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Correlation of End-Tidal Carbon Dioxide with Arterial Carbon Dioxide in Mechanically Ventilated Patients

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Background: Patients undergone mechanical ventilation need rapid and reliable evaluation of their respiratory status. Monitoring of End-tidal carbon dioxide ($ETCO_2$) as a surrogate, noninvasive measurement of arterial carbon dioxide ($PaCO_2$) is one of the methods used for this purpose in intubated patients.

Objectives: The aim of the present trial was to study the relationship between end-tidal CO_2 tensions with $PaCO_2$ measurements in mechanically ventilated patients.

Materials and Methods: End-tidal carbon dioxide levels were recorded at the time of arterial blood gas sampling. Patients who were undergoing one of the mechanical ventilation methods such as: synchronized mandatory mechanical ventilation (SIMV), continuous positive airway pressure (CPAP) and T-Tube were enrolled in this study. The difference between $ETCO_2$ and $PaCO_2$ was tested with a paired t-test. The correlation of end-tidal carbon dioxide to ($ETCO_2$) CO_2 was obtained in all patients.

Results: A total of 219 arterial blood gases were obtained from 87 patients (mean age, 71.7 ± 15.1 years). Statistical analysis demonstrated a good correlation between the mean of $ETCO_2$ and $PaCO_2$ in each of the modes of SIMV, CPAP and T-Tube; SIMV (42.5 ± 17.3 and 45.8 ± 17.1; r = 0.893, $P < 0.0001$), CPAP (37 ± 9.7 and 39.4 ± 10.1; r = 0.841, $P < 0.0001$) and T-Tube (36.1 ± 9.9 and 39.4 ± 11; r = 0.923, $P < 0.0001$), respectively.

Conclusions: End-tidal CO_2 measurement provides an accurate estimation of $PaCO_2$ in mechanically ventilated patients. Its use may reduce the need for invasive monitoring and/or repeated arterial blood gas analyses.

▸ *Implication for health policy/practice/research/medical education:*

Substitution of $ETCO_2$ monitoring as a noninvasive assessment of mechanical ventilation instead of $PaCO_2$ measurement which is an invasive assessment of mechanical ventilation.

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1. Background

End-tidal CO_2 monitors are used to estimate arterial CO_2 pressure ($PaCO_2$), but appropriate use of this noninvasive method of assessing blood gases in ventilated patients remains unclear. It has been used extensively in operating rooms, intensive care units, emergency departments and in pre-hospital setting (1-4). In a study that was conducted by Flanagan *et al.*, end-tidal CO_2 measurement provided

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an accurate estimation of $PaCO_2$, even during episodes of severe hypocarbia (5). One study indicated that measurements of end-tidal carbon dioxide concentrations correlated well with $PaCO_2$ values in non-intubated patients presenting with a variety of conditions to emergency departments (6). End-tidal carbon dioxide measurements may be sufficient measures of $PaCO_2$ in selected patients and obviate the need for repeat arterial blood gas determination. In a study that was carried out in ventilated head trauma patients, end-tidal $PaCO_2$ monitoring correlated well with $PaCO_2$ in patients without respiratory complications or without spontaneous breathing (7). However, its clinical validity is questionable in patients who have the greatest need for end-tidal $PaCO_2$ monitoring (i.e., patients who have respiratory distress or who are breathing spontaneously and overriding the ventilator). Noninvasive end-tidal carbon dioxide pressure ($ETCO_2$) monitoring may adequately predict $PaCO_2$ in non-intubated emergency department patients with respiratory distress, who are able to produce a forced expiration (8). $ETCO_2$ is a less accurate measure of $PaCO_2$ with tidal volume breathing and in patients with pulmonary disease. $PaCO_2$ cannot be estimated by the $ETCO_2$ method in a pre-hospital setting (9). There is wide variation in the gradient between $PaCO_2$ and $ETCO_2$ depending on the patient's condition, and this relationship does not remain constant over time, thus it is not useful in pre-hospital ventilation management. These data do not support routine monitoring of end-tidal CO_2 during short transportation times in adult patients requiring mechanical ventilation. However, the monitor may prevent morbidity in patients requiring tight control of $PaCO_2$ (10). One study reported that, $PaCO_2$ gives a poor estimate of $PaCO_2$ in patients with respiratory failure (11). In another study, that was carried out in mechanically ventilated patients with multisystem trauma, trends in the arterial to end-tidal carbon dioxide gradient magnitude were not reliable, and concordant direction changes in $ETCO_2$ and $PaCO_2$ are not assured (12).

2. Objectives

The aim of the present trial was to study the relationship between end-tidal CO_2 tensions with $PaCO_2$ measurements in mechanically ventilated patients.

3. Materials and Methods

This was a cross-sectional study conducted on 219 arterial blood gases in 87 adult patients with respiratory failure admitted to the Intensive Care Unit (ICU) of Shahid Beheshti Hospital, Kashan University of Medical Sciences, Iran, between March 2008 and February 2010. The mean age of the patients was 71.7 ± 15.1 years, 46 of the patients were male, and 43 were female. The study was approved by the local hospital Ethics Committee and informed consent was obtained. Blood samples were drawn by radial arterial puncture. Samples were immediately analyzed for $PaCO_2$ using a blood gas analyzer (AVL-995, AVL Medical Instruments, Graz, Austria). The arterial to end-tidal CO_2 gradient was determined. The $ETCO_2$ was measured using an end-tidal CO_2 analyzer (CAPNOGARD, Respironics, California, Inc. Carisbad, CA, USA), on the expiratory side of the circuit's endotracheal tube connector. After proper calibration and an equilibration time of 20 minutes with stable hemodynamic and respiratory variables, $ETCO_2$ were determined and the highest reading was recorded. Patients who were undergoing one of the mechanical ventilation methods such as; synchronized intermittent mandatory ventilation (SIMV), continuous positive airway pressure (CPAP) and T-Tube were enrolled in this study. The Mean ± SD of $PaCO_2$, $ETCO_2$ values and $PaCO_2$ - $ETCO_2$ gradients in all of the three groups were determined. The correlation between $PaCO_2$ and $ETCO_2$ in one of three modes of ventilation, SIMV, CPAP or T-tube, was done using linear regression. Paired t-test and a Kruskal-Wallis test were used to compare the gradients between $PaCO_2$, and $ETCO_2$ in each of the SIMV, CPAP and T-tube conditions. Data are presented as Mean ± SD. $P < 0.05$ was considered to indicate a significant difference.

4. Results

A total of 219 arterial blood gases were obtained from the 87 patients. The patients were ventilated with SIMV for 97 (44.3%) gas measurements, CPAP with support pressure for 70 (32%), and T-tube for 52 (23.7%). Statistical analysis demonstrated a good correlation between the mean of $ETCO_2$ and $PaCO_2$ in each of the modes of SIMV, CPAP and T-Tube; SIMV (42.5 ± 17.3 and 45.8 ± 17.1; r = 0.893, $P <$ 0.0001), CPAP (37 ± 9.7 and 39.4 ± 10.1; r = 0.841, $P < 0.0001$) and T-Tube (36.1 ± 9.9 and 39.4 ± 11; r = 0.923, $P < 0.0001$), respectively (*Table 1*). In each of these modes the $ETCO_2$ was generally lower than the $PaCO_2$. The mean difference between the arterial to end-tidal carbon dioxide tension gradients were measured in each of the modes, SIMV, CPAP and T-Tube (*Table 2*). A positive correlation between

Table 1. Comparison of $PaCO_2$ with $ETCO_2$ in Patients with Various Modes of Ventilation

	$PaCO_2$ [a], Mean ± SD	$ETCO_2$ [a], Mean ± SD	R	R^2	*P* value
Ventilation Setting					< 0.0001
SIMV [a] (n = 97)	45.8 ± 17.1	42.5 ± 17.3	0.893	0.798	
CPAP [a] (n = 70)	39.4 ± 10.1	37 ± 9.7	0.841	0.707	
T-tube [a] (n = 52)	39.4 ± 11	36.1 ± 9.9	0.923	0.852	

[a] Abbreviations: $PaCO_2$, partial arterial carbon dioxide tension; $ETCO_2$, end-tidal carbon dioxide; SIMV, synchronized mandatory mechanical ventilation; CPAP, continuous positive airway pressure

$PaCO_2$ and $ETCO_2$ was found with each of the SIMV, CPAP and T-tube modes, indicating statistical significance (*Figure 1, Figure 2* and *Figure 3*).

The relationship between $PaCO_2$ (mmHg) and $ETCO_2$ (mmHg) in CPAP mechanically ventilated patients is shown in *Figure 2*. There is a significant correlation (r = 0.841, $P < 0.0001$). The relationship between $PaCO_2$ (mmHg) and $ETCO_2$ (mmHg) in T-Tube ventilated patients is shown in *Figure 3*. There is a significant correlation (r = 0.923, $P < 0.0001$).

Table 2. Comparison of Mean Difference between $PaCO_2$ and $ETCO_2$ in Three Different Modes of Ventilation

	$PaCO_2$ [a] - $ETCO_2$ [a], Mean ± SD	95% CI
SIMV [a] (n = 97)	3.37 ± 7.93	1.77 - 4.97
CPAP [a] (n = 70)	2.32 ± 5.62	0.98 - 3.67
T-tube [a] (n = 52)	3.31 ± 4.26	2.13 - 4.50

[a] Abbreviations: $PaCO_2$, partial arterial carbon dioxide tension; $ETCO_2$, end-tidal carbon dioxide; SIMV, synchronized mandatory mechanical ventilation; CPAP, continuous positive airway pressure

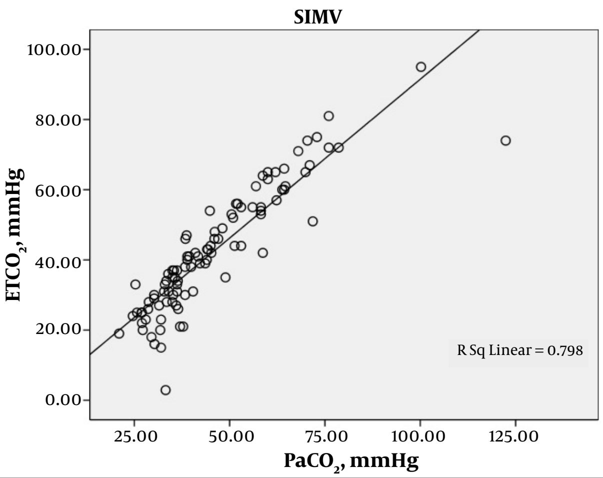

Figure 1. Relationship between $PaCO_2$ (mmHg) and $ETCO_2$ (mmHg) in SIMV Mechanically Ventilated Patients, Showing a Significant Correlation (r = 0.893, $P < 0.0001$)

5. Discussion

Our results clearly show a strong correlation between arterial $PaCO_2$ and $ETCO_2$ in critically ill patients undergoing mechanical ventilation, and it provides a clinically reliable estimate of ventilation levels. Measurements of $ETCO_2$ is an accepted standard of care for the monitoring of mechanically ventilated patients and this is often used during the ventilation of critically ill patients with respiratory failure (13). In healthy subjects there are close correlation between $PaCO_2$ and $ETCO_2$, and it is commonly accepted that $PaCO_2$ measurements vary approximately 2-5 mmHg above $ETCO_2$ values (14). Generally, $PaCO_2$ is expected to exceed $ETCO_2$ levels. Some studies have reported the correlation between $ETCO_2$ and $PaCO_2$ among ventilated patients and critical states (7, 13). Generally, $ETCO_2$ measurements are affected by $PaCO_2$ levels, dead space fraction, and pulmonary perfusion. $ETCO_2$ is dependent on alveolar CO_2 ($PACO_2$) and the site of sampling. Non-uniform alveoli CO_2 emptying patterns, in patients with large ventilation perfusion result in mismatching $PACO_2$, and underestimation of $PaCO_2$ levels (13). A high ventilation/perfusion ratio and dead space tends to cause low $ETCO_2$ levels relative to $PaCO_2$, whereas a low ventilation/perfusion ratio and shunt has little effect on causing a smaller $ETCO_2$ measure relative to $PaCO_2$. Among critically ill patients, increased intrapulmonary shunting from pulmonary parenchymal disease is relatively common. Yamanaka *et al.*, reported that an admixture of this blood into the arterial circulation contributes to increased $ETCO_2 - PaCO_2$ gradients (11). This increase may be up to 20 mmHg in patients with severe pulmonary or major systemic disease. In other words, $ETCO_2$ monitoring tends to underestimate $PaCO_2$ levels. In a study that was conducted by Sivan *et al.*, these discrepancies started to occur be-

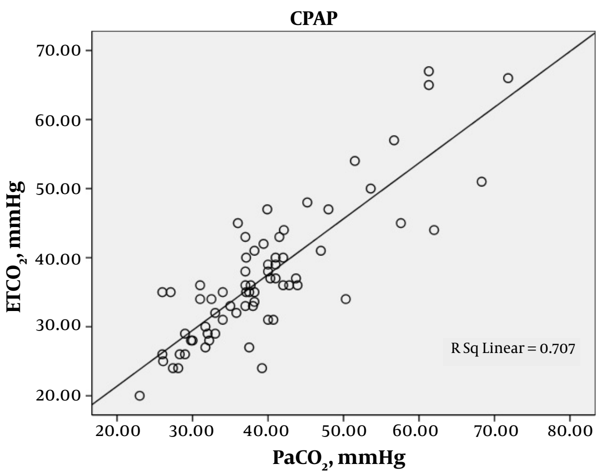

Figure 2. Relationship between $PaCO_2$ (mmHg) and $ETCO_2$ (mmHg) in CPAP Mechanically Ventilated Patients, Showing a Significant Correlation (r = 0.841, $P < 0.0001$)

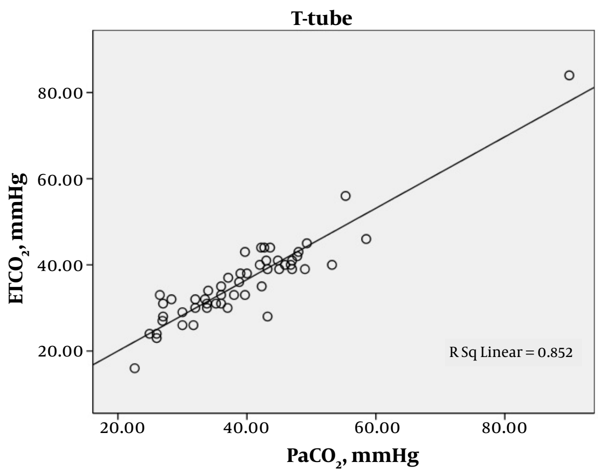

Figure 3. Relationship between $PaCO_2$ (mmHg) and $ETCO_2$ (mmHg) in T-Tube Ventilated Patients, Showing a Significant Correlation (r = 0.923, $P < 0.0001$)

low a PaO_2/PAO_2 ratio of 0.3 (15). Although $ETCO_2$ measurements have been identified as an invaluable tool to monitor airway patency and confirm endotracheal intubation, recent studies have suggested that it may also be used to guide ventilation as a surrogate measure of $PaCO_2$ (16). Previous studies have shown conflicting results concerning the correlation between $PaCO_2$ and $ETCO_2$ in different clinical settings. McDonald *et al.,* concluded that $ETCO_2$ correlates with $PaCO_2$ in critically ill patients undergoing conventional ventilation via an endotracheal tube and provides a clinically reliable estimate of ventilation (r^2 = 0.716 and $P < 0.001$) (17). In their study $ETCO_2$ (39.9 ± 12.7 mmHg) was lower than the $PaCO_2$ (45.5 ± 14.1 mmHg). In the current study the values of $ETCO_2$ and $PaCO_2$ overall in the patients were 39.2 ± 13.9 mmHg versus 42.2 ± 14.1 mmHg. Kerr et al., reported that $ETCO_2$ and $PaCO_2$ correlated well (r^2 = 0.77) in adults with traumatic brain injury, who did not have lung disease (defined as positive end-expiratory pressure of < 5 cm/H_2O), however, they did not correlate when a lung injury was present (7). Good correlation was also observed in a study that included adults with and without lung disease (18). Barton *et al.,* also reported that measurements of end-tidal carbon dioxide concentrations correlate well with $PaCO_2$ values in non-intubated patients presenting with a variety of conditions to the emergency room (6). End-tidal carbon dioxide measurements may be sufficient measures of $PaCO_2$ in selected patients and obviate the need for repeated arterial blood gas determination (6). Tobias and Meyer, concluded that measurement of transcutaneous CO_2 was a more accurate predictor of $PaCO_2$ than $ETCO_2$ (19). The difference between transcutaneous CO_2 and $PaCO_2$ was less than the difference between $ETCO_2$ and $PaCO_2$, 2.3 ± 1.3 mmHg versus 6.8 ± 5.1 mmHg (19). Continuous monitoring of SpO_2 (saturation of peripheral oxygen) and $ETCO_2$ can be used to wean patients safely and effectively after coronary artery bypass grafting. $ETCO_2$ was a good indicator of $PaCO_2$ (r = 0.76), its sensitivity to detect hypercarbia ($PaCO_2$ less than 45 mmHg) was 95% (20). In a study that was conducted on anesthetized, mechanically ventilated patients, transcutaneous monitoring of CO_2 partial pressure gave a more accurate estimation of $PaCO_2$ than $ETCO_2$ monitoring (r^2 = 0.73, and 0.50 respectively) (21). Weinger and Brimm measured arterial to end-tidal carbon dioxide gradient values of 4.24 ± 4.42 mmHg during intermittent mandatory ventilation (22). They reported good correlation between $ETCO_2$ and $PaCO_2$ in 25 adults with and without pulmonary disease (22). In patients without lung disease, ventilated either mechanically or spontaneously via a tracheal tube, the arterial to end-tidal carbon dioxide gradient values were 0.8-3.5 mmHg (23, 24). In the present study the difference between $PaCO_2$ and $ETCO_2$ in each of the SIMV, CPAP, and T-tube modes of the ventilator were; 3.37 ± 7.93 mmHg, 2.32 ± 5.62 mmHg, and 3.31 ± 4.26 mmHg, respectively. The objective of our study was to show that monitoring of $ETCO_2$ provides a clinically useful and effective method for assessing ventilation. Several studies have indicated a poor correlation of $ETCO_2$ with $PaCO_2$ in an emergency setting (9, 25, 26). Russell and Graybeal, reported that in mechanically ventilated neurointensive care patients, there is significant variability in the relationship between $PaCO_2$ and $ETCO_2$ (27). The $ETCO_2$ – $PaCO_2$ gradients were reported as 6.9 ± 4.4 mmHg. In another study that was conducted by Russsell *et al.,* during intraoperative craniotomies, this value was reported to be 7.2 ± 3.3 mmHg (28). They concluded that $ETCO_2$ may not provide a statistically stable estimation of $PaCO_2$ in mechanically ventilated neurosurgical patients undergoing craniotomies (28). Patients with respiratory failure and multisystem trauma have a much wider difference of 14 ± 11 mmHg (12). In a recent report, Warner *et al.,* evaluated 180 intubated patients with isolated traumatic brain injury and demonstrated a poor correlation between $ETCO_2$ and $PaCO_2$ (r^2 = 0.277) (29). In another study, in spite of a good correlation between $ETCO_2$ and $PaCO_2$ (r = 0.78, $P < 0.001$) in 20 intubated patients with respiratory failure, the changes in delta ETCO2 did not correlate as well with delta $PaCO_2$ (r = 0.58, $P \leq 0.001$) (30). The results of another study indicated that hypercapnia may be underestimated when $ETCO_2$ is substituted for $PaCO_2$ in patients breathing spontaneously via a cuffed oropharyngeal airway (31). Belpomme *et al.,* concluded that in a pre-hospital setting, $PaCO_2$ cannot be estimated by $ETCO_2$ levels (9). Moreover, there is a wide variation in the gradient between $PaCO_2$ and $ETCO_2$ depending on the patient's condition, and over time, this relationship does not remain constant and thus it is not useful in pre-hospital ventilation management (9). In a study that was conducted on hyperventilated neurosurgical patients, the values of $ETCO_2$ showed a moderately acceptable correlation with $PaCO_2$ measurements. However, changes in end-tidal carbon dioxide values failed to correlate with simultaneous changes in arterial carbon dioxide tension measures (32). Palmon *et al.,* compared two groups of patients as no-monitor and monitor-blind groups that were under controlled with a capnograph during transport (10). The results of their study do not support routine monitoring of end-tidal CO_2 during short transport times in adult patients requiring mechanical ventilation. However, the monitor may prevent morbidity in patients requiring tight control of $PaCO_2$ (10). Kavanagh *et al.*, found poor correlation between end-tidal and arterial $PaCO_2$, as well as poor correlation between transcutaneous and arterial $PaCO_2$ in extubated, spontaneously breathing patients recovering from general anesthesia (33). In conclusion, end-tidal CO_2 measurement provides an accurate estimation of $PaCO_2$ in mechanically ventilated patients. $ETCO_2$ monitoring in adult ventilated patients may be a useful tool in their management. Its use may limit the need for invasive monitoring and/or repeated arterial blood gas analyses. The results of this study shows that $ETCO_2$ monitoring accurately reflects $PaCO_2$ during mechanical ventilation. A comparison of mean differences between $PaCO_2$ and $ETCO_2$ in three different modes of ventilation did not show any statistical significance. Additional studies in relation to the efficiency of CO_2 monitoring during various phases of mechanical ventilation are recommended.

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Authors' Contribution

Ebrahim Razi (Study design and method), Gholam Abbass Moosavi (statistical analysis), Keivan Omidi (Data collection), Ashkan Khakpour Saebi (Data collection) and Armin Razi (Draft writing).

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