Clinical Nutrition ESPEN 63 (2024) 856–869

Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: http://www.clinicalnutritionespen.com

Educational Paper

How to interpret and apply the results of indirect calorimetry studies: A case-based tutorial

Mette M. Berger [a, *], Elisabeth De Waele [b], Leah Gramlich [c], Jennifer Jin [d], Olivier Pantet [e], Claude Pichard [f], Ashlee Jean Roffe [g], Lindsey Russell [h], Pierre Singer [i], Paul E. Wischmeyer [j]

[a] Faculty of Biology & Medicine, Lausanne University, Lausanne, Switzerland
[b] Department of Clinical Nutrition, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel, Brussels, Belgium
[c] Department of Medicine, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta Canada
[d] Division of Gastroenterology, Royal Alexandra Hospital, 10240 Kingsway Avenue, Edmonton, Alberta, Canada
[e] Department of Adult Intensive Care, Lausanne University Hospital (CHUV), Lausanne, Switzerland
[f] Department of Clinical Nutrition, Geneva University Hospital, Geneva, Switzerland
[g] Nutrition Department, Endeavor Health Swedish Hospital, Chicago IL, USA
[h] Department of Gastroenterology, Hepatology, and Nutrition, Digestive Disease & Surgery Institute, Cleveland Clinic, Cleveland, OH, USA
[i] Intensive Care Unit, Herzlia Medical Center and Department of General Intensive Care and Institute for Nutrition Research, Rabin Medical Center, Beilinson Hospital, Sackler School of Medicine, Tel Aviv University, Tel Aviv, and Intensive Care Unit, Herzlia Medical Center, Israel
[j] Department of Anesthesiology and Surgery, Duke University School of Medicine, Durham, NC, USA

ARTICLE INFO

Article history:
Received 14 May 2024
Accepted 28 July 2024

Keywords:
Energy expenditure
Indirect calorimetry
Respiratory quotient
Overfeeding
Enteral nutrition
Parenteral nutrition
Critical care
Obesity

SUMMARY

Evidence is growing that the individual adjustment of energy targets guided by indirect calorimetry (IC) can improve outcome. With the development of a new generation of devices that are easier to use and rapid, it appears important to share knowledge and expertise that may be used to individualize nutrition care. Despite the focus of this tutorial being on one contemporary device, the principles of IC apply across existing devices and can assist tailoring the nutrition prescription and in assessing response to nutrition therapy. The present tutorial addresses its clinical application in intubated mechanically ventilated and spontaneously breathing adult patients (canopy), i.e. it covers the range from critical illness to outpatients.

The cases that are presented show how the measured energy expenditure (mEE), and the respiratory quotient (RQ), i.e. the ratio of expired CO_2 to consumed O_2, should be applied in different cases, to adapt and individualize nutrition prescription, as it is a good marker of over- or underfeeding at the different stages of disease. The RQ also informs about the patient's body's capacity to use different substrates: the variations of RQ indicating the metabolic changes revealing insufficient or excessive feeding. The different cases reflect the use of a new generation device as a metabolic monitor that should be combined with other clinical observations and laboratory biomarkers. The tutorial also points to some shortcomings of the method, proposing alternatives.

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Abbreviations: BEE, Basal energy expenditure; BW, Body Weight; DIT, Diet-induced thermogenesis; EE, Energy expenditure; EPI, exocrine pancreatic insufficiency; FMI, Fat Mass Index; HBE, Harris and Benedict equation; IC, Indirect calorimetry; mEE, Measured energy expenditure; REE, Resting energy expenditure; RQ, Respiratory quotient; VAP, Ventilator-associated pneumonia; VCO_2, Carbon dioxide production; VO_2, Oxygen consumption.

* Corresponding author.
E-mail addresses: Mette.Berger@unil.ch (M.M. Berger), Elisabeth.DeWaele@uzbrussel.be (E. De Waele), lg3@ualberta.ca (L. Gramlich), jennifer.jin@ualberta.ca (J. Jin), olivier.pantet@chuv.ch (O. Pantet), claude.pichard@hcuge.ch (C. Pichard), ARoffe@schosp.org (A.J. Roffe), russell5@ccf.org (L. Russell), pierre.singer@gmail.com (P. Singer), paul.wischmeyer@duke.edu (P.E. Wischmeyer).

https://doi.org/10.1016/j.clnesp.2024.07.1055
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1. Introduction

The centenary of the Harris and Benedict equation (HBE) was celebrated in 2019 [1]. This first predictive equation of basal energy expenditure (BEE) (Table 1A) was based on the measurement of respiratory gas exchange [2]. Since this landmark equation was developed, it has become obvious that despite estimating BEE, it was not directly applicable in clinical settings, being designed for resting healthy individuals. Moreover, it remains an estimation which does not integrate metabolic changes. The inaccuracy of the HBE further increases when "activity factors" are applied (Table 1B).

In the 1930s technical progress enabled easy measurements of oxygen (O_2) and carbon dioxide (CO_2) concentrations, as well as of the volume of respiratory gases and heat production of living organisms. In 1949, J.B. Weir developed an equation based on the O_2 consumption (VO_2) and CO_2 production (VCO_2), derived from first principles for the energy (kcal) value of a litre of O_2 metabolizing a mixture of carbohydrate, protein and fat [3]. The value of protein oxidation derived from urea excretion (uN_2) is negligible. Importantly if applied in a patient on continuous feeding this equation reflects total energy expenditure (TEE), i.e. the sum of the basal energy expenditure (EE) and the diet induced thermogenesis (DIT) (see Section 2). Indeed heat production is tightly correlated with both gases according to the type of energy substrate that is metabolized [4,5].

How much energy should the patient depending on medical nutrition therapy (MNT) be fed? Aiming at optimizing artificial feeding, numerous equations have been developed over the last decades, but they have repeatedly been shown to have a limited accuracy, of no more than 70% of values measured by indirect calorimetry (IC) [2,8–10].

Moreover, both overfeeding and underfeeding are recognized to be harmful [11–13]. Therefore, optimizing nutrition support to the patient's individual needs is mandatory, although some timing questions persist [14,15]. Prior studies have highlighted the wide discrepancies between predictive equations and IC measurements [16]. With the availability of the latest-generation devices, IC use is finally spreading, enabling individualized MNT based on objective measurements. The individual adjustment of energy targets guided by IC can improve outcome, with trends to reduced mortality, as shown by the available meta-analysis [17–19]: the mechanisms supporting this improvement include the prevention of both under- and over-feeding, but also reduction of the inflammatory response linked to inexact feeding [20]. Another meta-analysis showed nutrition provision closer to energy targets was achieved when guided by IC compared to predictive equations [21]. Based on physiology and clinical evidence energy provision based on the precise measurement of EE by IC is strongly recommended by international European [22], American, and Canadian guidelines [23,24].

Centres with longstanding experience in the use of IC integrated the required training in their local nutrition teams, but practical training is not widely available in centres with less experience. The present paper aims at providing clinical examples of the use of a contemporary IC device (Q-NRG ®, Cosmed, Italy), to show how teams with training apply and interpret the measured values. The focus of the cases is on energy only and does not detail protein nutriture or feeding route. Importantly, given that the discussion regarding energy expenditure (measured) and requirements (prescribed) is predicated upon substrate metabolism and the energy physiology, the proposed considerations may be applied to any IC device.

Table 1A
The historical equations for basal energy expenditure (BEE) and calculation of EE based on gas exchange.

Harris & Benedict	BEE men = 66 + (13.7 × BW kg) + (5 × Height cm) − (6.8 × age) BEE women = 655 + (9.6 × BW kg) + (1.8 × Height cm) − (4.7 × age)
Weir equation	REE = [(VO_2 × 3.941) + (VCO_2 × 1.11) + (u N_2 × 2.17)] × 1440.

Table 1B
The Activity factors proposed by the original authors for the H&B equation [1], and which are commonly used, and should not be, as these factors were never validated by indirect calorimetry [6,7].

Activity Level	Activity Factor
Little exercise (sporadic)	BEE × 1.2
Light exercise (1–3 days/week)	BEE × 1.375
Moderate exercise (3–5 days/week)	BEE × 1.55
Heavy exercise (6–7 days/week)	BEE × 1.725
Very heavy exercise (2× a day)	BEE × 1.9

2. The physiology of energy expenditure determination

Four different methods enable measuring EE [4]: 1) direct calorimetry, 2) thermodilution (Fick method), 3) doubly labelled water, and finally 4) indirect calorimetry.

- **Direct calorimetry** measures heat production in a closed chamber, and is not applicable in clinical settings [8].
- **Thermodilution** requires a pulmonary artery catheter enabling cardiac output and arterial and mixed venous blood sample measurement.

$$EE = \text{Cardiac Output} \times Hb \times (SaO_2 - SvO_2) \times 95.18$$

where Sa and Sv = arterial and venous blood saturations (%), and Hb is haemoglobin (g/l).

The technique has its own limitations (variability due to cardiac output variation in the respiratory cycle and blood shunting over the bronchial arteries). Moreover, the indication to these invasive catheters' insertion is limited, reducing the availability of this option.

- The **doubly labelled water technique**, first published in 1955, has the advantage that it can be used in any environment and given orally. The method involves enriching the body water of a subject with heavy hydrogen (^2H) and heavy oxygen (^{18}O), and then determining the difference in washout kinetics between both isotopes, being a function of CO_2 production. Test starts with a baseline evaluation of the body liquids (urine, saliva, and blood), with a 2nd determination 7–12 days later (see Westerterp [25]). The calculations are based on assumptions such as steady-state CO_2 and H_2O turnover, and constant body water pool size during the measurement period, which may not be applicable for critically ill patients, as fluid volume shifts together with large changes in CO_2 production are frequently observed. It has been used in major burns though [26]. The delay to obtain the results limits its use to research.
- **Indirect calorimetry** is based on the direct application of the Weir equation, measuring VO_2 and VCO_2 to calculate EE [8] (Priem S, Sensors 2023), generally omitting the minor impact of nitrogen. The Deltatrac II® (Datex, Finland) has long been the

reference tool, validated both in vitro and in vivo. Other devices are available on the market, and have been compared to the Deltatrac II®, showing the superiority of the latter [27,28]. But this reference device is no longer available. After long efforts [8], a validated replacement device which meets criteria related to accuracy, ease of use, reliable measurement, and safety is now available. The Q-NRG® device has been validated both in vitro [29] and in clinical settings [30,31] with the ability to measure both spontaneous breathing and ventilated patients.

The physical condition of the patients during EE measurement must be recorded in the report, as they deeply influence the results. For healthy individuals, basal EE is measured in a resting state that is free of physical and psychological stress, a thermally neutral environment, i.e. at temperature ranges where energy used for the body temperature maintenance is minimal, and a fasting state (also called postabsorptive state), i.e. no oral intake for more than 8 h prior to the measurement, to avoid the EE related to physical activity and diet-induced thermogenesis (DIT).

Total daily EE is composed of three parts [32]: a) the basal EE (the minimum maintaining metabolic activity), b) the diet induced thermogenesis (DIT) which is the EE required to metabolize nutritional substrates, and c) the EE resulting from physical activity, which is the most variable and can been minimal in a recumbent patient but extremely elevated in healthy subjects such as lumber workers in Finland [33]. The DIT values are higher at a relatively high protein intake and lower at a high fat consumption. The exact individual DIT value determination requires to repeat the IC before and after feeding, which is impractical in the ICU. Therefore, the recommendation is to do the measurements in the fed state in intubated bed-ridden patients to include the DIT, thereby directly reflecting the patient's total energy needs and avoiding any estimated DIT addition.

There are some clinical scenarios that preclude an accurate IC assessment (Table 2) including agitation, air leakages in the respiratory circuit, use of other gases (helium) and specific ventilator settings (PEEP >10, FiO_2 >80%, non-invasive ventilation) [34]. Patients on ECMO, dialysis or continuous renal replacement therapy also challenge the interpretation of the IC results, as these techniques impact on VCO_2 and VO_2, making them less reliable. In these scenarios as well as changes in clinical status repeated IC measurements should be conducted as metabolic demands change throughout stages of critical illness [14,34].

- **Respiratory quotient (RQ):**

The ratio of VCO_2 to VO_2 is “dimensionless”, called RQ, is a piece of essential information retrieved from IC. It reflects the macronutrients being metabolized, as different energy pathways are used for fats, carbohydrates, and protein. Its application in clinical settings has generated debate [35], due to some degree of incertitude accompanying the measures (principally air leaks, and oxygen cell dysfunction). The sensitivity and specificity of RQ are certainly not 100% [35], but sufficiently precise to orient the analysis of the organism's metabolic utilization of substrates. Being more difficult to interpret, some authors have recommended ignoring values < 0.70 or >1.0, considering them non-physiologic which is inexact, as the physiologic range of RQ is 0.66–1.2 [36]. These values should be used for understanding of the patient's metabolic condition and in context of the clinical scenario, and the substrates that are metabolized (Fig. 1).

Many metabolized substances are compounds containing only the elements carbon, hydrogen, and oxygen. The chemical equation of their complete oxidation is:

$$C_xH_yO_z + (x + y/4 - z/2)\ O_2 \rightarrow \times\ CO_2 + (y/2)\ H_2O$$

and thus, metabolism of this compound gives an RQ of:

$$\frac{x}{(x + y/4 - z/2)}$$

For **glucose** ($C_6H_{12}O_6$), the complete oxidation equation is:

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$$

resulting in a RQ of 1: $6\ CO_2/6\ O_2 = 1$

For **proteins**, the RQ varies between 0.8 and 1.0. For **fats**, the RQ depends on the specific fatty acids present. Amongst the most common, RQ varies from 0.692 (stearic acid) to as high as 0.759 for the very long fatty acids (docosahexaenoic acid) [4]. Values below 0.70 reflect a starving condition, and insufficient energy, or the use of ketogenic diets with values as low as RQ = 0.66 [37]. For **ketone bodies**, the RQ is low, around 0.7 [38,39], and alcohol an RQ = 0.67. At the opposite range, citrate, which is widely used in continuous renal replacement therapy has an RQ = 1.33.

The food quotient will directly influence the RQ especially during short measures in fed state, such as generally done in the ICU. Making the fat and carb proportions vary out of usual ranges, Westerterp showed food quotients between 0.77 and 0.92 [39]. Stapel et al. calculated a standard feeding solution's RQ (16% protein, 49% carbs, 35% fat) to be 0.86 assuming respective substrate RQs to be 0.8, 1.0, and 0.7) [40], while Kagan et al. used an RQ of 0.80, 0.85, and 0.89 depending on the solution [41]. The RQ of a given feeding solution can be checked using calculators available on the web (seek “Thermic Effect of Food calculator”).

Table 2
A: The Fleisch equation [54] is an alternative predictive equation to HBE for the general population that includes total body surface area.
2B: Toronto equation for major burn injuries [55]: the equation includes further specific factors.

Reference	Factor included in equation	Equation
A: Fleisch [54]	Gender, age	EE (M) = 24 × (54.337821 − (1.19961 × Age) + (0.02548 × Age2) − (0.00018 × Age3)) EE (F) = 24 × (54.74942 − (1.54884 × Age) + (0.03580 × Age2) − (0.00026 × Age3))
B. Allard et al. [55]	Basal EE by Harris & Benedict, total burned BSA, previous 24hr energy intake, body temperature, time after injury	EE = −4343 + (10.5 × % burned surface area) + (0.23 × energy intake (kcal)) + (0.84 × EBEE) + (114 × body temperature (°C)) - (4.5 × post burn days)

Abbreviations: BSA = body surface area, EBEE = estimated basal EE by Harris & Benedict, CI = Previous 24hr Energy intake.

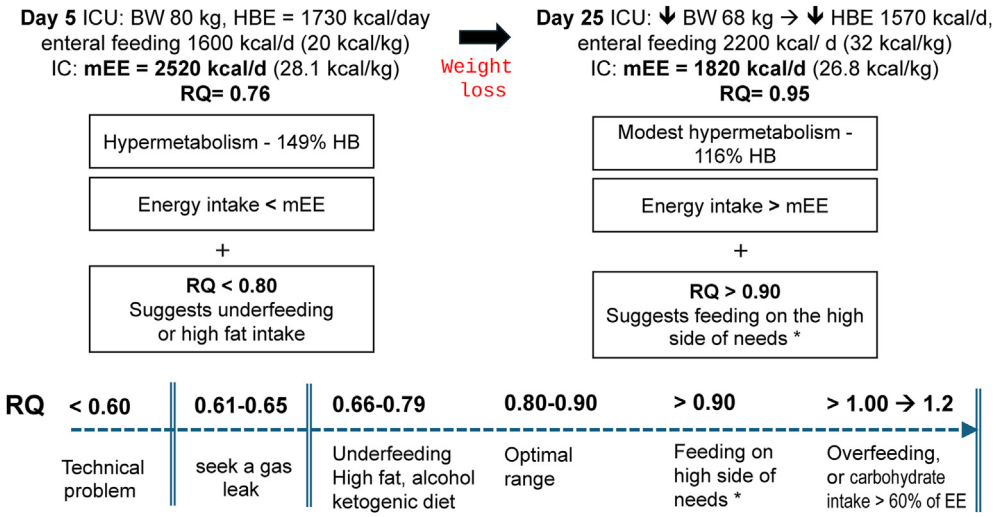


Fig. 1. Algorithm to assist the interpretation of mEE and RQ using the case of a young 45 years-old major trauma patient as example: pre-injury BW 80 kg, height 1.75 m, BMI 26.1 kg/m^2.
*: feeding with an RQ of 0.9–1.0 is often needed during rehabilitation to achieve weight gain.

Normally, subjects who are in energy balance are also in substrate balance with the RQ measured over a 24 h period being equal to the FQ. The RQ for omnivorous adults has been shown to be 0.845 ± 0.013 (mean ± sd) and a little higher in vegetarian, vegan and Asian diets with 0.86–0.88 [42].

Much of the knowledge about the interpretation of RQ is derived from research on obesity [43]. Insulin increases lipid storage and decreases fat oxidation, and is positively associated with increases in the RQ [43], and in weight gain [36,44]. A positive energy balance increases the RQ [43]. Thus, an RQ exceeding 1.0, reflects storage and ongoing lipogenesis. Energy intake in excess of an individual's EE, be it from carbohydrates or lipids, results in de novo lipogenesis both during oral feeding [43] and parenteral nutrition [45]. On the other side, values below 0.80 in a fed patient should raise the suspicion of underfeeding. Figure 1 provides an algorithm for the suggested interpretation of an RQ.

Thus, variations in the RQ in response to the feeding regimen reflect the adequacy of feeding, or its in adaptation to the metabolic level of a patient [35]. Values over 0.9 should raise the suspicion of overfeeding. The high values may also reflect inadvertent administration of substrates (glucose) delivered as drug dilution outside and in excess of the nutrition prescription: such a finding may help picking an imbalance in substrate delivery. As most enteral and many parenteral feeding solutions come as fixed combinations, a high RQ should not lead to attempting to change this composition, but rather to adjust the total energy intake, and probably reduce it.

The persistence of low RQ between 0.70 and 0.79 should raise the question of malabsorption/maldigestion, as feeding adequacy may be compromised by the presence of an undiagnosed exocrine pancreatic insufficiency (EPI) being present in 52% of patients, as shown by Wang et al. in 563 critically ill patients: the EPI diagnosis was based on faecal elastase-1 [46]. The identified risk factors included shock, sepsis, invasive mechanical ventilation and haemodialysis, which are frequently present. Importantly, the incidence of steatorrhea (8.8%) and diarrhoea (11%) were poor indicators of EPI. But intestinal losses, and particularly diarrhoea, can result in major losses of energy as shown by a study in patients on full enteral feeding using bomb calorimetry to analyse the fecal energy content [47]: the production of more than 350 g feces/day (627 kcal/day), resulted in significantly negative energy balances, and might become an indication to PN.

The very low RQ values reflect technical problems such as O_2 or CO_2 cell calibration issues, leaks (see Figure 1 and 4.11), and hence invalidity of the measure. Classical conditions where errors are predictable are acute acid/base disturbances [35], and COPD patients during a gas retention episode, conditions during which no measure should be made.

Finally leaks compromise the reliability of the RQ. This problem is frequent in children ventilated with uncuffed endotracheal tubes, as shown by paediatric studies [48,49] that indicate that despite this problem, the EE value remains clinically relevant to avoid both under- and overfeeding.

3. Differences between intubated and spontaneously breathing patients

Patients mainly differ by the severity of their clinical condition: the intubated patients often suffer more than one organ failure as compared to spontaneous breathers with canopy use (the case of high flow O_2 therapy is not addressed herein). Further most of these patients present with an important inflammatory response, and related alterations of their metabolism, with a variable degree of hypermetabolism being present in about 50% [50].

In the 1990s i.e. the early years of the clinical use of IC, the recommendation was to measure EE in post-absorptive state, i.e. after 8–10 h of fasting. In critically ill patients, this led to undue interruptions of feeding particularly with enteral nutrition, contributing to worsening the energy deficit. Worse, this practice transforms a measure into an estimation as 10–15% to the mEE must be added to account for the DIT and obtain a proxy of total EE. Therefore, since the 2000s, measuring in the fed state is recommended in intubated patients [51]. It avoids having to do an inexact estimation of DIT, and enables applying the measured value, as the

activity factor in critically ill patients is negligible even during active mobilisation [52].

In patients under canopy, the metabolic situation is different. Generally, the worst acute phase of disease is behind, and other problems may have developed that render feeding inefficient, ranging from massive malabsorption to intense physical activity, and requiring the expertise of a dietitian or nutritionist. Frequently in outpatient clinics, the measurements are done in fasted and rested patients. In these cases, an arbitrary DIT value (usually 10%) is applied, and the intensity of the physical activity must be appreciated. The latter physically activity, is highly variable ranging from 5 to 30% of total EE. Its estimation will remain empiric and requires a careful history and discussion with the patient to determine the interpretation of the measured EE: initial target will be set between 10 and 20% over the measured value, together with a monitoring of the tolerance (blood triglycerides, glycemia), In patients who appear "resistant to nutrition", the strategy will be to continue increasing energy delivery, and not stay stubbornly linked to a theoretical value. This occurs frequently in chronic IBD patients: if the weight does not start to increase with prescribed values, the latter is considered insufficient. In these cases, the measure EE serves to ensure the minimal feeding, but not the recovery needs.

It is important to note that current IC technology limits the ability to complete canopy studies in patients requiring supplemental O_2; thus, this technology is often reserved for those that have more fully recovered from their acute illness.

3.1. In critically ill patients

IC aims at avoiding gross underfeeding and preventing overfeeding. Hypermetabolism exists during some phases of diseases, especially the early phases, but the rapid muscle loss will change the requirements, as muscle represents roughly 40% of body weight. The current guidelines propose meeting 70% of measured or predicted EE within the first 3–4 days of ICU and advancing to target after that [22]. During these first days of feeding progression, there is no risk of overfeeding while hemodynamic and respiratory instability is maximal.

Hence the first IC study should be done by day 4–5 after admission, ideally before extubating mechanically ventilated patients, as dependence on nasal O_2 supplements after extubation will compromise a measure. Ideally measures should be repeated every 4–7 days, depending on patients' stability, with the last measure 1–2 days before ICU discharge.

The drugs used for treatment may significantly alter the EE: sedatives and muscle relaxants decrease the EE [53], as does the non-selective betablocker propranolol which is standard treatment after major burns after the initial fluid resuscitation (case 4.5). The RQ is a reliable indicator of the metabolic state, values below 0.75 likely indicating an insufficient energy intake (case 4.11). Values RQ < 0.6 do reflect a technical problem (suspect gas leak already <0.65). RQ values > 1.0 do occur in case of carbohydrate or lipid overload and should urge reconsideration of feeding, glucose for drug dilution, and sedation (potentially a lot of propofol?).

3.2. Ward patients

These patients are in an intermediary metabolic situation: still sufficiently sick to stay in hospital, but improving with less inflammation, and especially for some, carrying out rehabilitation program exercising, and being therefore difficult to assess as to their energy needs. The measures are done under canopy, frequently in fasted condition. Therefore, the mEE needs to be multiplied by an arbitrary thermogenesis and activity factor.

3.3. Outpatients

As EE is measured in resting conditions, the patients lying generally flat and breathing calmly under the canopy, this does not reflect their real level of activity. The activity factor cannot be determined precisely. This is particularly true in cancer patients and in patients with malabsorption, requiring clinical experience with a careful follow up of BW: a declining weight will encourage prescribing above mEE. Case 4.10 shows a lack of weight gain despite "adequate" energy provision which is characteristic of cachexia, which in this case is multifactorial and includes altered metabolism, hypogonadism, and ongoing inflammation with intra-abdominal sepsis.

3.3.1. How to prescribe in case of technical limitations

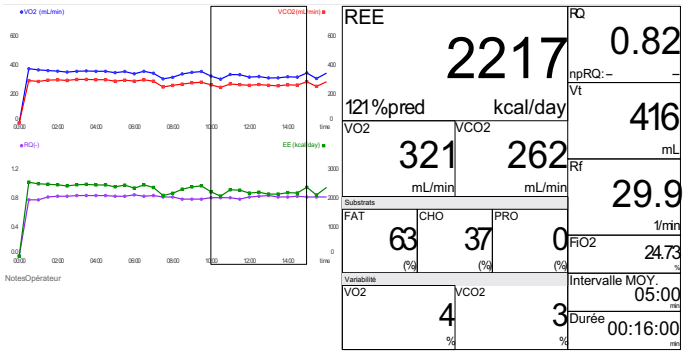
The teams which are trained with IC and using it frequently become experts in clinical evaluation and estimation of energy needs.

4. Clinical cases: from the ICU (intubated) to rehab and home care (canopy)

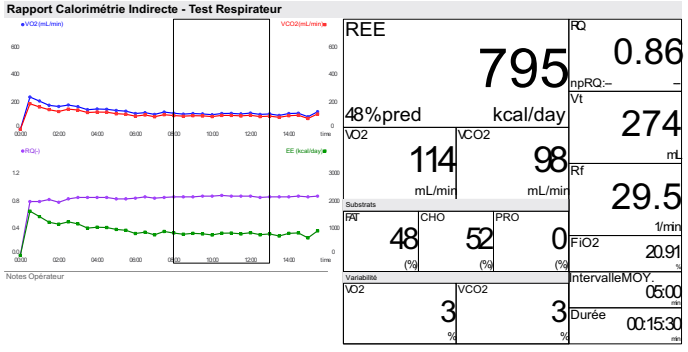
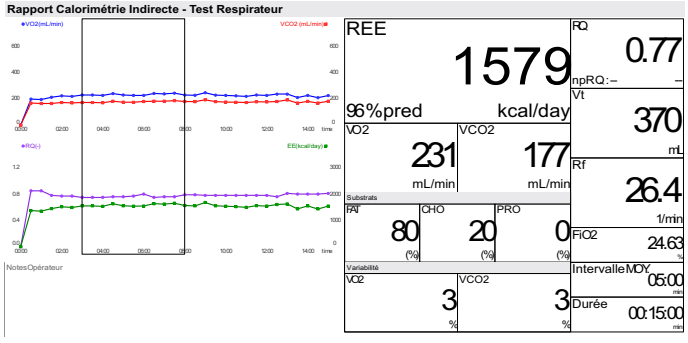
Hereafter 11 exemplar real case studies are presented. For each one there is a short summary of the history and clinical evolution, with the steps of the nutrition therapy, and how decisions were assisted by indirect calorimetry. The focus is on energy and the application of the IC generated values, while protein nutrition is not discussed in detail. As the previous 24 h' feeding determines total EE and includes DIT, the value of energy really delivered/prescribed will be provided, as total energy provision (total of feeds and non-nutritional sources). Route of feeding will not be discussed. Only labs and physiological values relevant for energy prescription will be reported: type of mechanical ventilation, PEEP, FiO2, fever, insulin dose, urea). The style will be telegraphic. Every case will be followed by a brief comment.

Practically: The Q-NRG® device offers in the upper box called REE a comparison with a basal EE prediction: the value should be inserted upon commissioning the device. Our recommendations is to insert either the HBE or the Fleisch equations (developed in 1951 by a Swiss physiologist [54]) which provides an estimate of basal metabolism enabling appreciating the metabolic levels that is measured during the IC (Table 2A). Major burns (cases 4.5 and 4.6) are indications to IC despite having an equation developed from IC (Table 2B).

4.1. Case of unexpected high EE in a sedated neuro patient

History	Indirect calorimetry
A 44-year-old man is admitted after embolization of a ruptured basilar artery aneurysm. Decompressive craniectomy was required on Day 3 and a posterior craniectomy on Day 4 Admission status: estimated body weight (BW): 75 kg. Height 1.80 m, afebrile *Treatment*: Volume Controlled Ventilation, FIO_2 0.25, deep sedation. *Initial energy target* prescription 1400 kcal (20kcal/kg/d of estimated BW). **Day 6**: intubated deeply sedated, Nutrition: Received only 535 kcal/1400 kcal previous 24h. No insulin. No weight available. IC is contraindicated (uncontrolled intracranial hypertension). Nutrition is increased to target. **Day 9:** intubated (FIO_2 25%) deeply sedated, Received only 1215/1440 kcal during previous 24 hours (gastroparesis), No insulin. Weight (real): 81.0 kg (but with oedema) Decision ↑ target to 2200 kcal. Addition of PN was proposed but not done. **Day 14:** Weight: 65.4 kg, intubated, FIO_2 21%, deeply sedated, Prescribed target 2200 kcal/day (was maintained). He received 2496 /2200 kcal during previous 24 hours, No insulin. Urea increased to 68 mg/dL (11.4 mmol/l), The patient was tracheotomized and ventilated for 19 days	**Day 9:** mEE 2217 kcal/d, RQ = 0.82  **Comment**: Unfortunately, due to the initial underestimation of the BW which resulted in low energy target, and prolonged immobilization, the patient suffered an important 12% weight loss (75 kg to 65.4kg). An earlier IC would have identified the elevated energy needs and stimulated the use of supplemental PN since day 4-7 as recommended [22,24].

4.2. Technical problems and/or beta-blocker impact in a neuro patient

History	Indirect calorimetry
A 78-year-old patient admitted to ICU after a cardiac arrest on ventricular fibrillation. The neuro-prognostication at 72h is in the grey zone (irritative EEG, low NSE = neuron-specific enolase) Admission data: estimated BW 80 kg, height 1.85 m: *Treatment*: deeply sedated, Volume Controlled Ventilation PEEP 10 cm H_2O, FIO_2 50%. *Initial prescribed energy target* 1600 kcal/d (20kcal/kg) increased to 1800 kcal by day 10. **Day 16**: Intubated, Stable, metoprolol 40mg/d. No sedation since day 3 (RASS -4). BW: 85.5 kg. (RASS = Richmond Agitation-Sedation Scale) Nutrition: Received 2060 kcal /1800 kcal last 24h, with a RQ=0.86, reflecting a nice mixed substrate solution. **Decision:** Despite the measure looking technically ok, and the effective betablockade, result of IC was discarded. ↓ target to 1700 kcal/d (about 20 kcal/kg) as an increase in VO_2 is expected in the coming days in the context of a possible awakening.	**Day 16**: mEE: 795 kcal/day, RQ =0.86 
Day 25: Intubated, FiO2 21%, No sedation, still very drowsy (RASS -3). Eye opening. Weight 85 kg Actual target 1700 kcal. Patient unfed (nasogastric tube accidentally removed). No insulin. Prealbumin 0.20 g/l **Decision**: Keep target 1700 kcal/24h (i.e. 1579 kcal +10% to cover DIT) **Evolution**: Due to the poor neurological evolution, comfort care is finally undertaken. **Comment**: This case illustrates how the energy needs may change over time. IC results must be interpreted critically considering the context. In the event of unexpected results, the examination must be repeated.	**Day 25:** mEE: 1579 kcal/day, RQ 0.77 

4.3. Unpredictable EE in obesity

History: A 69-year-old male, Class 1 obesity (BMI 34.6 kg/m2, BW 10<0 kg, 1.70 m, ideal BW 66 kg and adjusted weight 80 kg), admitted 5 days after gastric bypass for fever and suspected intra-abdominal sepsis, a CT-scan with contrast product was performed, showing a leak of the upper and lower anastomosis requiring re-surgery. The comorbidities were Diabetes Mellitus type 2 and terminal renal failure

Treatment: Ventilation: Assist Control, FIO_2 0.35, PaO_2/FIO_2 272, Sedated.

Day after day, energy intake could be increased reaching 70% at day 3 and 100% within the first week according to guidelines [24].

The potential energy needs bay on predictive equations were:

- Harris-Benedict **1826 kcal/d**
- Faisy-Fagon **2155 kcal/d**
- 25 kcal/kg/day **2500 kcal/d**
- Adjusted weight **2000 kcal/d**
- A.S.P.E.N obese [56]: 11–14 kcal/kg actual BW/day **1100 to 1400 kcal/d**

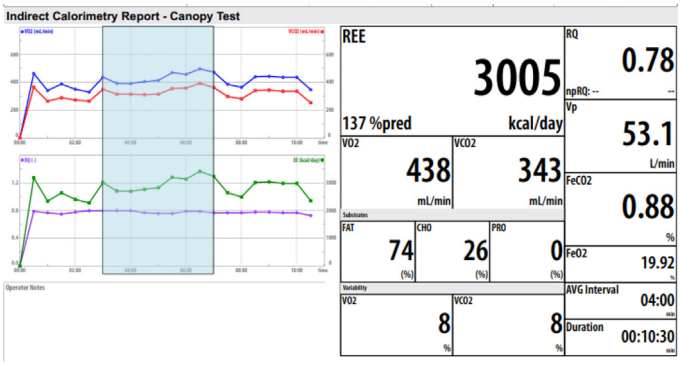
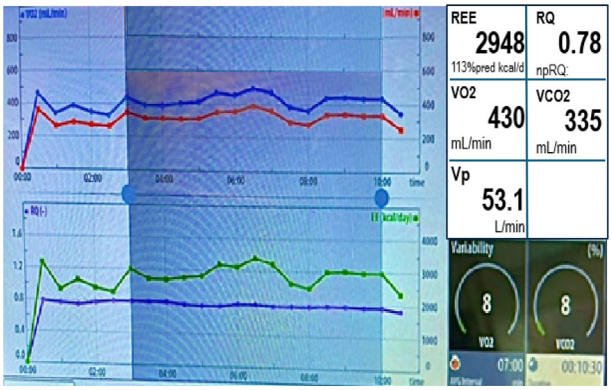
Indirect calorimetry measured EE 1660 kcal/d with an RQ=0.81

Decision: the target 1600 kcal/d was maintained.

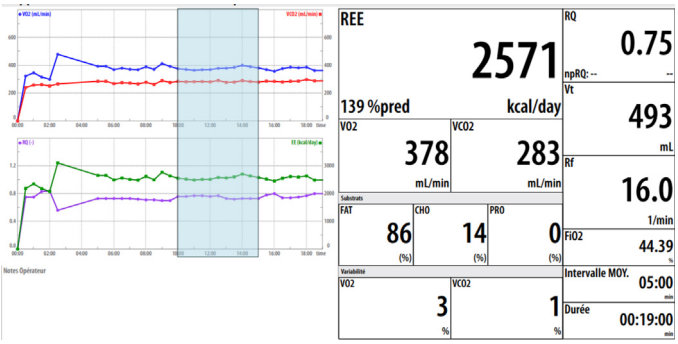
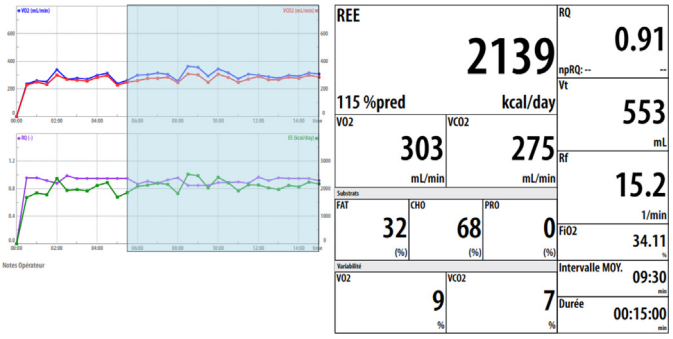
The use of predictive equations would have caused overfeeding (HBE, Faisy-Fagon, adjusted weight based) or underfeeding (ASPEN recommendations) [6,57]. Both over and underfeeding are leading to increased complications and mortality [13]. The SCCM-ASPEN guidelines [24] recommend feeding 60-70% of measured EE. So, if 1660 kcal is measured, the ASPEN guidelines would be to feed 990-1160 kcals/day, i.e. perform underfeeding.

Comment: The gold standard for evaluating EE is IC measurement [14,24]. Energy targets based on weight are challenging in obese patients since increased fat mass and sarcopenia may lead to misevaluation of the metabolically active tissue.

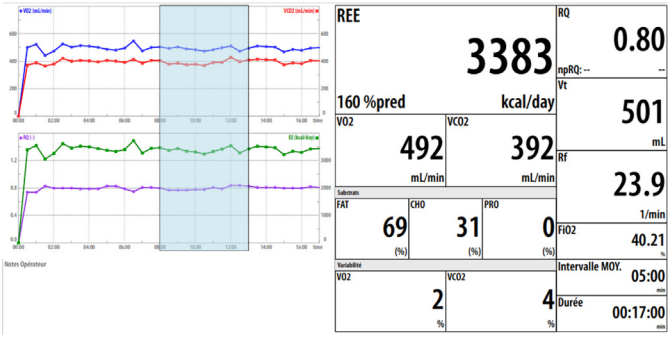
4.4. Unexpected high EE in "muscular" surgical patient

History	Indirect calorimetry
A 55-year-old male with short bowel syndrome admitted to ICU after a 13-hour abdominal surgery (recurrent bowel obstructions with history of 24 previous abdominal surgeries) **Pre-op IC pre-op clinic:** BW 104 kg, height 1.85m, mEE 3005 kcal/d. The RQ=0.78 points to a suboptimal low energy intake. **Day 2:** Patient started on TPN at 3000 kcal/d, based on pre-operative IC. **Day 3:** Emergency reop. for anastomotic leak fever and sepsis – bowel perforations were closed and patient back to ICU. **Day 5:** Emergency reop for recurrent bowel leak. Back to ICU intubated. **Day 7:** Patient extubated, septic, with minor weight loss (104 kg to 100 kg). IC shows similar REE at 2948 kcal/d with RQ= 0.78 reflecting adequate feeding. **Decision:** PN maintained at 3000 kcal/day. Patient restarted on intramuscular testosterone due to pre-op testosterone deficiency resulting from the short bowel syndrome. **Day 10:** Patient begins intensive rehabilitation and physical therapy in hospital walking 2-3 miles (3,3-4.8 km) per day and begins exercise band exercises, squats, sit/stands, biking on stationary bike (Peloton®), and small weights (5 kg or less) strength training. **Decision:** Increase PN to 4000 kcal/day due to estimated activity factor of 1.3-1.4 * (Table 1B) of measurement: this activity adjustment comes from the original HBE publication in healthy adults and ranges from 1.2 (sedentary lifestyle) to 1.5 (moderately active), to higher for very active subjects [7], but has never been validated. Adequacy will be verified on the next IC studies. **Comment**: the appreciation of the activity needs is often difficult. Using a face mask to measure VO_2 during stationary bike exercise can provide a more precise evaluation.	**Pre-OP (canopy mode):** mEE =3005 kcal/d, RQ= 0.78, 137% of HBE  **Day 7**: mEE=2948 kcal/d, RQ: 0.78, 133% of HBE 

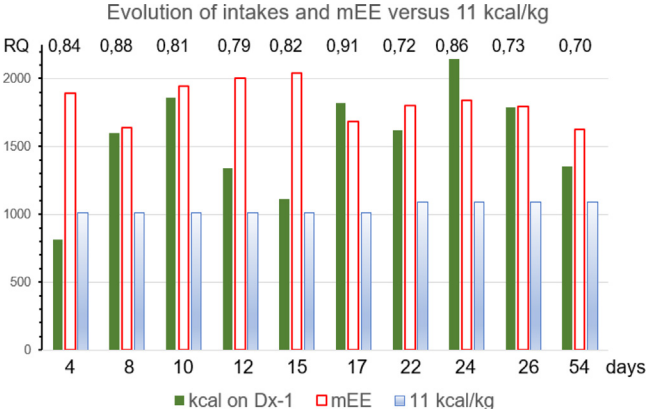
4.5. Impact of betablocker in major burns

History	Indirect calorimetry
A 23-year-old male, admitted for major thermal burns affecting 57% BSA (51% BSA surgical) with inhalation injury, in hypothermia (34.9°C), requiring intubation for 32 days. Admission: BW 78 kg, height 1.74m Nutrition: initial target = 2200 kcal/day. **Day 3:** ventilator-associated pneumonia **Day 5:** stable, intubated (FIO_2 45%), 36.0°C, sedated, weight 95 kg (+17 kg water). Propranolol was introduced (see below comment). The patient received 2260kcal /2200 kcal during previous 24 hrs, Insulin 0.5 UI/h. **Decision after IC:** ↑ Prescribed **target** to 2600kcal/d as RQ=0.75 is on the low side, reflecting moderate underfeeding. **Day 15:** weight 81.0 kg, Intubated, FIO_2 40%, stable but agitated 38.3°C, Received 2630 of the 2600 kcal in previous 24 hrs, Insulin 2.0 UI/h. **Decision after IC:** ↑ **the target** to 2700kcal/d The HBE equation with 1860 kcal would have resulted in underfeeding. The Toronto equation [55] (Table 2B), is close to the mEE on days 5 and 15.	**Day 5: mEE =2570 kcal/d, RQ= 0.75**, 138% of HBE, **Toronto 2417** kcal  **D15: mEE = 2721 kcal/d,** RQ= 0.89,147% of HBE, **Toronto 2737** kcal/d
Day 21: weight 78.2 kg stable, Intubated (FIO_2 34%), Prescribed target 2700 kcal/day. The patient received only 2320/2700 kcal (fasting 2hrs for hydrotherapy) during previous 24 hrs, zero Insulin. Under propranolol. **Decision** after IC: ↓ the target to 2300kcal/d **Evolution:** The patient was discharged after 40 days, still requiring EN (target 2300 kcal) and under propranolol **Comment:** On day 21, the Toronto equation overestimated the needs, as EE was lowered by propranolol. Betablockade is not integrated into the equation and justifies the continued use of IC. Moreover, the RQ=0.91 was increasing indicating that the feeding was on the upper side of the needs (but not massively as no insulin was required), enabling decreasing the target. The use of the non-selective betablocker propranolol belongs to good clinical practice after major burns. It was introduced in the early 2000s, aiming at reducing EE due to its direct effect on the sympathetic catecholamine burst (β1): the β2 effects are more metabolic with stimulation of hepatic glycogenolysis and gluconeogenesis, ketogenesis and lipolysis, and pancreatic release of glucagon: it also has psychological effects by stress reduction [58,59]	**Day 21: mEE =2139 kcal/d**, **RQ= 0.91,** 115% of HBE, **Toronto 2858** kcal/d 

4.6. Burn ICU – thermal major burns without betablockade

History	Indirect calorimetry
A 55-year-old male, BW 111 kg, height 1.98m, BMI 28 kg/m2, admitted to the ICU for major burns affecting 73% BSA (all surgical), moderate inhalation injury, requiring intubation, 40 days of mechanical ventilation and a tracheotomy. **Day 3**: Pneumonia (VAP). A complicated clinical course resulted from an intestinal haemorrhage required parenteral nutrition for 3 weeks. Betablockers could not be introduced as usual. **Day 9**: weight 122.5 kg (+11.5 kg water). unstable febrile, sedated, intubated (FIO_2 40%) **Prescribed target 3000** kcal/day: he was receiving 2960 kcal, Insulin 14 UI/h. After hemodynamic stabilization, Propranolol was finally introduced on day 28. **Decision:** ↑ the target to 3200 kcal/d Energy needs (without betablocker): the Toronto equation, gave very close values. Especially with high mEE, checking the RQ is essential: an RQ of 0.8 reflects a balanced feeding (no deficit, no excess). In the present case, the energy target was therefore increased despite the high insulin dose, but to a value slightly below the mEE, considering the fever that increases EE [60].	**Day 9**: mEE **3383 kcal/d,** RQ 0.80, 155% of HBE. **Toronto 3326** kcal  **Evolution:** was discharged after 119 days, still on enteral feeding (target 2900 kcal, combined oral and enteral feeding) and on propranolol. **Comments:** In absence of betablockade, the Toronto equation which integrates time after injury and previous 24 hours' feeding, performs nicely: its use is recommended in absence of IC because it was developed on regressions from IC studies [47,49]. Note that the stress factors often applied to HBE are not validated [6,7], nor is the 2 times HBE in major burns.

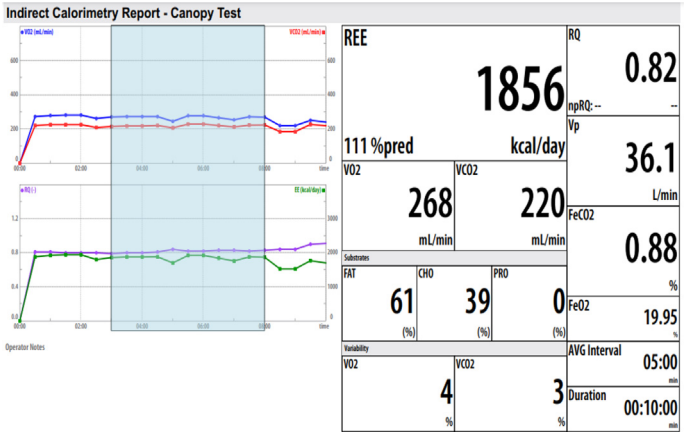
4.7. ICU to rehabilitation: value of repeated measured EE

History	Indirect calorimetry
62-year-old male presented in respiratory distress: with the diagnosis of pneumonia, he was intubated and oro-gastric tube was placed. *History*: COPD in a heavy smoker (one PPD for >45 years), chronic heart failure and kidney disease, Admission: BW 91.6 kg, Height 1.73 m, BMI 31 kg/m2. *Nutrition history*: The patient was nil PO for 3 days with a decreasing intake before that. Hence patient was considered as at risk of refeeding and at the edge of malnutrition *Initial nutrition plan*: trophic feeds initiated and advanced per ASPEN [24] ESPEN, and ESICM guidelines [22,61]. Figure shows evolution over 54 days of mEE, intakes of the previous day and the weight-based recommendations for obese patients. **Day 4** first IC, and repeated q2-5 days until extubation. Tube feeding quantity was adjusted accordingly. Extubated after 1 month. EN continued until PO exceeded 60% of needs. **Days 17 and 24:** feeding above mEE result in higher but still adequate RQ (0.91 and 0.86), which there reliably reflects the metabolic level, and enable adjusting intake. Feeding was subsequently reduced. While the patient was eating ad libitum, the IC results were used to add fortified foods and oral nutrition supplements to cover mEE. **Day 54**: Canopy IC showed mEE only 63% of low-end estimated needs (30-35 kcal/kg); increased to 120% of this value; literature notes rehab needs are 150% of mEE [62]. The low RQ of 0.7 reflects insufficient intake, could be used to infer a need to increase nutrition provision in addition to estimated actual PO intake. The patient required supplemental nasal O_2 and ventilation overnight; Feeding adjusted to 80% of mEE in attempt to encourage PO intake (Comment: the EN reducing strategy does not work, not even in children [63]).	 **Comments:** The weight-based equation of 11-14kcal/kg (ASPEN for obesity [24,56,64]) would have significantly underfed patient throughout the ICU stay; measured kcal/kg needs ranged from 18-22 kcal/kg; while this falls within the ASPEN 2021 guidelines of 12-25kcal/kg, this range is broad and does not truly individualize nutrition care

4.8. Evolution of EE in severe pancreatitis

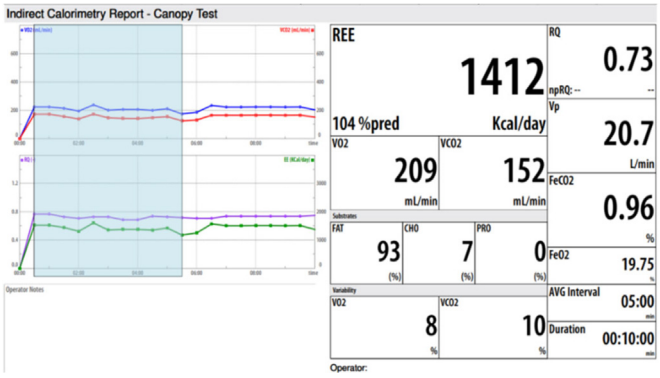
History: A 32-year-old male with a history of hepatic steatosis presents with severe abdominal pain due to pancreatitis and requires ICU admission due to shock and multisystem organ failure and severe metabolic perturbation. Admission: BW 88kg, height 1.73m; BMI 29.6 kg/m2.
Blood Glucose >40 mmol/L, insulin resistance requiring over 100 UI/d.
Development into persistent critical illness with repeated surgeries (12 over 3 months) for abdominal compartment syndrome and duodenal perforation ICU acquired polyneuropathy, renal failure requiring dialysis and ongoing intestinal failure. ICU stay spanned 6 months and was characterized by ongoing intra-abdominal sepsis and cachexia.
ICU: Early (weeks 1-12) ongoing severe catabolism and GI Tract not functional, acute kidney failure under dialysis:
Initial PN Prescription was 1800 kcal/d
IC: mEE=2823 kcal, RQ=0.78: the RQ<0.8 suggests underfeeding and burning fat stores, which reflects the current prescription below REE.
ICU: Late (weeks13-24)
IC: mEE=2150kcal/d, RQ=0.92, which suggests appropriate mixed fuel substrate. The patient receives PN: 2450 kcal/d,
Cachexia with 25 kg weight loss (63.5 kg) develops by 4 months post ICU admission despite being fed above mEE target. PN maintained and dialysis could be stopped.
Surgical recovery on the surgical ward for 2 months
IC: MEE=1832, RQ=0.84 → PN: 2450 kcal/d
Rehabilitation Early: still PN dependent receiving 2450 kcal/d (more than mEE due to activity with RQ 0.82); he eats ice chips. Plan: feed above mEE given resolution of inflammation and goal of weight gain
Rehabilitation Late: Weight is 67.4 kg,
IC: mEE 1923 kcal, RQ 0.93 indicating high feeding which was desired for rehabilitation and PN was maintained at 2500kcal/d
Oral intake is 500kcal/d: increased over 3 months with Plan to continue feeding in excess of mEE.
He rehabilitated over his final month in hospital and was transitioned to home PN. He was discharged to home after 9 months and weaned from PN.

Rehabilitation: IC: mEE 1856 kcal, RQ 0.82

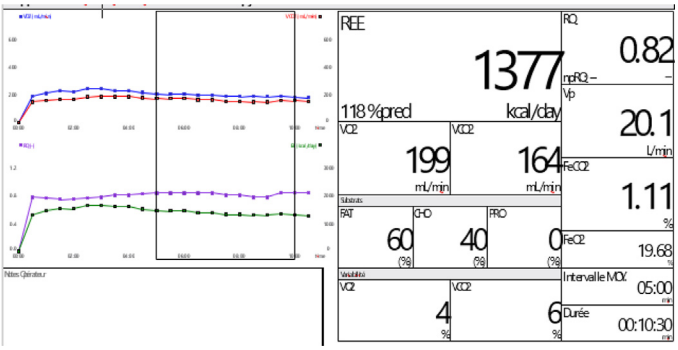


Comment: Lack of weight gain in the presence of adequate energy provision is characteristic of cachexia, which in this case is multifactorial and includes altered metabolism, hypogonadism, and ongoing inflammation with intra-abdominal sepsis.

4.9. ICU to home PN: adapting to low weight and physical activity

History	Indirect calorimetry
A 24-year-old man was treated for functional dyspepsia, gastroparesis and a psychological component leading to malnutrition for two years with enteral nutrition. A continuous weight loss (BMI 15.5, height 1.8m, BW 50.2kg) was observed, and referred for home PN. Laboratory: low albumin (31 g/L) without signs of inflammation. Nutrition Screening: NRS2002 >3, GLIM + Physical exam: cachectic, thenar muscle wasting, frail hair, and nails. Physical activity: low (2400 steps/day, Activity factor 1.2) Food diary analysis: unbalanced intake of 1450 kcal/d and 8 g/d protein. **Nutrition plan:** mEE =1412 kcal/d (28.1 kcal/d). PN containing 1070 kcal/d is prescribed. The low RQ=0.73 reflects a lowish intake. No signs of refeeding syndrome appeared, and treatment was built up to 1600kcal/d (nightly manner, 7/7 days). **Monitoring:** Good blood glucose control, nomal liver function test and one catheter related infection was observed in 2 years treatment. IC was repeated at 6 months and 2 years showing a parallel increase of BW and mEE, with a rather low (RQ=0.73) leading to increase in energy for an optimal RQ=0.80.	**Initial I.C: mEE 1412 kcal/d, RQ =0.73**  **After 6 months**: BMI 17.5 kg/m2 FMI 1.3 kg/m2, increase of mEE ¼ 1648kcal/day with RQ to 0.79 **After 2 years:** BMI 19.3 kg/m^2 FMI 2.3, increase of mEE 1864 kcal/d with RQ =0.80. **Comments:** Using IC enables a home PN therapy based on biophysical profiling and facilitates objective follow-up with changes to provisions reflection in IC measurements

4.10. Outpatient: cancer patient with resistance to nutrition therapy

History	Indirect calorimetry
A 49-year-old woman, 2 months after gastrectomy and combined chemo/radiotherapy for gastric cancer T4N1M1 was referred due to the persistence of cachexia. She was dependent on home PN for BW maintenance due to severe anorexia since the 3rd postoperative week with BW loss of 22% of the pre-disease BW. Observations: BW 45.3 kg, BMI 17.3 kg/m2, bioelectrical-derived fat-free mass (FFM) 88.3 % and fat mass (FM) 11.3%. Hb 123 g/L, Albumin 36 g/L, CRP 0.5 mg/L. The initial energy target was set 20% above the mEE (1650 kcal = 36 kcal/kg) and home-PN was administered 7 nights /week. **After 4 weeks**, BW remained stable (+0.5 kg), without changes of FFM and FM, mEE and RQ: mEE increased to 1491 kcal/d and RQ=0.84. **Decision:** Energy target was increased to 1800 kcal/d. **After further 3 weeks**, BW remained unchanged, while mEE increased to 1678 kcal/d with RQ =0.83. Liver tests remained within normal range, and anorexia and fatigue persisted. A tentative new energy target was set at 2100 kcal/d (46 kcal/kg) and home-PN was prescribed accordingly. No weight change was observed for the next 9 weeks, suggesting resistance to nutrition despite the very high level of energy administration, as reflected by unchanged BW and body composition. **After 4 weeks**: mEE = 1491 kcal/d, and ↑ RQ to 0.84 **Further 3 weeks later:** mEE ↑1678 kcal/d with stable RQ =0.83.	Initial measured energy expenditure (mEE) under canopy: 1377 kcal (118% of HBE predicted EE, 30kcal/kg), RQ=0.82  **Comments**: Measuring EE by IC is recommended in cancer patients, but measured in resting conditions, mEE does not reflect total EE. The mixed fuel RQ allows us to advance energy delivery beyond mEE to support weight gain through delivering energy in excess of requirements. In outpatients, the energy target should integrate the additional needs related to physical activity and/or refeeding: exceeding the mEE under close supervision is then required. It also shows that IC does not allow for optimizing nutrition support in all cancer patients

4.11. Impact of gas leaks

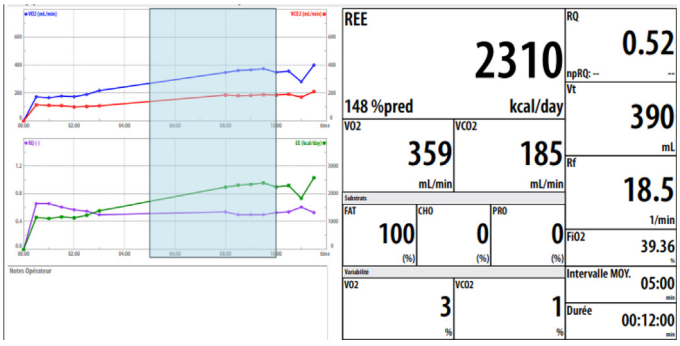
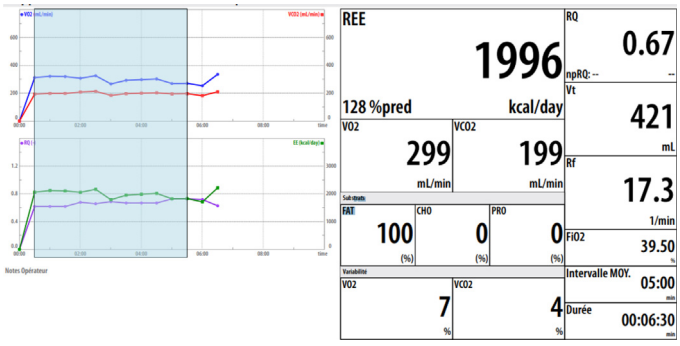
History	Indirect calorimetry
A 73-year-old man (79 kg, BMI 25.5, NRS 4) admitted after cardiac arrest Initial energy target: 1600 kcal/d (20 kcal/kg) **Day 9 – first IC**: Figure A shows a very low RQ=0,52 caused by gas leaks resulting in abnormally low VCO_2. The IC was repeated a few minutes later after some adjustments (Figure B), with values of mEE=1996 kcal with a still low RQ=0.67. This RQ was interpreted as reflecting starvation, as the patient was fed much below his then prescribed target of 1600 kcal/day. **Decision**: the energy target and feeding were increased. **Day 16**: stable mEE of 1966 kcal with a RQ=0.72 while fed 1800 kcal/day. Target was further increased to 2000 kcal/day. The patient was discharged to neuro-rehab. **Comments:** RQ<0.60 is not physiologic (first image) and leaks or technical issues with the measurement should be explored, as was done: the unstable increasing value of both gases is a signal.	Day 9 -A  Day 9 -B 

Table 3
Categories of patients likely to benefit from energy intake adjustment by IC, and conditions in which IC results are inaccurate, with factors limiting the feasibility of measures.

Classical indications to IC	Feasibility limitations- Inaccuracy
Obesity	Air leakages in respiratory circuit
Inflammatory bowel disease	Mechanical ventilation with PEEP >10 cmH_2O
High output intestinal fistula	Mechanical ventilation with FiO_2 > 80%
Anorexia nervosa	Non-invasive ventilation or high flow O_2
Long-term medical nutrition therapy, especially PN	Ventilation with helium
Chronic obstructive pulmonary disease	Supplemental O_2 in spontaneous breathing patient
Chronic kidney disease	ECMO
Chronic fibrotic pancreatitis	Hyperventilation (hypocapnia)
Diabetes mellitus (type 2)	Metabolic acidosis or alkalosis
Cancer	Agitation
Liver cirrhosis	Myorelaxants and heavy sedation
Neuromuscular degenerative diseases	Fever
Hyperthyroidism	Vasoactive drug (dopamin, dobutamine) adjustments during measurement
Pheochromocytoma	
Persistent critical illness	
Difficult/failed weaning from ventilator	

5. Application field

The above cases show how IC results have been applied in a broad range of clinical situations. Ideally such metabolic information should be available for all patients requiring medical nutrition therapy, as many types of diseases impact on EE, but this is wishful thinking [34], as IC devices are not available in numerous institutions, and numerous situations exists for which IC cannot be performed. Table 3 shows the classical indications to IC: the patients most likely to benefit from IC are those with very high or low BW, those with wasting diseases as they may be hypermetabolic, abnormal muscle function, endocrine diseases and inflammatory conditions (IBD, etc). Some technical problems may either impeach IC or reduce the quality of the measure (2nd column). Note that IC can be used in continuous renal replacement therapy (CRRT), with an error <5% on CO_2 with bicarbonate-based dialysate [65–67].

6. Conclusion

Several IC devices exist which have a variable precision as shown by studies comparing different devices [27,28]. The above text focuses on one single device (Q-NRG®) which has been shown to be extremely precise [29], and is used by the authors of this text. Despite some differences existing between devices, the principal data provided (VO_2, VCO_2, RQ and EE) are the same across devices, enabling the analysis of the measurement results: therefore, the above case analysis extends to other available IC devices. IC is a tool that provides metabolic information far beyond the only value of EE. With the RQ, it tells exactly how the patient is handling the received amount of energy: low values < 0.80 reflect insufficient feeding and values over 1.0 indicate too much. IC is a metabolic monitor, not only a guide of energy target and has a wide range of applications in clinical practice. Training is required as numbers should not be applied blindly.

Grants and funding

There was no financial support for this teaching project.

Statement of authorship

M.M. Berger (MMB) and L. Gramlich (LG) equally contributed to the conception and design of the research; all authors (MMB, EdW, LG, JJ, OP, CP, AJR; LR, PS, PEW) contributed to the acquisition and analysis of the clinical cases; all authors contributed to the interpretation of the data; and MMB and LG drafted the manuscript. All authors critically revised the manuscript, agreed to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript, including the revision.

Declaration of competing interest

None of the authors declares any conflict of interest.

Acknowledgments

Four co-authors (MMB, LG, LR, AJR) participated in a webinar organized by Baxter in 2022: the lack of specific education was the main conclusion of the meeting and the trigger for this educational paper which was written without any further financial support. We are grateful to Jeroen Molinger and Megan Beyer from Dpt of Anesthesiology (Duke University School of Medicine, Durham, NC, USA) for assistance in data extraction.

References

[1] Harris JA, Benedict FG. A biometric study of human basal metabolism. Proc Natl Acad Sci U S A 1918;4:370–3. https://doi.org/10.1073/pnas.4.12.370.
[2] Bendavid I, Lobo DN, Barazzoni R, Cederholm T, Coeffier M, de van der Schueren M, et al. The centenary of the Harris-Benedict equations: how to assess energy requirements best? Recommendations from the ESPEN expert group. Clin Nutr 2021;40:690–701. https://doi.org/10.1016/j.clnu.2020.11.012.
[3] Weir JB. deV. New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol 1949;109:1–9.
[4] Livesey G, Elia M. Estimation of energy expenditure, net carbohydrate utilization, and net fat oxidation and synthesis by indirect calorimetry: evaluation of errors with special reference to detailed composition of fuels. Am J Clin Nutr 1988;47:608–28.
[5] Jéquier E. The influence of nutrient administration on energy expenditure in man. Clin Nutr 1986;5:181–6. https://doi.org/10.1016/0261-5614(86)90022-1.
[6] Zusman O, Kagan I, Bendavid I, Theilla M, Cohen J, Singer P. Predictive equations versus measured energy expenditure by indirect calorimetry: a retrospective validation. Clin Nutr 2019;38:1206–10. https://doi.org/10.1016/j.clnu.2018.04.020.
[7] Douglas CC, Lawrence JC, Bush NC, Oster RA, Gower BA, Darnell BE. Ability of the Harris Benedict formula to predict energy requirements differs with weight history and ethnicity. Nutr Res 2007;27:194–9. https://doi.org/10.1016/j.nutres.2007.01.016.
[8] Oshima T, Berger MM, De Waele E, Guttormsen AB, Heidegger CP, Hiesmayr M, et al. Indirect calorimetry in nutritional therapy. A position paper by the ICALIC study group. Clin Nutr 2017;36:651–62. https://doi.org/10.1016/j.clnu.2016.06.010.
[9] De Waele E, Opsomer T, Honore PM, Diltoer M, Mattens S, Huyghens L, et al. Measured versus calculated resting energy expenditure in critically ill adult

patients. Do mathematics match the gold standard? Minerva Anesthesiol 2015;81:272–82.
[10] De Waele E, Jonckheer J, Wischmeyer PE. Indirect calorimetry in critical illness: a new standard of care? Curr Opin Crit Care 2021;27:334–43. https://doi.org/10.1097/MCC.0000000000000844.
[11] Faisy C, Llerena M, Savalle M, Mainardi JL, Fagon JY. Early ICU energy deficit is a risk factor for Staphylococcus aureus ventilator-associated pneumonia. Chest 2011;140:1254–60.
[12] Dissanaike S, Shelton M, Warner K, O'Keefe GE. The risk for bloodstream infections is associated with increased parenteral caloric intake in patients receiving parenteral nutrition. Crit Care 2007;11:R114. https://doi.org/10.1186/cc6167.
[13] 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.
[14] Singer P, Reintam-Blaser A, Berger MM, Alhazzani W, Calder PC, Casaer M, et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr 2019;38:48–79. https://doi.org/10.1016/j.clnu.2018.08.037.
[15] Wischmeyer PE. Tailoring nutrition therapy to illness and recovery. Crit Care 2017;21:316. https://doi.org/10.1186/s13054-017-1906-8.
[16] Tatucu-Babet OA, Ridley EJ, Tierney AC. Prevalence of underprescription or overprescription of energy needs in critically ill mechanically ventilated adults as determined by Indirect Calorimetry: a systematic literature review. JPEN - J Parenter Enter Nutr 2016;40:212–25. https://doi.org/10.1177/0148607114567898.
[17] Duan JY, Zheng WH, Zhou H, Xu Y, Huang HB. Energy delivery guided by indirect calorimetry in critically ill patients: a systematic review and meta-analysis. Crit Care 2021;25:88. https://doi.org/10.1186/s13054-021-03508-6.
[18] Pertzov B, Bar-Yoseph H, Menndel Y, Bendavid I, Kagan I, Glass YD, et al. The effect of indirect calorimetry guided isocaloric nutrition on mortality in critically ill patients-a systematic review and meta-analysis. Eur J Clin Nutr 2021;76:5–15. https://doi.org/10.1038/s41430-021-00919-0.
[19] Singer P, De Waele E, Sanchez C, Ruiz Santana S, Montejo JC, Laterre PF, et al. TICACOS international: a multi-center, randomized, prospective controlled study comparing tight calorie control versus Liberal calorie administration study. Clin Nutr 2020. https://doi.org/10.1016/j.clnu.2020.05.024.
[20] Berger MM, Pantet O, Jacquelin-Ravel N, Charriere M, Schmidt S, Becce F, et al. Supplemental parenteral nutrition improves immunity with unchanged carbohydrate and protein metabolism in critically ill patients: the SPN2 randomized tracer study. Clin Nutr 2019;38:2408–16. https://doi.org/10.1016/j.clnu.2018.10.023.
[21] Tatucu-Babet OA, Fetterplace K, Lambell K, Miller E, Deane AM, Ridley EJ. Is energy delivery guided by indirect calorimetry associated with improved clinical outcomes in critically ill patients? A systematic review and meta-analysis. Nutr Metab Insights 2020;13:1178638820903295. https://doi.org/10.1177/1178638820903295.
[22] Singer P, Blaser AR, Berger MM, Calder PC, Casaer M, Hiesmayr M, et al. ESPEN practical and partially revised guideline: clinical nutrition in the intensive care unit. Clin Nutr 2023;42:1671–89. https://doi.org/10.1016/j.clnu.2023.07.011.
[23] Dhaliwal R, Cahill N, Lemieux M, Heyland DK. The Canadian critical care nutrition guidelines in 2013: an update on current recommendations and implementation strategies. Nutr Clin Pract 2014;29:29–43. https://doi.org/10.1177/0884533613510948.
[24] Compher C, Bingham AL, McCall M, Patel J, Rice TW, Braunschweig C, et al. Guidelines for the provision of nutrition support therapy in the adult critically ill patient: the American Society for Parenteral and Enteral Nutrition. JPEN - J Parenter Enter Nutr 2022;46:12–41. https://doi.org/10.1002/jpen.2267.
[25] Westerterp KR. Doubly labelled water assessment of energy expenditure: principle, practice, and promise. Eur J Appl Physiol 2017;117:1277–85. https://doi.org/10.1007/s00421-017-3641-x.
[26] Goran MI, Peters EJ, Herndon DN, Wolfe RR. Total energy expenditure in burned children using the doubly labeled water technique. Am J Physiol 1990;259:576–85. https://doi.org/10.1152/ajpendo.1990.259.4.E576.
[27] Graf S, Karsegard VL, Viatte V, Heidegger CP, Fleury Y, Pichard C, et al. Comparison of three indirect calorimetry devices in mechanically ventilated patients: which device compares best with the Deltatrac II? A prospective observational study. Clin Nutr 2015;34:60–5. https://doi.org/10.1016/j.clnu.2014.01.008.
[28] Sundström M, Tjader I, Rooyackers O, Wernerman J. Indirect calorimetry in mechanically ventilated patients. A systematic comparison of three instruments. Clin Nutr 2013;32:118–21. https://doi.org/10.1016/j.clnu.2012.06.004.
[29] Oshima T, Dupertuis YM, Delsoglio M, Heidegger CP. Pichard C in vitro validation of indirect calorimetry device developed for the ICALIC project against mass spectrometry. Clin Nutr ESPEN 2019;32:50–5. https://doi.org/10.1016/j.clnesp.2019.05.004.
[30] Oshima T, Delsoglio M, Dupertuis YM, Singer P, De Waele E, Veraar C, et al. The clinical evaluation of the new indirect calorimeter developed by the ICALIC project. Clin Nutr 2020;39:3103–11. https://doi.org/10.1016/j.clnu.2020.01.017.
[31] Dupertuis YM, Delsoglio M, Hamilton-James K, Berger MM, Pichard C, Collet TH, et al. Clinical evaluation of the new indirect calorimeter in canopy and face mask mode for energy expenditure measurement in spontaneously breathing patients. Clin Nutr 2022;41:1591–9. https://doi.org/10.1016/j.clnu.2022.05.018.
[32] Westerterp KR. Diet induced thermogenesis. Nutr Metab 2004;1:5. https://doi.org/10.1186/1743-7075-1-5.
[33] Karvonen MJ, Turpeinen O. Consumption and selection of food in competitive lumber work. J Appl Physiol 1954;6:603–12. https://doi.org/10.1152/jappl.1954.6.10.603.
[34] Delsoglio M, Achamrah N, Berger MM, Pichard C. Indirect calorimetry in clinical practice. J Clin Med 2019;8:1387. https://doi.org/10.3390/jcm8091387.
[35] McClave SA, Lowen CC, Kleber MJ, McConnell JW, Jung LY, Goldsmith LJ. Clinical use of the respiratory quotient obtained from indirect calorimetry. JPEN - J Parenter Enter Nutr 2003;27:21–6.
[36] Ellis AC, Hyatt TC, Hunter GR, Gower BA. Respiratory quotient predicts fat mass gain in premenopausal women. Obesity 2010;18:2255–9. https://doi.org/10.1038/oby.2010.96.
[37] Johnston CS, Tjonn SL, Swan PD, White A, Hutchins H, Sears B. Ketogenic low-carbohydrate diets have no metabolic advantage over nonketogenic low-carbohydrate diets. Am J Clin Nutr 2006;83:1055–61. https://doi.org/10.1093/ajcn/83.5.1055.
[38] Schutz Y, Ravussin E. Respiratory quotients lower than 0.70 in ketogenic diets. Am J Clin Nutr 1980;33:1317–9. https://doi.org/10.1093/ajcn/33.6.1317.
[39] Westerterp KR. Food quotient, respiratory quotient, and energy balance. Am J Clin Nutr 1993;57. https://doi.org/10.1093/ajcn/57.5.759S. 759S-64S; discussion 64S-65S.
[40] Stapel SN, de Grooth HJ, Alimohamad H, Elbers PW, Girbes AR, Weijs PJ, et al. Ventilator-derived carbon dioxide production to assess energy expenditure in critically ill patients: proof of concept. Crit Care 2016;19:370. https://doi.org/10.1186/s13054-015-1087-2.
[41] Kagan I, Zusman O, Bendavid I, Theilla M, Cohen J, Singer P. Validation of carbon dioxide production (VCO(2)) as a tool to calculate resting energy expenditure (REE) in mechanically ventilated critically ill patients: a retrospective observational study. Crit Care 2018;22:186. https://doi.org/10.1186/s13054-018-2108-8.
[42] Black AE, Prentice AM, Coward WA. Use of food quotients to predict respiratory quotients for the doubly-labelled water method of measuring energy expenditure. Hum Nutr Clin Nutr 1986;40:381–91.
[43] Galgani JE, Moro C, Ravussin E. Metabolic flexibility and insulin resistance. Am J Physiol Endocrinol Metab 2008;295:E1009–17. https://doi.org/10.1152/ajpendo.90558.2008.
[44] Nakaya Y, Ohnaka M, Sakamoto S, Niwa Y, Okada K, Nomura M, et al. Respiratory quotient in patients with non-insulin-dependent diabetes mellitus treated with insulin and oral hypoglycemic agents. Ann Nutr Metab 1998;42:333–40. https://doi.org/10.1159/000012753.
[45] Tappy L, Schwarz JM, Schneiter P, Cayeux C, Revelly JP, Fagerquist CK, et al. Effects of isoenergetic glucose-based or lipid-based parenteral nutrition on glucose metabolism, *de novo* lipogenesis, and respiratory gas exchanges in critically ill patients. Crit Care Med 1998;26:860–7.
[46] Wang S, Ma L, Zhuang Y, Jiang B, Zhang X. Screening and risk factors of exocrine pancreatic insufficiency in critically ill adult patients receiving enteral nutrition. Crit Care 2013;17:R171. https://doi.org/10.1186/cc12850.
[47] Wierdsma NJ, Peters JH, Weijs PJ, Keur MB, Girbes AR, van Bodegraven AA, et al. Malabsorption and nutritional balance in the ICU - faecal weight as a biomarker: a prospective observational pilot study. Crit Care 2011;15:R264.
[48] Dokken M, Rustoen T, Stubhaug A. Indirect calorimetry reveals that better monitoring of nutrition therapy in pediatric intensive care is needed. JPEN - J Parenter Enter Nutr 2015;39:344–52. https://doi.org/10.1177/0148607113511990.
[49] Hulst JM, Joosten KF, Tibboel D, van Goudoever JB. Causes and consequences of inadequate substrate supply to pediatric ICU patients. Curr Opin Clin Nutr Metab Care 2006;9:297–303. https://doi.org/10.1097/01.mco.0000222115.91783.71.
[50] McClave SA, Lowen CC, Kleber MJ, Nicholson JF, Jimmerson SC, McConnel JW, et al. Are patients fed appropriately according to their caloric requirements? JPEN (J Parenter Enteral Nutr) 1998;22:375–81. https://doi.org/10.1177/014860719802200637 5.
[51] Singer P, Berger MM, Van den Berghe G, Biolo G, Calder P, Forbes A, 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.
[52] Hickmann CE, Roeseler J, Castanares-Zapatero D, Herrera EI, Mongodin A, Laterre PF. Energy expenditure in the critically ill performing early physical therapy. Intensive Care Med 2014;40:548–55. https://doi.org/10.1007/s00134-014-3218-7.
[53] Bruder N, Raynal M, Pellissier D, Courtinat C, Francois G. Influence of body temperature, with or without sedation, on energy expenditure in severe head-injured patients. Crit Care Med 1998;26:568–72. https://doi.org/10.1097/00003246-199803000-00033.
[54] Fleisch A. Le métabolism basal standard et sa détermination au moyen du Metabocalculator. Helv Med Acta 1951;18:23–44.
[55] Allard JP, Pichard C, Hoshino E, Stechison S, Fareholm L, Peters WJ, et al. Validation of a new formula for calculating energy requirements of burn patients. JPEN - J Parenter Enter Nutr 1990;14:115–8. https://doi.org/10.1177/0148607190014002115.

[56] Mogensen KM, Andrew BY, Corona JC, Robinson MK. Validation of the society of critical care medicine and American society for parenteral and enteral nutrition recommendations for caloric provision to critically ill obese patients: a pilot study. JPEN - J Parenter Enter Nutr 2016;40:713–21. https://doi.org/10.1177/0148607115584001.
[57] Choban P, Dickerson R, Malone A, Worthington P, Compher C, American Society for Parenteral. A.S.P.E.N. Clinical guidelines: nutrition support of hospitalized adult patients with obesity. JPEN - J Parenter Enter Nutr 2013;37:714–44. https://doi.org/10.1177/0148607113499374.
[58] Ali A, Herndon DN, Mamachen A, Hasan S, Andersen CR, Grogans RJ, et al. Propranolol attenuates hemorrhage and accelerates wound healing in severely burned adults. Crit Care 2015;19:217. https://doi.org/10.1186/s13054-015-0913.
[59] Rousseau AF, Losser MR, Ichai C, Berger MM. ESPEN endorsed recommendations: nutritional therapy in major burns. Clin Nutr 2013;32:497–502. https://doi.org/10.1016/j.clnu.2013.02.012.
[60] Baracos VE, Whitmore WT, Gale R. The metabolic cost of fever. Can J Physiol Pharmacol 1987;65:1248–54. https://doi.org/10.1139/y87-199.
[61] van Zanten ARH, De Waele E, Wischmeyer PE. Nutrition therapy and critical illness: practical guidance for the ICU, post-ICU, and long-term convalescence phases. Crit Care 2019;23:368. https://doi.org/10.1186/s13054-019-2657-5.
[62] Smith-Ryan AE, Hirsch KR, Saylor HE, Gould LM, Blue MNM. Nutritional considerations and strategies to facilitate injury recovery and rehabilitation. J Athl Train 2020;55:918–30. https://doi.org/10.4085/1062-6050-550-19.
[63] Zambelli L, Aumar M, Ley D, Antoine M, Coopman S, Morcel J, et al. Home enteral nutrition does not decrease oral feeding in children during the first year of nutritional support. Clin Nutr 2024;43:781–6. https://doi.org/10.1016/j.clnu.2024.02.001.
[64] Dickerson RN, Andromalos L, Brown JC, Correia Mitd, Pritts W, Ridley EJ, et al. Obesity and critical care nutrition: current practice gaps and directions for future research. Crit Care 2022;26:283. https://doi.org/10.1186/s13054-022-04148-0.
[65] Honore PM, De Waele E, Jacobs R, Mattens S, Rose T, Joannes-Boyau O, et al. Nutritional and metabolic alterations during continuous renal replacement therapy. Blood Purif 2013;35:279–84. https://doi.org/10.1159/000350610.
[66] Honore PM, Redant S, Preseau T, Kaefer K, Barreto Gutierrez L, Anane S, et al. Indirect calorimetry is the gold standard to assess REE in ICU patients: some limitations to consider. Crit Care 2021;25:406. https://doi.org/10.1186/s13054-021-03817-w.
[67] Ostermann M, Lumlertgul N, Mehta R. Nutritional assessment and support during continuous renal replacement therapy. Semin Dial 2021;34:449–56. https://doi.org/10.1111/sdi.12973.