

ETCO₂ PaCO₂ Gradient and its Correlation with Chest Radiographic Findings in Mechanically Ventilated Patients

Naveen Mohan¹, Prannoy George Mathen², Indresh Kumar³, Sona Kurian⁴, Gireesh Kumar K.P⁵, K.R. Sundaram⁶, Anu Vasudevan⁷

Author's Affiliation:

¹Assistant Professor, ²⁻⁴Senior Resident, ⁵Professor and HOD, ⁶Professor and Head of Department of Biostatistics, ⁷Biostatistician, Department of Emergency Medicine, Amrita School of Medicine (Kochi), Amrita University, Kerala, 682041, India.

Corresponding Author:

Prannoy George Mathen, Senior Resident, Dept of Emergency Medicine, Amrita Institute of Medical Sciences, Kochi, Kerala, 682041, India.

E-mail: prannoygeorge@live.com

Received on 14.04.2020

Accepted on 05.06.2020

Abstract

Context: There exists a deficiency in literature regarding the impact of chest radiographic findings on PaCO₂ ETCO₂ gradient. **Aim:** To evaluate PaCO₂ ETCO₂ gradient and its 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 PaCO₂ recorded. Highest ETCO₂ values and chest radiographic findings, also recorded simultaneously. Mean ETCO₂ and PaCO₂ values were compared with chest radiographic findings for radiopaque and radiolucent CXR groups. ETCO₂ PaCO₂ gradient was analyzed using unpaired Student t test, and ETCO₂ PaCO₂ 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 PaCO₂ 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 ETCO₂ showed no significant variations between the two groups (p 0.261). ETCO₂ PaCO₂ 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 PaCO₂ and ETCO₂ values were obtained in radiolucent CXR (r= 0.928, p<0.001) as compared to radiopaque CXR (r=0.718, p<0.001). **Conclusion:** ETCO₂ values can reliably predict PaCO₂ 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.

How to cite this article:

Naveen Mohan, Prannoy George Mathen, Indresh Kumar et al. ETCO₂ PaCO₂ Gradient and its Correlation with Chest Radiographic Findings in Mechanically Ventilated Patients. Indian J Emerg Med 2020;6(2):79-86.

Introduction

Background/Rationale

End-tidal carbon dioxide (ETCO₂), measures the concentration of carbon dioxide in exhaled air at the end of expiration; expressed as partial pressure in

mmHg (PETCO₂) measured through capnography, utilizing the selective absorption property of specific wavelength of infrared radiation by the CO₂ gas. Sudden changes in systemic CO₂ levels are reflected in ETCO₂ 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 - ($\text{PaCO}_2 - \text{ETCO}_2$) 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. ETCO₂ PaCO₂ gradient (PaCO₂ minus ETCO₂) 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 - ETCO₂ as well as PaCO₂ values were recorded in mmHg, for all the patients and the difference (PaCO₂-ETCO₂) calculated, analyzed and interpreted with regard to chest radiographic findings.

Statistical analysis

The mean ± SD of PaCO₂, ETCO₂ values, PaCO₂ - ETCO₂ gradients and PaCO₂ ETCO₂ correlation, were determined for both radiolucent and

radiopaque study groups. Statistical analysis was done using the IBM SPSS 20 software. The PaCO₂ - ETCO₂ gradient in the study groups were computed using unpaired Student t test. The correlation between PaCO₂ and ETCO₂, 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

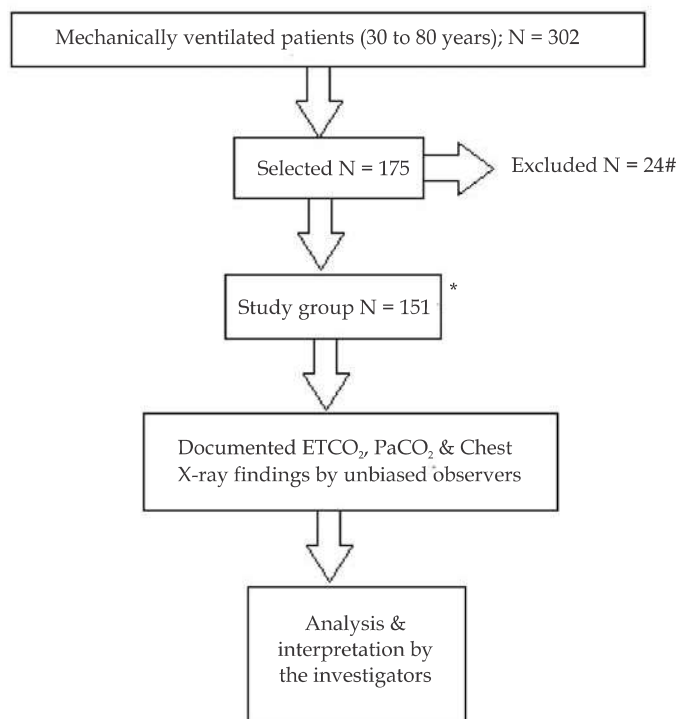
Participants

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 PaCO₂, ETCO₂ and chest X-ray were disregarded (as mentioned earlier) because our prime interest was to study the relevance of PaCO₂ and ETCO₂ discrepancy with regard to chest radiographic findings.

Flow Diagram



* Determined by pilot study

As per exclusion criteria

Outcome data

Table 1: Comparison of ETCO₂ Measurement with Chest Radiographic Findings

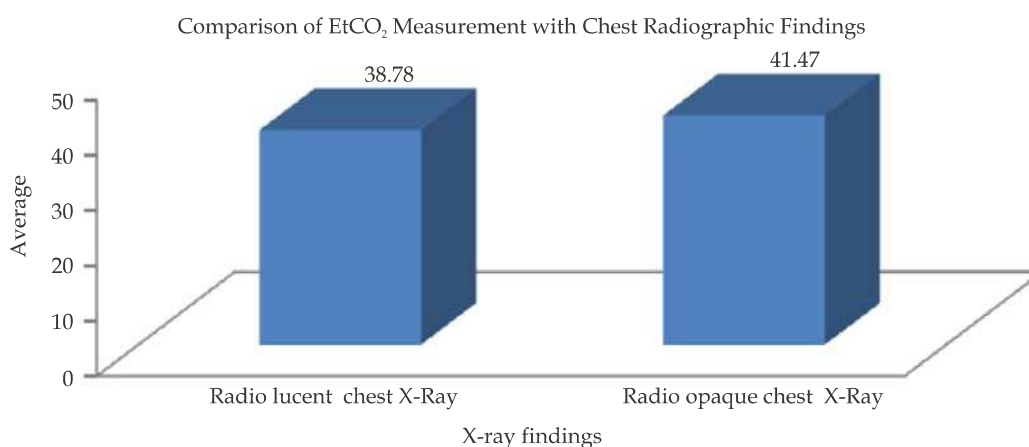
X-ray Finding	N	Mean ± SD (mmHg)	p value
Radiolucent chest X-Ray	85	38.78 ± 15.45	0.261
Radiopaque chest X-Ray	66	41.47 ± 17.39	

Mean value of ETCO₂ 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].

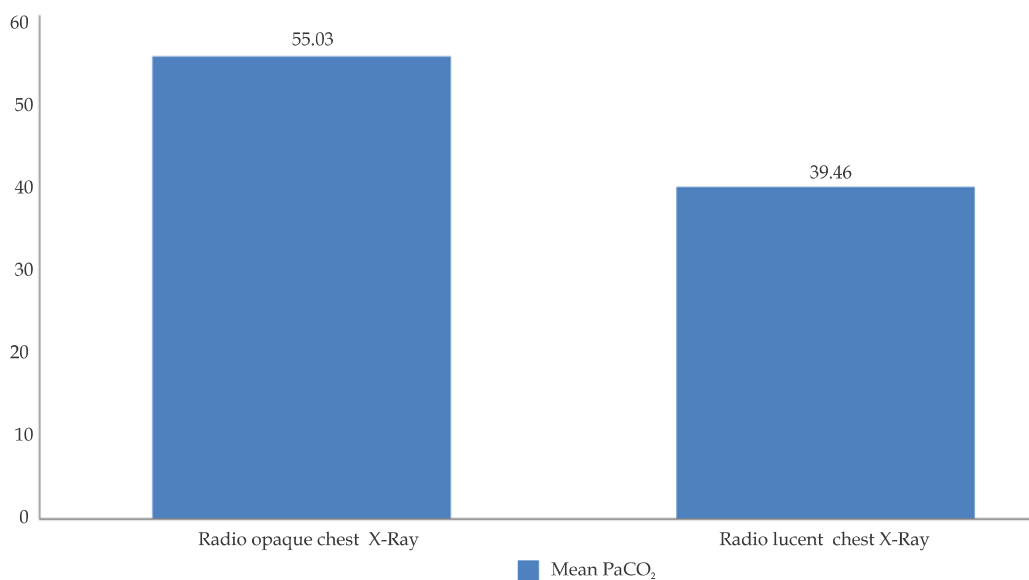
Table 2: Comparison of PaCO₂ Measurement with Chest Radiographic Findings

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 PaCO₂ 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 EtCO₂ PaCO₂ 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	

ETCO₂ PCO₂ gradient showed significant variation among the radiolucent and radiopaque groups. p value < 0.001 Table 3, Graph 3

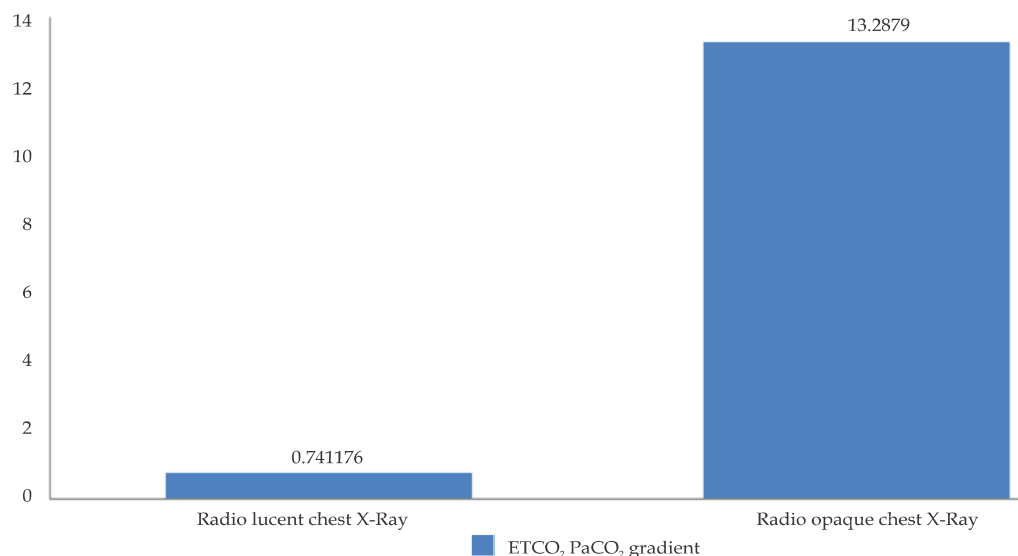
Statistical analysis revealed a good correlation between ETCO₂ and PaCO₂ (Correlation coefficient 0.928, p<0.001) in patients with radiolucent lung fields (Table 3). A relatively poor correlation

(Correlation coefficient 0.718, p<0.001) was noticed in patients with radiopaque lung fields as compared to the radiolucent group (Table 4).

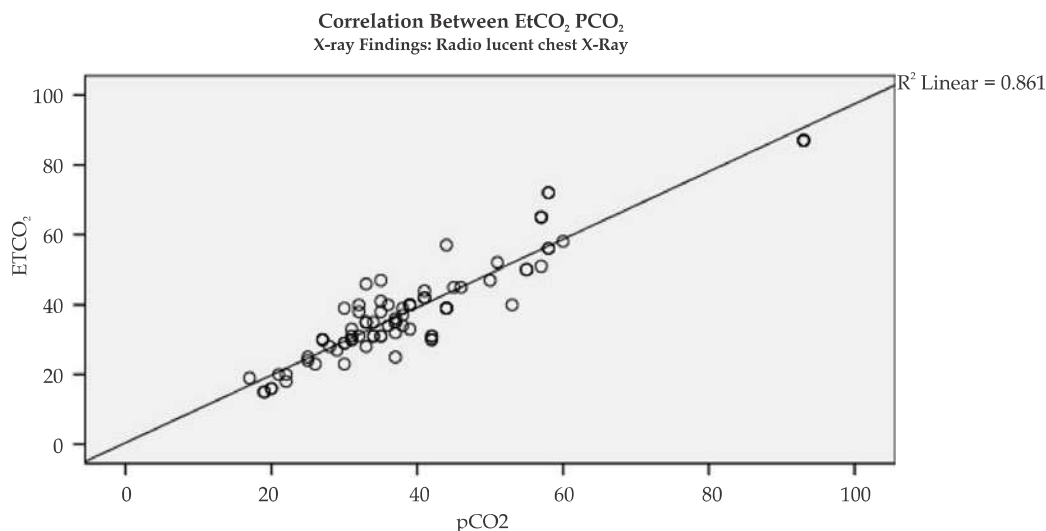
Table 4: EtCO₂ PaCO₂ Correlation against Chest Radiographic Findings

Radiolucent chest X-Ray	N	PaCO ₂ Correlation coefficient	p value
ETCO ₂	85	0.928	<0.001
Radiopaque chest X-Ray			
ETCO ₂	66	0.718	<0.001

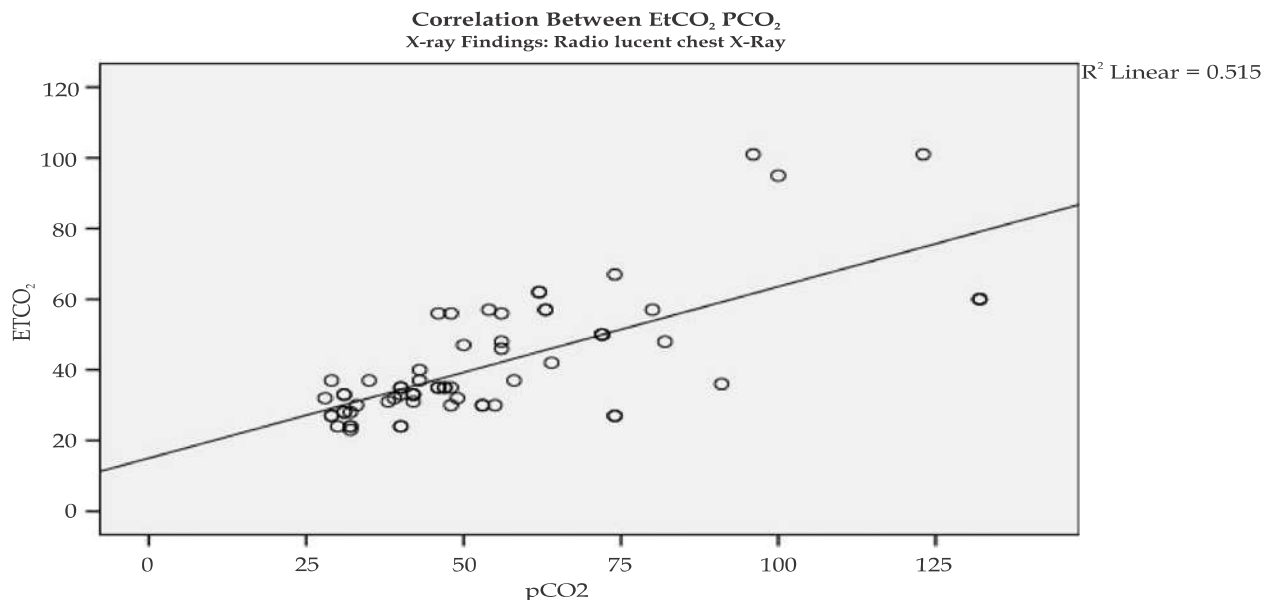
In Radiolucent chest X-Ray group, both ETCO₂ and PaCO₂ shows perfect positive correlation (r=0.928, p<0.001) and it's statistically significant. Graph 4



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 $\text{pETCO}_2 - \text{PaCO}_2$ difference was found to be ≥ 10 mmHg 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 ETCO₂ and PaCO₂ 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). ETCO₂ PaCO₂ gradient increased predictably with increasing V(D)/V(T).⁶

Kerr et al. got a good correlation between ETCO₂ and PaCO₂ in a subset of sedated paralyzed ventilated head trauma patients without respiratory complications (PEEP < 5 cm H₂O).³

Morley TF et al. concluded that PETCO₂ was less sensitive to changes in PaCO₂ 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 ETCO₂ correlated well with PaCO₂ in non-intubated patients having varied diagnosis, and found ETCO₂ values 3.5 mmHg lower than PaCO₂ values on an average.⁸ Another study by MC Plewa et al. (1995) in 29 non intubated patients with respiratory distress, revealed that PaCO₂-ETCO₂ was significantly higher in patients with pulmonary disease (9.9 +/- 4.2 torr), than without pulmonary disease (3.5 +/- 4.1 torr). PETCO₂ could predict PaCO₂ in only those patients capable of forced expiration.⁹

Ebrahim Razi et al. has found a good correlation between ETCO₂ and PaCO₂ in 87 patients mechanically ventilated using SIMV, T Tube and CPAP modes of ventilation. Mean PaCO₂-ETCO₂ 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 PETCO₂ and PaCO₂ in 25 post cardiectomy patients who were being weaned out of the ventilator.⁴ Whitesell et al also found good correlation between peak expired pCO₂ and PaCO₂ 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 PETCO₂ in computing PaCO₂ 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, pO₂/FiO₂ 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.

ETCO₂ measurements are affected by PaCO₂ levels, dead space fraction, pulmonary perfusion, and the site of sampling. PaCO₂ levels may be underestimated in conditions of PaCO₂ mismatch, secondary to large ventilation perfusion ratio, resultant from non-uniform alveoli CO₂ emptying.¹¹ A high ventilation/perfusion ratio and dead space may reduce ETCO₂ levels relative to PaCO₂. On the contrary, a low ventilation/perfusion ratio and shunt has little effect on causing a smaller ETCO₂ measure, relative to PaCO₂.

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 PaCO₂ 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 ETCO₂ value as compared to the arterial PaCO₂ 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 ETCO₂ recordings. This information may be utilized to limit frequent chest radiography and arterial puncture for PaCO₂ determination. It

may also help prediction of PaCO₂ for ventilator weaning purposes as well, in patients with radiolucent chest X-rays.

In short, the end tidal carbon dioxide levels (ETCO₂) correlated well with partial pressure of carbon dioxide in arterial blood gases (PaCO₂) in all mechanically ventilated patients irrespective of lung field opacities, diagnosis or hemodynamic status. As the variation was tremendous in radio opaque cases, ETCO₂ in these cases cannot be relied upon for predicting PaCO₂ values with precision. On the other hand, ETCO₂ values can be effectively and reliably used to predict PaCO₂ in mechanically ventilated patients having radiolucent lung fields in chest radiography.

Funding: Nil

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

Acknowledgement: Nurses, Emergency Medicine technicians and doctors of Dept of Emergency Medicine, Amrita Institute of Medical Sciences (Kochi) for their constant help in data collection.

References

1. Website-capnography.com. Bhavani Sankar Kodali MD [Accessed May 11 2019]. Available from: <http://www.capnography.com/123-lectures/316-capnography-lecture-powerpoint-bhavani-shankar-kodali-md>.
2. MJ McDonald MJ, Montgomery VL, Cerrito PB, et al. Comparison of end-tidal CO₂ and PaCO₂ in children receiving mechanical ventilation. *Pediatr Crit Care Med* 2002 Jul;3(3):244-49.
3. Kerr ME, Zempsky J, Sereika S, et al. Relationship between arterial carbon dioxide and end-tidal carbon dioxide in mechanically ventilated adults with severe head trauma. *Crit Care Med* 1996 May;24(5):785-90.
4. Weinger MB, Brimm JE. End-tidal carbon dioxide as a measure of arterial carbon dioxide during intermittent mandatory ventilation. *J Clin Monit* 1987;3(2):73-9.
5. Whitesell R, Asiddao C, Gollman D, et al. Relationship between arterial and peak expired carbon dioxide pressure during anesthesia and factors influencing the difference. *Anesth Analg* 1981;60(7):508-12.
6. Steven D. McSwain, Donna S. Hamel, RRT FAARC, et al. End tidal and arterial carbon dioxide measurements correlate across all levels of physiologic dead space. *Respir Care* 2010 Mar; 55(3):288-93.
7. Morley TF, Giaimo J, Maroszan E et al. Use of capnography for assessment of the adequacy of alveolar ventilation during weaning from mechanical ventilation. *Am Rev Respir Dis* 1993;148(2):339-44.
8. Barton CW, Wang ES. Correlation of end-tidal CO₂ measurements to arterial PaCO₂ in nonintubated patients. *Ann Emerg Med* 1994;23(3):560-3.
9. Plewa MC, Sikora S, Engoren M et al. Evaluation of capnography in non intubated emergency department patients with respiratory distress. *Acad Emerg Med* 1995. Oct 2(10):901-8.
10. Ebrahim Razi, Gholam Abbass Moosavi, Keivan Omidi et al. Correlation of End-Tidal Carbon Dioxide with Arterial Carbon Dioxide in Mechanically Ventilated Patients; *Arch Trauma Res* 2012 Summer;1(2):58-62.
11. Bhavani-Shankar K, Moseley H, Kumar AY, et al. Capnometry and anaesthesia. *Can J Anesth* 1992;39(6):617-32.