Dynamics of Carbon Dioxide Elimination Following Ventilator Resetting*

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Background: Carbon dioxide elimination (VCO₂) at steady state corresponds to the metabolic rate. A change in tidal ventilation will lead to a transient response in VCO₂ if other determinants of VCO₂ are constant. This principle may be applied in the critical care unit to resets ventilators.

Objective: To define and characterize the transient response of VCO₂ to a well-defined change in ventilation.

Methods: Forty-four patients in stable condition receiving volume-controlled mechanical ventilation had trend recordings of ventilator pressures, flow, volumes, VCO₂, and end-tidal CO₂ (ETCO₂) for 20 min. At time t₀, the minute ventilation was either increased (n=22) or decreased (n=22) by 10% after which these parameters were monitored over 30 min. Blood gas values were measured at 5 and 20 min after the change in ventilation and the dead space fractions were computed using the single breath—CO₂ test.

Data analysis: The first ten breaths (till t₁) after a change in ventilation were excluded. The time constant (τ) of the relative change in VCO₂ (ΔVCO₂) was calculated by fitting exponential regressions to ΔVCO₂ for periods up to 20 min after t₁.

Results: The ΔVCO₂ at t₁ was proportional to the relative change in tidal volume (ΔVt). The proportionality decreased gradually during 20 min. The proportionality of the relative change in ETCO₂ (ΔETCO₂) or PaCO₂ (ΔPaCO₂) with ΔVt was minimal at t₁ and increased during the 20 min. τ increased progressively when calculated over longer periods (p<0.001). τ was similar in the groups with increased and decreased ventilation up to 5 min, after which it was longer in the group with decreased ventilation (p<0.05). The ΔPaCO₂ after 20 min correlated best with ΔVCO₂ at t₁ (r=−0.8) and with ΔETCO₂ at the end of 20 min (r=0.8).

Conclusions: Noninvasively monitored VCO₂ provides an instantaneous indication of the change in alveolar ventilation in well-sedated, mechanically ventilated patients in stable condition without significant cardiovascular disease. (CHEST 1995; 108:196-202)

CaCO₂=arterial content of CO₂; Cst=static lung compliance; CVCO₂=venous content of CO₂; ETCO₂=end-tidal CO₂; ΔETCO₂=relative change in ETCO₂; PEEP=positive end-expiratory pressure; Pp=pressure; ΔPaCO₂=relative change in PaCO₂; SBTCO₂=single breath test for CO₂; t=τ=time constant of ΔVCO₂; t₀=instant of change of ventilation; t₁=after ten breaths after t₀; VCO₂=alveolar dead space percent; Vdaw=alveolar dead space percent; Vp=physiologic dead space percent; ΔVt=relative change in tidal volume

Key words: CO₂ elimination; mechanical ventilation; models; ventilator resetting

Determining the optimal ventilator settings in the critically ill, mechanically ventilated patients is at times difficult and time consuming. Arterial blood gases conventionally are used to assess the adequacy of gas exchange after a change in ventilator settings. The drawbacks of arterial blood gases include the use of indwelling catheters, expense, and lag period during which a patient’s safety is compromised. The patient’s status may have changed during the period from resetting to blood sampling. Continuous intraarterial fluoroptic blood gas systems are increasingly used to detect precipitous changes in cardiopulmonary function almost instantaneously.1 There is a need for noninvasive alternatives that rapidly and reliably indicate the utility of a change in ventilation.2,3

Variations of end-tidal CO₂ (ETCO₂) are known to correlate poorly with PaCO₂ changes after resetting the ventilator.4,5 Carbon dioxide elimination (VCO₂) has been used to evaluate the effect of a change of ventilation on gas exchange during high-frequency ventilation.6 During steady state, VCO₂ corresponds to the metabolic rate. Any improvement in alveolar ventilation or perfusion or matching between ventilation and perfusion will transiently increase VCO₂ and lower PaCO₂. After
some time, a new steady state will be established at which \( \dot{V}_{CO_2} \) again equals the metabolic rate. The use of \( \dot{V}_{CO_2} \) for monitoring of mechanically ventilated patients and during resetting the ventilation in the experimental setting has been described previously. However, the instantaneous response of \( \dot{V}_{CO_2} \) has not been systematically evaluated for the estimation of gas exchange after resetting ventilators. An expected problem in the use of \( \dot{V}_{CO_2} \) is the variations caused by changes in perfusion, body position, and other irrelevant factors that will lead to a high noise of the signal. The utility of the \( \dot{V}_{CO_2} \) response depends on the nature of the transient change, which needs to be defined so as to allow optimal separation of the signal from noise.

The objective of the present study was to determine the magnitude and time course of the transient \( \dot{V}_{CO_2} \) response after a well-defined change in alveolar ventilation. This was studied in a group of mechanically ventilated patients in reasonably stable conditions.

**Materials and Methods**

**Patients**

Forty-four patients without clinically significant cardiopulmonary disease were divided into two groups and studied mainly after elective surgery (Table 1). All patients were receiving volume-controlled ventilation with a ventilator (Servo Ventilator 900C, Siemens Elema, Solna, Sweden). They were adequately oxygenated with an FIO2 of less than 0.6 and a positive end-expiratory pressure (PEEP) of less than 8 cm H2O. The ETCO2 and \( \dot{V}_{CO_2} \) were monitored with a CO2 analyzer (930 CO2 Analyzer, Siemens Elema). The CO2 analyzer was calibrated prior to each measurement with a gas of known CO2 concentration. Blood gases were measured using an automated blood gas analyzer (ABL 300, Radiometer A/S, Copenhagen, Denmark) that was cross calibrated with the CO2 analyzer using the same gas. The initial ventilation parameters, pulmonary compliance, blood gases, and dead space fractions (Table 2) were monitored over a period of 20 min and the study was pursued only if the variability of the observed \( \dot{V}_{CO_2} \) was less than 3%. Stability was further defined as "constant temperature, constant hemodynamics and normal blood gases." Patients were adequately sedated with midazolam (2 to 10 mg/h) and fentanyl (0.1 to 0.3 mg/h) so that no spontaneous respiratory efforts were observed. This dose, which was titrated during the initial observation period, was adequate also for the period when changes in ventilation were introduced.

**Signal Sampling**

Signals from the ventilator and CO2 analyzer were sampled at two different rates and fed through an interface into two personal computers equipped with A/D converters.

**Single Breath — CO2 Test**: The pressure and flow signals from the ventilator and the CO2 signal from the CO2 analyzer were recorded at 200 Hz over 30 s intermittently, at specific instants during the study. The flow and CO2 signals were used for detailed dead space analysis according to the single breath — CO2 test described by Fletcher et al.

**Trend Recordings**: The peak pressure, end-inspiratory pause pressure (\( P_{pa} \)), expiratory tidal volume, and ETCO2 were continuously sampled, one value for each breath. The value of \( \dot{V}_{CO_2} \) from the analyzer is intrinsically filtered by a low-pass filter that has a variable time constant equal to 2.5 breaths. Further analysis was carried out using a software package (Microsoft Excel 4).

**Table 1—Clinical Profile of Patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>65 (19-80)*</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>38/6</td>
</tr>
<tr>
<td>Body mass index</td>
<td>23.6 (15.9-50.9)*</td>
</tr>
<tr>
<td>Initial blood pressure, mm Hg</td>
<td>120/60 (90/45-156/80)*</td>
</tr>
<tr>
<td>Duration of mechanical ventilation, h</td>
<td>8 (6-74)*</td>
</tr>
<tr>
<td>Diagnoses, n</td>
<td></td>
</tr>
<tr>
<td>Aortic surgery, bifemoral bypass</td>
<td>29</td>
</tr>
<tr>
<td>Polytrauma</td>
<td>6</td>
</tr>
<tr>
<td>Septicemia of unknown origin</td>
<td>5</td>
</tr>
<tr>
<td>Liver resection</td>
<td>2</td>
</tr>
<tr>
<td>Renal artery stenosis</td>
<td>1</td>
</tr>
<tr>
<td>Guillain-Barré syndrome</td>
<td>1</td>
</tr>
</tbody>
</table>

*Median with range in parentheses.
### Table 2—Ventilation Parameters and Blood Gas Values at Onset (Baseline) and 20 min After Change of Ventilation (Experimental)*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Experimental</th>
<th>Baseline</th>
<th>Experimental</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal volume, mL/kg</td>
<td>8.1 ± 1.5</td>
<td>8.9 ± 1.6</td>
<td>8.9 ± 1.6</td>
<td>7.9 ± 1.5</td>
</tr>
<tr>
<td>Peak pressure, cm H₂O</td>
<td>23.5 ± 4.2</td>
<td>25.3 ± 4.3</td>
<td>25.8 ± 4.8</td>
<td>23.7 ± 4.2</td>
</tr>
<tr>
<td>Compliance, mL/cm H₂O</td>
<td>48.1 ± 17.5</td>
<td>47.0 ± 14.7</td>
<td>44.3 ± 10.4</td>
<td>43.4 ± 9.57</td>
</tr>
<tr>
<td>PaO₂, kPa/FIO₂</td>
<td>38.8 ± 11.3</td>
<td>40.5 ± 11.4</td>
<td>38.6 ± 14.5</td>
<td>38.6 ± 10.8</td>
</tr>
<tr>
<td>PaCO₂, kPa</td>
<td>5.2 ± 0.7</td>
<td>4.8 ± 0.7</td>
<td>4.8 ± 0.7</td>
<td>5.0 ± 0.7</td>
</tr>
<tr>
<td>pH</td>
<td>7.43 ± 0.1</td>
<td>7.45 ± 0.1</td>
<td>7.45 ± 0.2</td>
<td>7.45 ± 0.1</td>
</tr>
<tr>
<td>V̇Daw, % of V̇t</td>
<td>15.1 ± 10.7</td>
<td>15.3 ± 11.6</td>
<td>14.9 ± 11.5</td>
<td>12.9 ± 10.4</td>
</tr>
<tr>
<td>V̇Dalv, % of V̇t</td>
<td>28.6 ± 7.1</td>
<td>26.5 ± 6.2</td>
<td>26.7 ± 6.4</td>
<td>28.9 ± 6.9</td>
</tr>
<tr>
<td>V̇pḢphys, % of V̇t</td>
<td>43.7 ± 11.5</td>
<td>41.8 ± 12.1</td>
<td>41.2 ± 11.7</td>
<td>41.7 ± 10.9</td>
</tr>
</tbody>
</table>

*Data are expressed as mean ± SD.

*p<0.001 compared with baseline value in same group.

*p<0.05 compared with baseline value in same group.

*p<0.05 intergroup comparison of baseline values.

### Procedure

Stability was confirmed over 20 min in a well-sedated patient receiving mechanical ventilation. During this period trend recordings were obtained and arterial blood gas values were measured during a single breath — CO₂ test. The minute ventilation was then randomly either increased (n=22) or decreased (n=22) by 10% at time t₀. Trend recordings were then collected for 30 min under the new “experimental” settings. Blood gases and single breath — CO₂ tests were repeated at t₀+5 and t₀+20 min. At t₀+30 min, the minute ventilation was brought back to initial settings and the study was terminated.

**Analysis of the Transient V̇CO₂ Response**: Baseline V̇CO₂ and ETCO₂ were the mean values of breaths immediately preceding t₀ (Fig 1). The first ten breaths after t₀ until time t₁ were ignored. ΔV̇CO₂ was defined as the relative change in V̇CO₂ during experimental settings.

\[ \Delta V̇CO₂ = (V̇CO₂(V) - V̇CO₂(B)) \]  

(Eq 1)

\[ \Delta V̇t, \Delta ETCO₂, \text{ and } \Delta PaCO₂ \text{ were similarly calculated. The relative change of } \Delta V̇CO₂ \text{ to } \Delta V̇t \text{ was determined as } \frac{\Delta V̇CO₂}{\Delta V̇t}. \]

Similarly, \[ \frac{\Delta ETCO₂}{\Delta V̇t} \text{ and } \frac{\Delta PaCO₂}{\Delta V̇t} \text{ were calculated.} \]

The time constant (τ) of decline of ΔVCO₂ was calculated by fitting exponential regressions to ΔVCO₂, starting from t₁ and lasting from 1 to 20 min, assuming that ΔVCO₂ declined mono-exponentially toward zero. Thus,

\[ ΔV̇CO₂(t) = ΔV̇CO₂(t₁)e^{-t/τ} \]  

(Eq 2)

The regressions were extrapolated backwards to t₀ to calculate ΔVCO₂(t₀).

**Calculation of Change in the Fractions of Dead Space**: A single breath test for CO₂ (SBT-CO₂) depicting the expired CO₂ fraction against expired tidal volume was plotted together with the fraction of CO₂ in equilibrium with arterial blood. Physiologic dead space fraction (V̇pḢphys) comprising airway dead space fraction (V̇naw) and alveolar dead space fraction (V̇Dalv) was computed from the SBT-CO₂.[12-14]

**Calculation of Lung Compliance**: Static lung compliance (Cst) was determined as:

\[ Cst = \frac{V}{(P_{p pause} - P_E)} \]  

(Eq 3)

where \( P_{p pause} \) represents the pressure measured by the transducer in the expiratory circuit during a postexpiratory pause hold, ie, PEEP + auto-PEEP.

### Statistical Analysis

Both groups were similarly distributed with respect to age, sex, diagnoses, body mass index, and duration of mechanical ventilation. There were no changes in the patients’ clinical status (blood pressure, heart rate, temperature, or mental status) during the study. All the baseline ventilator and gas exchange parameters with the exception of PaCO₂ were similar in the two groups (Table 2). After 5 min of experimental ventilation, within each group, there was a change in the PaCO₂ and V̇Daw. The pH changed in the expected direction, although it was not statistically significant. After increased ventilation, the decreased V̇Daw resulted in a significant reduction in V̇pḢphys, whereas after decreased ventilation, there was an increase in V̇Daw and decrease in V̇Daw so that V̇pḢphys was nearly constant.

In the V̇CO₂ trend recording, each point (Fig 1) represents one breath, and is at a fixed frequency, proportional to the volume of tidal expired CO₂ corresponding to the area under the SBT-CO₂ (Fig 2). Similarly, each value from the trend recording of
ETCO₂ represents one breath.

After an increase in ventilation, ΔVCO₂/ΔVT was close to 1 at t₁ and fell to 0.3 at t₁+20 min. ΔETCO₂/ΔVT changed from −0.17 to −0.65 during the same period (Table 3). The course after a decrease in ventilation was similar to that after an increase up to and including t₁+5 min. Later the changes in both parameters were significantly slower after a step reduction of ventilation compared with a step increase (Table 4).

τ was normally distributed in either group only when calculated for the period up to t₁+20 min when it was 17.1 ± 9.9 min (mean ± SD) after increased ventilation compared with 35.1 ± 10.7 min after decreased ventilation. This difference is significant (p<0.05). τ at t₁+20 min in either group did not correlate with age, body mass index, sex, diagnoses, baseline compliance, and baseline PaCO₂. τ calculated over shorter periods after a change of ventilation was lower (p<0.001 by Friedman’s nonparametric test and Table 4). τ in both groups was similar up to t₁+5 min but longer after that in the group with decreased ventilation (p<0.001).

ΔVCO₂(t₀) calculated from data up to t₁+1 min correlated with ΔPaCO₂ determined after 20 min (r=−0.8). The correlation did not improve when ΔVCO₂(t₀) was calculated over periods longer than 1 min. Accordingly, ΔPaCO₂ after 20 min may be expressed in terms of either ΔVCO₂(t₀) or ΔVCO₂(t₁).

<table>
<thead>
<tr>
<th>ΔVCO₂ =±10%</th>
<th>Vt</th>
<th>ΔVCO₂/ΔVT</th>
<th>Vt</th>
<th>ΔVCO₂/ΔVT</th>
<th>Vt</th>
<th>ΔVCO₂/ΔVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>t₀</td>
<td>1.01 ± 0.3</td>
<td>t₁+1 min</td>
<td>0.97 ± 0.2</td>
<td>t₁+2 min</td>
<td>0.95 ± 0.3</td>
<td>t₁+5 min</td>
</tr>
<tr>
<td>Vt =−10%</td>
<td>ΔETCO₂/ΔVT</td>
<td>0.73 ± 0.6</td>
<td>ΔPaCO₂/ΔVT</td>
<td>0.74 ± 0.2</td>
<td>ΔETCO₂/ΔVT</td>
<td>0.53 ± 0.2</td>
</tr>
</tbody>
</table>

*Data are expressed as means ± SD.

**DISCUSSION**

Arterial blood gas analyses remain the mainstay for determination of optimal ventilator strategy in a modern critical care unit. The search for an optimal ventilator strategy, particularly in a patient with complex abnormalities, may involve a series of resettings that may be inefficient and time-consuming if each resetting is to be judged by a delayed blood gas result. During this wait, any change in patient status not related to the mode of ventilation may obscure the result of resetting. There is a need for an immediate assessment of gas exchange after ventilator resetting. Continuous intra-arterial fluoroptic
blood gas systems are being increasingly used to detect precipitous changes in cardiopulmonary function almost instantaneously. \(^1\) ETCO\(_2\), which has been used to monitor ventilation,\(^15\) has the advantage of being noninvasive. However, a number of studies show limitations of ETCO\(_2\) due to technical factors like concentration profiles, sample flow rates, and sample tube dimensions\(^6-18\) or patient-related factors such as the presence of intrinsic lung disease or a change in the arterial-ETCO\(_2\) gradient.\(^5,19\) The latter problem implies that a fall in ETCO\(_2\) may be caused by a desired decrease in PaCO\(_2\) or by a detrimental effect on the pulmonary circulation when it does not reflect an increased PaCO\(_2\).

VCO\(_2\) that is monitored breath by breath with the CO\(_2\) analyzer reflects at steady state the metabolic rate. Any change in effective alveolar ventilation will lead to a temporary deviation from this value. The CO\(_2\) dynamics after a change in the minute ventilation have been theoretically elucidated by Farhi and Rahn,\(^20,21\) Cherniack et al,\(^22\) and Henneberg et al.\(^23\) The events after a change of ventilation can be followed in a simplified version of their models (Fig 3). During steady state at rest, about 200 mL CO\(_2\) is cleared by the lungs every minute. This represents only 8% of the CO\(_2\) flux through the lungs. The important content of CO\(_2\) in the blood and the low extraction rate of CO\(_2\) in the lungs imply that an increase in minute ventilation by 10% leads to an in-

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### Table 4—\(\tau\) in the Two Groups During Different Durations of Calculation After \(t_1\)*

<table>
<thead>
<tr>
<th>Time, min</th>
<th>Increased Ventilation</th>
<th>Decreased Ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.65 (−3.55−17.80)</td>
<td>7.20 (3.50−13.87)</td>
</tr>
<tr>
<td>2</td>
<td>7.95 (5.27−13.62)</td>
<td>9.12 (5.53−17.92)</td>
</tr>
<tr>
<td>3</td>
<td>7.98 (5.58−15.02)</td>
<td>11.73 (7.90−19.27)</td>
</tr>
<tr>
<td>4</td>
<td>14.02 (7.93−21.53)</td>
<td>12.42 (9.80−22.15)</td>
</tr>
<tr>
<td>5</td>
<td>12.65 (8.93−19.35)</td>
<td>14.47 (10.08−21.48)</td>
</tr>
<tr>
<td>10</td>
<td>14.18 (10.57−18.85)</td>
<td>22.40 (17.17−38.15)</td>
</tr>
<tr>
<td>15</td>
<td>16.45 (12.13−19.12)</td>
<td>30.85 (22.75−43.92)</td>
</tr>
<tr>
<td>20</td>
<td>17.10 (11.07−23.05)</td>
<td>35.08 (27.98−43.62)</td>
</tr>
</tbody>
</table>

*Data are median (25th to 75th percentiles). \(^p<0.05\) intergroup comparison (by Mann-Whitney).

\(^p<0.001\) within-group comparison with the \(\tau\) value at 5 min (Wilcoxon matched-pairs signed ranks test).

\(^p<0.001\) intergroup comparison (by Mann-Whitney).

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**Figure 3.** A simplified model of CO\(_2\) dynamics after a change in ventilation in a normal subject. According to Fick’s principle, the CO\(_2\) eliminated by the lungs (VCO\(_2\)) is equal to the product of (CvCO\(_2\)−CaCO\(_2\)) and the cardiac output. Panel A represents the steady state. After a 10% increase in minute ventilation (B), VCO\(_2\) increases by 10% to 220 mL/min. According to Fick’s principle, arterial CO\(_2\) content falls by 4 mL/L to 476 mL/L. This modest reduction will be further dampened in the peripheral tissues where the total store of CO\(_2\) is about six times higher than in blood. As shown, venous CO\(_2\) content will change by only 0.1% during the first circulation time. The front of the first pass is depicted on the venous side. At a new steady state, all contents of CO\(_2\) will be reduced by 10% compared with panel A.
stantaneous and nearly proportionate increase in the \( VCO_2 \), i.e., about 20 mL/min. The immediate fall of alveolar, end-tidal, and arterial \( CO_2 \) will be trivial. During the first circulation time after a change in ventilation, the fall in arterial content of \( CO_2 \) (Ca-\( CO_2 \)) corresponds to only 0.8% of its initial value. The tissue stores of \( CO_2 \) will further dampen this fall. Accordingly, the venous content of \( CO_2 \) (Cv\( CO_2 \)) will fall by only 0.1% of its previous value during the first circulation time after the step change. The changes in Pa\( CO_2 \) and ETCO\(_2\) would be proportionate to \( VCO_2 \) only after a prolonged washout time of blood and tissue \( CO_2 \) stores while \( VCO_2 \) returns to the value corresponding to metabolic rate. This theoretical model forms the basic rationale for the use of the transient \( VCO_2 \) response in resetting the ventilator.\(^{7,11}\)

A detailed analysis of the \( CO_2 \) dynamics after a change of ventilation would need attention to pH changes. An increase of ventilation leads to alkalinization of body fluids that will buffer the changes in partial pressures of \( CO_2 \) and delay attainment of a new steady state.

The very first breaths after resetting represent the reaction time of the ventilator to the change of its function, dilution of alveolar gas, and probably a fast adaptation of pulmonary circulation to the new mean alveolar pressure. In addition, the \( VCO_2 \) signal is subjected to a filtering within the analyzer. Therefore, the first ten breaths after a change in ventilator settings were ignored and exponential regressions were fitted to data points from \( t_1 \) to \( t \) where \( \Delta VCO_2 \) would theoretically be smaller than true value if calculated at \( t_1 \) since \( \Delta VCO_2 \) decreases with time after a step change (Table 3). We corrected this by extrapolating the exponential backwards over ten breaths to \( t_0 \). Notably, determination errors or individual variation of \( \tau \) used in the extrapolation from \( t_1 \) to \( t_0 \) does not importantly affect the calculated value for \( \Delta VCO_2(t_0) \) because the extrapolation distance was small and the step change was as large as 10%. \( \Delta VCO_2(t_0) \) and \( \Delta VCO_2(t_1) \) gave similar results as predictors of \( \Delta PaCO_2 \). The advantages of the former appear accordingly only to be theoretical.

The results accorded closely with the theoretical model. In the present study, a proportionality equal to 1 between the change in PVC\(_2\) and the change in \( VT \) was observed at \( t_1 \). This proportionality could be observed for about 2 min after which a slow decrease toward baseline PVC\(_2\) became evident. ETCO\(_2\) and Pa\( CO_2 \), on the other hand, showed small initial changes. Nunn has shown that it takes half as much time for ETCO\(_2\) to stabilize after a step increase in ventilation compared with that after a step decrease.\(^{24-26}\) However, our data on PVC\(_2\) and ETCO\(_2\) indicate these time courses to be similar during the first 5 min and as expected according to the model.

A difference as shown by Nunn was seen in observations covering more than 5 min (Tables 3 and 4). This may be due to adaptive changes in vivo such as redistribution of perfusion to various body compartments and pH regulation. Clinical algorithms needed to generate and interpret ventilator resettings based on observation of \( \Delta VCO_2 \) could be similar for both step increases and decreases, since the important response after a step change should be observed during the initial minutes when the time course of stabilization is similar.

Progressively higher values of \( \tau \) over longer periods of time are in keeping with the multicompartmental model of \( CO_2 \) dynamics. It implies that the well-perfused body compartments equilibrate at higher rates than those poorly perfused. Theoretically, adaptive changes of perfusion could also play a role.

A prerequisite for proportionality between \( \Delta VCO_2 \) and \( \Delta VT \) at a change of ventilation is an almost constant ventilation/perfusion relationship that would leave physiologic dead space largely unchanged. This was so in our study population and in keeping with our intention to study patients in stable condition with no expected inadvertent reaction to a 10% change in ventilation. The reverse finding would indicate that a change in ventilation had somehow affected the ventilation/perfusion relationship in the lung, in which case better alveolar ventilation would not translate into a proportional \( \Delta VCO_2 \). However, even this situation would accurately sum up the cardiopulmonary and gas exchange status of that population.

V\(_{CO_2}\) is known to increase linearly with \( VT \) in studies with high-frequency ventilation.\(^{27}\) This transient linearity of V\(_{CO_2}\) has been used experimentally to tailor the ventilatory settings during high-frequency ventilation\(^{7,27}\) and during special modes of ventilation.\(^{28}\) The present study shows that V\(_{CO_2}\) does reflect the change in efficient alveolar ventilation within a minute of resetting a conventional ventilator in subjects in quasi-stable condition. It allows an adequate prediction of Pa\( CO_2 \) resulting from the change. However, when this technique is applied, one must ensure that simultaneous changes of parameters unrelated to ventilation do not occur. These include sudden onset of arrhythmias, spasm and shivering, and change of cardioprotective treatment. \( \Delta VCO_2/\Delta VT \) showed an important scatter around the mean value of 1 (Table 3). If this scatter is due to noise that is not proportional to V\(_{CO_2}\), it would make it difficult to detect a change of alveolar ventilation much below 10% in individual patients. While resetting a ventilator with a certain goal such as to decrease Pa\( CO_2 \) with this technique, one must accordingly make the step of a sufficiently large magnitude.
so that it results in a detectable change in \( V_C02 \).

The usefulness of \( ETC02 \) is limited by its inherently slow reaction to a change of alveolar ventilation. As seen in Figure 1, the shift from baseline is less discernible for \( ETC02 \) compared with \( \Delta V_C02(t_0) \). Furthermore it represents one point in the capnogram, whereas \( V_C02 \) represents the area under the curve in the SBT-\( C02 \). \( V_C02 \) thus incorporates and adds to the information provided by \( ETC02 \).

This study, done in a quasi-stable clinical population, shows \( V_C02 \) after a change of alveolar ventilation to behave as expected from theoretical models. Accordingly, it allows instant, cheap, and noninvasive determination of effective gas exchange provided that the step change in ventilation is sufficiently large. It could, in conjunction with noninvasive oximetry, provide rapid and reliable guidelines toward the utility of a change in ventilator settings.

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