Intensive Care Med (1989) 15:274–278

Intensive Care Medicine

Techniques

Validation of a new closed circuit indirect calorimetry method compared with the open Douglas bag method

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Received: 20 May 1988; accepted: 16 December 1988

Abstract. New equipment designed for the routine measurement of oxygen uptake ($\dot{V}O_2$) using a closed circuit method has been validated by comparing it with a standard Douglas bag method. The equipment (The Caloric Measurement Unit, CMU) has been tested in 10 critically ill patients during mechanical ventilation (MV) and in 10 spontaneously breathing healthy subjects. Determinations of $\dot{V}O_2$ and of the resting energy expenditure (REE) were measured in duplicate with the standard method and once with the CMU. Six additional patients receiving MV were studied with the CMU to evaluate the reproducibility and the effect of $FIO_2 = 1$ vs $FIO_2 = 0.43$ on $\dot{V}O_2$ measurements. Considering the whole group of 10 patients and 10 subjects, the mean difference of $\dot{V}O_2$ between both methods was -2 ± 21 ml/min (95% confidence interval, -11.8 to 7.8 ml/min, $p = 0.6$) standard deviation. Both methods had a similar reproducibility and the mean difference of $\dot{V}O_2$ measured at the two different FIO_2 with the CMU was -3.2 ± 11 ml/min (95% confidence interval, -14.7 to 8.4 ml/min, $p = 0.5$). No statistically significant difference was found between derived REE values obtained from either method. These data show a good correlation between the two methods suggesting that CMU may be used in place of the standard method with the same accuracy in measurement of $\dot{V}O_2$ even at $FIO_2 = 1$.

Key words: Oxygen uptake – Resting energy expenditure – Closed circuit method – Mechanical ventilation – FIO_2

Several studies have shown that optimum nutritional support plays an important role in decreasing morbidity and mortality of hospitalized patients and in reducing the time spent in hospital [2, 18]. On the other hand, since there are no simple ways of measuring it, considerable controversy exists concerning the best methods of assessing nutritional status. A recent study has shown that judgements based on clinical history and physical examination are as effective in assessing the nutritional status as using the different objective tests [3].

Instead of using equations such as that of Harris-Benedict and adding an arbitrary factor for the presumed energy needs of injury and infection [11, 15], investigators with extensive experience have proposed the use of indirect calorimetry to measure the energy expenditure and calculate the caloric nutritional intake. The former practice has resulted, particularly in some critically ill patients, in an excessive caloric input which may lead to undesirable complications [1, 8]. For any individual patient, this method can produce inaccurate results [7, 20]. This is especially true in critically ill patients who show the greatest individual variations in energy expenditure, especially when they are receiving treatment with drugs such as morphine [17], barbiturates [10] or during mechanical ventilation [14].

Recently new equipment (Caloric Measurement Unit, ICOR, Bromma, Sweden) has been especially designed for the routine measurement of oxygen consumption ($\dot{V}O_2$) using a closed circuit method and the calculation of the resting energy expenditure (REE). This equipment is reported to be accurate and easy-to use in clinical practice. Like most of the open circuit systems available [5, 9] this new equipment can be used both in spontaneously breathing patients and in patients on mechanical ventilation, at any FIO_2 and during any ventilatory mode.

The aim of the present study was to validate the $\dot{V}O_2$ values obtained with the CMU, comparing them with those obtaiend with a standard open-circuit method using a Douglas bag in critically ill patients undergoing mechanical ventilation and in spontaneously breathing healthy subjects. The reproducibility and the effect of measuring $\dot{V}O_2$ at two different FIO_2 with the CMU were also examined.

Material and methods

Patients

Ten healthy subjects and 10 patients undergoing treatment with mechanical ventilation were investigated to compare the values measured with both methods. There were 5 females and 5 males in the healthy group, all volunteers from the nursing and medical staff of our ICU, with a mean age of 30 years (range, 26–33 years). There were 9 males and 1 female in the patients' group (Group A) with a mean age of 44 years (range 26–76 years). Their primary diagnoses are listed in Table 1.

Six additional patients (Group B, Table 1) with a mean age of 54 years (range 15–77 years) were studied to assess the repeatibility and the effects of two different FIO_2 values on measurements with the CMU during mechancial ventilation.

All patients receiving mechanical ventilation were studied with a CPU ventilator (Ohmeda), adapting an external air/oxygen (O_2) mixer (Bennett-AO mixer) to provide a stable FIO_2 [6]. The mixed gas was directed to both the O_2 and air ports of the ventilator and the ventilator FIO_2 dial set to 1. These patients were sedated with diazepam or morphine. They were on a high IMV rate (mean = 15 breath/min range 13 to 20 breath/min). Enteral or parenteral nutrition were continued during the measurements.

Protocol

Healthy subjects were studied after resting for 30 min in a supine position and in a quiet environment. They were breathing room air through a mouth piece connected to a Rudolph value of low resistance. A noseclip was fitted during the period of measurement. Patients had been resting for at least 30 minutes and no voluntary muscle activity or agitation were permitted during the study.

Table 1. Clinical diagnosis and demographic data of patients

No.	Sex	Age	Diagnosis
Group A			
1	M	61	Head trauma
2	M	26	Head trauma
3	M	26	Head trauma
4	M	43	Cerebral haemorrhage
5	M	43	Cerebral thrombosis
6	M	76	Tetanus
7	M	48	Multi-organ failure
8	F	42	Pneumonia
9	M	28	Head trauma
10	M	51	Rhabdomyolysis
Group B			
1	F	40	Cerebral aneurysm
2	M	15	Head trauma
3	M	64	Pneumonia
4	M	64	Cerebral neoplasm
5	M	64	Pneumonia
6	M	77	Pneumonia

To compare both methods we began with selecting the order of each method with a table of randomization for every subject and patient. We did two measurements of $\dot{V}O_2$ with the standard method and one measurement with the CMU.

In group B, we measured $\dot{V}O_2$ with the CMU at different FIO_2 in the following way: $\dot{V}O_2$ was initially measured with FIO_2 of 0.43 (range, 0.3 to 0.5) and the measurement was repeated at the same FIO_2 20 min later. Afterwards, the patient was ventilated with a FIO_2 of 1 and $\dot{V}O_2$ was measured after 20 min.

Description of CMU

The caloric measurement Unit (CMU) is a new device for the routine measurement of a patient's oxygen uptake ($\dot{V}O_2$) and corresponding caloric expenditure. The CMU uses the principle of closed-circuit indirect calorimetry and measures $\dot{V}O_2$ by continuously monitoring the change in the volume of the gas in a closed breathing circuit.

The principal components (Fig. 1) are a bellows, mounted inside a sealed pressure chamber, a special carbon dioxide (CO_2) absorber attached to the outside of the CMU and an ultrasonic sensor. The CO_2 produced by the patient is removed by the absorber and as the patient consumes O_2 the volume of gas in the closed circuit decreases. This decrease in volume is detected by the ultrasonic sensor and constant calibrated pulses of O_2 from an external source are fed into the closed circuit until the volume of gas is restored to its original value. The amount of O_2 added to the closed breathing circuit to replenish the oxygen absorbed by the patient is $\dot{V}O_2$. A microprocessor calculates the average oxygen consumed by the patient over a five-breath period and $\dot{V}O_2$ (STPD) may be presented as an average of 50, 100, or 250 breaths.

Calibration of the equipment

There is an external calibration system that determines exactly how much the bellows move for any particular change in the breathing circuit. An internal calibration system determines the actual volume of 20 replenishment pulses of O_2.

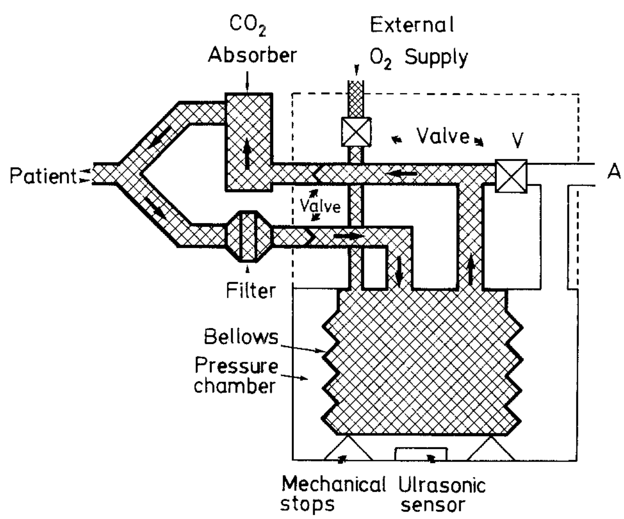

Fig. 1. Description of the CMU. The cross-hatched area represents the part of the circuit connected to the patient during the period of measurement. The mechanical ventilator is adapted to A and during measurement the CMU functions as a bag-in-a-bottle, the bellows being compressed by the ventilator after closing the valve (*V*)

The CMU can be used with spontaneously breathing patients, with or without endotracheal tubes and at any desired FIO_2. When the CMU is used during mechanical ventilation, it is connected between the patient and the ventilator. The system works according to the bag-in-a-bottle principle and can be used equally well with any type of ventilation mode.

The specified accuracy of the CMU in measuring $\dot{V}O_2$ is $\pm 8\%$. Once $\dot{V}O_2$ has been determined, the CMU calculates the energy expenditure using a modification of Weir's formula [19]: REE = 1.44 $(3.941 \times \dot{V}O_2 + 1.106 \times \dot{V}O_2)$.

Since the respiratory quotient, (RQ), is equal to $\dot{V}CO_2/\dot{V}O_2$, the value RQ $\times$ $\dot{V}O_2$ can be substituted for $\dot{V}CO_2$ and the equation becomes: REE $= 1.44 \times \dot{V}O_2\ (3.941 + 1.11 \times RQ)$.

The value for $\dot{V}O_2$ is measured and an estimated value for the RQ between 0.7 and 1 is entered on the keyboard. In practice, the error introduced by substituting an assumed value for RQ is very small, not exceeding 7%, when the RQ is changed from 0.7 to 1. We used an RQ value of 0.85 and the $\dot{V}O_2$ value was an average of 50 breaths (3–5 min of measuring time).

Description of the standard open-circuit method

The FIO_2 of the ventilator is measured by collecting inspired gas in a Douglas bag for 5 min. The Douglas bag is connected to the expiratory port of the ventilator or to the expiratory side of a Rudolph valve in spontaneously breathing subjects, and is washed once with expired gases before each collection. Afterwards, the expired gases are collected for 3–5 min and immediately analysed for volume and gas fractions.

The Douglas bag volume was measured with a Wright spirometer, aspirating the gas with a vacuum pump adjusted to give flow rates through the spirometer of 20 l/min. The volume meter was calibrated with the aid of a 1.5 l syringe. The expected accuracy of such procedure to measure the minute expired volume ($\dot{V}E$) is $\pm 0.5\%$. Volume is corrected to STPD and expressed in ml/min.

The oxygen uptake ($\dot{V}O_2$) is calculated according to the following formula:

$$\dot{V}O_2 = VE \left[\frac{(1 - FEO_2 - FECO_2)}{(1 - FIO_2)} FIO_2 - FEO_2 \right]$$

The analysis of FIO_2 and FEO_2 was done with a polarographic electrode (IL 1312). The linearity of the O_2 electrode was checked by analysis in the 12%–50% range of O_2. The expected accuracy is $\pm 2\%$. For analysis of mean $FECO_2$, an infrared CO_2 analyzer (Engström Eliza) was used which has an expected accuracy of ± 1 mmHg. The linearity of this equipment was checked with gas fractions of CO_2 from 0% to 4.9%. The elimination of carbon dioxide ($\dot{V}CO_2$) is calculated according to the formula ($\dot{V}CO_2 = \dot{V}E \times FECO_2$.

The value of energy expenditure was calculated using the Weir formula [19] described above.

Statistical analysis

The mean and standard deviation are reported. An unpaired t-test was used to detect significant differences between $\dot{V}O_2$ values obtained from healthy subjects and those from patients. A paired *t*-test was used to test the null hypothesis that assumes no difference between the two methods when the first $\dot{V}O_2$ measurement with the standard method was compared with $\dot{V}O_2$ obtained with the CMU. A linear regression analysis was done relating both methods and the regression coefficients and the standard deviation from regression were calculated. The study of the degree of agreement between both methods and the repeatability of each method was done according to the analysis proposed by Bland and Altman [4].

Results

The reproducibility of the PO_2 electrode in terms of the coefficient of variation based on multiple measurements of gases was very small, less than 0.2%. The air-oxygen mixer adapted to the CPU ventilator produced a stable FIO_2, with a coefficient of variation of 0.2% with repeated measurements of $FIO_2 = 0.401$. The reproducibility of the CO_2 analyzer was less than 4%.

Oxygen consumption values

There was no statistically significant difference between $\dot{V}O_2$ values obtained from patients (group A) and those from healthy subjects so we pooled all these data together to compare the CMU with the standard method. All the individual values of $\dot{V}O_2$ are given in Table 2.

No statistically significant difference was found with $\dot{V}O_2$ values obtained from the standard method and those from the CMU (232 ± 41.6 versus 234 ± 39.2 ml/min). The mean difference between $\dot{V}O_2$ obtained with both methods was -2 ± 21 ml/min, $t = -0.48$, degrees of freedom = 19, $p = 0.6$, (95% confidence interval of -11.8 to 7.8 ml/min). There was a high degree of statistical correlation between both methods (Fig. 2).

The derived REE values obtained from the standard method (1620 ± 272.7 kcal/day) were not signifi-

Table 2. Individual values of $\dot{V}O_2$ (ml/min) measured with the standard method and the CMU

No.	Resp	1st $\dot{V}O_2$	2nd $\dot{V}O_2$	$\dot{V}O_2$ (CMU)
1	MV	216	234	235
2	MV	248	249	260
3	MV	276	266	258
4	MV	205	205	218
5	MV	202	186	194
6	MV	201	201	204
7	MV	262	277	249
8	MV	216	235	256
9	MV	255	262	286
10	MV	324	302	301
11	SB	185	205	198
12	SB	172	174	178
13	SB	256	265	282
14	SB	236	241	272
15	SB	247	237	224
16	SB	190	181	189
17	SB	264	257	241
18	SB	236	233	223
19	SB	294	265	268
20	SB	165	165	159

RESP, type of respiration; *MV*, mechanical ventilation; *SB*, spontaneous breathing

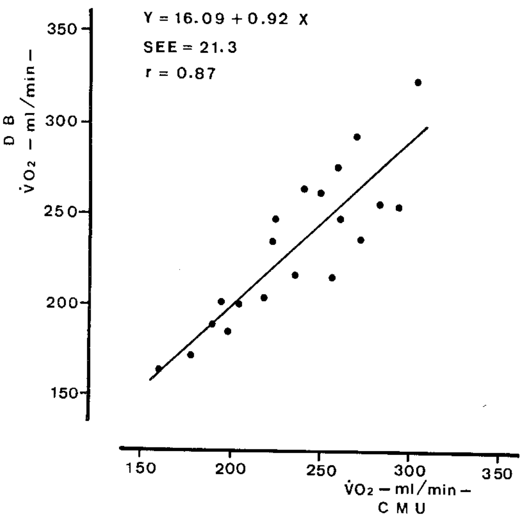

Fig. 2. Regression analysis of the $\dot{V}O_2$ measured with both methods in the whole group of healthy subjects and the patients of group A. The results of the standard method (*DB*) are shown on the *ordinate* and those of the CMU on the *abscissa*

Table 3. Individual values of $\dot{V}O_2$ (ml/min) measured with the CMU at two different FIO_2 in group B patients

	$FIO_2 = 0.43$		$FIO_2 = 1$
No.	1st $\dot{V}O_2$	2nd$\dot{V}O_2$	3rd $\dot{V}O_2$
1	180	187	189
2	187	173	175
3	237	243	237
4	191	198	192
5	242	247	263
6	210	216	210

cantly different from those obtained with the CMU (1641±273.9 kcal/day).

Reproducibility of standard and CMU methods

The mean difference between duplicate measurements of $\dot{V}O_2$ with the standard method was 0.5±13.3 ml/min, t = 0.17, df = 19, P = 0.87 (95% confidence interval of −5.6 to 6.7 ml/min). The mean difference obtained with the CMU at $FIO_2 = 0.43$ was −2.8± 8.3 ml/min t = −0.84, df = 5, $p = 0.4$, (95% confidence interval −11.5 to 5.85 ml/min).

Effect of two different FIO_2 on CMU values

There was no statistically significant difference in $\dot{V}O_2$ measured with $FIO_2 = 0.43$ versus $FIO_2 = 1$ (Table 3). The mean difference between both values was −3.2±11 ml/min, t = −0.7, df = 5, $p = 0.5$ (95% confidence interval −14.7 to 8.4 ml/min).

Discussion

The measurement of $\dot{V}O_2$ with new equipment (CMU) was compared with an established technique to see whether they agreed sufficiently for the CMU to replace the rather time-consuming standard open-circuit method. The results of this clinical study show that both methods can be used interchangeably to measure $\dot{V}O_2$ and REE.

The usual statistical approach to assessing the degree of agreement between two measurement methods is by using correlation coefficients, which only measure the strength of a relation between two variables but not the agreement between them. In fact, the true values remain unknown in clinical validation and it is always difficult to accept a 'gold standard' against which compare the new technique. We have performed the analysis outlines above [4] examining $\dot{V}O_2$ differences between both methods by plotting each difference against its mean and we observed a good agreement between the standard and CMU methods. The discrepancies between the two methods was summarized by calculating the mean difference, the standard deviation of the differences and the 95% confidence interval of the mean difference [18]. This difference appears small enough to allow the use of the CMU in place of the standard method. The reproducibility of both methods was studied in the same way, giving similarly small variations between them.

Measurements with the CMU required minimal user interaction at any breathing mode. We found the process of calibration particularly easy in contrast with other sophisticated computer techniques, in which accurate calibrated gas mixtures are needed to calibrate the O_2 and CO_2 analyzers [16]. The closed system described in this study does not use an O_2 analyzer and can be used over a wide range of oxygen concentrations, including $FIO_2 = 1$, without introducing the errors arising from measuring high levels of FIO_2 [22].

Carbon dioxide production is not measured with the present configuration of the CMU and the RQ value was estimated as 0.85. The associated error assuming such an RQ value is unikely to exceed 3.5%, which represents a minor error on the calculation of energy expenditure.

The closed circuit indirect calorimetry is subject to errors from air leaks and is not suitable for use during anesthesia. Although it is not a continuous method of measuring $\dot{V}O_2$, the CO_2 absorber supplied with the CMU has been especially designed to be completely gas-tight and have a low resistance. It has an useful life for 1 h measuring time which means 6−12 measurements of 5−10 min each. In our experience this CO_2 absorber was very effective in removing all the expired

CO_2 coming from the patient, since the CO_2 analyzer did not detect CO_2 at the outlet part of the absorber.

The open circuit method using a Douglas bag is also subject to errors from loss of volume or gas contamination during collection and analysis. However, in spite of being a laborious technique that needs a lot of expertise, we believe that it is a useful method in the ICU, because most of units have the basic equipment needed. It is important to measure both FIO_2 and FEO_2 and ensure a stable FIO_2 during the whole procedure of measurement during mechanical ventilation. This can be accomplished by placing an external blender connected to the O_2 and air port of the ventilator.

In contrast with compact systems that analyze gas and measure volume on a continuous basis, the CMU as well as the open Douglas bag method provides only a single value from each measurement. There is some controversy about how well short period measurements of energy expenditure correspond to longer periods of measurements. Some authors [12, 21] have found that resting energy expenditure can be measured at any time of day, providing that measurement conditions are closely regulated. The difference between REE and total energy expenditure measured during an eight-hour period averaged only 5% in one study [21]. However, other authors recommend that energy expenditure monitoring be performed continuously on a 24 h basis since it may vary considerably from one hour to another in the critically ill patient [7].

In conclusion, we found the design of the CMU to be useful and accurate to measure $\dot{V}O_2$ and REE either during spontaneous breathing or during mechanical ventilation. The CMU is well suited to measure $\dot{V}O_2$ at any FIO_2 and can replace the standard method for routine clinical monitoring in the ICU.

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