Effect of Ventilatory Settings on Accuracy of Cardiac Output Measurement Using Partial CO2 Rebreathing

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Background: Recently, a new device has been developed to measure cardiac output noninvasively using partial carbon dioxide (CO2) rebreathing. Because this technique uses CO2 rebreathing, the authors suspected that ventilatory settings, such as tidal volume and ventilatory mode, would affect its accuracy; they conducted this study to investigate which parameters affect the accuracy of the measurement.

Methods: The authors enrolled 25 pharmacologically paralyzed adult post–cardiac surgery patients. They applied six ventilatory settings in random order: (1) volume-controlled ventilation with inspired tidal volume (Vt) of 12 ml/kg; (2) volume-controlled ventilation with Vt of 6 ml/kg; (3) pressure-controlled ventilation with Vt of 12 ml/kg; (4) pressure-controlled ventilation with Vt of 6 ml/kg; (5) inspired oxygen fraction of 1.0; and (6) high positive end-expiratory pressure. Then, they changed the maximum or minimum length of rebreathing loop after establishing steady-state conditions (15 min), they measured cardiac output using CO2 rebreathing and thermodilution via a pulmonary artery catheter. Finally, they repeated the measurements during pressure support ventilation, when the patients had restored spontaneous breathing. The correlation between two methods was evaluated with linear regression and Bland-Altman analysis.

Results: When Vt was set at 12 ml/kg, cardiac output with the CO2 rebreathing technique correlated fairly with that measured by thermodilution (y = 1.02x, R = 0.63; bias, 0.28 l/min; limits of agreement, −1.78 to +2.34 l/min), regardless of ventilatory mode, oxygen concentration, or positive end-expiratory pressure. However, at a lower Vt of 6 ml/kg, the CO2 rebreathing technique underestimated cardiac output compared with thermodilution (y = 0.70x; R = 0.70; bias, −1.66 l/min; limits of agreement, −5.90 to +0.58 l/min). When the loop was fully retracted, the CO2 rebreathing technique overestimated cardiac output.

Conclusions: Although cardiac output was underreported at small Vt values, cardiac output measured by the CO2 rebreathing technique correlates fairly with that measured by the thermodilution method.

Although there is controversy over the cost benefit of pulmonary artery catheterization,1,2 cardiac output (CO) is commonly monitored when treating critically ill patients. Recently, a new device, the NICO2 system (Novametrix Medical Systems Inc., Wallingford, CT), has been developed to measure CO noninvasively using partial carbon dioxide (CO2) rebreathing.3,4 This device uses periodic partial CO2 rebreathing to create a CO2 disturbance, which is then used in a differential Fick CO2 equation to calculate CO.5

There have been few studies to investigate how well the results obtained by CO2 rebreathing correlate with those obtained by the conventional thermodilution technique.5–7 Furthermore, it remains to be clarified which ventilatory or hemodynamic parameters affect the measured values when the CO2 rebreathing technique is used. Because noninvasive CO measurement depends on CO2 rebreathing and assumes constant dead space and mixed venous CO2 content through the CO2 rebreathing procedure,5,4 we suspected that change in ventilatory settings might affect accuracy of the CO measurement. Consequently, we performed a prospective comparative study to evaluate the effects of tidal volume (Vt), ventilatory mode, inspired oxygen fraction (FIo2), and positive end-expiratory pressure (PEEP) on the accuracy of the measurement. The NICO2 system uses a rebreathing loop in which volume is adjustable according to tidal volume. We suspected that a too-short loop may affect the accuracy due to poor signal-to-noise ratio. Therefore, we investigated, as a factor of the machine itself, the effect of adjusting the length of the rebreathing loop.

Subjects and Methods

The study was approved by the institutional ethics committee of the National Cardiovascular Center (Osaka, Japan), and written informed consent was obtained from each patient.

Patients

Twenty-five adult patients aged 48–78 yr (median, 61 yr) who had undergone cardiac surgery (table 1) were enrolled in this study. Enrollment criteria were (1) insertion of a Swan-Ganz catheter; (2) stable hemodynamics in the intensive care unit; and (3) no leakage around the endotracheal tube. We excluded candidates who (1) had central nervous system disorders; (2) might be adversely affected by induced hypercapnia (risk of severe pulmonary hypertension or increased intracranial pressure); or (3) demonstrated severe tricuspid regurgitation on intraoperative examination of transesophageal echocardiography, which interferes with the accuracy of thermodilution CO measurement. Arterial blood pressure, heart rate, pulmonary artery pressure, central venous pressure, and pulse oximeter signal (PM–1000; Nellcor Inc., Hayward, CA) were continuously monitored in all pa-
CO MEASUREMENT BY PARTIAL CO 2 REBREATHING

Table 1. Patient Profile

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>25</th>
</tr>
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<tr>
<td>M/F</td>
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<tr>
<td>Age (yr)</td>
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<td>Height (cm)</td>
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<td>Body Weight (kg)</td>
<td>63 ± 11</td>
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<td>Coronary artery disease</td>
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<td>Acquired valve disease</td>
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<td>Thoracic aortic aneurysm or dissection</td>
<td>4</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>2</td>
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</table>

Measurements

We measured CO using two methods. Values for CO derived from a thermodilution technique (CO30) were obtained using a Swan-Ganz catheter (7.5 French; Abbott Laboratories, North Chicago, IL). Injection of 10 ml cold saline (0°C) was performed in triplicate, and the values were averaged. Because the CO measurement varies depending on when in the respiratory cycle the measurement is initiated,\(^3\) we standardized the timing of bolus injection after the first half of the expiratory phase. We confirmed the injection timing by watching the waveform of airway pressure versus time on the graphic monitor of a ventilator (Bird Corp., Palm Springs, CA). Noninvasive measurement of CO (CO30) was performed with a NICO2 system (software version 3.1, fast mode). This procedure has been presented in detail elsewhere.\(^3\) Briefly, on a breath-by-breath basis, CO2 production (\(\dot{V}_{CO2}\)) is calculated from the flow and CO2 concentration at the airway opening. Then, to establish the relation between \(\dot{V}_{CO2}\) and CO, the Fick principle is applied as follows:

\[
\dot{V}_{CO2} = CO \times (C\dot{V}_{CO2} - C_{acaco}), \tag{1}
\]

where \(C\dot{V}_{CO2}\) and \(C_{acaco}\) represent the CO2 content in mixed venous and arterial blood, respectively. In the NICO2 system, CO2 rebreathing is performed for 50 s every 3 min using a disposable sensor (Novametrix Medical Systems). A brief period of CO2 rebreathing caused a change in Paco2 and a change in \(\dot{V}_{CO2}\) but little or no change in \(C\dot{V}_{CO2}\) in anesthetized dogs,\(^5\) probably because the quantity of CO2 stores in the body is large, and new equilibrium levels are attained after 20–30 min.\(^6\) Assuming that CO and \(C\dot{V}_{CO2}\) remained constant during the CO2 rebreathing procedure, the following equation can be substituted for the previous one:

\[
\Delta\dot{V}_{CO2} = CO \times (-\Delta C_{acaco}), \tag{2}
\]

where \(\Delta\dot{V}_{CO2}\) is the change in \(\dot{V}_{CO2}\) between normal breathing and CO2 rebreathing, and \(\Delta C_{acaco}\) is the change in arterial CO2 content. Assuming here that dead space fraction (\(V_d/V_t\)) remains constant during the CO2 rebreathing and that \(\Delta C_{acaco}\) is proportional to changes in arterial carbon dioxide pressure (Paco2) and end-tidal CO2 pressure (PETCO2), the following equation can be plotted:

\[
CO = \Delta\dot{V}_{CO2}/S \times \Delta PETCO2, \tag{3}
\]

where \(\Delta PETCO2\) is the change in PETCO2 between normal breathing and CO2 rebreathing, and S is the slope of the CO2 dissociation curve from hemoglobin. The constant S can be expressed as a function of hemoglobin concentration and Paco2 as follows:\(^5\)

\[
S = (1.34 \times [Hb] + 18.34)/(1 + 0.193 \times Paco2) \tag{4}
\]

where [Hb] is hemoglobin concentration.

Before the start of the study protocol, the NICO2 system was calibrated for zero CO2 by opening the system to the atmosphere, according to the manufacturer’s instructions. We entered the results of arterial oxygen pressure (Pao2), Paco2, FIO2 (0.4–0.7), and hemoglobin concentrations (7.9–11.9 g/dl) into the machine when each patient was under the baseline ventilation. Calculation of these parameters is used to calculate shunt fraction (Pao2 and FIO2), alveolar dead space (Paco2), and the slope of the CO2 dissociation curve (hemoglobin).\(^3\)

Study Protocol

We used Bird 8400STi ventilators (Bird Corp.). At the time of admission to the intensive care unit, initial ventilatory settings were as follows: synchronized intermittent mandatory ventilation mode; volume-controlled ventilation (VCV); inspired \(V_t\) of 10 ml/kg; decelerating flow pattern; respiratory rate of 10–12 breaths/min; and inspiratory time of 1.0 s. The FIO2 was adjusted by attending physicians to maintain a Pao2 greater than 100 mmHg. Baseline PEEP was set at 4 cm H2O in 23 patients; because of hypoxemia, the remaining 2 patients needed PEEP of 6 and 8 cm H2O, respectively. With the patients maintained in the supine position, sedated with continuous intravenous injection of propofol (2–3 mg · kg\(^{-1}\) · h\(^{-1}\)), and paralyzed with bolus administration of vecuronium bromide (4–8 mg), we started the measurement protocol.

In random order, we applied six ventilatory settings to all of the 25 patients, and then we applied three additional settings in a fixed order (table 2). To test the effects of ventilatory mode and \(V_t\), we chose VCV with inspired \(V_t\) of 12 or 6 ml/kg and pressure-controlled ventilation (PCV) with the same \(V_t\) settings. The FIO2 and respiratory rate were fixed identical to baseline. The PEEP was also fixed identical to the baseline measurement (4 cm H2O in 23 patients, 6 cm H2O in 1, and 8 cm H2O in 1). The inspiratory time was set to 1.0 s for both VCV and PCV. The level of pressure control was adjusted.

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to obtain the same $V_T$ during VCV. The rebreathing loop was sized according to the manufacturer’s instructions recommended for set tidal volume of 12 ml/kg. To examine the effects of FIO$_2$, we increased the FIO$_2$ to 1.0 with VCV and 12 ml/kg $V_T$. To examine the effects of high PEEP, we increased PEEP to 12–15 cm H$_2$O with VCV and 12 ml/kg $V_T$, depending on the patient’s hemodynamic stability. The order of these six conditions was randomized. Then, to examine the effects of varying the length of the rebreathing loop, in 17 patients, measurements were performed with the loop maximally expanded (400 ml) or fully retracted (150 ml) while VCV and 12 ml/kg $V_T$ were used. After the measurements were completed, vecuronium infusion was stopped. When the patient recovered stable spontaneous breathing, we switched the ventilatory mode to continuous positive airway pressure of 4 cm H$_2$O plus pressure-support ventilation (PSV) of 10 cm H$_2$O. After establishing steady-state conditions (approximately 15 min) at each setting, we measured both CO$_{sl}$ and CO$_{TD}$. We limited ourselves perform only nine measurements (one measurement for each ventilatory setting) per patient. Arterial blood samples were analyzed with a calibrated blood gas analyzer (ABL 505; Radiometer, Copenhagen, Denmark). Hemodynamic data were also recorded. $V_T$/$V_T$ and venous admixture fraction

<p>| Table 3. Respiratory and Hemodynamic Parameters at Each Ventilatory Setting |
|---------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|</p>
<table>
<thead>
<tr>
<th>Ventilatory Setting</th>
<th>VCV Large $V_T$</th>
<th>VCV Small $V_T$</th>
<th>PCV Large $V_T$</th>
<th>PCV Small $V_T$</th>
<th>VCV FIO$_2$ 1.0</th>
<th>VCV High PEEP</th>
<th>VCV Long Loop</th>
<th>VCV Short Loop</th>
<th>PSV</th>
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<tr>
<td>V$_T$ (ml/kg)</td>
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<td>$3.0 \pm 2.0$</td>
<td>$3.0 \pm 2.0$</td>
<td>$3.0 \pm 2.0$</td>
<td>$3.0 \pm 2.0$</td>
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<tr>
<td>PEEP (cm H$_2$O)</td>
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<td>pH</td>
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<td>$0.93 \pm 0.93$</td>
<td>$0.93 \pm 0.93$</td>
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<td>Paco$_2$ (mmHg)</td>
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<td>$39.2 \pm 6.0$</td>
<td>$39.2 \pm 6.0$</td>
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<td>HR (beats/min)</td>
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<td>$92 \pm 7$</td>
<td>$92 \pm 7$</td>
<td>$92 \pm 7$</td>
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<td>BP (mmHg)</td>
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<td>$79 \pm 9$</td>
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<td>PaCO$_2$ (mmHg)</td>
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<td>$7.9 \pm 2.5$</td>
<td>$7.9 \pm 2.5$</td>
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<td>PCWP (mmHg)</td>
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<td>PVR (dyn · s · cm$^{-5}$)</td>
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<td>$158 \pm 89$</td>
<td>$158 \pm 89$</td>
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<tr>
<td>SVR (dyn · s · cm$^{-5}$)</td>
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<td>$1,162 \pm 372$</td>
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<tr>
<td>$\overline{SVO}_2$ (%)</td>
<td>$72 \pm 7$</td>
<td>$72 \pm 7$</td>
<td>$72 \pm 7$</td>
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* $P < 0.05$ versus volume-controlled ventilation (VCV)–large tidal volume ($V_T$), pressure-controlled ventilation (PCV)–large $V_T$, fraction of inspired oxygen (FIO$_2$) 1.0, high positive end-expiratory pressure (PEEP), long loop, short loop, and pressure-support ventilation (PSV). $\dagger P < 0.05$ versus other ventilatory settings. $\ddagger P < 0.05$ versus VCV–large $V_T$, PCV–small $V_T$, and PSV. $\S P < 0.05$ versus VCV–large $V_T$, PCV–large $V_T$, FIO$_2$ 1.0, long loop, short loop, and PSV. $\overline{P} P < 0.05$ versus PCV–large $V_T$, long loop, short loop, and PSV. $\overline{S} P < 0.05$ versus PCV–large $V_T$, PCV–small $V_T$, PCV–low, FIO$_2$ 1.0, high PEEP, and short loop. $\overline{**} P < 0.05$ versus PCV–large $V_T$ and short loop. $\overline{\dagger} P < 0.05$ versus PCV–large $V_T$ and FIO$_2$ 1.0. $\overline{\ddagger} P < 0.05$ versus PCV–large $V_T$, PCV–large $V_T$, high PEEP, and PSV.

$V_T$ = minute ventilation; PEEP = peak inspiratory pressure; Paco$_2$ = arterial carbon dioxide tension; P/F = ratio of arterial oxygen tension to FIO$_2$; CO$_{sl}$ = cardiac output with thermodilution; CO$_{ne}$ = cardiac output with carbon dioxide rebreathing; VCO$_2$ = carbon dioxide production; PETCO$_2$ = end-tidal carbon dioxide pressure; $V_{ET}/V_T$ = dead-space fraction; Q$_O_2$/Q$_{CO}_2$ = venous admixture fraction; HR = heart rate; BP = mean artery pressure; PA = mean pulmonary artery pressure; CPR = central venous pressure; PCWP = pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance; SVR = systemic vascular resistance; $SVO_2$ = mixed venous oxygen saturation.

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(\dot{Q}_s/\dot{Q}_T) were calculated using the following equations\textsuperscript{10,11}:

\[ V_D/V_T = 1 - (0.863 \cdot V\dot{CO}_2)/(V_E \cdot Pa\dot{CO}_2) \quad (5) \]

and

\[ \dot{Q}_s/\dot{Q}_T = (Cc'\dot{O}_2 - Ca\dot{O}_2)/(Cc'\dot{O}_2 - C\dot{V}_\dot{O}_2), \quad (6) \]

where \( V_E \) is minute ventilation, \( Cc'\dot{O}_2 \) is oxygen content at the pulmonary capillary, \( Ca\dot{O}_2 \) is arterial oxygen content, and \( C\dot{V}_\dot{O}_2 \) is mixed venous blood oxygen content. Assuming that pulmonary capillary blood is fully saturated with oxygen and that oxygen content is roughly proportional to oxygen saturation, the second equation can be revised as follows:

\[ \dot{Q}_s/\dot{Q}_T = (1 - Sa\dot{O}_2)/(1 - S\dot{V}_\dot{O}_2), \quad (7) \]

where \( Sa\dot{O}_2 \) and \( S\dot{V}_\dot{O}_2 \) are oxygen saturation at the artery and mixed venous blood, respectively.

**Statistical Analysis**

Data are presented as mean ± SD. Using analysis of variance with repeated measures, mean values were compared across different settings. When significance was observed, the mean values were tested by multiple comparison with the Bonferroni correction. We evaluated the correlation between \( CO_{NI} \) and \( CO_{TD} \) with linear regression and Bland-Altman analysis.\textsuperscript{12,13} To investigate which parameters contributed to the discrepancy between \( CO_{NI} \) and \( CO_{TD} \), we also performed linear multiple regression analysis among \( Fo_2, V_T, V_E, PEEP, peak\, inspiratory\, pressure, pH, PaO_2, \dot{P}aCO_2, PETCO_2, V\dot{CO}_2, \) and \( S\dot{V}_\dot{O}_2 \). Statistical significance was set at \( P < 0.05 \).

**Results**

Blood gas and hemodynamic results are summarized in table 3. Minute ventilation was stable at all 12-ml/kg \( V_T \) settings. Regardless of ventilatory mode, the 6-ml/kg \( V_T \) settings resulted in higher \( PaCO_2 \), higher \( PETCO_2 \), and less \( V\dot{CO}_2 \), compared with the 12-ml/kg \( V_T \) settings. During PSV, \( V_T \) values (8.8 ± 2.6 ml/kg) decreased to between those for 12- and 6-ml/kg \( V_T \) settings, whereas minute ventilation was similar to that at the 12-ml/kg \( V_T \) settings. \( CO_{TD} \) values were similar at each 12-ml/kg \( V_T \) setting, although \( CO_{TD} \) values at the 6-ml/kg \( V_T \) settings were slightly larger in comparison. At high PEEP, \( CO_{TD} \) values were lower.

![Fig. 1. Agreement between cardiac output measurements obtained by carbon dioxide rebreathing (\( CO_{NI} \)) and those obtained by thermodilution technique (\( CO_{TD} \)). (A) Large tidal volumes (\( V_T, 12 \) ml/kg) during both volume-controlled ventilation and pressure-controlled ventilation. (B) Same modes, but with small tidal volumes (6 ml/kg). Equations and result curves for linear regression analysis are also shown.](http://anesthesiology.pubs.asahq.org/pdfaccess.ashx?url=/data/journals/jasa/931225/ on 06/23/2017)
Levels of pressure control were 24 ± 7 (16–36) cm H₂O with inspired Vₜ of 12 ml/kg and 13 ± 4 (8–22) cm H₂O with Vₜ of 6 ml/kg. As a result, there was no difference in peak inspiratory pressure for VCV and PCV at either Vₜ setting (table 3).

Results of Bland-Altman analysis and linear regression analysis are shown in table 4 for each ventilatory setting. When Vₜ values were the same, Bland-Altman analysis characteristics between CO TD and CO NI were almost identical (bias and precision: 12-ml/kg Vₜ VCV, 0.18 and 1.04; 12-ml/kg Vₜ PCV, 0.37 and 1.17; 6-ml/kg Vₜ VCV, −1.67 and 1.06; and 6-ml/kg Vₜ PCV, −1.64 and 1.19, table 4). Consequently, for the same Vₜ values, CO data during both VCV and PCV were analyzed together.

When Vₜ was 12 ml/kg, a fair correlation was observed between CONI and COTD (fig. 1). The slope of linear regression was 1.02 (R² = 0.63, fig. 1), and bias was small (0.28 l/min, fig. 2), although limits of agreement were wide (−1.78 to +2.34 l/min, fig. 2). This is the case with ventilatory setting of high FlO₂ or high PEEP (table 4). By contrast, when Vₜ was small (6 ml/kg), the CONI underestimated the COTD with a slope of 0.70 (fig. 1), a bias of −1.66 l/min, and limits of agreement of −3.9 to +0.54 l/min (fig. 1). During PSV, the correlation between CO NI and CO TD was also close to identical (slope = 1.07, R = 0.63, bias = 0.52 l/min, table 4). With the loop maximally expanded, the CO NI correlated moderately with CO TD (slope = 1.05, bias = 0.48, table 4); however, with the loop fully retracted, CO NI overestimated CO TD (slope = 1.23, bias = 1.50, table 4). Linear multiple regression analysis revealed that the setting most affecting the discrepancy between CO NI and CO TD was minute ventilation (R = 0.616).

Figure 3 shows a relation between changes in cardiac output measurements obtained by thermodilution technique and those obtained by carbon dioxide rebreathing technique (CO TD) during both volume-controlled ventilation and pressure-controlled ventilation. (A) Same modes, but with small tidal volumes (6 ml/kg). Dotted lines show bias and limits of agreement between the two methods.

Discussion

The main findings of this study are as follows. (1) During mechanical ventilation with large constant Vₜ or during PSV, CO measurements obtained by CO₂ rebreathing technique correlate with those obtained by thermodilution method. (2) When minute ventilation is large, the accuracy of the CO₂ rebreathing technique is not affected by a selection of VCV, PCV, spontaneous breathing (PSV), PEEP, or FlO₂. (3) When Vₜ and minute ventilation are reduced, the CO₂ rebreathing technique
underreports CO. (i) CO measurements are accurate when the rebreathing loop is maximally expanded but is overestimated when the loop is fully retracted.

**Clinical Implications**

Using partial CO₂ rebreathing, CO can be measured noninvasively.³,⁴ However, there have been few clinical reports, on the accuracy of this technique.⁵⁻⁷ We need to confirm that it provides effective monitoring for critically ill patients and discover parameters that might affect accuracy. Our results suggest that at a large VT setting and with constant minute ventilation, CO measurements obtained from this technology correlate fairly with those from the thermodilution method. When inspired VT is set at 12 ml/kg and respiratory rate is set at 10–12 breaths/min, which results in an actual minute ventilation of 0.13–0.14 L/min⁻¹/kg⁻¹, the linear regression slopes for CO NI and CO TD were almost identical (1.01:1.05). Bias analysis also indicated small bias and moderate precision (fig. 2), while accuracy was consistent regardless of ventilatory mode (VCV or PCV), PEEP, or FiO₂. Correlation of results from CO NI and CO TD was also satisfactory during PSV (table 4). These observations suggest that this CO₂ rebreathing technique is reliable both with large constant VT and during PSV. In addition, because the maximally expanded loop did not affect accuracy (table 4), rather than it being necessary to strictly adjust the loops, there may be some leeway in adjusting them for the maximal expected VT. In contrast, when the rebreathing loop was set too short for a given VT, CO NI measurements had greater values than those obtained by CO TD (table 4). This may be due to the small changes in PETCO₂ that occur with the shortest loop during CO₂ rebreathing, when a slight amount of noise would likely generate large errors.

To our surprise, when VT was small (6 ml/kg), CO NI measurements showed consistently lower values than those produced by CO TD, resulting in a linear regression slope of 0.70 and a negative value of bias (figs. 1 and 2). Low VT (6 ml/kg) is currently recommended for ventilator management in acute respiratory failure,¹⁴ so attention needs to be drawn to the lack of reliable measurement using CO NI at the low VT setting. Reasons for these discrepant results have not been clarified, but there are several possible explanations.

First, after we adjusted the length of rebreathing loops for high VT, when VT was decreased, results may have been affected because the loop had become relatively too long. However, we found that the maximally expanded loop did not make CO NI measurements less accurate (table 4). This finding suggests that the combination of long loop and small VT are unlikely to impair the accuracy of CO NI.

Second, at small VT settings, PETCO₂ increased to almost 60 mmHg in several patients. The software (version 3.1) that we used suspends rebreathing when the baseline PETCO₂ is greater than 65 mmHg or PETCO₂ is greater than 80 mmHg during CO₂ rebreathing. It could be that the linearity between Ca CO₂ and PETCO₂ is less accurate when PETCO₂ is extremely high.

Finally, the assumed constancy of mixed venous CO₂ content may be false for some time after VT and minute ventilation are changed. The measured values of VCO₂ were smaller at low VT than at high VT (table 3). Although we waited for 15 min, this may not have been enough time for CO₂ stores to reach a steady state, which is 100 times larger than oxygen stores.⁹ In addition, the time course of the increase in PaCO₂ after abrupt decrease of ventilation is much slower than the rate of decrease after abrupt increase of ventilation.⁹ These facts suggest that CO₂ stores and mixed venous CO₂ content may continue to change even after PaCO₂ and PETCO₂ seem to have reached plateau values. If this is the case, the accuracy of the CO₂ rebreathing technique may be compromised when there are abrupt changes in minute ventilation and VCO₂. Further study is needed to find out exactly what happens after these sudden changes and whether these mechanisms affect the accuracy of the CO₂ rebreathing technique.

**Limitations**

The current study has several limitations. First, the patients in our study were sedated and paralyzed initially, resulting in constant VT and stable VCO₂. Even during PSV, they breathed quietly with small variation in VT. Therefore, our results may not be directly extrapolated to populations of patients whose VT and VCO₂ are changing.⁶ Secondly, our patients had relatively normal lung mechanics (respiratory system compliance, 45.4 ± 12.8 ml/cm H₂O; resistance, 11.2 ± 4.1 cm H₂O·s⁻¹), and their hemodynamics had been stabilized at time of entry into the study. In more seriously compromised patients, the accuracy may be quite different. To corroborate the relevance of our findings for acutely ill and ventilator-dependent patients, it is prudent to perform further studies. Third, we did not examine how the ventilatory pattern alterations affect the assumptions underlying the fundamental equation of the NICO₂ technique: e.g., constant VT/V̇, constant CO₂, and constant mixed venous CO₂ content during the CO₂ rebreathing procedure. Finally, it remains to be clarified whether the impaired accuracy of CO NI with small VT results from small VT itself or from reduced minute ventilation. During PSV, when VT was smaller (8.8 ± 2.6 ml/kg) but minute ventilation was similar to that at the high VT settings, CO NI and CO TD values correlated fairly (y = 1.07x); we speculate that if normocapnia is sustained by adjusting the respiratory rate, the accuracy of the CO NI technique can be maintained at small VT.

In conclusion, noninvasive measurement of CO using CO₂ rebreathing is reliable with a bias of less than 0.5 l/min and a precision of 1 l/min when the tidal
volume is large and constant, regardless of ventilatory modes. However, at small tidal volume, the rebreathing system underreports CO₂, compared with the conventional thermodilution technique.

References


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