

RESEARCH

Open Access



Continuous and repeat metabolic measurements compared between post-cardiothoracic surgery and critical care patients

Koichiro Shinozaki^{1,2,3,4*}, Pey-Jen Yu⁵, Qiuping Zhou⁶, Hugh A. Cassiere⁷, Stanley John⁷, Daniel M. Rolston^{2,3}, Nidhi Garg^{2,8}, Timmy Li², Jennifer Johnson³, Kota Saeki^{1,9}, Taiki Goto¹⁰, Yu Okuma¹, Santiago J. Miyara¹, Kei Hayashida¹, Tomoaki Aoki¹, Vanessa K. Wong¹, Ernesto P. Molmenti^{1,11}, Joshua W. Lampe^{1,12} and Lance B. Becker^{1,2,3}

Abstract

Objective Using a system, which accuracy is equivalent to the gold standard Douglas Bag (DB) technique for measuring oxygen consumption (VO_2), carbon dioxide generation (VCO_2), and respiratory quotient (RQ), we aimed to continuously measure these metabolic indicators and compare the values between post-cardiothoracic surgery and critical care patients.

Methods This was a prospective, observational study conducted at a suburban, quaternary care teaching hospital. Age 18 years or older patients who underwent mechanical ventilation were enrolled.

Results We included 4 post-surgery and 6 critical care patients. Of those, 3 critical care patients died. The longest measurement reached to 12 h and 15 min and 50 cycles of repeat measurements were performed. VO_2 of the post-surgery patients were 234 ± 14 , 262 ± 27 , 212 ± 16 , and 192 ± 20 mL/min, and those of critical care patients were 122 ± 20 , 189 ± 9 , 191 ± 7 , 191 ± 24 , 212 ± 12 , and 135 ± 21 mL/min, respectively. The value of VO_2 was more variable in the post-surgery patients and the range of each patient was 44, 126, 71, and 67, respectively. SOFA scores were higher in non-survivors and there were negative correlations of RQ with SOFA.

Conclusions We developed an accurate system that enables continuous and repeat measurements of VO_2 , VCO_2 , and RQ. Critical care patients may have less activity in metabolism represented by less variable values of VO_2 and VCO_2 over time as compared to those of post-cardiothoracic surgery patients. Additionally, an alteration of these values may mean a systemic distinction of the metabolism of critically ill patients.

Keywords Indirect calorimetry, Oxygen consumption, Carbon dioxide generation, Respiratory quotient, Douglas bag

*Correspondence:
Koichiro Shinozaki
shino@gk9.so-net.ne.jp
Full list of author information is available at the end of the article



Introduction

Oxygen consumption (VO_2), carbon dioxide generation (VCO_2), and respiratory quotient (RQ), which is the ratio of VCO_2 to VO_2 , are important measures of the metabolism in humans [1–3]. These measurements are widely used for patients with a variety of conditions, including post-surgery [1], shock [4], pulmonary and cardiac diseases [5], and critical illness requiring mechanical ventilation [2, 6, 7]. Indirect calorimetry is a non-invasive method, in which VO_2 and VCO_2 are measured from concentrations of oxygen and carbon dioxide of inhalation and exhalation [8–10]. Since it is non-invasive, indirect calorimetry has been widely used by clinicians [11, 12] as well as animal studies [13–16]. However, due to the lack of a gold standard, the accuracy has been questioned for nearly 100 years [6, 7, 17, 18].

One of the traditional but standard methods is the Douglas Bag (DB) collection technique, which was first introduced by a physiologist, Claude Gordon Douglas, in 1911 [19]. This technique is still the most reliable gold standard these days [18]. Central focus of the DB method is the accuracy of gas concentrations of inhalation and exhalation. Errors are propagated particularly when a high oxygen concentration gas is used [10]. The DB technique is a method using collection bags that equilibrate concentrations of gases inside a bag. The DB technique exerts higher accuracy if a gas concentration dynamically changes. The concentrations of oxygen and carbon dioxide in exhalation change dynamically during each breath. Therefore, the DB method enables reliable measurements when the accuracy of VO_2 , VCO_2 , and RQ is in need [18]. However, a complexity of the method and lengthy processing time limit the number of measurements that can be performed at bedside.

We developed an automation device that enables continuous and repeat measurements of VO_2 , VCO_2 , and RQ in patients undergoing mechanical ventilation [20]. The accuracy was validated, and it was equivalent to that of the DB technique. To the best of our knowledge, this is the first study that applied repeat measurements of VO_2 , VCO_2 , RQ by using a method equivalent to the DB technique and we will demonstrate the results of continuous metabolic measurements in post-cardiothoracic surgery and critical care patients.

Materials and methods

Study design

This was a prospective, observational study conducted at a suburban, quaternary care teaching hospital. Age 18 years or older patients who underwent mechanical ventilation were enrolled. The study protocol was approved by the Institutional Review Board

(16–615-North Shore University Hospital). Written informed consent for participation was obtained from patients or next of kin prior to the procedures. If a patient did not hold a capacity for consent or did not have a legally authorized representative or next of kin, the patient was enrolled with waived consent. We excluded patients whose positive end-expiratory pressure (PEEP) setting was higher than 10 cm H_2O due to an expected gas leak from the mechanical ventilation circuit. Our method and calculation algorithm enabled measurements of VO_2 , VCO_2 , and RQ at a variety range of fraction of inspired oxygen (F_iO_2) [21] and therefore, no upper limit was made on an F_iO_2 setting of mechanical ventilation.

Automation system

We previously reported the detail of our methods [20]. This is a unique technique, for which we have devoted most of our time to validate its accuracy and the results can be found in the other report [20]. In brief, ten minutes were given to all patients for acclimating to the apparatus before starting a measurement. For the measurements of VO_2 , VCO_2 , and RQ, inhalation and exhalation were independently analyzed. A commercially available gas analyzer (GF-210R Multi-Gas Module, Nihon Kohden Corporation, Irvine, CA, USA) was used. The gases were sampled from a mechanical ventilator (AVEA[®] ventilator, CareFusion, San Diego, CA, USA) and the gas concentrations of oxygen and carbon dioxide were measured by the gas analyzer. By using these values, we calculated fraction of expired oxygen (F_EO_2) and fraction of expired carbon dioxide (F_ECO_2) from the concentrations measured at the exhaust port (F_{exh}O_2 and $\text{F}_{exh}\text{CO}_2$, respectively). The measurement was performed at bedside, which enabled a real-time and continuous collection of data. A dehumidification device (DHU-1000 Dehumidification Unit, Nihon Kohden Corporation, Tokyo, Japan) was set in conjunction with the gas analyzer: the dehumidification unit was intended for use in dehumidifying a sample gas. We have validated the accuracy of this automation system [20]. The validation included (i) a system response time; (ii) sensor accuracy of gas concentrations; (iii) the performance of mixing chamber; (iv) the calculation algorithm of our automation system; (v) and VO_2 , VCO_2 , and RQ in healthy volunteers compared between the device and the DB methods.

The gas concentrations of inhalation and exhalation were measured alternately, and the duty cycle was 15 min. The gas concentration in inhalation was measured at the first 6 min of the duty cycle. A valve switched the sampling port from inhalation to exhalation and 9 min were given for F_EO_2 and F_ECO_2 measurements.

Calculations and analysis

$F_I O_2$, $F_E O_2$, $F_I CO_2$ (fraction of inspired carbon dioxide), $F_E CO_2$, in-circuit humidity and temperature in the dehumidification device, and ambient pressure and temperature around the mechanical ventilator circuit were measured. A minute ventilation volume of exhalation (V_E), inhalation to exhalation (I:E) ratio, and bias flow setting were recorded from the mechanical ventilator. For the automation system, $F_E O_2$ and $F_E CO_2$ were calculated from the gas concentrations measured at the ventilator exhaust port. The following equations are used in this study:

$$R = V_I / V_E \quad (1)$$

$$VO_2 = V_I \times F_I O_2 - V_E \times F_E O_2 \quad (2)$$

$$VCO_2 = V_E \times F_E CO_2 - V_I \times F_I CO_2 \quad (3)$$

where V_I is a minute ventilation volume of inhalation and V_E is that of exhalation. $F_I CO_2$ is zero since the inhalation gas does not contain CO_2 . RQ , VO_2 , and VCO_2 are then transformed to equations as follows:

$$VO_2 = (R \times F_I O_2 - F_E O_2) \times V_E \quad (4)$$

$$VCO_2 = F_E CO_2 \times V_E \quad (5)$$

$$RQ = VCO_2 / VO_2 \quad (6)$$

R is generally derived from the Haldane transformation with the assumption that nitrogen is neither produced nor retained by the body, and that no gases are present other than O_2 , CO_2 , and nitrogen [22]. Because the denominator includes $F_I O_2$ and it goes to zero as $F_I O_2$ increases to 1.0, R increases to infinite number when $F_I O_2$ is 1.0. Therefore, the Haldane transformation limits $F_I O_2$ generally up to 0.6. This is a significant limitation in critical care, in which patients normally require a high level $F_I O_2$. Therefore, we developed a method for measuring R and sought the number of R by using our rodent model [21]. Our results suggested that R was not 1.0 and so V_I was not equal to V_E . While our result is in line with the concept of the Haldane transformation that helps us interpret $V_I \neq V_E$, the data from our rodent model also indicates that R may be constant as opposed to dependent on $F_I O_2$ as the calculation from the Haldane transformation outputs. We sought a value of human R calculated from the values obtained from previous human reports [22, 23] and determined it as 1.0097 in this study.

Statistical analysis

We reported data as mean and standard deviation and descriptive statistics were used. The values were reported as standard temperature and pressure and dry (STPD). Spearman's rho and correlation coefficients were calculated, and Mann–Whitney U tests were used for comparison between two groups. Generalized linear mixed model, in which covariates include survival outcomes and number of measurements, was used to estimate the effects on continuous and repeat measurements. Prism for Mac version 9 (GraphPad Software, San Diego, CA) and SPSS version 27 (IBM, Armonk, NY) were used for statistical analysis, and P values less than 0.05 was considered statistically significant.

Results

Data from 10 patients were analyzed in this study. Table 1 shows baseline characteristics of the study subjects. Out of 10 subjects, 4 were patients post cardiothoracic surgery, 5 were patients in the intensive care units (ICU), and 1 was in the emergency room (ER). Sequential organ failure assessment (SOFA) score, blood lactate level (mmol/L), and P/F ratio (arterial partial oxygen pressure to $F_I O_2$) were obtained at ICU admission. Female patients had significantly lower weights and heights than male ($p < 0.05$ and $p < 0.05$, respectively). None of the post-cardiothoracic surgery patients had major adverse events nor died. This study included 6 critical care patients, whose metabolic measurements were performed in the ER or ICU, and 3 were died.

Initial metabolic values

Table 2 demonstrates values of initial metabolic measurements. SOFA score negatively correlated with RQ (-0.657 , $p < 0.05$). Initial blood lactate levels negatively correlated with VCO_2 (-0.671 , $p < 0.05$) but adjusting it by body weight rejected the significance. $F_I O_2$ negatively correlated with RQ (-0.696 , $p < 0.05$) (Supplement).

Continuous and repeat metabolic measurements

We performed continuous and repeat metabolic measurements by the automation device and Fig. 1 and Table 2 show the results. The minimum number of measurements were 5 cycles for 75 min occurred in ER and the longest measurement lasted for 12 h and 15 min and 50 cycles of repeat measurements were performed. Figure 1 A shows the trend of $F_I O_2$ over time. There was a downward trend of $F_I O_2$ in the post-surgery patients because all patients were weaned off from mechanical ventilation during the post-day 1 of surgery. In contrast, there was no consistent pattern of $F_I O_2$ in the critical care patients.

Table 1 Characteristics of study subjects and fraction of inspired oxygen when starting the measurements

Subject	Site	Age	Gender	Weight (kg)	Height (cm)	BMI (kg/m ²)	Diagnosis	SOFA	Lactate (mmol/L)	F _O ₂	Ve (L/min)	P/F ratio	PEEP (cmH ₂ O)	Discharge Outcome
1	CTICU	52	Male	76	173	25	CAD	3	2	1.00	6.9	233	5	Alive
2	CTICU	63	Male	106	185	31	CAD	3	1.7	1.00	5.1	155	5	Alive
3	CTICU	72	Male	82	167	29	Aortic Aneurysm, Aortic Valve Stenosis	5	1.7	1.00	4.3	207	5	Alive
4	CTICU	62	Male	72	175	24	CAD	7	1.9	1.00	9.0	296	10	Alive
5	ER	85	Female	35	152	15	Aspiration Pneumonia, Respiratory Arrest	6	7.1	1.00	6.4	277	5	Death
6	MICU	76	Male	63	178	20	Multiple Myeloma, Renal Failure	9	1.4	0.60	8.2	392	5	Death
7	MICU	62	Male	84	170	29	Cirrhosis, Pulmonary Fibrosis, Respiratory Failure	12	2.9	1.00	7.7	68	10	Death
8	MICU	92	Male	69	178	22	Pneumonia, Vocal Cord Paralysis, Respiratory Failure	4	1.1	1.00	7.6	260	5	Alive
9	MICU	70	Female	55	165	20	Airway Compromise, Aspiration Pneumonia	0	1	0.30	7.1	403	5	Alive
10	MICU	71	Female	62	152	27	COPD exacerbation, Hypercapnia	0	5.7	0.25	4.1	633	5	Alive

Sequential Organ Failure Assessment (SOFA) score, blood lactate level, and arterial partial oxygen pressure / F_O₂ (P/F) ratio were calculated from the values at ICU admission. Ve is a minute ventilation volume measured at the exhaust port and the values are expressed as BTPS (body temperature, pressure, water vapor saturated)

CTICU stands for cardiothoracic intensive care unit, ER emergency room, MICU medical intensive care unit, CAD coronary artery disease, COPD chronic obstructive pulmonary disease

Table 2 Metabolic values

Subject	Initial Values				Repeat Measurements						
	VO2 (ml/min)	VCO2 (ml/min)	VO2/BW (ml/kg/min)	VCO2/BW (ml/kg/min)	RQ	# of samples	Length (min)	VO2 (ml/min)	VCO2 (ml/min)	VO2/BW (ml/kg/min)	VCO2/BW (ml/kg/min)
1	249	144	3.28	1.89	.58	17	270	234±14	160±9	3.08±0.18	2.11±0.12
2	202	133	1.91	1.25	.66	33	540	262±27	184±20	2.47±0.25	1.74±0.19
3	158	106	1.93	1.29	.67	24	390	212±16	149±14	2.58±0.20	1.82±0.17
4	238	139	3.31	1.93	.58	26	435	192±20	131±6	2.67±0.28	1.82±0.08
5	132	63	3.77	1.80	.48	5	75	122±20	58±9	3.49±0.57	1.65±0.26
6	210	133	3.33	2.11	.63	48	735	189±9	133±5	3.00±0.14	2.11±0.08
7	181	96	2.15	1.14	.53	14	300	191±7	107±5	2.27±0.08	1.27±0.06
8	236	133	3.42	1.93	.56	10	210	191±24	129±3	2.77±0.35	1.87±0.04
9	213	149	3.87	2.71	.70	18	330	212±12	155±7	3.85±0.22	2.82±0.13
10	117	92	1.89	1.48	.78	17	300	135±21	103±16	2.18±0.34	1.66±0.26

The values of repeat measurements are expressed as means and standard deviations
 BW stands for body weight, RQ respiratory quotient

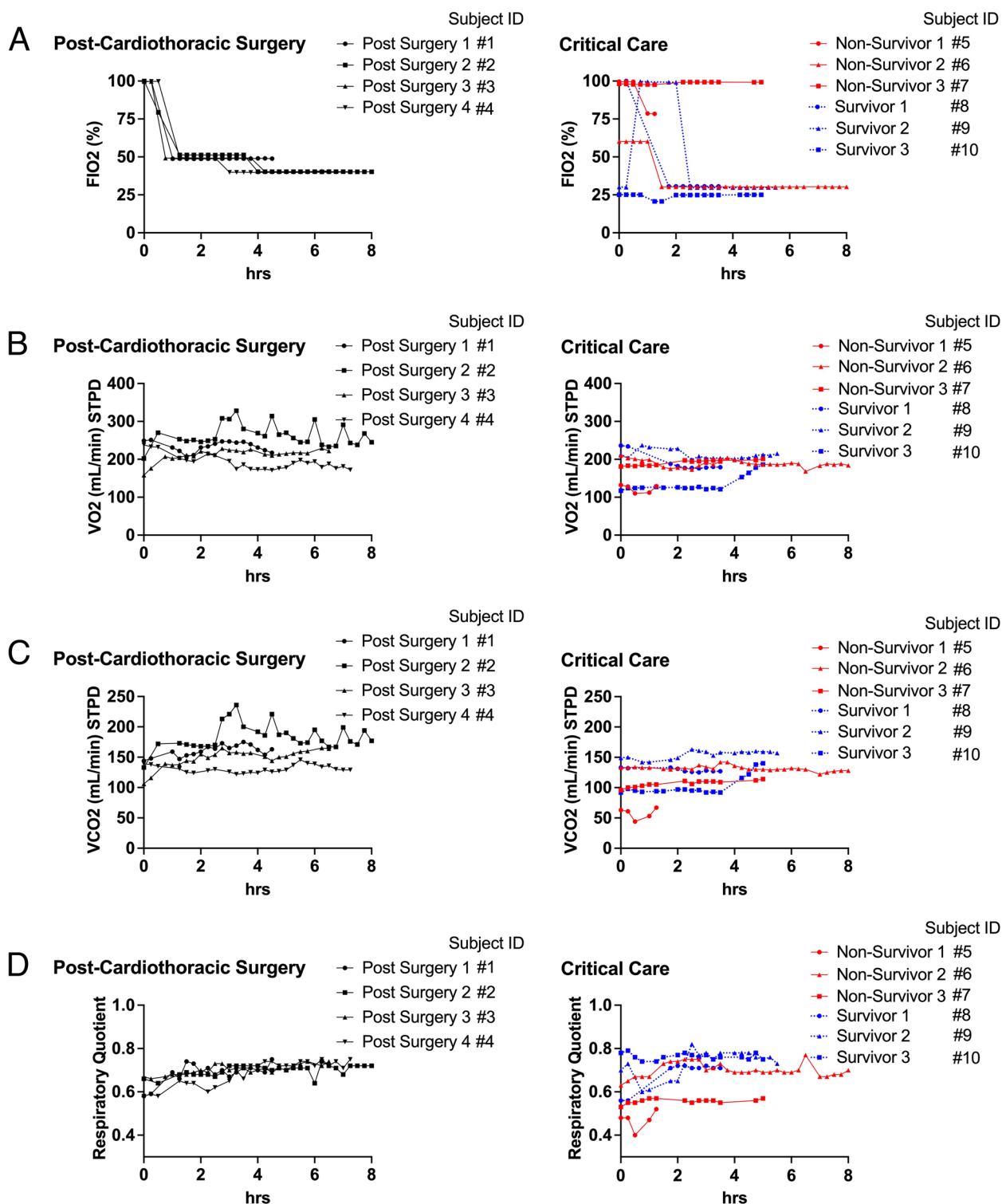


Fig. 1 Continuous and Repeat Metabolic Measurements. The measurements were started from the admission to the cardiothoracic intensive care unit for post-surgical patients. For critical care patients, the measurements were started from the earliest possible timing after enrollment. **A** Fraction of inspired oxygen (FIO₂). **B** VO₂ at standard temperature and pressure and dry (STPD). **C** VCO₂ at STPD. **D** RQ. *n* = 4 for post-surgery, *n* = 6 for critical care patients. Subjects IDs are corresponding to those in Table 1

The mean VO_2 in the 4 post-surgery patients were 234 ± 14 , 262 ± 27 , 212 ± 16 , and 192 ± 20 mL/min, respectively. Those in the critical care patients were 122 ± 20 , 189 ± 9 , 191 ± 7 , 191 ± 24 , 212 ± 12 , and 135 ± 21 mL/min, respectively. The value of VO_2 was variable in the post-surgery patients and the range was 44, 126, 71, and 67, respectively. These values seemed more variable than those (22, 42, 20, 60, 38, 69) of critical care patients. The range of non-survivors (22, 42, 20) appeared to be less than those (60, 38, 69) of survivors.

The mean VCO_2 in the 4 post-surgery patients were 160 ± 9 , 184 ± 20 , 149 ± 14 , and 131 ± 6 mL/min, respectively. Those in critical care patients were 58 ± 9 , 133 ± 5 , 107 ± 5 , 129 ± 3 , 155 ± 7 , and 103 ± 16 mL/min, respectively. The value of VCO_2 was variable in 4 post-surgery patients and the range was 31, 103, 59, and 24, respectively. These values seemed more variable than those (23, 21, 18, 8, 21, 48) of critical care patients. Figure 2 shows the result of detailed analysis on VCO_2 . According to Eq. (5), VCO_2 is derived from V_E and $F_E CO_2$. The higher VO_2 found in post-surgery patients seemed associated with both variables. Non-survivors had lower $F_E CO_2$

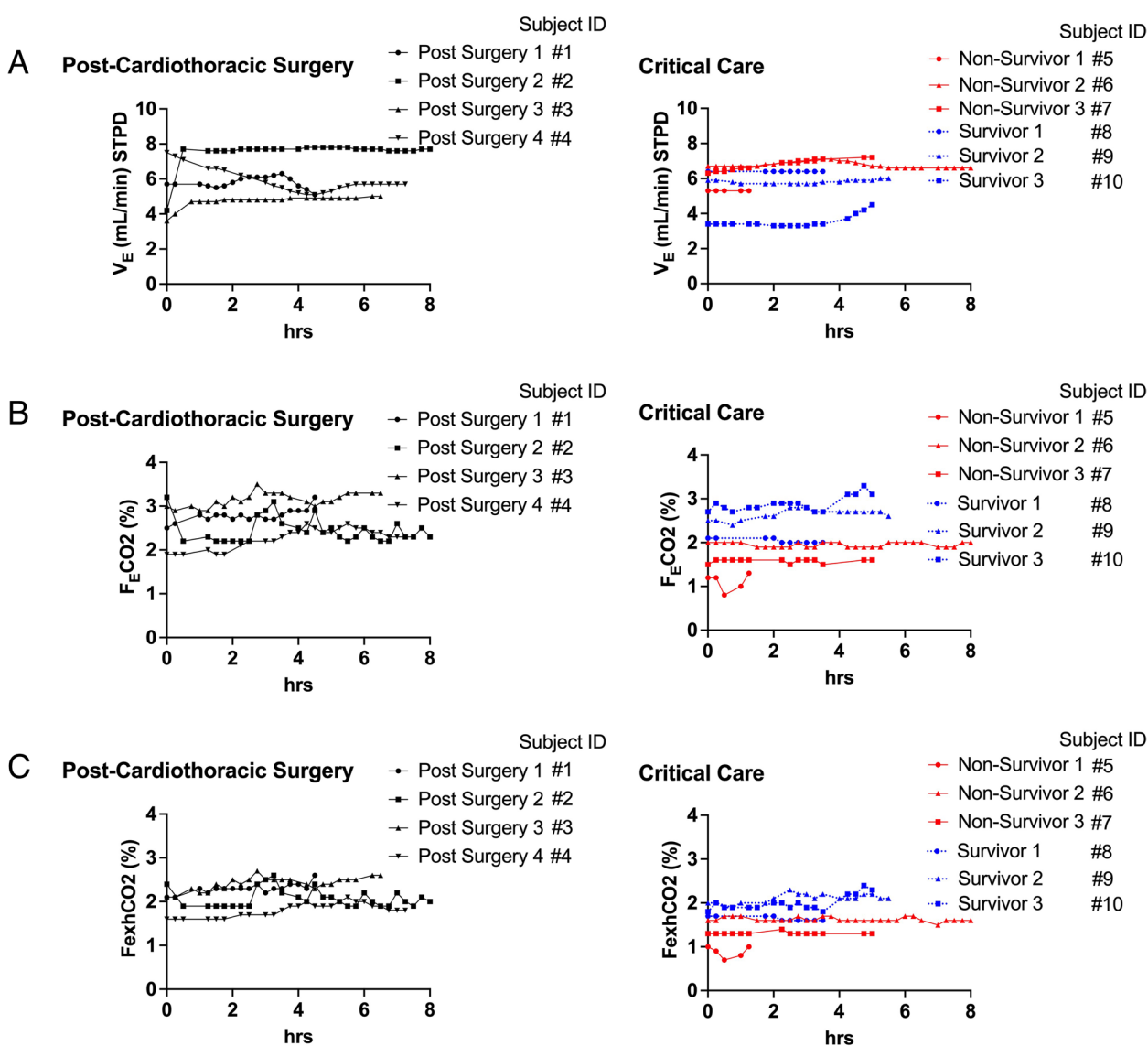


Fig. 2 Ventilation and Carbon Dioxide Levels. **A** Minute ventilation volume (SPTD) measured at the exhaust port. **B** Fraction of expired carbon dioxide ($F_{E}CO_2$). **C** Fraction of expired carbon dioxide measured at the exhaust port. $n=4$ for post-surgery, $n=6$ for critical care patients. Subjects IDs are corresponding to those in Table 1

than survivors and the same trend was found by the plots in fraction of CO₂ at exhaust port of the mechanical ventilator (F_{exh}CO₂). Generalized linear mixed model identified the effects of outcome on VO₂ ($p < 0.05$), VCO₂ ($p < 0.01$), and VCO₂ per weight ($p < 0.01$), but not on VO₂ per weight.

The mean RQ in the 4 post-surgery patients were 0.69 ± 0.05 , 0.70 ± 0.02 , 0.70 ± 0.02 , 0.69 ± 0.06 respectively. Those in critical care patients were 0.47 ± 0.04 , 0.71 ± 0.03 , 0.56 ± 0.01 , 0.68 ± 0.06 , 0.73 ± 0.06 , 0.76 ± 0.01 , respectively. The range of RQ of the post-surgery patients were 0.17, 0.10, 0.08, 0.17 and those of the critical care patients were 0.12, 0.14, 0.04, 0.16, 0.22, and 0.05, respectively.

Discussion

We developed a system for measuring F_IO₂, F_EO₂, and F_ECO₂ in humans undergoing mechanical ventilation. These gas concentrations are critical components when seeking accurate VO₂, VCO₂, and RQ. The accuracy of our system was equivalent to the gold standard DB collection technique [20]. Our automation system allows for continuous and repeat measurements, to which the DB technique has a significant limitation due to the complexity of its procedure. By using our automation system, we successfully collected continuous values of VO₂, VCO₂, and RQ in post-surgical and critical care patients.

The volume ratio of inhalation to exhalation defined as R in this study is an essential component of calculating VO₂. However, there is a significant technical difficulty of measuring the small differences between V_I and V_E. Therefore, V_I is commonly calculated by using the Haldane transformation, which limits the use of F_IO₂ up to 0.6. Assuming V_I equals V_E and ignoring this small difference eliminate the concern. However, failure to account for this small difference can erroneously decrease VO₂ by 17% [10], if V_I is actually not equal to V_E, and the error propagates at higher F_IO₂ levels. The adequacy of the Haldane transformation [22] supports that V_I is not equal to V_E.

We have developed a method for measuring the small differences between V_I and V_E [21]. Our results from the rodent model showed that R ranged from 1.0081 ± 0.0017 to 1.0092 ± 0.0029 at F_IO₂ 0.3 and 1.0, respectively, indicating that V_I is not equal to V_E ($R \neq 1.0000$). While our results were in line with the concept of the Haldane transformation supporting the idea of V_I \neq V_E, our data revealed that R is an independent value from F_IO₂ as opposed to that calculated by the Haldane transformation, which includes F_IO₂ in its equation. We sought a value of human R calculated from the values obtained from previous human reports [22, 23] and determined it as 1.0097 in this study. These data justify the use of

$R = 1.0097$ to all calculations that include various F_IO₂ levels that depend on patient's condition.

Our automation system allows for continuous and repeat measurements of VO₂, VCO₂, and RQ. The data of 10 patients were evaluated in this study. Post-surgical patients had higher VO₂ and VCO₂ and appeared to have more variable numbers as compared to those of critical care patients. It is inferred that the post-surgical patients had more active metabolism than critical care patients, which might be attributed to purposefully minimized sedatives to wean off the patients from mechanical ventilation. The greater variability of metabolic values argues the unmet need of continuous measurements. In other words, one point measurement such as the traditional DB technique, even though it is accurate and reliable, may not be sufficient to identify an important signal that varies over time. We also found that non-survivors appeared to have low F_ECO₂. This is inferred that patients who are critically ill may have less activity in metabolism.

Differences in study values were observed between survivors and non-survivors at the beginning of the measurements. This suggests that significant systemic distinctions occurred at the starting period of our measurements and those could induce changes in the values. Indeed, SOFA scores were higher in non-survivors and there was a negative correlation of VCO₂ with the initial value of blood lactate, while there was no statistically significant correlation between SOFA and VCO₂. Both SOFA scores and blood lactate are known to indicate the severity of diseases but the difference of the correlation patterns of VCO₂ with these values may be led by a mechanistic response. Moreover, our study subjects include female patients, whose weights and heights were significantly lower than male. Adjusting VCO₂ by weight rejected the correlation of VCO₂ with blood lactate, meaning it might be confounded by the body size. On the other hand, RQ is not affected by the body size as its calculation cancels the effect of body weight. Indeed, there were negative correlations of RQ with SOFA and F_IO₂. We found that high F_IO₂ leads to lower RQ due to the increase in VO₂ [20]. Therefore, this finding might mean that the lowered RQ could be led by the distinctions of the patients or high F_IO₂ or both. However, due to the small number of our study population, we could not draw a conclusion. Further studies may warrant the investigation of these mechanisms.

This study is subject to several limitations. The number of samples, first and foremost, is limited in this study owing to the nature of explanatory design of our current work. Second, the study lacks a mechanistic information. More detailed information such as the dose of inotropes, vasoactive inotropic score, and nutrition would help with identifying specific characteristics or reasons that

alter VO_2 , VCO_2 , or RQ in the ICU settings. Particularly because nutrition [3] and/or disease conditions [24, 25] may alter RQ, more focused information on these variables needs to be investigated. The automation system aids clinicians to collect more information on metabolism of patients. Moreover, our method enables the gas concentration measurements that are equivalent to the gold standard DB method. Therefore, we expect to see more metabolic data from patients in the future.

Conclusions

We developed an automation system that enables repeat measurements of VO_2 , VCO_2 , and RQ. Critical care patients may have less variability of VO_2 and VCO_2 as compared to the post-cardiothoracic surgery patients.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12890-023-02657-4>.

Additional file 1: Table S1. Differences of values between post-surgery and critical care patients. **Table S2.** Differences of values between survivors and non-survivors. **Table S3.** Differences of values between male and female patients. **Table S4.** Correlation between study values. **Table S5.** Mechanical ventilator settings.

Acknowledgements

None.

Authors' contributions

K. Shinozaki has full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis; K. Shinozaki, K. Saeki, J. W. Lampe, L. B. Becker designed the conception of the study; K. Shinozaki, P. J. Yu, Q. Zhou, D. M. Rolston, J. Johnson, and Y. Okuma performed acquisition of data and K. Shinozaki analyzed data; all authors made interpretations of data; all authors added intellectual content of revisions to the paper and gave full approval of the version to be published.

Funding

This research was supported by the research grant of Nihon Kohden Corporation.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due the current sponsorship made with Nihon Kohden Corporation but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The Northwell Health Human Research Protection Program is guided by the ethical principles as set forth in the 1979 report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (entitled: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, the "Belmont Report"), following the Declaration of Helsinki, which has been revised several times since 1964.

The study protocol was approved by the Institutional Review Board (16–615-North Shore University Hospital). Written informed consent for participation was obtained from patients or next of kin prior to the procedures.

Consent for publication

Not applicable.

Competing interests

Saeki belongs to Nihon Kohden Innovation Center, INC and Goto to Nihon Kohden Corporation as employee. This does not invade the authors' adherence to all the Journal's policies. Shinozaki and Becker own intellectual property of metabolic measurement in critically ill patients. Shinozaki has grant/research supported by Grants-in-Aid for Scientific Research (KAKEN, 23K19643) and Nihon Kohden Corp. Becker has grant/research supported by Philips Healthcare, the National Institutes of Health, Nihon Kohden Corp., BeneChill Inc., Zoll Medical Corp, Medtronic Foundation, and patents in the areas of hypothermia induction and perfusion therapies. All the other authors have no disclosures.

Author details

¹The Feinstein Institutes for Medical Research, Northwell Health, Manhasset, NY, USA. ²Department of Emergency Medicine, Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY, USA. ³Department of Emergency Medicine, North Shore University Hospital, Manhasset, NY, USA. ⁴Department of Emergency Medicine, Kindai University Faculty of Medicine, Osaka-Sayama, Osaka, Japan. ⁵Department of Cardiothoracic Surgery, North Shore University Hospital, Manhasset, NY, USA. ⁶Division of Critical Care Medicine of Emergency Medicine, Long Island Jewish Medical Center, New Hyde Park, NY, USA. ⁷Division of Critical Care Medicine, Department of Medicine, North Shore University Hospital, Manhasset, NY, USA. ⁸Department of Emergency Medicine, South Shore University Hospital, Bay Shore, NY, USA. ⁹Nihon Kohden Innovation Center, Cambridge, MA, USA. ¹⁰Nihon Kohden Corporation, Tokyo, Japan. ¹¹Department of Surgery, Medicine, and Pediatrics, Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY, USA. ¹²ZOLL Medical, Chelmsford, MA, USA.

Received: 12 November 2022 Accepted: 13 September 2023

Published online: 16 October 2023

References

- Gump FE, Kinney JM, Price JB Jr. Energy metabolism in surgical patients: oxygen consumption and blood flow. *J Surg Res.* 1970;10:613–27.
- Manthous CA, Hall JB, Olson D, Singh M, Chatila W, Pohlman A, Kushner R, Schmidt GA, Wood LD. Effect of cooling on oxygen consumption in febrile critically ill patients. *Am J Respir Crit Care Med.* 1995;151:10–4.
- 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 Enteral Nutr.* 2003;27:21–6.
- Siegel JH, Fabian M, Smith JA, Kingston EP, Steele KA, Wells MR, Kaplan LJ. Oxygen debt criteria quantify the effectiveness of early partial resuscitation after hypovolemic hemorrhagic shock. *J Trauma.* 2003;54:862–80 (discussion 880).
- Guazzi M, Adams V, Conraads V, Halle M, Mezzani A, Vanhees L, Arena R, Fletcher GF, Forman DE, Kitzman DW, Lavie CJ, Myers J. EACPR/AHA scientific statement. clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations. *Circulation.* 2012;126:2261–74.
- Sundstrom 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.
- Graf S, Karsegard VL, Viatte V, Heidegger CP, Fleury Y, Pichard C, Genton L. Evaluation of three indirect calorimetry devices in mechanically ventilated patients: which device compares best with the Deltatrac II((R))? A prospective observational study. *Clin Nutr.* 2015;34:60–5.
- Matarese LE. Indirect calorimetry: technical aspects. *J Am Diet Assoc.* 1997;97:5154–160.
- da Rocha EE, Alves VG, da Fonseca RB. Indirect calorimetry: methodology, instruments and clinical application. *Curr Opin Clin Nutr Metab Care.* 2006;9:247–56.
- Branson RD, Johannigman JA. The measurement of energy expenditure. *Nutr Clin Pract.* 2004;19:622–36.
- Soussi S, Vallee F, Roquet F, Bevilacqua V, Benyamina M, Ferry A, Cupaciu A, Chaussard M, De Tymowski C, Boccarda D, Mimoun M, Chaouat M, Anstey J, Mebazaa A, Legrand M. Measurement of oxygen consumption

- variations in critically ill burns patients: are the fick method and indirect calorimetry interchangeable? *Shock*. 2017;48:532–8.
12. Hensel M, Kox WJ. Increased intrapulmonary oxygen consumption in mechanically ventilated patients with pneumonia. *Am J Respir Crit Care Med*. 1999;160:137–43.
 13. Musch TI, Bruno A, Bradford GE, Vayonis A, Moore RL. Measurements of metabolic rate in rats: a comparison of techniques. *J Appl Physiol*. 1985;1988(65):964–70.
 14. van Klinken JB, van den Berg SA, van Dijk KW. Practical aspects of estimating energy components in rodents. *Front Physiol*. 2013;4:94.
 15. Yo K, Yu YM, Zhao G, Bonab AA, Aikawa N, Tompkins RG, Fischman AJ. Brown adipose tissue and its modulation by a mitochondria-targeted peptide in rat burn injury-induced hypermetabolism. *Am J Physiol Endocrinol Metab*. 2013;304:E331–341.
 16. Even PC, Nadkarni NA. Indirect calorimetry in laboratory mice and rats: principles, practical considerations, interpretation and perspectives. *Am J Physiol Regul Integr Comp Physiol*. 2012;303:R459–476.
 17. Hagedorn HC. An apparatus for the graphic recording of oxygen consumption and carbon dioxide output, especially adapted for clinical work. *Biochem J*. 1924;18:1301–7.
 18. Black C, Grocott MP, Singer M. Metabolic monitoring in the intensive care unit: a comparison of the Medgraphics Ultima, Deltatrac II, and Douglas bag collection methods. *Br J Anaesth*. 2015;114:261–8.
 19. Shephard RJ. A critical examination of the Douglas bag technique. *J Physiol*. 1955;127:515–24.
 20. Shinozaki K, Yu PJ, Zhou Q, Cassiere HA, Stanley J, Rolston DM, Garg N, Li T, Johnson J, Saeki K, Goto T, Okuma Y, Miyara SJ, Hayashida K, Aoki T, Wong V, Molmenti EP, Lampe JW, Becker LB. An automation system equivalent to the Douglas bag technique enables continuous and repeat metabolic measurements in patients undergoing mechanical ventilation. *Clin Ther*. 2022;44:1471–9.
 21. Shinozaki K, Okuma Y, Saeki K, Miyara SJ, Aoki T, Molmenti EP, Yin T, Kim J, Lampe JW, Becker LB. A method for measuring the molecular ratio of inhalation to exhalation and effect of inspired oxygen levels on oxygen consumption. *Sci Rep*. 2021;11:12815.
 22. Wilmore JH, Costill DL. Adequacy of the Haldane transformation in the computation of exercise VO₂ in man. *J Appl Physiol*. 1973;35:85–9.
 23. Herron JM, Saltzman HA, Hills BA, Kylstra JA. Differences between inspired and expired minute volumes of nitrogen in man. *J Appl Physiol*. 1973;35:546–51.
 24. Shinozaki K, Becker LB, Saeki K, Kim J, Yin T, Da T, Lampe JW. Dissociated oxygen consumption and carbon dioxide production in the post-cardiac arrest rat: a novel metabolic phenotype. *J Am Heart Assoc*. 2018;7:e007721.
 25. Uber A, Grossestreuer AV, Ross CE, Patel PV, Trehan A, Donnino MW, Berg KM. Preliminary observations in systemic oxygen consumption during targeted temperature management after cardiac arrest. *Resuscitation*. 2018;127:89–94.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

