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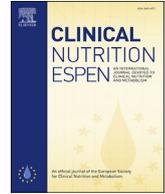
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Original article

Energy requirements of long-term ventilated COVID-19 patients with resolved SARS-CoV-2 infection



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SUMMARY

Background & aims: Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can rapidly progress into acute respiratory distress syndrome accompanied by multi-organ failure requiring invasive mechanical ventilation and critical care treatment. Nutritional therapy is a fundamental pillar in the management of hospitalized patients. It is broadly acknowledged that overfeeding and underfeeding of intensive care unit (ICU) patients are associated with increased morbidity and mortality. This study aimed to assess the energy demands of long-term ventilated COVID-19 patients using indirect calorimetry and to evaluate the applicability of established predictive equations to estimate their energy expenditure.

Methods: We performed a retrospective, single-center study in 26 mechanically ventilated COVID-19 patients with resolved SARS-CoV-2 infection in three independent intensive care units. Resting energy expenditure (REE) was evaluated by repetitive indirect calorimetry (IC) measurements. Simultaneously the performance of 12 predictive equations was examined. Patient's clinical data were retrieved from electronic medical charts. Bland-Altman plots were used to assess agreement between measured and calculated REE.

Results: Mean mREE was 1687 kcal/day and 20.0 kcal relative to actual body weight (ABW) per day (kcal/kg/day). Longitudinal mean mREE did not change significantly over time, although mREE values had a high dispersion (SD of mREE \pm 487). Obese individuals were found to have significantly increased mREE, but lower energy expenditure relative to their body mass. Calculated REE showed poor agreement with mREE ranging from 33 to 54%.

Conclusion: Resolution of SARS-CoV-2 infection confirmed by negative PCR leads to stabilization of energy demands at an average 20 kcal/kg in ventilated critically ill patients. Due to high variations in mREE and low agreement with calculated energy expenditure IC remains the gold standard for the guidance of nutritional therapy.

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1. Introduction

Since its first outbreak in December 2019, the worldwide spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was paralleled by increasing hospitalization and ICU

admission of coronavirus disease 2019 (COVID-19) patients. In 5–12% of COVID-19 infections, intensive care unit (ICU) admission is necessary, mostly due to respiratory failure [1,2]. Among ICU

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Abbreviations

ABW	actual body weight	mREE	measured resting energy expenditure
ACCP	American College of Chest Physicians	NRS score	Nutritional Risk Screening score
AdjBW	adjusted body weight	PC	polymerase chain reaction
BMI	body mass index	PEEP	positive end-expiratory pressure
COVID-19	coronavirus disease 2019	pREE	predicted resting energy expenditure
ECMO	extracorporeal membrane oxygenation	REE	resting energy expenditure
ESPEN	European Society for Clinical Nutrition and Metabolism	RQ	respiratory quotient
F _I O ₂	inspiratory oxygen fraction	RT-PCR	real-time polymerase chain reaction
HB	Harris-Benedict	SARS-CoV-2	severe respiratory syndrome coronavirus 2
IC	indirect calorimetry	SD	standard deviation
ICU	intensive care unit, kcal kilocalories	SAPS score	Simplified Acute Physiology Score
IQR	interquartile range	SOFA score	sequential organ failure assessment score
mNUTRIC score	modified Nutritional Risk in the Critical ill score	VCO ₂	volume of carbon dioxide produced per minute
		VO ₂	volume of oxygen consumed per minute
		WHO	world health organization

patients with COVID-19, up to 91% require invasive mechanical ventilation [3].

More than 60% of severely and critically ill COVID-19 patients have a high nutritional risk, which is accompanied by an increased ICU admission rate and in-hospital mortality [4,5]. These findings substantiate the necessity of adequate nutritional support during every stage of hospitalization.

In-depth knowledge of COVID-19 patient's energy demands along their clinical course is essential to provide adequate nutritional therapy. Current data on the time-course dependent metabolic phenotype of patients suffering from SARS-CoV-2 infection are sparse and focusses on patients with an acute infection requiring mechanical ventilation [6,7]. Currently to our knowledge no study investigates energy requirements in COVID-19 patients after resolution of SARS-CoV-2 infection and post-COVID-19 patients respectively.

The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends to determine COVID-19 critically ill patients' energy demands using indirect calorimetry (IC) [8]. The American Society for enteral and parenteral nutrition states that although IC can ideally determine energy requirements in COVID-19 patients it bears the risk of potential contamination and exposition of healthcare providers to increased viral loads. The society recommends the use of weight-based equations instead [9]. A predictive equation recommending 20 kcal/kg/day can be used and 80–100% of target energy supply should be reached by day 4 [8,10].

Since safety for healthcare providers has utmost priority when performing IC, specific considerations have to be taken into account including most thorough planning of measurements, apnea mode and tube clamping during connection and disconnection of the calorimeter and disinfection and storage of the equipment [11].

An accurate equation to predict energy expenditure would be a valuable instrument to avoid potential harm in aggressively ventilated critically ill patients by disrupting the ventilation circuit to perform IC and to minimize the risk of infection with SARS-CoV-2 for operators.

In this study, we conducted a retrospective observational analysis to investigate the energy requirements of COVID-19 critically ill patients after confirmed resolution of SARS-CoV-2 infection and the potential role of equations to predict caloric demands.

2. Material & methods

This retrospective observational study was approved by the Institutional Ethics Board of the University of Technology Dresden,

Dresden, Germany (BO-EK-222052020) and complied with the declaration of Helsinki. The study was conducted on three intensive care units of the University Hospital Carl Gustav Carus at the University of Technology Dresden.

IC was performed by trained operators during clinical routine following established recommendations published elsewhere [12] using a Q-NRG + calorimeter (COSMED, Rome, Italy). Following a 20-min resting period, IC was performed until variability was $\leq 10\%$. Calorimeters were calibrated and warmed up before each measurement. All consecutive patients meeting the following criteria were included: age ≥ 18 years, confirmed COVID-19 by PCR in history, invasive mechanical ventilation, and terminated isolation for SARS-CoV-2 infection according to European Centre for Disease Prevention and Control recommendations [13]. RT-PCR was performed every other day. Patients were considered SARS-CoV-2 negative when two consecutive RT-PCR showed cycle threshold values ≥ 30 . Nevertheless, special precautions were undertaken to minimize risks of SARS-CoV-2 transmission, including apnea mode and tube clamping during connection and disconnection [11]. Patients on extracorporeal membrane oxygenation (ECMO) were excluded from our study. IC was performed every other day. When the patient's respiratory condition was unstable IC was skipped. From January 11th 2021 to February 21st 2021 twenty-six consecutive patients meeting the inclusion criteria were included in the final analysis. Relative mREE was defined as mREE in kcal per kg ABW. In our study we used predictive equations that have been established for use in critically ill patients. Equations derived from healthy adults (Harris-Benedict [14], Owen [15], and Mifflin St. Jeor [16]), from hospitalized ventilated and spontaneously breathing patients (Ireton-Jones 1997 [17]), or critically ill (Penn State [18], and Swinamer [19]). The complete equations are listed in [Supplementary Table 1](#).

Mean of differences was calculated as mean of pREE subtracted from mREE. Percent difference was defined as the difference divided by measurements mean. Absolute difference and absolute percent difference were calculated with the respective absolute values. Agreement was defined as prediction between 85% and 115% of patient's mREE, and calculated as mean pREE divided by mean mREE.

2.1. Data collection

Demographic data, medical records, scores, comorbidities, laboratory findings, arterial blood gas analysis, ventilator settings,

calorimetry results, and clinical outcomes were retrieved from patient’s electronic medical charts.

2.2. Statistical analysis

Demographic and medical data following normal distribution were represented as mean ± standard deviation (SD). Data with a skewed distribution were presented as median and interquartile range (IQR). Categorical variables were described as frequency rates and percentages. Student’s t-test was performed for continuous parameters. P-values < 0.05 were considered statistically significant. Bland-Altman plots were conducted as described previously [20]. All analyses were performed using R software (The R Foundation, <http://www.r-project.org>, version 4.0.0) and GraphPad Prism (GraphPad Software, Inc. version 8).

3. Results

3.1. Baseline characteristics of included individuals

Baseline characteristics from 26 patients are shown in Table 1. Among included individuals 18 were male (69.2%), the median age was 62.4 years and median length of mechanical ventilation until isolation for SARS-CoV-2 was suspended was 17.3 days. 68% of patients showed significant comorbidities (≥2). 57.7% were obese (BMI ≥30 kg/m²). At the end of the study period ICU mortality rate was 20% (n = 5), 48% of patients were transferred to skilled nursing facilities under mechanical ventilation, and 32% remained under intensive care.

Table 1

Patient baseline characteristics and clinical data at the time of isolation cessation and clinical outcomes until end of study.

(a) Baseline characteristics (n = 26)				
Age (years) ^a	63.4 (9.66)			
BMI (kg/m ²) ^a	30.5 (6.08)			
Sex ratio (M:F)	18:8			
Obese (BMI ≥ 30)				
no	11 (42.3%)			
yes	15 (57.7%)			
Number of Comorbidities				
0	1 (4.00%)			
1	7 (28.0%)			
≥2	17 (68.0%)			
SAPS Score ^a	41.3 (9.19)			
IC measurements per patient ^a	4 (3)			
(b) Clinical data (n = 26)				
SOFA Score ^{a,d}	11.3 (2.46)			
Ventilator days ^{a,d}	17.3 (11.9)			
Pulmonary artery embolism				
no	22 (84.6%)			
yes	4 (15.4%)			
Deceased ^b	5 (19.2%)			
Continued ICU hospitalization ^b	9 (34.6%)			
Transferred to skilled nursing facility ^b	12 (46.2%)			
Use of steroids	16 (62%)			
Use of neuromuscular blocker	0 (0%)			
(c) Energy expenditure data (n = 105)				
	all patients	Obese	Non-Obese	P value ^c
RQ	0.91 (0.19)	0.93 (0.16)	0.90 (0.20)	0.348
Measured REE per day (kcal/day)	1687 (487)	1878 (411)	1539 (494)	<0.001
Measured REE per kg actual BW (kcal/kg/day)	20.0 (5.52)	21.1 (6.55)	18.5 (3.37)	0.010

Values in parentheses are percentages unless indicated otherwise.

^a Values are mean (SD).

^b Disposition on the end of the study period.

^c Obese vs. Non-Obese, P-values indicate comparison of Obese and Non-Obese groups; Student’s t-Test was performed for continuous parameters.

^d As calculated on the day of the first measurement.

3.2. Longitudinal energy expenditure following resolution of SARS-CoV-2 infection

105 IC measurements from 26 COVID-19 ICU patients after cessation of isolation are summarized in Fig. 1 and Table 1C. The mean number of measurements per patient was 4 (±3). Overall mean mREE was 1687 kcal/day with a standard deviation of ±487 (Table 1C). Mean mREE normalized to bodyweight was 20.0 kcal/kg/day (±5.52). Total mREE and relative mREE did not change significantly throughout the measurement period (Fig. 1A and B). Obese individuals (BMI ≥ 30 kg/m²) have a higher risk for malnutrition and a lower basal metabolic rate relative to their body weight. Therefore, we compared absolute and relative energy expenditure of obese and non-obese patients. Indeed, the total mREE of obese individuals was significantly higher compared to non-obese patients’ mREE, while mREE relative to body weight was significantly lower in the obese group (Fig. 1D and E).

3.3. Comparison of mREE with predictive equations

To validate equation precision, we calculated pREE for all 105 measurements using 12 most commonly applied equations (Table 2). Although differences between mean mREE and mean pREE were low and ranged between 3 kcal/day (Mifflin St. Jeor) and 131 kcal/day (Penn State (HB)), a substantial discrepancy between calculated and measured resting energy expenditure in individual measurements led to poor agreement between mREE and pREE for all tested equations (Table 3). Mifflin St. Jeor achieved the highest agreement of mREE with pREE (defined as 85–115% of mREE) (54%), and Penn State (HB) was the worst with

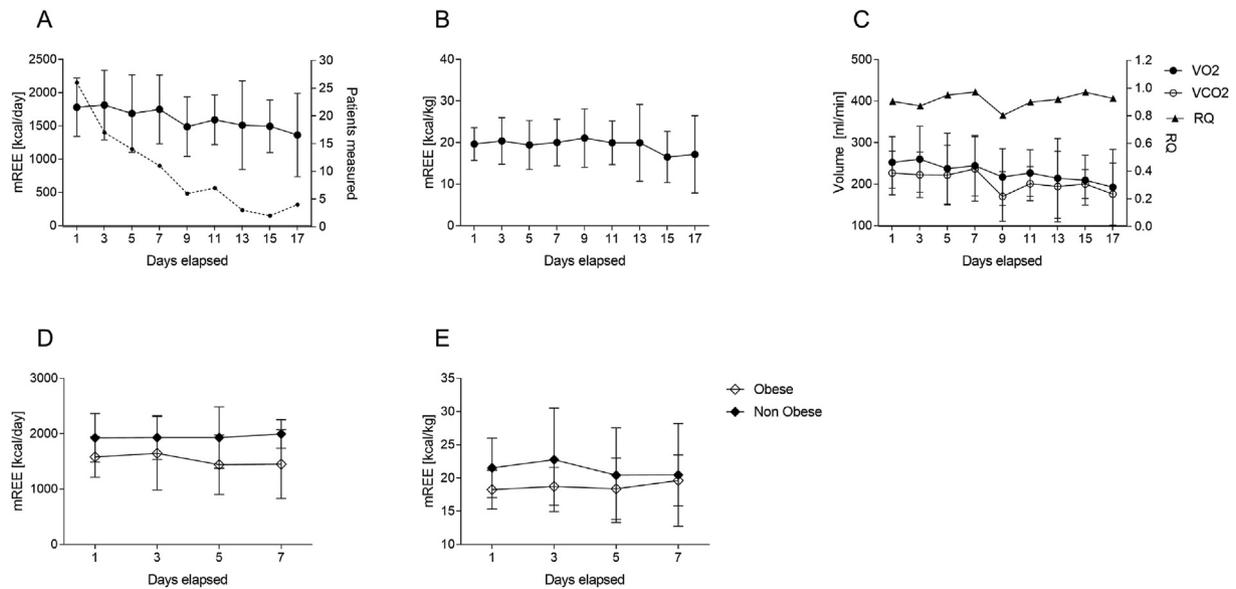


Fig. 1. Longitudinal energy expenditure, VO₂, VCO₂, and RQ in intubated COVID-19 ICU patients since cessation of isolation for SARS-CoV-2 infection. **A** Total resting energy expenditure per day over time since cessation of isolation. **B** Relative energy expenditure over time per kilogram ABW. **C** Oxygen consumption (VO₂), carbon dioxide production (VCO₂), and respiratory quotient (RQ) over time. **D** Total resting energy expenditure per day over time in Obese and Non-Obese patients. **E** Relative resting energy expenditure over time per kilogram ABW in obese and non-obese patients.

Table 2
Performance metrics of predictive equations. Numbers in brackets indicate SD.

Equation	Mean of pREE kcal/day	Mean of difference kcal/day	Mean of absolute difference kcal/day	% difference	% absolute difference
Mifflin St. Jeor	1684 (256)	2.91 (399)	317 (241)	-7.24 (31.4)	22.1 (23.4)
WHO	1609 (329)	78.1 (429)	335 (278)	-2.15 (31.7)	22.2 (22.6)
Swinamer	1868 (352)	-183.7 (416)	356 (281)	-18.99 (37.8)	27.2 (32.4)
Penn State (Mifflin – St. Jeor)	1690 (329)	-5.66 (396)	318 (233)	-7.20 (32.3)	22.4 (24.3)
Harris-Benedict	1652 (379)	35.5 (440)	356 (259)	-4.48 (32.2)	23.7 (22.2)
Owen	1660 (306)	27.3 (460)	373 (269)	-6.25 (36.2)	25.6 (26.3)
ACCP	1690 (246)	-3.09 (482)	382 (291)	-9.13 (38.8)	26.8 (29.4)
Müller	1678 (331)	8.71 (445)	359 (261)	-6.91 (34.5)	24.6 (25.1)
HB (Roza & Shizgal)	1665 (375)	22.0 (445)	360 (259)	-5.50 (33.1)	24.2 (23.2)
Iretton - Jones 1997	1675 (231)	11.8 (444)	354 (267)	-7.64 (35.0)	24.8 (25.8)
ESPEN 20 kcal/kg	1730 (453)	-42.61 (461)	377 (266)	-8.72 (33.8)	25.3 (24.0)
Penn State (HB)	1556 (396)	128 (426)	365 (253)	1.83 (31.0)	23.4 (20.3)

Table 3
Agreement of equations with measured REE. Agreement is presented as percent patient agreement meeting defined ranges.

Equation	85%–115% agreement	Less than 85% (underfeeding)	More than 115% (overfeeding)	95%–105% agreement	75%–125% agreement
Mifflin St. Jeor	54%	19%	27%	12%	73%
WHO	48%	31%	21%	17%	67%
Swinamer	47%	12%	41%	14%	67%
Penn State (Mifflin – St. Jeor)	44%	25%	31%	17%	70%
Harris-Benedict	40%	30%	30%	11%	68%
Owen	40%	29%	31%	8%	63%
ACCP	40%	29%	31%	22%	64%
Müller	40%	28%	32%	9%	67%
HB (Roza & Shizgal)	40%	30%	30%	11%	68%
Iretton - Jones 1997	39%	28%	33%	16%	67%
ESPEN 20 kcal/kg	38%	27%	35%	10%	66%
Penn State (HB)	33%	41%	26%	15%	58%

only 33% agreement. The calculated mean of absolute differences varied between 317 kcal/day (±241) for Mifflin St. Jeor and 377 kcal/day (±266) using 20 kcal/kg/day recommended by ESPEN. Further, Mifflin St. Jeor also showed the lowest absolute percent difference compared to mREE.

In line with these findings, Bland Altman plots comparing mREE and pREE show broad scattering of differences (mREE – pREE/2) despite low deviation of mean differences (see Fig. 2).

In summary, all tested equations predicted overfeeding or underfeeding in 46%–67% of cases.

4. Discussion

4.1. Longitudinal mREE

Our study describes longitudinal mREE in COVID-19 ICU patients requiring long-term mechanical ventilation despite successfully resolving SARS-CoV-2 infection. To our knowledge, only one other

study reported longitudinal mREE during the early phase (first three weeks following intubation) of critical illness [6]. Whittle et al. analyzed IC data from 26 COVID-19 ICU patients, showing a median mREE of 2789 kcal/day. During the first week following ICU admission mREE was 19.2 kcal/kg in non-obese patients and 17.5 kcal/kg in obese individuals. This period was followed by a persistent hypermetabolic phase in weeks 2 and 3 with up to

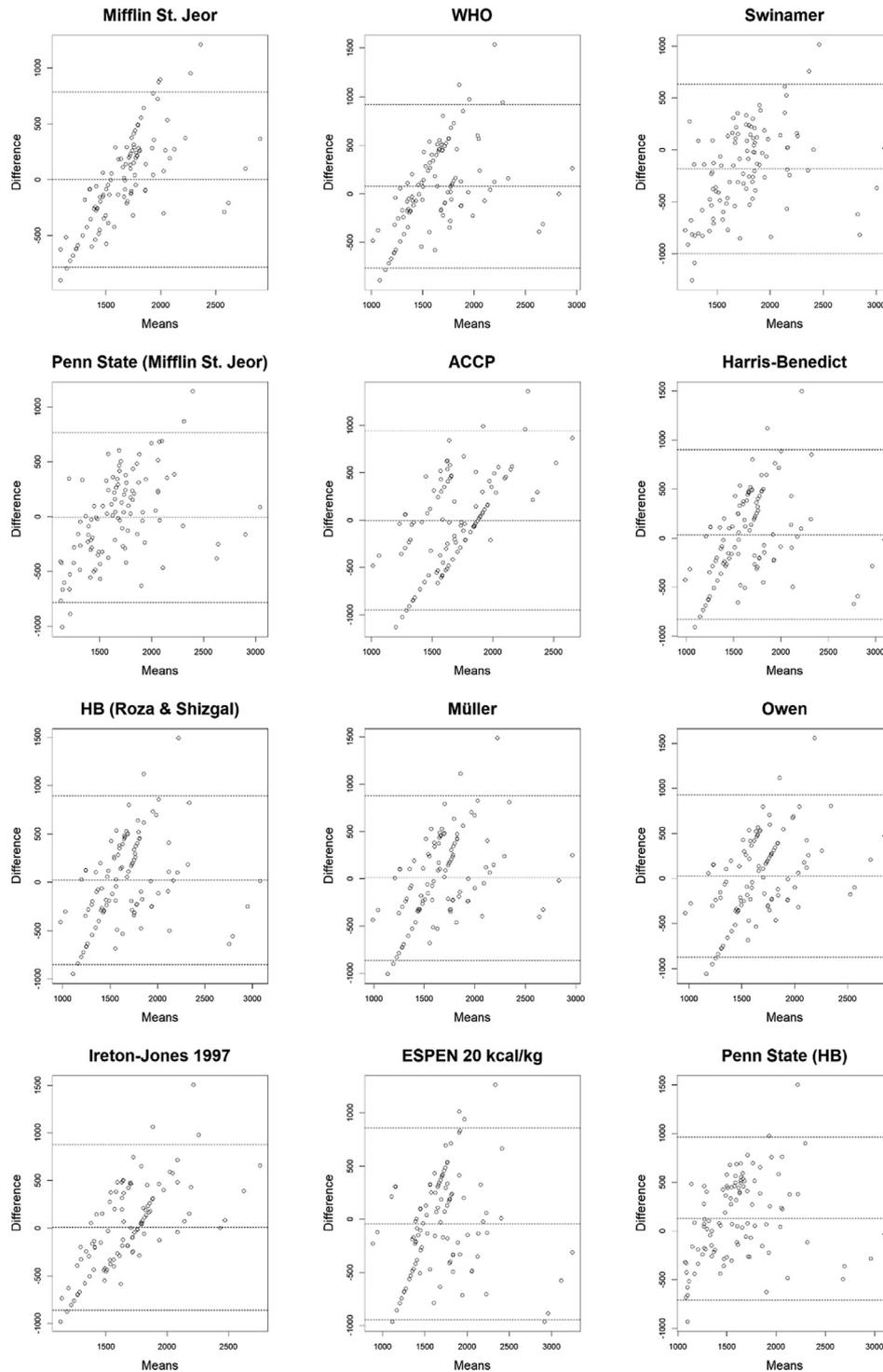


Fig. 2. Bland-Altman plots of the agreement between mREE by IC and pREE by Mifflin St. Jeor, WHO, Swinamer, Penn State (Mifflin St. Jeor), Harris-Benedict, Owen, ACCP, Müller, HB (Roza & Shizgal), Ireton-Jones, ESPEN 20 kcal/kg, and Penn State (HB) equations. X-axis marks mean of measurements (mREE and pREE) presented as kcal/day. Y-axis marks their difference presented as kcal/day.

29 kcal/kg and 31.5 kcal/kg for non-obese and obese patients respectively. mREE measured by Whittle and colleagues exceeded predicted EE (pREE) calculated using Harris-Benedict-Equation on an average of 150% [6]. End of isolation or negative RT-PCR tests were not reported. Therefore, the energy requirements of long-term ventilated COVID-19 patients and adaptations upon resolution of SARS-CoV-2 infection remained unknown. Yu et al. performed a single IC measurement of seven patients with confirmed COVID-19 pneumonia. The measurement time-point varied between day 8 and 55 of ICU admission. In line with the hypermetabolic state described by Whittle et al., they report a median mREE of 4044 kcal/day, 235% of pREE using the Penn State-Equation [7].

Metabolism in the critically ill is highly complex and subject of research for almost a century, independent of the current SARS-CoV-2 pandemic. Identifying a uniform course of energy expenditure in critically ill patients has failed [21]. The transition from early to late acute phase and consecutively post-acute phase in predefined time intervals as suggested in literature [10,21] does not seem to be applicable in COVID-19 patients.

Taken together, the previously described hypermetabolism during active SARS-CoV-2 infection and our findings of a decline in energy demands upon resolution of infection imply that critical turning points in the course of COVID-19 (including ICU admission and cessation of isolation for infectiousness) rather than predefined phases should be used to reassess energy requirements and nutritional therapy.

4.2. Predictive equations are not feasible to estimate energy expenditure

A lack of availability, tight schedules and risk of infection lead to the widespread use of predictive equations for the guidance of nutritional therapy in ICU patients. Numerous equations have been described, but few have been validated for use in ICU patients. Nevertheless, it has been shown that pREE poorly correlates with mREE in critically ill adults in the pre-COVID-19 era, regardless of what equation was used [22]. Furthermore, no equation was validated in subjects that resemble COVID-19 critical illness. Previous studies found the Harris-Benedict and the Penn State equations to severely underestimate EE in COVID-19 patients in the early period of acute phase [6,7]. All equations under investigation proved to perform poorly in our cohort. The highest agreement was achieved when energy expenditure was calculated using Mifflin St. Jeor equation.

4.3. Clinical implications

Hypercaloric nutrition has been shown to be partly responsible for excessive carbon dioxide production (VCO₂) in mechanically ventilated patients [23–25]. Our data suggest that strong adherence to nutrient prescription according to measured energy requirements might alleviate detrimental hypercapnia in COVID-19 patients by preventing overfeeding.

4.4. Limitations

COVID-19 can rapidly deteriorate into severe hypoxemia and hypercapnia requiring escalation of respiratory support from inspiratory oxygen fraction (F_iO₂) > 70%, increasing positive end-expiratory pressure (PEEP) adjustment, nitric oxide use, and culminating in the necessity of ECMO, which renders measurement infeasible. Disrupting the ventilator circuit may further worsen patient's respiratory condition. Furthermore, IC is inaccurate in high F_iO₂ ranges [26,27]. Measuring a patient's energy requirement on ECMO is challenging since gas exchange occurs by

the patient's native lung and by the ECMO device. This needs sophisticated settings that are currently applicable for research purposes only [28].

Our study presents data from three independent intensive care units in a single clinic from a retrospective cohort of COVID-19 patients. Larger studies are warranted integrating long-term IC measurements starting from pre-ICU, over acute phase to convalescence phase to understand metabolism and changes in energy requirements during the COVID-19 disease course.

5. Conclusion

Compared with the caloric expenditure of up to 31.5 kcal/kg in the acute phase of SARS-CoV 2-infection infection described by Whittle et al., we observed a normalized mREE of 20.0 kcal/kg on average after resolution of infection in ventilated patients. Our findings suggest that the end of isolation for infection affirmed by negative PCR results represents an important clinical landmark to re-evaluate energy demands and nutritional support in critically ill COVID-19 patients. Predictive equations carry a high risk of over- and underfeeding due to poor agreement with mREE. The intra-variability of a patient's caloric requirements may vary during the clinical course, which many formulas cannot capture. None of the equations under investigation can sufficiently replace IC.

Declaration of competing interest

The authors declare that they have no conflict of interest. This investigator-initiated study was conducted independent of grant funding.

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Author's contribution

Conceived and designed the study: JvR, RM.
 Acquired the data: JvR, RM, SvB, HCH, RS.
 Analyzed the data: JvR, RM.
 Wrote the paper: JvR, RM.
 Critical review of the manuscript: AS, LS, JW, TW.
 Final approval of the manuscript: all authors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.clnesp.2021.06.016>.

References

- [1] Phua J, Weng L, Ling L, Egi M, Lim CM, Divatia JV, et al. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. *Lancet Respir Med* 2020;8:506–17. [https://doi.org/10.1016/S2213-2600\(20\)30161-2](https://doi.org/10.1016/S2213-2600(20)30161-2).
- [2] Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020;382:1708–20. <https://doi.org/10.1056/NEJMoa2002032>.
- [3] Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19). *J Am Med Assoc* 2020;324:782. <https://doi.org/10.1001/jama.2020.12839>.
- [4] Zhang P, He Z, Yu G, Peng D, Feng Y, Ling J, et al. The modified NUTRIC score can be used for nutritional risk assessment as well as prognosis prediction in critically ill COVID-19 patients. *Clin Nutr* 2021;40:534–41. <https://doi.org/10.1016/j.clnu.2020.05.051>.

- [5] Li G, Zhou C, Ba Y, Wang Y, Song B, Cheng X, et al. Nutritional risk and therapy for severe and critical COVID-19 patients: a multicenter retrospective observational study. *Clin Nutr* 2020. <https://doi.org/10.1016/j.clnu.2020.09.040>.
- [6] Whittle J, Molinger J, MacLeod D, Haines K, Wischmeyer PE, LEEP-COVID Study Group. Persistent hypermetabolism and longitudinal energy expenditure in critically ill patients with COVID-19. *Crit Care* 2020;24:581. <https://doi.org/10.1186/s13054-020-03286-7>.
- [7] Yu P-J, Cassiere H, DeRosa S, Bocchieri K, Yar S, Hartman A. Hypermetabolism and coronavirus disease 2019. *J Parenter Enteral Nutr* 2020;44:1234–6. <https://doi.org/10.1002/jpen.1948>.
- [8] Barazzoni R, Bischoff SC, Breda J, Wickramasinghe K, Krznaric Z, Nitzan D, et al. ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection. *Clin Nutr* 2020;39:1631–8. <https://doi.org/10.1016/j.clnu.2020.03.022>.
- [9] Martindale R, Patel JJ, Taylor B, Arabi YM, Warren M, McClave SA. Nutrition therapy in critically ill patients with coronavirus disease 2019. *JPEN - J Parenter Enteral Nutr* 2020;44:1174–84. <https://doi.org/10.1002/jpen.1930>.
- [10] Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, 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>.
- [11] Singer P, Pichard C, De Waele E. Practical guidance for the use of indirect calorimetry during COVID 19 pandemic. *Clin Nutr Exp* 2020;33:18–23. <https://doi.org/10.1016/j.clnex.2020.07.002>.
- [12] Oshima T, Berger MM, De Waele E, Guttormsen AB, Heidegger C-P, 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>.
- [13] European Centre for Disease Prevention and control. ECDC Guidance for discharge and ending of isolation of people with COVID-19. 2020.
- [14] Harris JA, Benedict FG. A biometric study of human basal metabolism. *Proc Natl Acad Sci* 1918;4:370–3. <https://doi.org/10.1073/pnas.4.12.370>.
- [15] Owen OE, Holup JL, D'Alessio DA, Craig ES, Polansky M, Smalley KJ, et al. A reappraisal of the caloric requirements of men. *Am J Clin Nutr* 1987;46:875–85. <https://doi.org/10.1093/ajcn/46.6.875>.
- [16] Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO. A new predictive equation for resting energy expenditure in healthy individuals. *Am J Clin Nutr* 1990;51:241–7. <https://doi.org/10.1093/ajcn/51.2.241>.
- [17] Ireton-Jones C, Jones JD. Improved equations for predicting energy expenditure in patients: the Ireton-Jones equations. *Nutr Clin Pract* 2002;17:29–31. <https://doi.org/10.1177/011542650201700129>.
- [18] Frankenfield DC, Coleman A, Alam S, Cooney RN. Analysis of estimation methods for resting metabolic rate in critically ill adults. *J Parenter Enteral Nutr* 2009;33:27–36. <https://doi.org/10.1177/0148607108322399>.
- [19] Swinamer DL, Grace MG, Hamilton SM, Jones RL, Roberts P, King EG. Predictive equation for assessing energy expenditure in mechanically ventilated critically ill patients. *Crit Care Med* 1990;18:657–61. <https://doi.org/10.1097/00003246-199006000-00017>.
- [20] Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* (London, England) 1986;1:307–10. <https://doi.org/10.1016/j.ajo.2008.09.032>.
- [21] Moonen HPFX, Beckers KJH, van Zanten ARH. Energy expenditure and indirect calorimetry in critical illness and convalescence: current evidence and practical considerations. *J Intensive Care* 2021;9:8. <https://doi.org/10.1186/s40560-021-00524-0>.
- [22] De Waele E, Opsomer T, Honoré PM, Diltor 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.
- [23] Herve P, Simonneau G, Girard P, Cerrina J, Mathieu M, Duroux P. Hypercapnic acidosis induced by nutrition in mechanically ventilated patients: glucose versus fat. *Crit Care Med* 1985;13:537–40. <https://doi.org/10.1097/00003246-198507000-00005>.
- [24] Talpers SS, Romberger DJ, Bunce SB, Pingleton SK. Nutritionally associated increased carbon dioxide production. *Chest* 1992;102:551–5. <https://doi.org/10.1378/chest.102.2.551>.
- [25] Dark DS, Pingleton SK, Kerby GR. Hypercapnia during weaning. *Chest* 1985;88:141–3. <https://doi.org/10.1378/chest.88.1.141>.
- [26] Phang PT, Rich T, Ronco J. A validation and comparison study of two metabolic monitors. *JPEN - J Parenter Enteral Nutr* 1990;14:259–61. <https://doi.org/10.1177/0148607190014003259>.
- [27] Takala J, Keinänen O, Väisänen P, Kari A. Measurement of gas exchange in intensive care: laboratory and clinical validation of a new device. *Crit Care Med* 1989;17:1041–7. <https://doi.org/10.1097/00003246-198910000-00015>.
- [28] De Waele E, Jonckheer J, Pen JJ, Demol J, Staessens K, Puis L, et al. Energy expenditure of patients on ECMO: a prospective pilot study. *Acta Anaesthesiol Scand* 2019;63:360–4. <https://doi.org/10.1111/aas.13287>.