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$ETCO_2$ $PaCO_2$ Gradient and its Correlation with Chest Radiographic Findings in Mechanically Ventilated Patients

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Abstract

Context: There exists a deficiency in literature regarding the impact of chest radiographic findings on $PaCO_2$ $ETCO_2$ gradient. *Aim*: To evaluate $PaCO_2$ $ETCO_2$ gradient and it's correlation with chest radiographic findings, in mechanically ventilated patients. *Materials and Methods:* A prospective observational study was undertaken on mechanically ventilated adult patients, at an Indian Emergency department. Minimum sample size was 151, derived through a pilot study, with a power of 80% and 95% confidence. Arterial blood gas samples were collected, one each, from selected patients, analyzed and $PaCO_2$ recorded. Highest $ETCO_2$ values and chest radiographic findings, also recorded simultaneously. Mean $ETCO_2$ and $PaCO_2$ values were compared with chest radiographic findings for radiopaque and radiolucent CXR groups. $ETCO_2$ $PaCO_2$ gradient was analyzed using unpaired Student t test, and $ETCO_2$ $PaCO_2$ correlation using Pearson's correlation coefficient. p value <0.05 was accepted as statistically significant. *Results*: Mean age of study group was 54.15 ± 17.714 years. Mean $PaCO_2$ was significantly elevated in the radiopaque CXR group (55.03 ± 25.70)mmHg , than radiolucent CXR group (39.46 ± 14.77)mmHg, p <0.001. Mean $ETCO_2$ showed no significant variations between the two groups (p 0.261). $ETCO_2$ $PaCO_2$ gradient in radiolucent CXR and radiopaque CXR respectively were (0.741 ± 5.77, p<0.001) and (13.28 ± 17.93; p < 0.001). A more statistically significant and promising correlation between arterial $PaCO_2$ and $ETCO_2$ values were obtained in radiolucent CXR (r= 0.928, p< 0.001) as compared to radiopaque CXR (r=0.718, p<0.001). *Conclusion*: $ETCO_2$ values can reliably predict $PaCO_2$, in mechanically ventilated patients with radiolucent chest radiographs.

Keywords: End tidal Carbon Dioxide monitoring; Arterial partial pressure of carbon dioxide; Mechanical ventilator; Radiopaque chest X-Ray and radiolucent chest X-Ray.

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Introduction

Background/Rationale

End-tidal carbon dioxide ($ETCO_2$), measures the concentration of carbon dioxide in exhaled air at the end of expiration; expressed as partial pressure in mmHg ($PETCO_2$) measured through capnography, utilizing the selective absorption property of specific wavelength of infrared radiation by the CO_2 gas. Sudden changes in systemic CO_2 levels are reflected in $ETCO_2$ readings, making capnography an important tool for monitoring early ventilatory

or circulatory compromise. With normal pulmonary blood flow and alveolar ventilation, the $ETCO_2$ levels approximate $PaCO_2$ levels, i.e. 35-45 mmHg. A decreased cardiac output leads to decreased pulmonary perfusion and thereby decreased $ETCO_2$.[1]

End tidal CO_2 measurements have shown excellent correlation with arterial $PaCO_2$ values, in studies conducted on ventilated pediatric and adult patients without pulmonary diseases and respiratory complications. The variation between the two, varied from 0.8 to 4.24 ± 4.42 mmHg in patients with normal lung, indicating that $ETCO_2$ values can reliably predict $PaCO_2$ values in such cases.[2–5] In patients with diseased lungs the variation ranged from 3.3 mmHg to 10 mmHg or above.[2,5]

But when it comes to clinical practice, physicians would very often notice that $ETCO_2$ readings are found to be unreliable in estimating arterial $PaCO_2$, especially in those with chest radiopacity. There is often, a necessity for repeated arterial blood gas sampling for assessment of the ventilatory status of mechanically ventilated patients, which often becomes a cumbersome and painful procedure, especially if an arterial line is not placed. This situation prompted us to undertake this specific study incorporating chest radiographic findings in conjunction with $PaCO_2$ $ETCO_2$ gradient to find out any possible correlation with the two. Ours is a pilot study.

Objectives

The primary objective of the study is to ascertain the correlation between $PaCO_2$ $ETCO_2$ gradient, and chest radiographic findings on lung field clarity. The secondary objective is to identify the relationship of mean $ETCO_2$ and mean $PaCO_2$ values with chest radiographic findings. We hypothesized that $PaCO_2$ and $ETCO_2$ values correlate well in all mechanically ventilated patients, irrespective of their chest radiographic status.

Materials and Methods

Study design

A prospective observational study on mechanically ventilated patients. The study was approved by the hospital ethics committee.

Setting

The study was conducted between September 2015 and February 2019 at the Emergency Medicine department and Emergency Intensive Care Unit (ICU) of an Indian Medical College Hospital with an annual emergency department patient load of around 50,000.

Participants

Randomly selected 151 mechanically ventilated patients in the age group 30 to 80 years admitted in the emergency department regardless of the gender, hemodynamic status, diagnosis or ventilator parameters were included in the study. Exclusion criteria: 24 Patients who were either pregnant and those with pneumothorax and those having inadequately exposed chest radiographs were excluded.

Variables

Quantitative variables - End tidal carbon dioxide concentration ($ETCO_2$), Arterial Partial pressure of carbon dioxide ($PaCO_2$). Measured in mmHg.

Qualitative variable - chest radiographic finding (documented as radiopaque or radiolucent).

Derived variable – ($PaCO_2$ – $ETCO_2$) for both radiolucent and radiopaque chest Xrays.

Data sources/measurement

Blood samples were collected through radial or femoral arterial punctures, maintaining sterile precautions. Samples were immediately analyzed for $PaCO_2$ using a pre-calibrated blood gas analyzer (Radiometer ABL800 FLEX) and results recorded. The $ETCO_2$ was measured using a side stream end-tidal CO_2 analyzer (Nihon Kohden, Cap-STAT OLG-2800), adjusted at low aspiration flow rate (50 ml min^{-1}) that will minimize dispersion of gases in the sampling tube, as well as avoids aspiration of condensed water and secretions, preventing occlusion issues. Precalibrated equipment was connected to the expiratory port of the circuit's endotracheal tube. After an equilibration time of 10 minutes, $ETCO_2$ was determined and the highest reading recorded. Then, portable chest X-Rays of the patients were taken, analyzed and classified as radiolucent CXR /radiopaque CXR, based on x ray absorption features.

Bias

The staff nurses as well as the emergency medical technicians during the respective shifts, gathered blood for arterial blood gas analysis and handed over to the principal investigator. The respective emergency physicians (on duty) reported the $ETCO_2$ values as well as the chest radiographic findings to the principal investigator, to reduce

observer bias. All data collectors were blinded to the study objective.

Study size

Absence of similar previous studies prompted us to undertake a pilot study on 20 randomly selected from 302 mechanically ventilated patients admitted in the emergency department. $ETCO_2$ $PaCO_2$ gradient ($PaCO_2$ minus $ETCO_2$) in radiolucent chest X-Ray was determined to be (4.78 ± 15.7)mmHg and (12.28 ± 28.3)mmHg in radiopaque chest X-Ray, based on which, the minimum sample size was determined as 151 (with a power of 80% and 95% confidence).

Quantitative variables

Both the quantitative variables - $ETCO_2$ as well as $PaCO_2$ values were recorded in mmHg, for all the patients and the difference ($PaCO_2$-$ETCO_2$) calculated, analyzed and interpreted with regard to chest radiographic findings.

Statistical analysis

The mean ± SD of $PaCO_2$, $ETCO_2$ values, $PaCO_2$ - $ETCO_2$ gradients and $PaCO_2$ $ETCO_2$ correlation, were determined for both radiolucent and radiopaque study groups. Statistical analysis was done using the IBM SPSS 20 software. The $PaCO_2$ - $ETCO_2$ gradient in the study groups were computed using unpaired Student t test. The correlation between $PaCO_2$ and $ETCO_2$, was analyzed by Pearson`s correlation analysis. Data was represented as mean ± SD, and a p value <0.05 was considered to be statistically significant.

Results

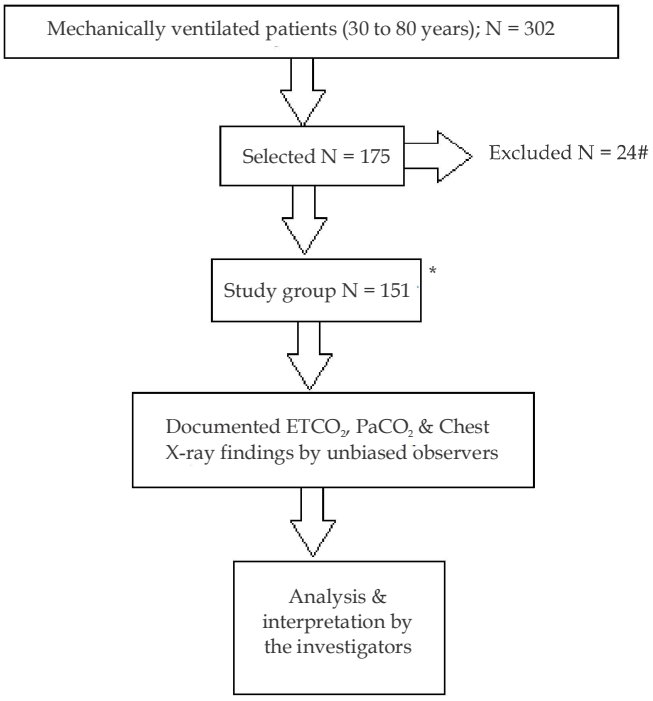
Participants

Participants were selected based on the flow diagram and the exclusion criteria mentioned previously.

Descriptive data

Mean age of our study group was 54.15 ± 17.714 years, all of whom were mechanically ventilated for various reasons, which were either pulmonological or non pulmonological. Other clinical profiles apart from $PaCO_2$, $ETCO_2$ and chest X-ray were disregarded (as mentioned earlier) because our prime interest was to study the relevance of $PaCO_2$ and $ETCO_2$ discrepancy with regard to chest radiographic findings.

Flow Diagram



* Determined by pilot study
\# As per exclusion criteria

Outcome data

Table 1: Comparison of $ETCO_2$ Measurement with Chest Radiographic Findings

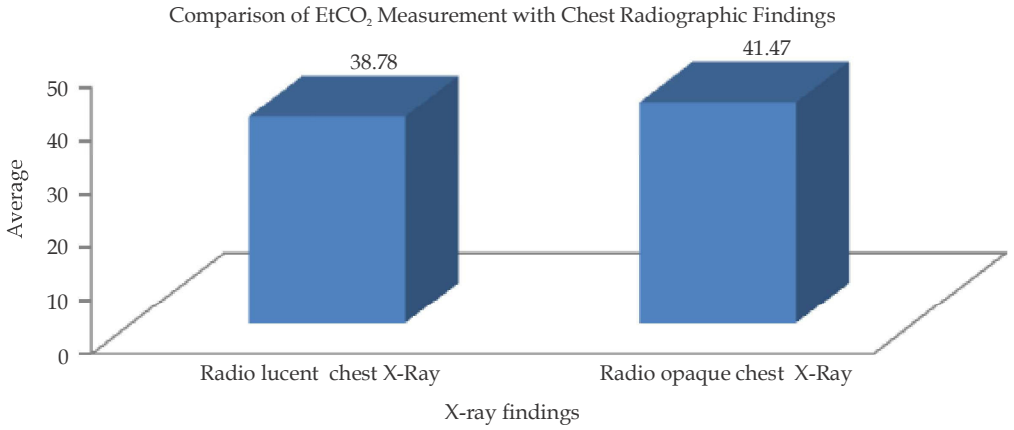
X-ray Finding	N	Mean ± SD (mmHg)	p value
Radiolucent chest X-Ray	85	38.78 ± 15.45	0.261
Radiopaque chest X-Ray	66	41.47 ± 17.39	

Mean value of $ETCO_2$ measured in radio lucent chest X-Ray group and that of radiopaque chest X-Ray group showed no significant variations. The p value was determined to be 0.261 [Table 1, Graph 1].

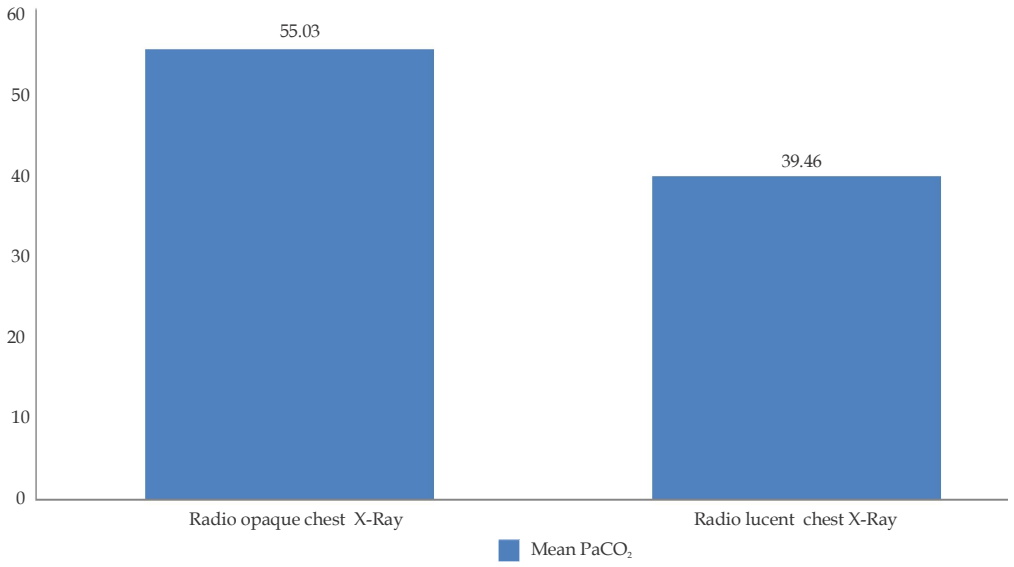
Table 2: Comparison of $PaCO_2$ Measurement with Chest Radiographic Findings

X-ray Finding	N	Mean ± SD (mmHg)	p value
Radiolucent chest X-Ray	85	39.46 ± 14.77	<0.001
Radiopaque chest X-Ray	66	55.03 ± 25.70	

Mean $PaCO_2$ was significantly elevated in the radiopaque chest X-ray group as compared to radiolucent chest X-ray group and p value was found to be significant p <0.001. Table 2, Graph 2



Graph 1:



Graph 2:

Main results

Table 3: Comparison of $EtCO_2$ $PaCO_2$ Gradient *vs* Chest Radiographic Findings.

X-ray Finding	N	Mean ± SD (mmHg)	p value
Radio lucent chest X-Ray	85	0.741 ± 5.77	<0.001
Radio opaque chest X-Ray	66	13.28 ± 17.93	

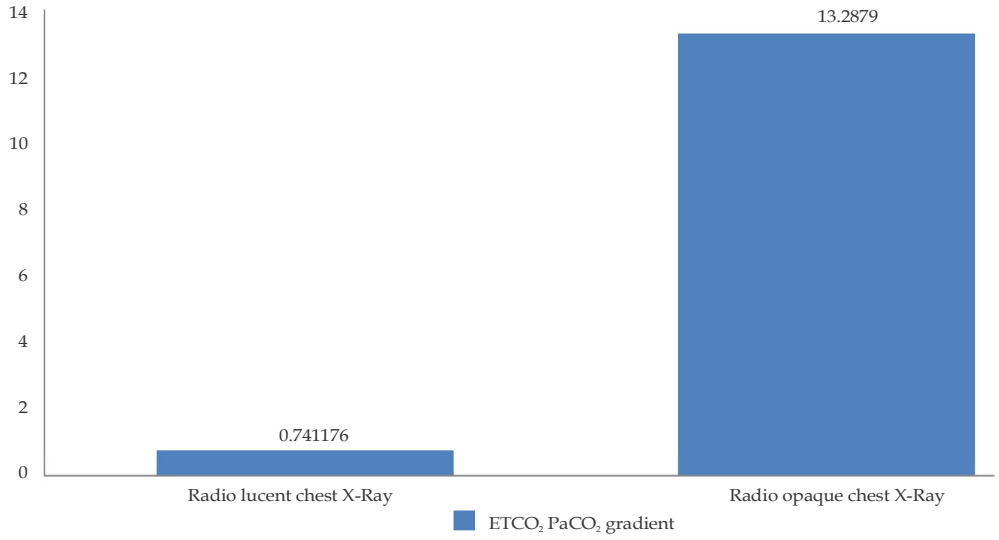
$ETCO_2$ PCO_2 gradient showed significant variation among the radiolucent and radiopaque groups. p value < 0.001 Table 3, Graph 3

Statistical analysis revealed a good correlation between $ETCO_2$ and $PaCO_2$ (Correlation coefficient 0.928, p<0.001) in patients with radiolucent lung fields (Table 3). A relatively poor correlation (Correlation coefficient 0.718, p<0.001) was noticed in patients with radiopaque lung fields as compared to the radiolucent group (Table 4).

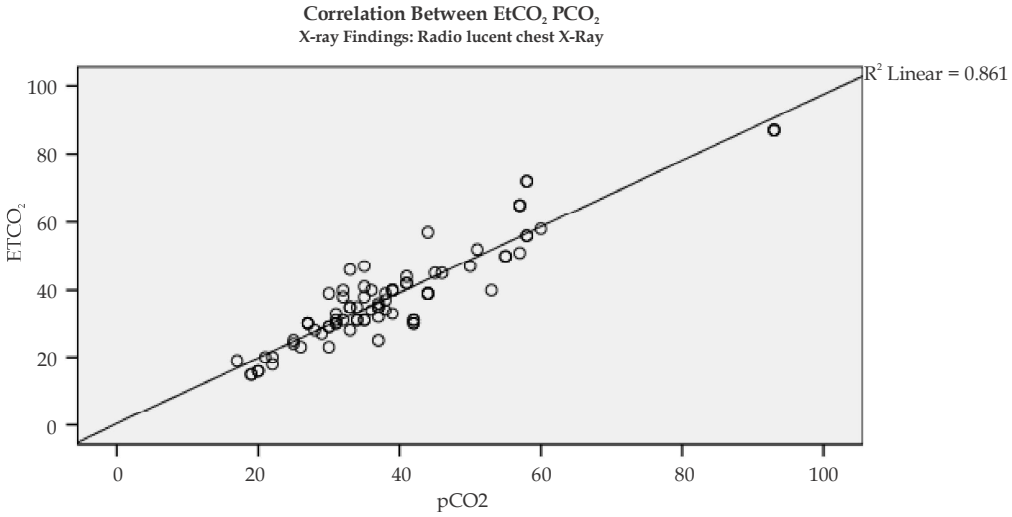
Table 4: $EtCO_2$ $PaCO_2$ Correlation against Chest Radiographic Findings.

Radiolucent chest X-Ray	N	$PaCO_2$ Correlation coefficient	p value
$ETCO_2$ Radiopaque chest X-Ray	85	0.928	<0.001
$ETCO_2$	66	0.718	<0.001

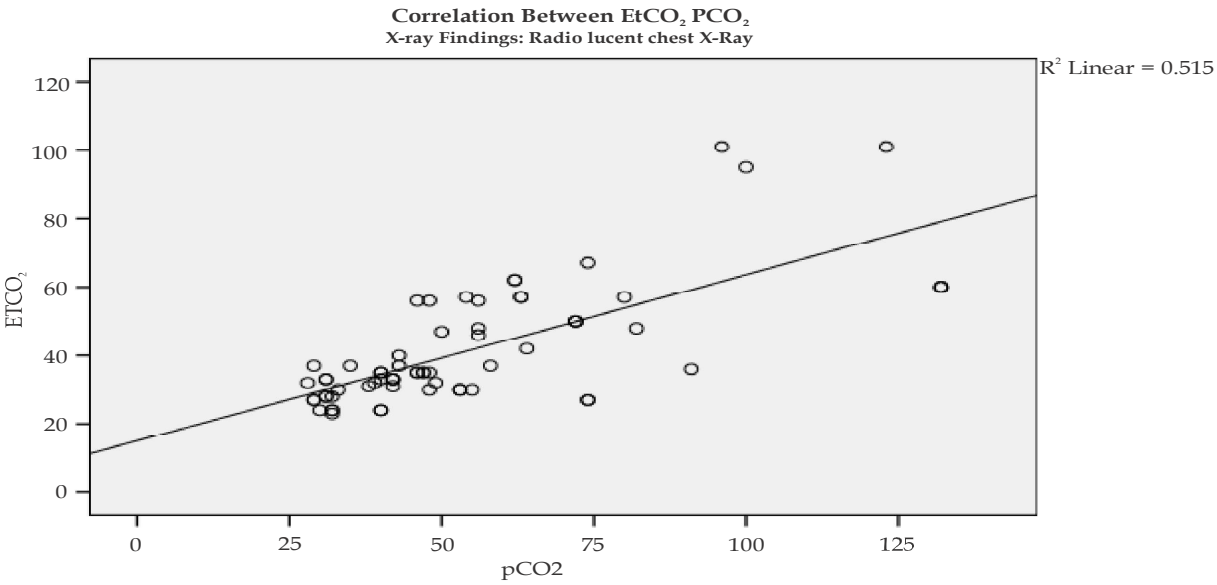
In Radiolucent chest X-Ray group, both $ETCO_2$ and $PaCO_2$ shows perfect positive correlation (r=0.928, p<0.001) and it's statistically significant. Graph 4



Graph 3:



Graph 4:



Graph 5:

In Radiopaque chest X-Ray group, $ETCO_2$ and $PaCO_2$ shows positive correlation($r = 0.718$, $p<0.001$) and is statistically significant Graph 5, though not as much reliable in predicting $PaCO_2$ as compared to the radiolucent group.

Discussion

Key results

Mean $PaCO_2$ was significantly elevated in the radiopaque chest X-ray group, as compared to radiolucent chest X-ray group ($p <0.001$), whereas mean $ETCO_2$ showed no significant variations between the two groups ($p = 0.261$). A statistically significant correlation between arterial $PaCO_2$ and $ETCO_2$ values were obtained ($r= 0.928$, $p< 0.001$ in radiolucent chest X-rays) and ($r=0.718$, $p<0.001$ in radiopaque chest X-rays) in our study, on mechanically ventilated patients. $PaCO_2$ $ETCO_2$ gradient obtained was 0.741 ± 5.77 mmHg ($p<0.001$) in radiolucent chest radiography and 13.28 ± 17.93 mmHg in radiopaque chest radiography.

Limitations

The major limitation was that the study was conducted in a single centre. We would recommend a multi center study with a larger number of recorders and interpreters for further validation. If oxygenation status and base deficit parameters are of primary concern in any ventilated patient, $ETCO_2$ measurement alone may not serve the purpose. A minor limitation in our study was that the population mostly consisted of patients who were on different modes of ventilator. And hence $ETCO_2$ values and pattern of graph may lack uniformity in some patients, depending on whether the breath was purely patient driven or ventilator driven. It would have been an advantage if $ETCO_2$ recordings were obtained exclusively on sedated and paralyzed patients, wherein all breaths were purely machine delivered. To reduce this bias, an equilibration time was provided, and the highest $ETCO_2$ values only were recorded.

Interpretation

$ETCO_2$ values correlated well with $PaCO_2$ values in both radiolucent and radiopaque study groups, proving our hypothesis true for all mechanically ventilated patients. The extent of variation between $PaCO_2$ and $ETCO_2$ was more in the radiopaque group as compared to the radiolucent group, indicating that $ETCO_2$ can accurately and reliably be used to predict $PaCO_2$, only when the chest radiography show radiolucency in lung fields. Similar studies were unavailable in literature.

McDonald et al., obtained a good correlation between $ETCO_2$ and $PaCO_2$ in critically ill pediatric patients undergoing conventional ventilation through an endotracheal tube, and found it clinically reliable for estimating ventilation ($r^2 = 0.716$ and $P < 0.001$). They used a mainstream $ETCO_2$ device for their study and $pETCO_2$ – $PaCO_2$ difference was found to be >=10mmHg in 35% of cases with pO_2/FiO_2 ratio <200 and 10% of cases with pO_2/FiO_2 ratio >200.[2] A moderate to strong correlation was

also observed between $ETCO_2$ and $PaCO_2$ for all V(D)/V(T) ranges(ranging from severe to minimal lung disease) in a study done by Steven D et al. on ventilated pediatric population (below 17 years). $ETCO_2$ $PaCO_2$ gradient increased predictably with increasing V(D)/V(T).[6]

Kerr et al. got a good correlation between $ETCO_2$ and $PaCO_2$ in a subset of sedated paralyzed ventilated head trauma patients without respiratory complications (PEEP<5cm H_2O).[3]

Morley TF et al. concluded that $PETCO_2$ was less sensitive to changes in $PaCO_2$ in patients with parenchymal lung disease especially emphysema and hence may not be reliable for weaning purposes.[7]

Barton CW et al., has reported that $ETCO_2$ correlated well with $PaCO_2$ in non-intubated patients having varied diagnosis, and found $ETCO_2$ values 3.5mmHg lower than $PaCO_2$ values on an average.[8] Another study by MC Plewa et al. (1995) in 29 non intubated patients with respiratory distress, revealed that $PaCO_2$-$ETCO_2$ was significantly higher in patients with pulmonary disease (9.9 +/- 4.2 torr), than without pulmonary disease (3.5 +/- 4.1 torr). $PETCO_2$ could predict $PaCO_2$ in only those patients capable of forced expiration.[9]

Ebrahim Razi et al. has found a good correlation between $ETCO_2$ and $PaCO_2$ in 87 patients mechanically ventilated using SIMV, T Tube and CPAP modes of ventilation. Mean $PaCO_2$-$ETCO_2$ was observed to be 3.37+- 7.93, 3.31 +- 4.26 and 2.32 +-5.62 respectively.[10] Weinger and Brimm found arterial to end-tidal carbon dioxide gradient values of 4.24 ± 4.42 mmHg during intermittent mandatory ventilation and reported good correlation between maximal $PETCO_2$ and $PaCO_2$ in 25 post cardiotomy patients who were being weaned out of the ventilator.[4] Whitesell et al also found good correlation between peak expired pCO_2 and $PaCO_2$ values in patients with and without lung diseases, and the arterial to end-tidal carbon dioxide gradient values were 3.3 torr and 0.8 torr respectively.[5]

Most of the studies stressed the significance of $PETCO_2$ in computing $PaCO_2$ values, in patients with normal lung, and without pulmonary diseases. Ironically, none of the studies excluded the chances of pulmonary disease through pulmonary function test or CT chest. Most of them used alternative parameters such as PEEP, pO_2/FiO_2 ratios or V(D)/V(T) to exclude a lung pathology.

Even though lung field radiolucency in chest radiograph is insufficient to exclude all pulmonary diseases, especially obstructive and restrictive lung diseases, it can indicate acute pathological changes manifesting as radiopacity in lung fields, like pneumonia and pulmonary oedema, causing numerous mortalities in the emergency setting, rather than acute non infective exacerbations of obstructive or restrictive lung diseases. In order to completely exclude a lung disease, a pulmonary function test and a CT chest are ideal, which is non feasible or impractical in the golden hours of an emergency setting.

$ETCO_2$ measurements are affected by $PaCO_2$ levels, dead space fraction, pulmonary perfusion, and the site of sampling. $PaCO_2$ levels may be underestimated in conditions of $PaCO_2$ mismatch, secondary to large ventilation perfusion ratio, resultant from non-uniform alveoli CO_2 emptying.[11] A high ventilation/perfusion ratio and dead space may reduce $ETCO_2$ levels relative to $PaCO_2$. On the contrary, a low ventilation/perfusion ratio and shunt has little effect on causing a smaller $ETCO_2$ measure, relative to $PaCO_2$.

Factors like baseline diagnosis, low cardiac output states, cardiogenic shock, pulmonary embolism, post cardiac arrest states , use of PEEP, varying modes of ventilators, varying ventilator brands, varying ventilator expiratory times, inaccurate calibration of capnometer, recording error etc were not taken into consideration in our study. A most likely explanation that can be offered for our findings are the large areas of dead space and high V/Q ratios which are often found in lung pathologies. Mixing of air in both perfused, underperfused and non perfused alveoli can alter the $PaCO_2$ levels to considerable extent, especially when they reach the larger airways on exhalation. The capnograph, being connected to the expiratory circuit of the ventilator will therefore record a lower $ETCO_2$ value as compared to the arterial $PaCO_2$ value.

Generalizability

Patients are mechanically ventilated for respiratory or mechanical insufficiency, ineffective gas exchange, for airway protection, for imaging, or for impending respiratory failure in neurological diseases. And they are subjected to frequent arterial blood sampling and frequent chest radiography.

Our findings may help emergency physicians and intensivists, working in a resource limited setting, to rapidly predict the possibility of a lung pathology (such as consolidation or pulmonary edema) from $ETCO_2$ recordings. This information may be utilized to limit frequent chest radiography and arterial puncture for $PaCO_2$ determination. It

may also help prediction of $PaCO_2$ for ventilator weaning purposes as well, in patients with radiolucent chest X-rays.

In short, the end tidal carbon dioxide levels ($ETCO_2$) correlated well with partial pressure of carbon dioxide in arterial blood gases ($PaCO_2$) in all mechanically ventilated patients irrespective of lung field opacities, diagnosis or hemodynamic status. As the variation was tremendous in radio opaque cases, $ETCO_2$ in these cases cannot be relied upon for predicting $PaCO_2$ values with precision. On the other hand, $ETCO_2$ values can be effectively and reliably used to predict $PaCO_2$, in mechanically ventilated patients having radiolucent lung fields in chest radiography.

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Research Quality and Ethics Statement:

The authors of this manuscript declare that this scientific work complies with reporting quality, formatting and reproducibility guidelines set forth by the EQUATOR Network. The authors also attest that this clinical investigation was determined to require the Institutional Review Board/Ethics Committee review, and the corresponding protocol/ approval number is [IRB-AIMS-2019-202]. We also certify that we have not plagiarized the contents in this submission and have done a Plagiarism Check.

Conflicts of interest: Nil

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