}_F = 1.69 \dot{V}_{O_2} - 1.69 \dot{V}_{CO_2} - 1.94 \dot{U}_N \tag{4}
\]

and protein oxidation rate ($dP$) is:

\[
dP = 6.25 \dot{U}_N \tag{5}
\]

Energy expenditure in steady state is the sum of oxidation rates multiplied by the caloric value of each substrate (Table 1):

\[
EE = 4.18 \dot{V}_{O_2} + 9.46 \dot{V}_F + 27 \dot{U}_N \tag{6}
\]

By substituting CHO and F by Eqs. (3) and (4), we get:

\[
EE = 3.82 \dot{V}_{O_2} + 1.22 \dot{V}_{CO_2} - 1.99 \dot{U}_N \tag{7}
\]

Due to differences in calorimetric values used, this equation differs slightly from the classical de Weir’s equation:

\[
EE/(kcal/24h) = 3.94 \dot{V}_{O_2} + 1.11 \dot{V}_{CO_2} - 2.17 \dot{U}_N
\]

where $\dot{U}_N$ is nitrogen excretion in the urine during 24 h.

It is also possible to derive REE from $\dot{V}_{O_2}$ alone if the patient is in steady state and not in respiratory failure:

\[
EE/(kcal/24h) = \dot{V}_{O_2} \cdot 4.838 \cdot 1.44
\]

**Inspired and expired volumes and the Haldane transformation**

The difference between expiratory and inspiratory content of $O_2$ and $CO_2$ is small and is difficult to

<table>
<thead>
<tr>
<th>Substrate</th>
<th>$O_2$</th>
<th>$CO_2$</th>
<th>RQ</th>
<th>Caloric value (kcal/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate (CHO)</td>
<td>0.829</td>
<td>0.829</td>
<td>1.00</td>
<td>4.18</td>
</tr>
<tr>
<td>Fat (F)</td>
<td>2.019</td>
<td>1.427</td>
<td>0.71</td>
<td>9.46</td>
</tr>
<tr>
<td>Protein (P)</td>
<td>0.966</td>
<td>0.782</td>
<td>0.81</td>
<td>4.32</td>
</tr>
<tr>
<td>Urea nitrogen</td>
<td>6.04</td>
<td>4.89</td>
<td></td>
<td>27.0</td>
</tr>
</tbody>
</table>

RQ, respiratory quotient.

Caloric values are given differently in the literature. The values given in the table are typical values.
measure with sufficient accuracy. Therefore, the Haldane transformation, based on the assumption that $[N_2]$ is the same in inspired and expired air, is used to measure inspiratory volumes ($\dot{V}_i$).

(a) $\dot{V}_{O_2} (l/min) = (\dot{V}_i \cdot F_{O_2}) - (\dot{V}_e \cdot F_{O_2})$

(b) $\dot{V}_{CO_2} (l/min) = (\dot{V}_i \cdot F_{CO_2}) - (\dot{V}_e \cdot F_{CO_2})$

$\dot{V}_i$: Inspired volume
$\dot{V}_e$: Expired volume
$F_i$: Oxygen, respectively CO$_2$ concentration in inspired air
$F_e$: Oxygen, respectively CO$_2$ concentration in expired air

(c) $\dot{V}_i = \frac{F_{CO_2}}{F_{O_2}} \cdot \dot{V}_e$

Equations (a) and (c) are used to prove this formula:

(d) $\dot{V}_{O_2}(l/min) = \dot{V}_e \left( \frac{F_{CO_2} \cdot (1 - F_{CO_2} - F_{CO_2})}{1 - F_{CO_2}} \right) - F_{CO_2}$

The higher the FiO$_2$, the more inaccurate the measurement will be.

**Resting energy expenditure**

Indirect calorimetry [15] is considered the most accurate method to measure REE. Before measurement, steady-state conditions must be achieved. If ventilation changes, it will take at least 1 h to gain a new steady-state condition. Two different techniques are used, the open and closed circuit. In the closed circuit, breathing is done from a closed gas mixture. CO$_2$ and water are removed from the expiratory gas and used for subsequent inspirations. The amount of oxygen added to the circuit corresponds to VO$_2$. In the open circuit, used in most indirect calorimeters, inspired and expired O$_2$, CO$_2$, and flow are measured. On the basis of these measurements, VO$_2$ and VCO$_2$ are calculated. REE [70% of total energy expenditure (TEE)] is measured from determining VO$_2$ and VCO$_2$ and applying Weir’s equation. Most of the clinical studies on indirect calorimetry in ICU patients have used an apparatus (Deltatrac II, Datex, Finland) developed about 30 years ago. Sale of Deltatrac II was discontinued 8 years ago and very few working units still remain. New instruments are in the market, but recent prospective studies have shown that new devices have insufficient precision, accuracy, and reproducibility. Therefore these machines are not recommended for clinical practice. Initiatives to develop new indirect calorimeters applicable for spontaneous ventilation, for patients on non-invasive ventilation (NIV) and on the ventilator are taken.

**CONCLUSION**

Nutritionists, intensive care specialists, researchers, and innovators must collaborate to develop a new indirect calorimeter to a reasonable cost (less than 10000 €) that gives reliable data and is easy to use in the clinical setting. Until then, we suggest to use The European Society for Clinical Nutrition and Metabolism guidelines, that is 20–25 kcal/kg in the acute phase and 25–30 kcal/kg in the recovery phase, to estimate energy requirement in the critically ill patient.

**Acknowledgements**

The input to the manuscript by Jørn Henrik Vold was highly appreciated.

**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES AND RECOMMENDED READING**

Papers of particular interest, published within the annual period of review, have been highlighted as:

● of special interest

★★ of outstanding interest


This article outlines an applicable guide for nutrition of the ICU patient.


Important reading before a new indirect calorimeter is implemented in clinical practice.


Important reading before a new indirect calorimeter is implemented in clinical practice.


This is the largest study comparing the effect of glutamine to standard of care. The results have to some extent changed standard of care.


