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Original article

Comparison of the Beacon and Quark indirect calorimetry devices to measure resting energy expenditure in ventilated ICU patients

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SUMMARY

Introduction: Critically ill patients in the Intensive Care Unit (ICU) should receive nutritional support matched to their metabolic needs as both under- and overfeeding energy has been shown to increase mortality. Critical illness can significantly affect metabolism. Consequently, resting energy expenditure (REE) can vary markedly during critical illness. Therefore, indirect calorimetry to estimate REE is recommended to determine energy requirements in individual ICU patients and to guide optimal nutritional support. Currently, the Quark metabolic monitor is considered the gold standard in our ICU, but novel mechanical support devices are also equipped with indirect calorimetry functionalities. This study aimed to evaluate the performance of a currently unevaluated device.

Methods: A cross-sectional analysis in mechanically ventilated patients was conducted in a mixed medical-surgical ICU. The primary outcome was a numerical and visual comparison of the performance of the Beacon indirect calorimeter to calculate REE compared to the Quark device using Bland Altman plots. Performance was evaluated using bias, precision, accuracy, and reliability. Secondary analysis included a comparison with REE estimated by predictive equations.

Results: Seventy-one measurements were obtained in 27 mechanically ventilated subjects. An underestimation by the Beacon device in calculated REE of −96.2 kcal/day (4.5%) was found. There was a bias towards higher VCO_2 and lower VO_2 values with Beacon as compared to Quark. The reliability of the Beacon was good, with an absolute intraclass correlation coefficient of 0.897 (95%CI 0.751–0.955; $p = 0.000$). There was a poor correlation (<0.40) between the separate indirect calorimetry devices and most predictive equations. Only the Faisy predictive equations had good reliability (ICC 0.687, $p = 0.002$).

Conclusions: Beacon indirect calorimetry accurately determined REE in mechanically ventilated critically ill patients compared to the gold standard in our ICU (Quark indirect calorimeter), although confidence intervals were wide. There was low bias and good reliability. On the other hand, predictive equations performed poorly compared to both devices, underestimating the true metabolic needs of mechanically ventilated ICU patients.

1. Introduction

Critically ill patients in the Intensive Care Unit (ICU) should receive nutritional support matched to their metabolic needs. In observational studies, both underfeeding and overfeeding energy increased morbidity and mortality among ICU patients [1–5]. Critical illness can significantly affect metabolism, and energy expenditure (EE) can vary markedly during critical illness [6]. Resting energy expenditure (REE) which accounts usually for 70% of total energy expenditure (TEE), can markedly increase after burns, sepsis, trauma, and surgery and in patients receiving vasopressors [4]. However, REE also can decrease because of sedation, analgesics, or neuromuscular blocking agents [7]. Predictive equations – such as the Harris-Benedict and Penn state University equations - are commonly used in clinical settings to predict REE [8–11]. However, predictive equations are population-based averages, have low accuracy rates compared with indirect calorimetry, and are unreliable to predict EE in individual patients [4,11–15]. This lack of adequate

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List of abbreviations

APACHE II	Acute Physiology And Chronic Health Evaluation II
ARDS	Acute Respiratory Distress Syndrome
BMI	Body Mass Index
95%CI	95% confidence interval
EE	Energy Expenditure
$EEVCO_2$	EE estimated by ventilator-derived carbon dioxide consumption
FiO_2	Fraction of Inspired Oxygen
FQ	Food Quotient
GCS	Glasgow Coma Scale
ICC	Intraclass Correlation Coefficient
ICU	Intensive Care Unit
IQR	Interquartile range
LoA	Limits of Agreement
PEEP	Positive End-Expiratory Pressure
PBQ	Patient-Beacon-Quark (measurement configuration)
PQB	Patient-Quark-Beacon (measurement configuration)
RASS	Richmond Agitation Sedation Scale
REE	Resting Energy Expenditure
RER	Respiratory Exchange Ratio
RQ	Respiratory Quotient
SD	Standard Deviation
SE	Standard Error
SOFA	Sequential Organ Failure Assessment
TEE	Total Energy Expenditure
VCO_2	Volume of carbon dioxide expired
VO_2	Volume of oxygen inspired
ZGV	Ziekenhuis Gelderse Vallei

methods to determine energy requirements poses a serious challenge to clinicians since these targets are used to guide nutritional support [16]. Therefore, the recent European Society for Clinical Nutrition and Metabolism (ESPEN) adult ICU guideline recommends indirect calorimetry to estimate EE during critical illness to determine the energy requirements in individual ICU patients and to guide optimal nutritional support [17].

1.1. Indirect calorimetry

REE can be estimated with the Weir equation via oxygen consumption (VO_2) and carbon dioxide production (VCO_2), measured with indirect calorimetry [18].

For decades, the Deltatrac Metabolic Monitor (Datex, Helsinki, Finland; hereafter: Deltatrac) was considered the “gold standard” indirect calorimeter for critical care patients because VO_2 and VCO_2 measurements in ventilated patients were equivalent to mass spectrometry results [19,20]. Unfortunately, Deltatrac is no longer manufactured, and several new devices have been introduced, relying on breath-by-breath analysis instead of the mixing chamber method used in the Deltatrac device. The QUARK RMR (COSMED, Rome, Italy; hereafter: Quark) has been validated – along with the CCM express (Medgraphics, Milano, Italy) – against the Deltatrac in mechanically ventilated patients [5,21–23]. However, the Quark is a cumbersome device, requiring a time and personnel consuming user-assisted calibration procedure before each use.

Currently, a novel mechanical support device designed as a continuously Intensive Care Clinical Advisory system for ventilated patients, was equipped with indirect calorimetry functionalities as well. This Beacon Care system (Mermaid Care Company, Denmark; hereafter called: Beacon) works with any ICU ventilator and requires no installation but only a virtual training of 1 h to use the system [24]. Until now, only one study has been published evaluating reliability and agreement between the Beacon and another indirect calorimetry device, i.e., Ecovx (GE Healthcare, Helsinki, Finland) [25]. It was concluded that Beacon measurements were within-day reliable up to FiO_2 fractions of 0.85. That study was conducted in healthy subjects in sitting positions and not in critically ill and mechanically ventilated ICU patients, which warrants further evaluation of the device.

Therefore the primary aim of the present study was to test the performance of the Beacon device in measuring VO_2 consumption and VCO_2 production, and determining REE, compared with the current gold standard in our ICU (the Quark). Additionally, measurements were compared with REE estimations by predictive equations.

2. Materials and methods

2.1. Study design and study participants

A cross-sectional analysis was conducted in critically ill ICU patients in Gelderse Vallei Hospital (ZGV) from September 17, 2018, till April 5, 2019. Adult patients (aged ≥18 years) being mechanically ventilated for ≥48 h were eligible. After signing the informed consent by the patient or legal representative, patients were enrolled. Patients with high levels of mechanical ventilatory support (i.e., fraction of inspired oxygen (FiO_2) >0.6 or positive end-expiratory pressure (PEEP) > 12 cmH_2O) or ventilated in prone position were excluded from the study for patient safety and technical reasons, as well as patients with an acute respiratory distress syndrome (ARDS) as defined by the Berlin definition [26]. Moreover, patients with unspecified amounts of air leakage (such as uncuffed tracheostomy cannula, endotracheal tube cuff leaks, tracheoesophageal fistulae, subcutaneous emphysema, or chest tube drainage) or a body temperature making an accurate measurement impossible (<36 or >42 °C) were excluded. Each subject served as his/her control. The Medical Ethical Committee of ZGV approved the study (protocol number 1807-131).

2.2. Study procedure

All measurements were performed by two investigators (SA and HSB), and study data were recorded. To ensure reliable, valid, and representative assessment of REE, subjects were not allowed to be engaged in any physical activity (such as physiotherapy) nor receive any form of renal replacement therapy as well as changes in ventilatory support (except for changes in FiO_2) 2 h before the measurements. Furthermore, no inhalation drugs were administered during actual measurements. For safety reasons, blood gasses were obtained before each measurement and indirect calorimetry was not performed when pH was below 7.3.

The measurements were performed with sampling lines from both Beacon and Quark calorimetry devices simultaneously in place. A pilot study on four subjects was performed to determine the optimal position for both devices. It was observed that REE calculations by the two devices were different based on the positions of the sampling lines (mean difference 224.3 kcal/day, SD 146.1 kcal/day). Therefore, two consecutive measurements in a computer-generated random order were performed, either Patient-Beacon-Quark (PBQ) configuration or Patient-Quark-Beacon (PQB) configuration (Fig. 1). Conditions remained unchanged between the separate configuration measurements. After reaching a steady-state, each measurement was performed for at least 15 min per configuration. Recordings from the first 5 min and unstable conditions were excluded. A set of two configurations was defined as a single measurement day.

Measurements were performed on three subsequent days. Room temperature was maintained between 20 and 22 °C during measurements. Both devices were calibrated (gas and flow/volume calibration procedures) before commencing measurements according to the user's manual provided by the manufacturer.

2.3. Study devices: the Quark and Beacon indirect calorimeters

Both Quark and Beacon functions are based on breath-by-breath gas analysis techniques [24,27]. The disposable flow sensors – attached to the patient-ventilator circuit – trap small amounts of inhaled and exhaled gases via gas sampling lines. This technique is used to measure flow: VCO_2 (in mL/min) and VO_2 (in mL/min). The inbuilt software uses these measurements to calculate the respiratory exchange ratio (RER: VCO_2/VO_2) and REE (kcal/day) in both devices. The RER is an estimate for the respiratory quotient (RQ) when ventilatory parameters and acid-base balance are stable [20]. RER ranges in physiologic circumstances between 0.67 and 1.2 and depends on the composition of (non)nutritional intake [20,28,29].

The formula used by the Quark device to calculate REE is similar to the Weir equation:

$$REE = [(3.9 \times VO_2(\text{in mL/min})) + (1.1 \times VCO_2(\text{in mL/min}))] \times 1440.$$

The Beacon used another equation:

$$REE = 5.5 \times VO_2(\text{in mL/min}) + 1.76 \times VCO_2(\text{in mL/min}) - 1.99 \times \text{urinary nitrogen (UN)}.$$

As UN was set to 13 by the manufacturer, this can be further simplified to:

$$REE = 5.5 \times VO_2(\text{in mL/min}) + 1.76 \times VCO_2(\text{in mL/min}) - 25.87$$

2.4. Data collection

Data collection from the electronic patient documentation system included demographic and clinical baseline characteristics and prognostic scores, such as Acute Physiology and Chronic Health Evaluation (APACHE) II and sequential organ failure assessment (SOFA) scores. Data extraction was performed using queries searching the ICU patient data management system (MetaVision; iMDsoft, Tel Aviv, Israel) and electronic patient record system (Neozis; MI Consultancy, Katwijk, The Netherlands). These parameters of interest are routinely collected during standard clinical care, and therefore imposed no burden to patients. During measurements, additional information regarding vital parameters, Glasgow Coma Scale (GCS) and ventilator mode and settings were recorded, including respiratory rate (breaths/min), body temperature (°C), PEEP (mmH_2O) and FiO_2 (%). Data verification was conducted manually.

2.5. Sample size

Using R software, a sample size of 20 patients was calculated (mean difference 224.3 kcal/day, standard deviation (SD) 146.1 kcal/day, alpha 0.05 and power of 0.8). As the study subjects are ICU patients, an estimated dropout rate of 10% was added to the calculated sample size. The final sample size was calculated as 22 patients.

2.6. Statistical analysis

All statistical analyses were conducted using IBM SPSS Statistics 24.0 (IBM Corporation, Armonk, NY, USA; 2016). Discrete variables were displayed as proportions. Continuous variables were reported as means, including standard deviations (SD) or, in the case of non-normal distribution, as medians with interquartile ranges (IQR). P-values below 0.05 were considered statistically significant.

2.6.1. Primary data analysis

Primary data analysis included a numerical and visual comparison (using Bland Altman plots) of the Beacon's performance compared to the Quark device in measuring VO_2 consumption, VCO_2 production and REE calculation. Because the conditions between the separate configuration measurements were kept constant and unaltered, only measurements from the configurations with the device of interest closest to the patient were used for final analysis to minimize the concurrent effect of gas sampling (i.e., PQB for the Quark and PBQ for the Beacon, respectively).

Bias and precision were calculated to assess accuracy. Bias was defined as the mean difference between both devices; a bias of

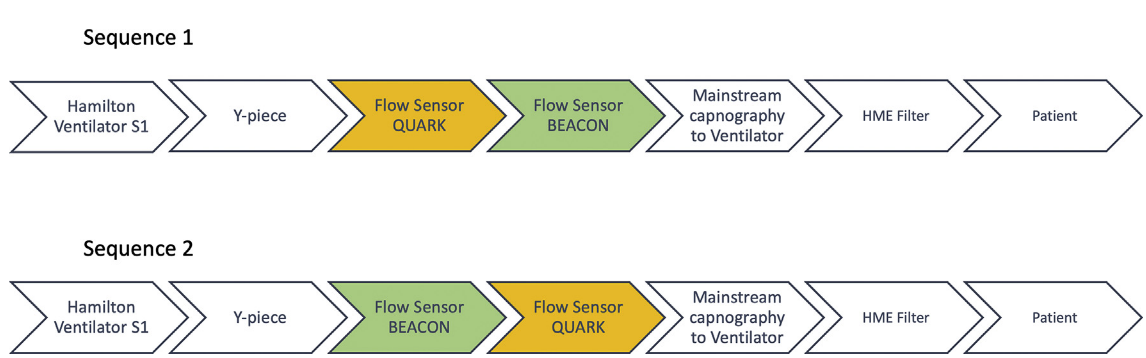

Fig. 1. Title: Measurement configurations. Legend: two consecutive measurements in a computer-generated random order were performed, either Patient-Beacon-Quark (PBQ) configuration or Patient-Quark-Beacon (PQB) configuration (and vice versa). Conditions remained unchanged between the separate configuration measurements.

<10% was considered acceptable. Precision was visualized by the upper and lower limits of the 95% confidence interval (95%CI) in the Bland Altman plots (limits of agreement, LoA). In addition, agreement (reliability) between both devices was assessed by calculating the absolute intraclass correlation coefficient (ICC). Reliability was considered poor with an ICC <0.4, fair when 0.4 ≤ ICC <0.6, good when 0.6 ≤ ICC <0.8 and excellent when ICC was ≥0.8.

All calculations were corrected for repeated measures using mixed models.

2.6.2. Secondary data analysis

Secondary data analysis included the performance of eight frequently used predictive equations compared Beacon and Quark indirect calorimetry. The FAO/WHO/UNU, Harris-Benedict, 25 kcal/kg/day, Penn State 1998 & 2003, Mifflin-St Jeor, Ireton-Jones and Faisy equations were used to calculate REE manually and compared to the REE calculations by the Beacon device and Quark [8,9,30–33]; (see Supplement 1).

Predictive equations were adjusted for under- and overweight patients with a Body Mass Index (BMI) of <18.5 or >27 kg/m^2, respectively. In these cases, weight was adjusted to ideal body weight at a BMI of 18.5 or 27 kg/m^2.

3. Results

During the study period, ninety-seven mechanically ventilated patients were eligible for inclusion; of these, informed consent was obtained from 28 patients or their legal representatives. One patient refused participation after the family initially signed informed consent, leaving a total of 27 patients in this study.

The demographic and baseline patient characteristics are summarized in Table 1. Twenty patients (74.1%) were male. The median age was 71 (IQR 61–78) years, and BMI varied between 20.2 and 44.4 kg/m^2 (median 27.8 kg/m^2; IQR 24.9–31.0). The median APACHE II and SOFA scores on ICU admission were 21 and 7, respectively. Admission types were unequally distributed among the population: 17 (63%) were medical, 10 (37%) were surgical.

Table 1
Baseline characteristics.

Gender (male)	*N (%)*	20 (74.1)
Age (years)	*Median [IQR]*	71 [61–78]
BMI on admission (kg/m^2)	*Median [IQR]*	27.8 [24.9–31.0]
Type of admission (medical)	*N (%)*	17 (63)
APACHE II score on admission	*Median [IQR]*	21 [17–24]
SOFA score on admission	*Median [IQR]*	7 [6–10]
NUTRIC score on admission	*Median [IQR]*	5 [4–6]
SAPS II score	*Median [IQR]*	45 [38–53]
Length of ICU stay (days)	*Median [IQR]*	15 [10–38]
Duration of mechanical ventilation (hours)	*Median [IQR]*	286.0 [148.6–588.8]
Intravenous sedation during measurements (yes)	*N (%)*	13 (48.1)
Ventilator mode during measurements	*N (%)*	
P-CMV		6 (8.3%)
ASV		6 (8.3%)
PS		60 (83.3%)
Type of feeding	*N (%)*	
Enteral		25 (92.6)
Enteral/parenteral		2 (7.4)
Parenteral		0 (0.0)

BMI = Body Mass Index.
APACHE II = Acute Physiology And Chronic Health Evaluation II.
SOFA = Sequential Organ Failure Assessment.
NUTRIC = Nutrition Risk in Critically Ill.
SAPS = Simplified Acute Physiology Score.
P-CMV = Pressure Controlled Mandatory Ventilation.
ASV = Adaptive Support Ventilation.
PS = Pressure Support.
IQR = InterQuartile Range.
SD = Standard Deviation.

Table 2
Mean measured VCO2 and VO2 (mL/min) and calculated REE (kcal/day) [over the measurement days].

		estimated means	SE	95% CI	
PQB	**Quark**				
	VCO2	229.9	26.8	176.5	283.3
	VO2	312.3	30.8	251.1	373.4
	REE	2118.1	211.9	1696.5	2539.8
	Beacon				
	VCO2	203.2	14.1	175.0	231.5
	VO2	244.8	16.1	212.5	277.0
	REE	1681.0	111.2	1457.7	1904.3
PBQ	**Quark**				
	VCO2	214.7	14.1	186.4	243.0
	VO2	294.7	16.1	262.5	326.9
	REE	1987.4	111.2	1764.2	2210.7
	Beacon				
	VCO2	246.9	8.2	229.0	264.8
	VO2	290.7	10.0	270.5	310.9
	REE	2022.0	69.5	1880.8	2163.1

PQB referring to configuration Patient-Quark-Beacon.
PBQ referring to configuration Patient-Beacon-Quark.
VCO2 = volume of carbon dioxide expired (in mL/min).
VO2 = volume of oxygen inspired (in mL/min).
REE = Resting Energy Expenditure (in kcal/day).
SE = Standard Error.
95%CI = 95% Confidence Interval.

3.1. Measurements

A total of 72 measurements was performed. One measurement was excluded for technical reasons (RER <0.6). Seventy-one measurements in 27 subjects were included for further analysis. Not all subjects could be measured on three consecutive days. In seven subjects, only one (n = 3) or two (n = 4) measurements were obtained: they were extubated before consecutive measurements or passed away. In 42 measurement sessions (59%), the configuration patient-Quark-Beacon was carried out first ($p = 0.377$).

Periprocedural, patients received intravenous sedation, analgesia, or anxiety-reducing medication during 78.9% (56/71) of the measurements. During 23 of these measurements, patients were deeply sedated with propofol or midazolam (Richmond Agitation Sedation Scales (RASS) −4/-5).

Over the measurement days, patients received less sedation and vasopressors and had decreasing leukocyte counts, although these

Table 3
Bias and precision of the Beacon device.

	Mean difference[a]	SE	SD	95%CI[b]	
REE	−96.2	32.6	274.6	−634.4	442.0
VCO2	17.0	4.1	34.1	−49.8	83.8
VO2	−21.5	4.7	39.2	−98.3	55.3
RQ	0.12	0.009	0.08	−0.04	0.28

REE = Resting Energy Expenditure (in kcal/day).
VCO2 = volume of carbon dioxide expired (in mL/min).
VO2 = volume of oxygen inspired (in mL/min).
RQ = Respiratory Quotient (VCO_2/VO_2).
SE = Standard Error.
SD = Standard Deviation.
95%CI = 95% Confidence Interval.
[a] Also defined as bias; Beacon compared to Quark device.
[b] *Also defined as precision (= bias ± (1,96 × SD)).*

differences were minor and not statistically significant (see Supplement 2).

3.2. Primary outcome: performance of the Beacon device

Quark measurements were used as reference. A significant interaction ($p = 0.000$) between the Beacon device and configuration type was found as illustrated in Supplement 3.

Mean measured VCO_2 were 229.9 (standard error (SE) 26.8) and 203.2 (SE 14.1) mL/min for Quark and Beacon, respectively, in configuration Patient-Quark-Beacon. For the configuration Patient-Beacon-Quark this was 214.7 (SE 14.1) and 246.9 (SE 8.8) mL/min, respectively (Table 2; Supplement 4a).

Concerning oxygen uptake measurements, mean measured VO_2 were 312.3 (SE 30.8) and 244.82 (SE 16.1) mL/min for Quark and Beacon, respectively, in configuration Patient-Quark-Beacon. For the configuration Patient-Beacon-Quark this was 294.7 (SE 16.1) and 290.7 (SE 10.0) mL/min, respectively (Table 2; Supplement 4b).

The mean difference in VCO_2 and VO_2 measurements by the Beacon device compared to Quark were +17.0 (SE 4.1) and −21.5 (SE 4.7) mL/min, respectively (Table 3). Bias and precision are visualized in the Bland–Altman plots (Fig. 2a-c). For the Bland–Altman plots, only measurements from the configurations with the device of interest closest to the patient were used to minimize the concurrent effect of gas sampling (i.e., for the Quark PQB and for the Beacon PBQ, respectively).

3.2.1. REE calculations

Mean calculated REE was 2118.1 (SE 211.9) and 2022.0 (SE 69.5) kcal/day for Quark and Beacon, respectively, in their configurations closest to the patient (Patient-Quark-Beacon and Patient-Beacon-Quark respectively; see also Table 2 & Supplement 4c). Comparisons between REE calculations are illustrated in Fig. 2d. The mean difference in REE calculation between Beacon and Quark was −96.2 (SE 32.6) kcal/day, resulting in a bias of 4.5%. When applying the same formula (Weir) for both devices to calculate REE, the mean difference reduced to −73.9 (SE 31.3) kcal/day. This corresponds with a bias of 3.5%.

The Beacon device under- and overestimated REE in respectively 62.0% and 36.6% of cases. Reliability was good with an absolute

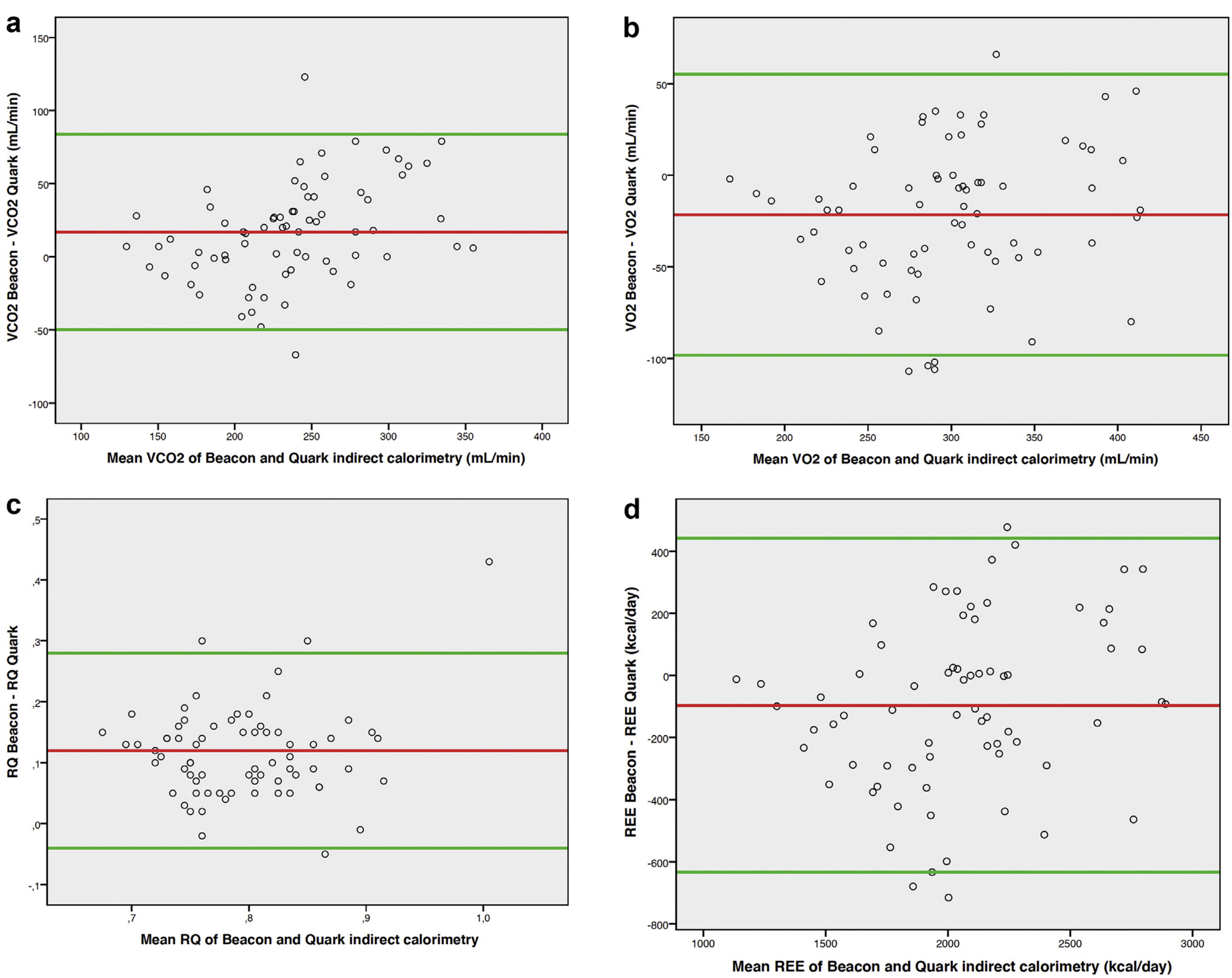

Fig. 2. a-c. Title: Bland–Altman plots of VCO_2, VO_2 and RQ by both indirect calorimeters. Legend: *Red line = mean difference = bias. *Green lines = limits of agreement = bias ± (1.96 × SD) = precision. d. Title: Bland–Altman plot of REE measured by Quark and Beacon indirect calorimeters. Legend: *Red line = mean difference = bias. *Green lines = limits of agreement = bias ± (1.96 × SD) = precision. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 4
Indirect calorimetry compared to predictive equations.

	Mean REE	Mean difference with ….		Absolute ICC			
		… REE Q	… REE B	Quark	*p-value*	Beacon	*p-value*
Quark	2118.1	NA	96.2	1.000	NA	0.897	0,000
Beacon	2021.9	−96.2	NA	0.897	0.000	1.000	NA
FAOWHO	1648.6	−469.4	−373.4	0.156	0.159	0.110	0.318
FAOWHO_IBW	1571.9	−546.1	−450.1	0.138	0.120	0.142	0.218
Harris Benedict	1602.8	−515.2	−419.2	0.158	0.152	0.147	0.249
Harris Benedict_IBW	1497.6	−620.4	−524.4	0.119	0.117	0.150	0.165
25 kcal/kg	2129.6	11.6	107.6	0.313	0.180	0.161	0.330
25 kcal/kg_IBW	1924.8	−193.2	−97.2	0.434	0.041	0.391	0.103
Penn1998	2018.1	−99.9	−3.9	0.530	0.027	0.468	0.062
Penn1998_IBW	1902.4	−215.6	−119.6	0.564	0.004	0.574	0.013
Penn2003	1846.2	−271.8	−175.8	0.480	0.013	0.467	0.042
Penn2008_IBW	1756.8	−361.2	−265.2	0.451	0.002	0.495	0.011
Mifflin	1546.8	−571.2	−475.2	0.153	0.112	0.148	0.214
Mifflin_IBW	1464.9	−653.1	−557.1	0.135	0.072	0.163	0.127
Ireton	1622.7	−495.3	−399.3	0.081	0.285	0.086	0.345
Ireton_IBW	1581.7	−536.3	−440.3	0.075	0.270	0.103	0.294
Faisy	2132.9	14.9	110.9	0.636	0.007	0.514	0.032
Faisy_IBW	2067.4	−50.6	45.4	0.687	0.002	0.605	0.011

NA = Not Applicable.
IBW = Ideal Body Weight.
REE = Resting Energy Expenditure.
Q = Quark.
B = Beacon.
ICC = Intraclass Correlation Coefficient (Two-Way Mixed, Absolute Agreement).

intraclass correlation coefficient of 0.897 (95%CI 0.751–0.955; p = 0.000).

3.3. Secondary outcomes: predictive equations

3.3.1. Predictive equations

Numerical comparisons between instruments and predictive equations are presented in Table 4. There was a poor correlation (<0.40) between the separate indirect calorimetry devices and most predictive equations. Reliability was fair for the weight adjusted Penn 1998 and Penn 2003 equations (ICC 0.574 and 0.495, respectively, compared to the Beacon device); only the Faisy and weight adjusted Faisy predictive equations performed good (ICC 0.636, p = 0.007 and ICC 0.687, p = 0.002, respectively, compared to the Quark device).

4. Discussion

The primary aim of this study was to evaluate the performance of the Beacon indirect calorimetry device in measuring VCO_2 and VO_2 and determination of REE in mechanically ventilated ICU patients. There was a bias towards higher VCO_2 and lower VO_2 values with Beacon compared to Quark (mean difference +17.0 mL/min and −21.5 mL/min respectively), although not statistically significant. Mean REE was underestimated by 96.2 kcal/day by the Beacon device compared to the reference Quark device; a bias of 4.5%. Of note, the indirect calorimeters use different formulas to calculate REE. When using the Weir formula for the Beacon device as well, this mean difference reduced to −73.8 (SE 31.3) kcal/day, lowering its bias to 3.5%. The Beacon device under- and overestimated the REE in respectively 62.0% and 36.6% of cases. Reliability was good with an absolute intraclass correlation coefficient of 0.897 (95%CI 0.751–0.955; p = 0.000).

Mean differences in REE calculations by Beacon compared to Quark were more prominent for the separate configurations: −437.2 (SE 31.0; p = 0.000) kcal/day and 34.5 (SE 30.4; p = 0.260) kcal/day, for PQB and PBQ respectively. This observation may be explained by the position of the flow sensors of both devices. In the PQB configuration, the Quark flow sensor is positioned closer to the patient than the Beacon flow sensor. In this way, the Beacon flow sensor is influenced by Quark's gas sampling, resulting in lower REE calculations (and vice versa for the PBQ configuration).

Because the conditions between the separate configuration measurements were kept constant and unaltered, only measurements from the configurations with the device of interest closest to the patient were used for the Bland–Altman plots to minimize the concurrent effect of gas sampling (i.e. for the Quark PQB and for the Beacon PBQ, respectively).

Calculated REE increased over the measurement days, especially between days 1 and 2 (+174.6 kcal/day for both devices). This may be due to less sedation and mechanical support and increased in condition (inflammatory parameters), although these changes were not statistically significant (Supplement 2).

To date, this is the first study of indirect calorimetry in ICU patients using the Beacon device. Poulsen et al. compared the Beacon device with another breath-by-breath indirect calorimeter (Ecovx) in healthy subjects (2019). They demonstrated that the Beacon device measured VO_2, and VCO_2 (and calculated REE) at 21%–85% FiO_2 reliably, but with increasing bias at FiO_2 levels of ≥85% [25]. We could extend this to the population of critically ill mechanically ventilated patients.

Furthermore, this is the first study comparing predictive equations with the Beacon indirect calorimeter. Predictive equations perform poorly, mainly because they contain static estimations of REE and do not reflect the (dynamic) energy demands of ICU patients.

It was observed that confidence intervals were wide, indicating that – although the mean difference between the two devices may be only 96.2 kcal/day – the Beacon can make a large measurement error. The large standard deviations (and wide 95% CI's) in our study are either due to the sensitivity of measurements in ICU patients, the relatively small and heterogeneous study sample, or a combination of both. Even minor disturbances resulted in patients' unrest or anxiety, ultimately increasing his/her energy expenditure. The standard errors were the largest for the Beacon device measurements over the separate days when in the closest position to the patient (configuration PBQ). This result might be due to different reliability or more variable/fewer stable measurements. A follow-up study will allow us to (re)evaluate measurement reliability, and the effect of the configuration and REE formula use.

4.1. Strengths

The main strength of the current study includes that it was performed in ICU patients, directly reflecting the (dynamic) metabolic needs of a patient group, which is insufficiently considered when using (static) predictive equations. Although the study population was relatively small, we could include repeated measurements for most study participants. Several aspects of the Beacons performance were highlighted, including bias, precision, accuracy, and reliability.

4.2. Limitations

The most important limitation of this study is the lack of validation with the absolute gold standard at the time of the study: the Deltatrac. However, the Quark has been validated against this device and was considered the gold standard in this study. The second limitation was measurements on three separate days, resulting in changes of the (clinical) condition leading to statistical bias. A final limitation of this study is its generalizability, as the two indirect calorimeters were compared in ICU subjects.

Repeating this study in healthy persons will allow evaluating accuracy, bias, and reliability without measuring confounders by disease and sedation. Moreover, as already suggested by Poulsen et al., further studies need to evaluate accuracy, bias and precision at high levels of FiO_2 ($\geq$85%) [25]. Finally, validation against next generation indirect calorimeters (Q-NRG) which are currently considered gold standard, is necessary [34].

5. Conclusion

Beacon indirect calorimetry is accurate compared to the current gold standard in our ICU (Quark indirect calorimeter), with a mean underestimation in calculated REE of only −96.2 kcal/day (4.5%). However, confidence intervals were wide, indicating the risk of large measurement errors. Moreover, there was bias towards higher VCO_2 and lower VO_2 values with Beacon compared with Quark, although not statistically significant. Reliability was good, with an absolute intraclass correlation coefficient of 0.897. In contrast, there was a poor correlation (<0.40) between the separate indirect calorimetry devices and most predictive equations. Therefore, predictive equations should not be used to estimate metabolic needs of mechanically ventilated ICU patients.

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Author contributions

HSB contributed to study design, measurements, data collection, data analysis, writing and revision of the manuscript. SA contributed in measurements and data collection and revision of the manuscript. MM contributed to data analysis and revision of the manuscript. AvZ contributed to the study design and revision of the manuscript.

Declaration of competing interest

Prof. Dr A.R.H. van Zanten reported receiving honoraria for advisory board meetings, lectures, research, and travel expenses from AOP pharma, Braun, Cardinal Health, Danone-Nutricia, Dim-3, Fresenius Kabi, Mermaid, Lyric, and Nestle-Novartis. The other authors have nothing to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2022.01.015.

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