Evaluation of the cardiopulmonary status using a noninvasive respiratory profile monitor in chronic obstructive lung disease patients during low-ventilation strategy

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**Background** Patients with chronic obstructive pulmonary disease (COPD) patients are susceptible to complications, especially volutrauma, during the period of mechanical ventilation; low ventilation is a safe strategy to avoid these complications. Noninvasive capnography is a suitable technique for monitoring and assessing the cardiac and the pulmonary status of these patients during the period of mechanical ventilation.

**Objectives** Assessment of the cardiac and the pulmonary status of two COPD patient groups receiving mechanical ventilation with a low tidal volume strategy using a noninvasive CO2 respiratory profile monitor (volumetric capnography).

**Patients and methods** Forty patients were recruited in the respiratory ICU of Abbassia Chest Hospital; these patients were divided into two groups: 20 COPD patients with the predominant pathology of chronic bronchitis (CB) and 20 patients with the predominant pathology of emphysema disease, who presented with clinical and radiological evidence of chronic obstructive lung disease and were in need of mechanical ventilation. All the patients in the study were followed up three times per day until weaning; data were recorded on admission, after 24 h and before weaning using volumetric capnography.

**Results** There was significant correlation between EtCO2 and arterial PCO2 during the whole period of mechanical ventilation in CB and emphysematous patients; the mean dead-space fraction was significantly higher in the emphysema group than in the CB group. There was a significant negative correlation between the mean values of VV/Vt and the pulmonary capillary blood flow on admission and after 24 h in the emphysema group. The mean cardiac output, the mean stroke volume, and the pulmonary capillary blood flow increased significantly before extubation in the CB group, in contrast to the emphysema group in which there was an insignificant difference.

**Conclusion** Volumetric capnography could be helpful in assessing the severity of functional disturbances, and the use of more refined noninvasive parameters will be of value in managing and monitoring COPD patients during the whole period of mechanical ventilation.

**Introduction** Invasive mechanical ventilatory support has two important considerations in respiratory failure caused by acute exacerbation of chronic obstructive pulmonary disease (COPD): they are minimizing regional overdistention and managing positive end-expiratory pressure (PEEP). Overdistention injury occurs when an excessive end-inspiratory alveolar ‘stretch’ physically damages alveolar structures and produces local and systemic inflammation (ventilator-induced lung injury). This stretch injury may be a consequence of excessive tidal volumes. This has led to recommendation to reduce tidal volumes (e.g. 5–7 ml/kg) to protect the lung in acute exacerbation of COPD [1]. Monitoring of the ventilated patient should focus on the assessment of patient response to and titration of mechanical ventilation, while avoiding complications [2]. The use of volumetric capnography in mechanically ventilated patients has the capability to monitor not only lung mechanics but also cardiac and respiratory interaction noninvasively [3].

**Patients and methods**

**Study design** Forty patients, who presented with clinical and radiological evidence of COPD with respiratory failure due to exacerbation and were in need of mechanical ventilation, were recruited in the respiratory ICU of Abbassia Chest Hospital in the period between 2011 and 2013. These patients were divided into two groups: 20 COPD patients with the predominant pathology of chronic bronchitis (CB) and 20 patients with the predominant pathology of emphysema disease; we used clinical criteria, clinical history with compatible physical findings, and evidence of hyperinflation on chest radiograph, in support of the diagnosis of COPD and for differentiation between
the two groups [4]. All patients were subjected to full history taking from a relative of the patient, clinical examination, chest radiography, computed tomography, ECG, echocardiography, and arterial blood gas measurement. Continuous infusion of midazolam and elective invasive mechanical ventilation and volumetric capnography monitoring were performed. All the patients in the study were followed up three times per day until weaning, and the data were recorded on admission, after 24 h and before weaning.

Monitoring
Variables measured included the cardiac output, the stroke volume, the pulmonary capillary blood flow (PCBF), EtCO₂, VCO₂, V̇/V̇̇, V̇̇̇/V̇̇̇̇, MV̇̇̇, Raw, PEEP, and compliance.

Data analysis
Analysis of data was performed using the Statistical Package for Social Sciences (SPSS version 15.0.1 for Windows; SPSS Inc., Chicago, Illinois, USA).

(1) Descriptive statistics:
   (a) Parametric data were expressed as range and mean ± SD.
   (b) Nonparametric data were expressed as frequency and percentage.

(2) Analytical statistics:
   (a) Paired t-test.
   (b) Independent sample t-test.
   (c) Analysis of variance test.

Results
Forty participants were chosen randomly. Twenty of them had CB: this group consisted of 85% men, with a mean age of 63.75 years; and 20 participants had emphysema: all of them in this group were men with a mean age of 59 years. CB patients in this study were successfully weaned from mechanical ventilation within 3–9 days, whereas emphysematous patients took longer (3–15 days). Tracheostomy operation was performed in 12.5% patients in the emphysematous group at a median time of 15 days from the beginning of mechanical ventilation; the main demographic data are illustrated in Table 1.

On admission, PO₂ in the CB group was significantly less than in the emphysema group with \( P \) value of 0.013 as shown in Fig. 1. Significantly better values of PH and PCO₂ were observed in the CB group than in the emphysema group after 24 h of mechanical ventilation, with \( P \) values of 0.014 and 0.009, respectively, as shown in Figs. 2 and 3.

In the CB group, there was significant improvement in the hemodynamic parameters during the whole period of mechanical ventilation with regard to blood pressure, pulse, and temperature. In the emphysema group, there were no significant differences in the hemodynamic parameters except for pulse, which showed significant improvement until trial of weaning. On comparison, there was no significant difference between the two groups.

| Table 1 Demographic data of the two groups (n = 20) | CB group | Emphysema group | \( P \) |
|-----------------------------------------------|---------|-----------------|-------|
| Sex [\( N \) (%)]                             |         |                 |       |
| Male                                          | 17 (85) | 20 (100)        | 0.22  |
| Female                                        | 3 (15)  | 0               |       |
| Age (years)                                   |         |                 |       |
| Range                                         | 53–86   | 45–79           | 0.13  |
| Mean ± SD                                     | 63.75 ± 10.06 | 59 ± 9.5     |       |
| Tracheostomy [\( N \) (%)]                    | 0       | 5 (25)          | 0.055 |
| Duration of MV (days)                         |         |                 |       |
| Range                                         | 3–9     | 3–15            | 0.0001|
| Mean ± SD                                     | 4 ± 1.5 | 8.1 ± 3.7       |       |

CB, chronic bronchitis; MV, mechanical ventilation.

Comparison between chronic bronchitis (CB) and emphysema groups regarding PO₂: a significant decrease was observed in PO₂ in the CB group compared with the emphysema group (\( t = 2.57, \ \( P = 0.013 \)).

Comparison between the two groups regarding PH after 24 h: a significant decrease in PH was observed in the emphysema group compared with the chronic bronchitis (CB) group (\( t = 2.86, \ \( P = 0.014 \)).
Regarding the cardiac parameters, pulmonary blood flow, cardiac output, and stroke volume, there was no significant difference between the two groups during the whole period of mechanical ventilation. At baseline in CB, the mean stroke volume and the cardiac index were 49.5 ml/beat and 2.43 l/min/m², respectively, and increased to 69.1 ml/beat ($P < 0.01$) and 3.1 l/min/m² ($P < 0.01$), respectively, before extubation; also, the mean PCBF level and the cardiac output were 3.6 and 5.2 l/min, respectively, at baseline compared with 4.2 l/min ($P < 0.05$) and 6.1 l/min ($P = 0.05$), respectively, before extubation. In emphysematous patients, only the stroke volume at baseline of 47.2 ml/beat increased significantly to 61.3 ml/beat ($P < 0.05$) before extubation as shown in Table 2.

On admission, the mean values of the dead-space fraction, the peak expiratory flow (PEF), and the PEEP measured among emphysema patients group were significantly higher than the values among patients in the CB group, with $P$ values of 0.000, 0.004, and 0.004, respectively, as shown in Fig. 4a, whereas the mean values of EtCO$_2$ and $V_t$ in the CB group were significantly higher than the values in the emphysema group, with $P$ values of 0.025 and 0.044, respectively, as shown in Fig. 4b.

After 24 h, the mean dead-space fraction, the PEF and the PEEP were significantly increased in the emphysema group compared with the CB group, with $P$ values of 0.000, 0.021, and 0.002, respectively, as shown in Fig. 5.

Before extubation, the mean dead-space fraction, the PEF, and the PEEP were significantly higher in the emphysema group than in the CB group, with $P$ values of 0.048, 0.015, and 0.002, respectively (Fig. 6).

With regard to the two groups studied, the end-tidal carbon dioxide was significantly correlated to the arterial partial pressure of carbon dioxide on admission, after 24 h and before extubation.

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### Table 2 Cardiac parameters of the chronic bronchitis and the emphysema groups by capnography

| Variables | Baseline (mean ± SD) | After 24 h (mean ± SD) | Before extubation (mean ± SD) | $P$  |
|-----------|----------------------|------------------------|-------------------------------|-----|
| **Chronic bronchitis** | | | |     |
| COP (l/min) | 5.25 ± 1.4 | 5.3 ± 1.3 | 6.1 ± 1.3 | 0.05 |
| SV (ml/beat) | 49.5 ± 14.8 | 54.6 ± 15.2 | 69.1 ± 16.5 | <0.01 |
| CI (l/min/m²) | 2.43 ± 0.5 | 2.5 ± 0.5 | 3.1 ± 0.7 | <0.01 |
| PCBF (l/min) | 3.6 ± 0.7 | 3.7 ± 0.8 | 4.2 ± 0.9 | <0.05 |
| **Emphysema** | | | |     |
| COP (l/min) | 5.3 ± 1.5 | 5.7 ± 1.2 | 5.4 ± 1.5 | >0.05 |
| SV (ml/beat) | 47.2 ± 17.8 | 59.3 ± 16.5 | 61.3 ± 16.9 | <0.05 |
| CI (l/min/m²) | 2.8 ± 0.7 | 2.8 ± 0.7 | 2.8 ± 0.8 | >0.05 |
| PCBF (l/min) | 3.7 ± 1.03 | 3.7 ± 0.9 | 3.5 ± 1.03 | >0.05 |

CI, cardiac index; COP, cardiac output; PCBF, pulmonary capillary blood flow; SV, stroke volume.
In the CB group, there was a highly significant negative correlation between the dead-space fraction and the cardiac output during all periods of mechanical ventilation. There was also a significant negative correlation between the two variables in the emphysema group on admission and after 24 h.

In the emphysema group, there was a highly significant negative correlation between dead-space fractions and PCBF on admission and it also had a significant negative correlation after 24 h (Tables 3–6).

**Discussion**

This study enrolled 40 COPD patients and differentiated them into two groups, according to the history, clinical findings, and radiological findings of each group: there were 20 COPD patients, with the predominant pathology of CB, and 20 patients with the predominant pathology of emphysema diseases. This selective methodology was partially in agreement with the methodology used by Farah and Makhoul [5], who enrolled COPD patients and dealt with them as one group without differentiating them into the CB and the emphysematous groups, but their study depended on history and clinical findings to diagnose the disease. Frazier et al. [6] measured the mean cardiac output by volumetric capnography, which was 5.3 l/min at baseline during mechanical ventilation and increased significantly to 6.5 l/min during the weaning trial by continues positive airway pressure (CPAP) trial ($P = 0.036$). These were in agreement with the results in the present study as there was a significant increase in the mean cardiac output measured by volumetric capnography of the CB group at baseline ($5.25 \pm 1.4$ l/min), which reached $6.1 \pm 1.3$ l/min before extubation, whereas in the emphysematous group, there was no significant difference between the two stages. In our study, the cardiac output of the two groups was recorded using the partial CO$_2$ rebreathing technique, which yielded a mean cardiac output at baseline of $5.25 \pm 1.4$ and $5.3 \pm 1.5$ l/min in the CB and the emphysematous groups, respectively. This coincides with the study of Jérôme et al. [7] which enrolled 20 consecutive mechanically ventilated patients who had acute respiratory distress syndrome (ARDS). They measured the cardiac output after a 2-h period of hemodynamic stability. The mean cardiac output value was $5.8 \pm 1.7$ l/min with the partial carbon dioxide rebreathing technique. Their study compared this method with thermodilution in which the mean cardiac output was $6.7 \pm 1.9$ l/min and there was significant correlation between the two methods. The mean stoke volume at baseline was $49.5 \pm 14.8$ and $47.2 \pm 17.8$ ml/beat, respectively, and increased significantly to $69.1 \pm 16.5$ and $61.3 \pm 16.9$ ml/beat in the CB and the emphysema groups, respectively, during weaning. These results were in agreement with Frazier et al. [6] who studied the hemodynamic function during baseline mechanical ventilation and during a trial of CPAP by the carbon dioxide rebreathing technique: the mean stroke volume was $52 \pm 36$ ml/beat at baseline during mechanical ventilation and increased significantly to $78 \pm 38$ ml/beat ($P < 0.001$) during the CPAP trial. The pulmonary blood flow was measured noninvasively by the partial
Table 3 Correlation between the end-tidal carbon dioxide and the arterial partial pressure of carbon dioxide

| \(\text{EtCO}_2/\text{PaCO}_2\) | On admission | After 24 h | Before extubation |
|----------------|-------------|-------------|-------------------|
| Chronic bronchitis | \(r\) | 0.7 | 0.9 | 0.8 |
| | \(P\) | 0.00 | 0.00 | 0.00 |
| Emphysema | \(r\) | 0.23 | 0.3 | 0.7 |
| | \(P\) | 0.3 | 0.1 | 0.00 |

Table 4 Correlation between external positive end-expiratory pressure and airway resistance

| External PEEP/Raw | On admission | After 24 h | Before extubation |
|-----------------|-------------|-------------|-------------------|
| Chronic bronchitis | \(r\) | −0.09 | −0.125 | −0.513 |
| | \(P\) | 0.66 | 0.58 | 0.021 |
| Emphysema | \(r\) | 0.12 | 0.14 | 0.33 |
| | \(P\) | 0.61 | 0.53 | 0.146 |

Table 5 Correlation between the dead-space fraction ratio \(V_d/V_t\) and the cardiac output

| \(V_d/V_t/\text{COP}\) | On admission | After 24 h | Before extubation |
|----------------|-------------|-------------|-------------------|
| Chronic bronchitis | \(r\) | −0.55 | 0.74 | −0.803 |
| | \(P\) | 0.008 | <0.0001 | <0.0001 |
| Emphysema | \(r\) | 0.59 | −0.48 | −0.12 |
| | \(P\) | 0.006 | 0.029 | 0.59 |

Table 6 Correlation between the dead-space fraction \(V_d/V_t\) and the pulmonary capillary blood flow

| \(V_d/V_t/\text{PCBF}\) | On admission | After 24 h | Before extubation |
|----------------|-------------|-------------|-------------------|
| Chronic bronchitis | \(r\) | 0.040 | 0.05 | −0.09 |
| | \(P\) | 0.86 | 0.8 | 0.69 |
| Emphysema | \(r\) | −0.6 | −0.5 | −0.1 |
| | \(P\) | 0.005 | 0.02 | 0.6 |

PCBF, pulmonary capillary blood flow.

\(\text{CO}_2\) rebreathing technique: the mean pulmonary blood flow was 3.6 ± 0.7 l/min in CB at baseline and it significantly increased before extubation to reach 4.2 ± 0.9 l/min, in contrast to the emphysema group, in which there was an insignificant difference, with a mean PBF of 3.7 ± 1.03 l/min at baseline and 3.5 ± 1.03 l/min before extubation. These results are in agreement with the study of Jérôme et al. [7], in which the mean value of PCBF was 4.6 ± 1.3 l/min by the carbon dioxide rebreathing technique. In this study, before extubation, the mean dead-space fraction measured by volumetric capnography in the emphysema group was 0.15 ± 0.1, which was significantly higher than that of the CB group (0.09 ± 0.06); this was in agreement with González-Castroa et al. [8] who enrolled 76 patients for mechanical ventilation, out of whom 14 patients were diagnosed to have COPD with exacerbation, nine patients were diagnosed to have pneumonia, and the remaining had other causes: the mean value of \(V_d/V_t\) in the 59 extubated patients was 0.48 ± 0.09, whereas in the 17 patients with failed extubation, the mean value of \(V_d/V_t\) was 0.65 ± 0.08. Our result demonstrated that the mean dead-space fraction measured by volumetric capnography on admission and before extubation reduced from 0.345 to 0.15, respectively, in the emphysema group, which was significantly higher than that of CB group, which was 0.14 and reduced to 0.09, respectively. These results were in agreement with Kallet et al. [9], who measured the ratio of the physiologic dead-space to tidal volume \(V_d/V_t\) with volumetric capnography before therapy with human recombinant activated protein C, and found a reduction in \(V_d/V_t\) from 0.55 to 0.27. In the present study, before extubation, there were two modes of weaning used: pressure support and \(T\) piece. There was no significant difference between the two modes between the two groups. The mean values of dynamic compliance were 41.05 and 43.00 ml/cmH\(_2\)O, the static compliance were 25.8 and 26.90 ml/cmH\(_2\)O, airway resistance was 24.30 and 26.75 cmH\(_2\)O/l/s, and the mean dead-space fraction values were 0.15 and 0.09 in the emphysema group and the CB group, respectively. These results were comparable to those of El Ghamrawy et al. [10] who used BIPAP compared with pressure support for the weaning of 32 COPD patients with acute respiratory failure. The respiratory system static, dynamic compliance, and the resistance were calculated by equations, but the ratio of dead-space to tidal volume was calculated automatically from capnography and displayed on the ventilator screen. They did not use the non-rebreathing \(\text{CO}_2\) monitor as in our study. The mean level of respiratory dynamic compliance with BIPAP was 21.8 ml/cmH\(_2\)O, which was significantly lower than its level with PS (25.0 ml/cmH\(_2\)O); the static compliance was 38.9 ± 11.3 ml/cmH\(_2\)O with BIPAP, which was insignificantly higher than its level with PS (39.3 ± 12.1 ml/cmH\(_2\)O); these values were less than our values, and this may be explained by the fact that they used the method of calculation. The mean level of resistance with bi-level positive air pressure (BIPAP) was 28.3 cmH\(_2\)O/l/s, which was significantly higher than the corresponding level with PS (22.8 cmH\(_2\)O); these values coincided with our result. The mean dead-space ventilation was 0.57 and 0.54 with BIPAP and PS, respectively, with no significant difference, but these results were slightly higher than our result. In the present study, the \(P(a-et)\) \(\text{CO}_2\) gradient decreased from 25.15 ± 13.6 on admission to 8.15 ± 6.2 before extubation in the emphysema.
group, and the \( P (a-eT) \) CO\(_2\) gradient decreased from 10.78 ± 10.84 to 5.35 ± 3.884 in the CB group. Defilippis et al. [11] studied the \( P (a-eT) \) CO\(_2\) gradient in 20 patients with severe dyspnea and hypercapnia undergoing noninvasive ventilation. The \( P (a-eT) \) CO\(_2\) gradient was measured at subsequent times: T0 (admission) was 60.7 ± 17.7 mmHg; it decreased progressively, reaching 8.4 ± 8 mmHg at T6 h and 4.7 ± 6.7 mmHg at T12 h, which was lower than the baseline value. A positive correlation was found between EtCO\(_2\) and PaCO\(_2\) values \((r = 0.89, P = 0.001)\). In the present study, with regard to the CB group, EtCO\(_2\) was significantly correlated to PaCO\(_2\) on admission \((r = 0.7, P = 0.00)\), after 24 h \((r = 0.9, P = 0.00)\), and before extubation \((r = 0.8, P = 0.00)\); however, in the emphysema group, the EtCO\(_2\) was significantly correlated to the PaCO\(_2\) only before extubation \((r = 0.7, P = 0.00)\). These results were in agreement with Yosefy et al. [12], who enrolled 73 patients in their study. The medical diagnosis included 55–75.3% patients with pulmonary edema, 14–19.2% patients with exacerbation of COPD, and 4–5.5% patients with exacerbation of bronchial asthma. Significant correlation was found between EtCO\(_2\) and arterial PCO\(_2\) \((r = 0.792)\). Razi et al. [13] confirmed a good correlation between the mean of EtCO\(_2\) and PaCO\(_2\) in each of the modes of SIMV, CPAP, and T-tube between EtCO\(_2\) tensions with PaCO\(_2\) measurements in mechanically ventilated patients with the following correlation coefficients and \(P\) values: SIMV \((r = 0.893, P < 0.0001)\), CPAP \((r = 0.841, P < 0.0001)\), and T-tube \((r = 0.923, P < 0.0001)\), respectively. In the present study, in the emphysematous group, there was a highly significant negative correlation between the mean values of dead-space fractions \(V/d/V\) at admission \((3.7 ± 1.03)\) and after 24 h. These results were in agreement with the result of Tusman et al. [14] who tested whether the \(V/d/V\) can detect states of low PBF in a noninvasive manner. Fifteen patients who had undergone cardiopulmonary bypass (CPB) were studied. During constant ventilation, volumetric capnography was performed and the \(V/d/V\) was recorded. Before CPB, \(V/d/V\) was 0.36 ± 0.05. During weaning from CPB, \(V/d/V\) decreased with increasing PBF. At CPBs of 80, 60, 40, and 20%, \(V/d/V\) values were 0.64 ± 0.06, 0.55 ± 0.06, 0.47 ± 0.05, and 0.40 ± 0.04, respectively \((P < 0.001)\). After CPB, \(V/d/V\) values were similar to that at baseline \((0.37 ± 0.04)\).

Traditional approaches to mechanical ventilation use tidal volumes of 10 to 15 ml/kg of body weight, which result in volutrauma [15]. A prospective cohort of 361 ICUs from 20 countries with a total of 5183 mechanically ventilated patients with limited tidal volumes 6–8 ml/kg were included in the study. This study found that barotrauma was present in 2.9% of the patients with COPD, 6.3% of the patients with asthma, 10.0% of the patients with chronic interstitial lung disease, 6.5% of the patients with acute respiratory distress syndrome, and 4.2% of the patients with pneumonia [16]. In the present study, barotrauma was not recorded in 40 patients in whom the low-ventilation strategy was used.

**Conclusion**

Low ventilation is a safe strategy to avoid complications such as volutrauma and barotrauma. Noninvasive capnography is a simple and safe bedside method for noninvasive estimation of pulmonary and cardiac parameters for monitoring COPD patients during the period of mechanical ventilation. There was significant correlation between EtCO\(_2\) and arterial PCO\(_2\) throughout the period of mechanical ventilation in CB and emphysematous patients; hence, monitoring PetCO\(_2\) provided a good noninvasive assessment of hypercapnic episodes during weaning from mechanical ventilation. The \( P (a-eT) \) CO\(_2\) gradient decreased before extubation in emphysematous and CB patients, and this indicates a change in perfusion to help with weaning. The mean dead-space fraction was significantly higher in the emphysema group than in the CB group throughout the period of mechanical ventilation. Also, there was a significant negative correlation between the mean values of dead-space fractions \(V/d/V\) and the PCBF in the emphysematous patients. Hence, early and repeated measurements of the pulmonary and the cardiac function by this monitor could provide clinicians with valuable information for prognosis and disease monitoring.

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**Conflicts of interest**

There are no conflicts of interest.

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