

ORIGINAL ARTICLE

Pediatrics

Bias between capnometry and venous carbon dioxide during initial assessment of pediatric emergency department patients: A video-based study

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Abstract

Objective: The bias of capnometry (ETCO₂) and venous carbon dioxide (vpCO₂) among pediatric emergency department (PED) patients triaged to critical care areas is unknown. We aimed to explore correlations and bias between ETCO₂ and vpCO₂ and identify predictors of bias.

Methods: This was an observational, video-based, retrospective study comparing ETCO₂ and vpCO₂. Pediatric patients with simultaneous ETCO₂ and vpCO₂ data were included. Our primary aim utilized linear regressions to determine correlations and Bland–Altman analysis to assess bias. Our secondary aim utilized multiple regression to identify clinical covariates contributing to bias. Covariates included age, respiratory rate, heart rate, mean arterial blood pressure, capnometry interface, PED diagnosis, and PED disposition.

Results: A total of 200 PED patients with ETCO₂ and vpCO₂ data were included. The median (interquartile range [IQR]) ETCO₂, vpCO₂, and ΔCO₂ in mmHg were 38 (32, 46), 49 (41, 61), and 11 (4, 20), respectively. ETCO₂ ($r = 0.76$) and ΔCO₂ ($r = 0.71$) were highly correlated with vpCO₂. The mean bias between ETCO₂ and vpCO₂ was -14.1 mmHg (95% confidence interval [CI], -41.9 – -13.7). The bias between ETCO₂ and vpCO₂ increased at higher values of each measure. ETCO₂ sampling interface was the only independent predictor of vpCO₂ in our multivariate analysis. Patients requiring bag-valve mask (BVM) ventilation had the highest median bias between ETCO₂ and vpCO₂ (29 mmHg, IQR 15, 37).

Conclusion: ETCO₂ and vpCO₂ were highly correlated. However, bias increased at higher levels of both ETCO₂ and vpCO₂. Among PED patients, ETCO₂'s ability to approximate vpCO₂ diminishes with worsening hypercarbic respiratory failure.

KEYWORDS

capnometry, pediatrics

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1 | INTRODUCTION

1.1 | Background

Derangements in venous carbon dioxide (vpCO₂) are common and potentially life-threatening among severely ill and injured children. End-tidal capnometry (ETCO₂) quantifies exhaled carbon dioxide (CO₂) continuously and non-invasively. In healthy spontaneously breathing children, ETCO₂ should approximate normal venous carbon dioxide levels of 35–45 mmHg of CO₂.¹ Ward et al. provide a framework of three variables that affect bias between ETCO₂ and serum CO₂: (1) ventilation-perfusion abnormalities, (2) respiratory patterns that inhibit complete alveolar emptying, and (3) poor sampling.² In acute illness in pediatric emergency department (PED) patients, all three factors may be present and influence the accuracy of ETCO₂. ETCO₂ has been shown to have clinical utility confirming endotracheal placement; assessing respirations during sedations, seizures, bronchiolitis, and asthma; detecting metabolic disturbances (diabetic ketoacidosis, sepsis, trauma, and dehydration); as well as detecting cardiac output in cardiac arrest.^{3–34} However, there is a gap in knowledge regarding the utility of ETCO₂ as a proxy for vpCO₂ during initial assessment of undifferentiated pediatric patients presenting to the emergency department (ED) with signs of critical illness.

1.2 | Importance

No study has utilized video recordings of real-world ETCO₂ data at the time of initial venous blood gas sampling among patients presenting to the PED. Video review uniquely allows the detailed study of PED resuscitations and supports accurate data collection of visible time-sensitive variables. We believe that a detailed video analysis of capnometry measurements during initial assessment of patients triaged to the PED critical care area will provide insight into the real time bias of ETCO₂ from vpCO₂ during initial assessment of critically ill children.

1.3 | Goals of this investigation

We aimed to utilize video recordings of ETCO₂ as viewed by the bedside clinician during the initial assessment of pediatric patients triaged to the PED critical care area. Our primary aim was to determine the correlation and bias between venous carbon dioxide (vpCO₂) with simultaneous ETCO₂ among a real-world PED patient during their initial evaluation in the PED resuscitation area. Our secondary aim was identifying clinical predictors of bias between ETCO₂ and vpCO₂.

The Bottom Line

In critical care pediatrics, the practitioner is increasingly dependent on data to make accurate clinical decisions regarding care. This study shows that capnometry can be used as a routine adjuvant alongside pulse oximetry unless the patient is in hypercarbic respiratory failure, most likely due to poor ventilation. More studies using capnometry in pediatric critically ill patients will be needed to further define its use.

2 | METHODS

2.1 | Study design and setting

This was a retrospective, video-based, observational study of pediatric patients undergoing initial evaluation and resuscitation in the critical care area of a PED. This study was determined to be exempt by our local institutional review board. The study site was a large urban tertiary free standing Children's Hospital. It is the major regional provider of emergency care to children and a level 1 pediatric trauma center, with approximately 62,000 annual encounters. A total of 4000 patients per year are evaluated in the critical care area. Each of the critical care bays is equipped with an audio-video recording system. There are three to four feeds for each resuscitation bay, one of which is the patient monitor. Capnometry data are included on the monitor, when used for the patient. Recordings are reviewed regularly for peer review and quality assurance activities, with strict policies for storage, review, and permanent deletion developed with medical center's legal counsel. Recordings occur continuously in all resuscitation bays and are available for review using a proprietary software program (Livecapture, B-Line Medical). The data collected from these recordings reflect real-world clinical data as experienced by the PED clinician during critical care. For this study, vpCO₂ and ETCO₂ were obtained as part of the patients care at the discretion of the treating clinician.

2.2 | Selection of participants

Patients ≤18 years of age were identified for inclusion from the complete ED registry of patients who received care in the critical care area.³⁵ Only clinical encounters from the critical care area with vpCO₂ assessed were reviewed for potential inclusion. Patients with ETCO₂ measurements within 5 min of venous blood gas that could be directly observed on video were included. Patients without both measures or those in cardiac arrest were excluded. Demographic information as

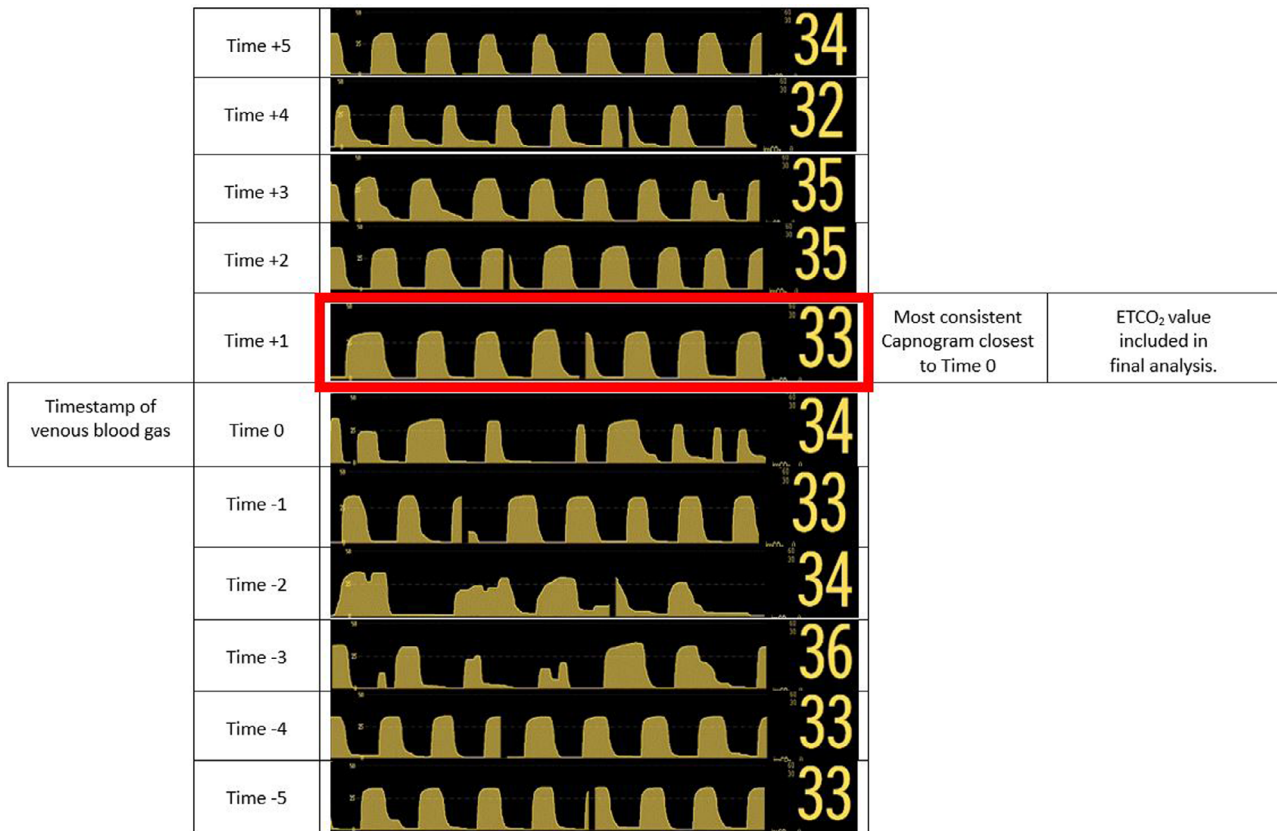


FIGURE 1 Example of sampled capnogram tracings and selection of ETCO₂ value included in final analysis. Time of venous blood gas sample, established as time zero (T_0). Capnogram tracings and capnometry values starting at T_0 were serially captured every minute for 5 min prior to T_0 and 5 min after T_0 . From these 11 time points, the most stable capnogram waveform that was closest in time to T_0 was included in final analysis. Consistency of waveforms was prioritized rather than their morphologic approximation of a normal waveform. In this example, Time = +1(T_1) was included in the final analysis for the most consistent capnogram closest to Time = 0.

well as results of venous blood gas assessment were exported from the electronic medical record (EPIC, Madison Wisconsin).

2.3 | Measurements

2.3.1 | Capnometry and venous blood gas

The clinical monitoring system used for capnometry assessment in the critical care area was the IntelliVue X2 by Phillips. Capnometry readings were obtained via video recordings of Phillips microstream, a side stream capnography system. Capnometry can be measured by nasal, tracheostomy, bag-valve mask (BVM), or endotracheal tube (ETT) interfaces. $vpCO_2$ values were obtained via I-STAT (Abbott Point of Care Inc.), a point-of-care blood analyzer. After the blood sample was placed in the I-STAT analyzer, blood gas analysis results were generally available within 2 min.

2.3.2 | Capnogram classification

The venous blood gas sample result time, as recorded in our electronic health record, was identified and established as time zero (T_0) for our

study. To determine which capnometry value was included in the final analysis, we serially captured the capnogram tracing and capnometry values starting at T_0 and then every minute for 5 min prior to T_0 and 5 min after T_0 . From these 11 time points, the most stable capnogram waveform that was closest in time to T_0 was included in final analysis (Figure 1). We categorized capnogram waveforms into categories of stability based upon the waveforms directly preceding the leading edge of the capnogram tracing. In instances where there were more than five waveforms displayed on the capnogram, we visually inspected the capnogram and categorized the five preceding waveforms as “stable” (four to five waveforms of similar morphology), “intermediate” (two to three similar waveforms), or “unstable” (zero to one waveforms of similar morphology). We prioritized the consistency of waveforms (rather than their morphologic approximation of a normal waveform) to make these characterizations.¹⁴

2.4 | Clinical outcomes

Our primary predictor was ETCO₂ value, and our primary outcomes were $vpCO_2$ and the difference between $vpCO_2$ and ETCO₂ (ΔCO_2). Secondary outcomes were covariates associated with bias between ETCO₂ and $vpCO_2$. Covariates included age, respiratory rate, heart

rate, mean arterial blood pressure, capnometry interface, PED diagnosis, and PED disposition.

2.5 | Data analysis

2.5.1 | Data storage and statistical software

Data from video review and the electronic health record were stored, organized, and merged in REDCAP and R-studio.^{36,37} Statistical testing was conducted using SAS.

2.5.2 | Statistical analysis

Descriptive statistics were used to describe a study sample. Linear regressions were performed, and Pearson correlation coefficients were calculated to determine correlation between continuous variables (ETCO₂, vpCO₂, and ΔCO₂). Multiple regression with backwards stepwise selection was performed to identify clinical covariates contributing to bias of ETCO₂ and vpCO₂. Covariates were selected a priori based upon presumed ability to influence ETCO₂ values and ability to reliably obtain covariates from video and electronic health record review of clinical encounters. Covariates included age, respiratory rate, heart rate, mean arterial blood pressure, capnometry interface, PED diagnosis, and PED disposition. Only significant covariates (*p*-value < 0.05) were included in the final model. A Bland-Altman plot was created to display the level of agreement (95% LOA) between ETCO₂ and vpCO₂.

2.5.3 | Missing data

To account for missing vital sign data for the covariates included in our multiple regression, we systematically replaced all the missing data by reviewing the images of the clinical monitor displaying the capnogram and capnometry data. If a vital sign was missing, the missing vital sign from the image of the clinical monitor that was closest in time to the missing value was included in final analysis. All missing vital sign data were able to be replaced with vital sign data from within 5 min of the time the venous blood gas resulted.

2.5.4 | Diagnostic categories

ICD-10 encounter diagnoses codes associated with the patient's presentation were grouped using the Pediatric Emergency Care Applied Research Network (PECARN) ICD-Based Diagnosis Grouping system (<https://pecarn.org/tools/>).³⁸ The PECARN Major Group Descriptions were utilized and encounters were classified into the following diagnostic categories: (1) neurologic disease; (2) trauma; (3) respiratory disease; (4) endocrine, metabolic, and nutrition. A fifth group called "Sepsis, Shock & Hypovolemia" was created to categorize ICD-10 codes

TABLE 1 Patient demographics, frequencies of capnometry interface observed and diagnostic categories.

| Characteristic | N = 200 |
|--|-------------------------------|
| Age (years) | 4.0 (1.0, 13.0 ^a) |
| Sex | |
| Female | 90 (45%) |
| Male | 110 (55%) |
| Capnometry Interface | |
| Nasal | 151 (76%) |
| Bag-valve mask | 38 (19%) |
| Endotracheal tube | 4 (2.0%) |
| Tracheostomy | 7 (3.5%) |
| Diagnostic categories | |
| Neurologic diseases | 126 (63%) |
| Respiratory diseases | 23 (12%) |
| Trauma | 22 (11%) |
| Sepsis, shock, and hypovolemia | 19 (9.5%) |
| Endocrine, metabolic, and nutritional diseases | 10 (5.0%) |
| Capnogram waveform morphology | |
| Consistent | 147 (74%) |
| Intermediate | 36 (18%) |
| Variable | 17 (8.5%) |

^aMedian (IQR); *n* (%).

TABLE 2 Description of ETCO₂, vpCO₂, and ΔCO₂ for entire study sample, reported in median (IQR) mmHg.

| Characteristic | Median (IQR) |
|-------------------|--------------|
| ETCO ₂ | 38 (32, 46) |
| vpCO ₂ | 49 (41, 61) |
| ΔCO ₂ | 11 (4, 20) |

that matched this clinical presentation. When ICD-10 codes were not associated with a Major Group Description or there were less than 15 instances of a given Major Group Description, ICD-10 description and chart review were utilized to categorize subjects into one of the above five categories. Upper airway and ear, nose, and throat presentations were included in respiratory disease. Toxic ingestions and psychiatric presentations were included in neurologic disease.

3 | RESULTS

We reviewed 428 consecutive clinical encounters with vpCO₂ obtained in the PED critical care area between December 2020 and August 2021 to constitute 200 patients meeting the required paired values of ETCO₂ and pvCO₂ observed on video. Our sample was 55% males. The median (interquartile range [IQR]) age in years was 4.0 (1.0, 13.0). Nasal capnometry was the interface utilized in

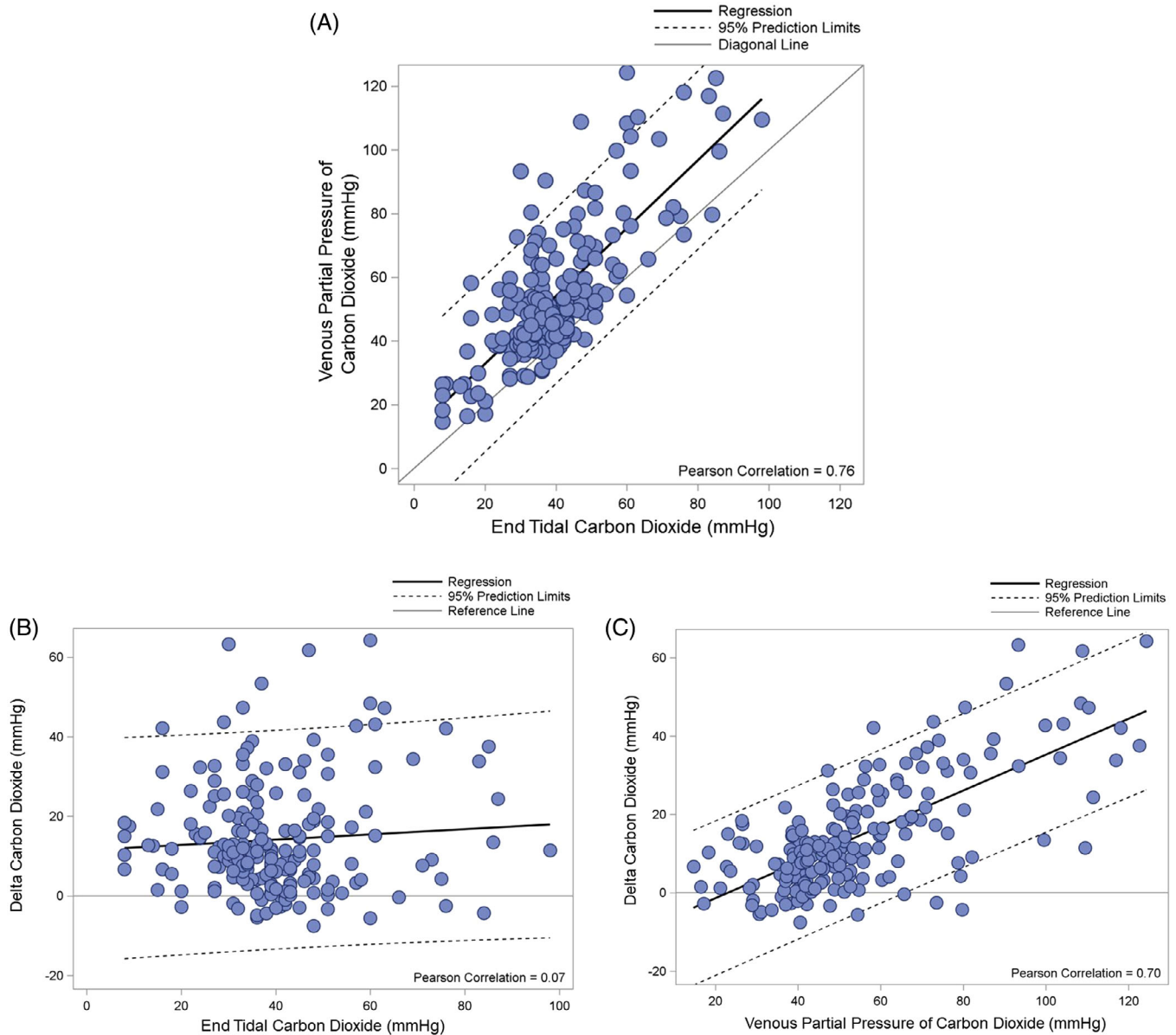


FIGURE 2 Univariate linear regressions: (A) correlation of capnometry (ETCO₂) value and venous partial pressure of carbon dioxide (vpCO₂), Pearson correlation of 0.75. (B) Correlation between ETCO₂ and ΔCO₂, Pearson correlation of 0.07. (C) Correlation between vpCO₂ and ΔCO₂, Pearson correlation of 0.7.

151 of 200 (75.5%) observations. Capnometry values from ETTs and tracheostomies were infrequently observed (5.5%). Capnometry was most frequently paired with a venous blood gas among patients presenting to the PED with concern for neurologic disease (63%). Capnometry values were associated with a stable capnography waveform in 74% of observations. (Table 1). In our sample, the median (IQR) values for our primary predictors and outcomes in mmHg were ETCO₂, 38 (32, 46), vpCO₂, 49 (41, 61), and ΔCO₂ 11 (4, 20) (Table 2).

Capnometry as a predictor of vpCO₂ was plotted using simple linear regression. These were highly correlated with a Pearson Correlation coefficient of 0.76 with a slope of 1.07. Of note, there was greater variance between ETCO₂ and vpCO₂ at higher values and less variance at lower ETCO₂ and vpCO₂ values (Figure 2a). The ETCO₂ and

ΔCO₂ are independent of each other with a Pearson correlation of 0.07 (Figure 2b). The vpCO₂ and ΔCO₂ are highly correlated with a Pearson correlation of 0.7 (Figure 2c). Bland-Altman analysis resulted in an estimated bias for the difference between ETCO₂ and vpCO₂ to be -14.1 mmHg with a 95% confidence interval of (-41.9 mmHg, 13.7 mmHg) (Figure 3). Visual inspections of the Bland-Altman plot display unequal bias between ETCO₂ and vpCO₂, with higher bias at higher mean values of ETCO₂ and vpCO₂.

To identify additional covariates associated with bias of ETCO₂ and vpCO₂, covariates (age, respiratory rate, heart rate, mean arterial blood pressure, capnometry interface, ED encounter diagnosis, and ED disposition) were modeled with a multiple regression with backwards stepwise elimination. Non-significant covariates were excluded

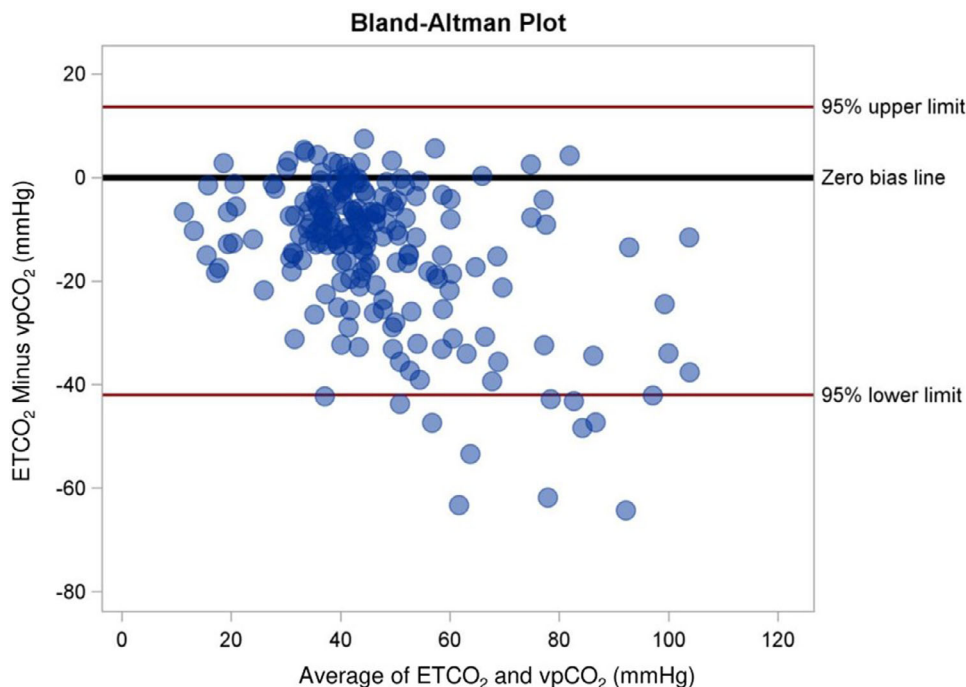


FIGURE 3 Bland–Altman plot of ETCO_2 compared with vpCO_2 . The mean bias between these two values was -14.1 mmHg with a 95% confidence interval of -41.9 and 13.7 mmHg. The bias between ETCO_2 and vpCO_2 increases at higher values of each measure.

TABLE 3 Description of ETCO_2 , vpCO_2 , and ΔCO_2 stratified by capnometry interface, reported in median (IQR) mmHg.

| Characteristic | Nasal, N = 151 | Bag-Valve mask, N = 38 | Endotracheal tube, N = 4 | Tracheostomy, N = 7 | p-value |
|---------------------|--------------------------|---------------------------|-----------------------------|--------------------------|---------------------|
| ETCO_2 | 36 (30, 42) ^a | 51 (38, 62) ^a | 33 (27, 38) ^a | 48 (34, 58) ^a | <0.001 ^b |
| vpCO_2 | 46 (39, 53) ^a | 76 (65, 93) ^a | 41 (40, 47) ^a | 60 (58, 83) ^a | <0.001 ^b |
| ΔCO_2 | 9 (3, 15) ^a | 29 (15, 37) ^a | 16 (6, 24) ^a | 20 (16, 32) ^a | <0.001 ^b |

^aMedian (IQR).

^bKruskal–Wallis rank sum test.

from the final model. Capnometry interface was the only significant covariate that was an independent predictor in our sample.

Median ETCO_2 , vpCO_2 , and ΔCO_2 were significantly different across capnometry interfaces. Of note, there were only 11 combined observations of ETCO_2 sampled by ETT and tracheostomy. BVM had higher median values of ETCO_2 , vpCO_2 , and ΔCO_2 (Table 3).

4 | LIMITATIONS

Our study has several limitations. The use of capnometry and obtaining of venous blood gas measurements during resuscitation in the PED was not set up in a standardized fashion. These data were available only retrospectively and were dependent on PED clinician practices. It should be noted that we were not able to determine a patient's tidal volume and include this in our analysis. We acknowledge that respiratory rate and tidal volume together fully assess a patient's ventilation. Our critical care area and video review of clinical encounters did not allow for feasible assessment of delivered tidal volume when assess-

ing both vpCO_2 and ETCO_2 . Our sample included a large proportion of neurologic-based clinical diagnoses more frequently than other important categories of illness or injury. We were only able to capture video recordings of patients in the critical care area and not standard PED care areas and therefore may not have included a full spectrum of patients in which capnometry was utilized. Additionally, our sample size was not large enough to draw generalizable conclusions across all ETCO_2 interfaces, specifically ETTs and tracheostomies, when compared to nasal and BVM values. Lastly, while blood gas measurements in PEDs are most commonly venous samples, findings from our study may be limited when compared to arterial measurements in other clinical settings.

5 | DISCUSSION

ETCO_2 and vpCO_2 were highly correlated in our sample of undifferentiated pediatric patients during initial evaluation and resuscitated in our PED. The high degree of correlation of ETCO_2 and vpCO_2 is consis-

tent with previous studies both inside and outside the PED.^{16,17,26-34} However, strong correlation alone does not fully explain the clinical utility of these two measures of CO₂. Our results suggest that the bias between ETCO₂ and vpCO₂ is dependent upon a patient's degree of respiratory failure, with greater bias at higher CO₂ values, and worsening respiratory failure. The bias between ETCO₂ and vpCO₂ increased at higher CO₂ levels when assessed by simple linear regression. ΔCO₂ values increased at higher vpCO₂ values. The ETCO₂ interface with the highest ΔCO₂ was among those patients presenting with respiratory failure requiring immediate BVM respiratory support. Our Bland-Altman analysis displayed that at higher ETCO₂ and vpCO₂ values, the bias between these two values increases, and ETCO₂ often underestimates vpCO₂ especially at higher CO₂ values. Our results when taken together suggest that ETCO₂'s ability to approximate vpCO₂ diminishes among patients presenting to the PED with worse hypercarbic respiratory failure. The emergency clinician, when utilizing ETCO₂ during the initial assessment of pediatric patients, should interpret the absolute value of ETCO₂ with caution among patients who display signs of respiratory failure and those patients who display elevated ETCO₂ values during initial assessment.

In this retrospective video-based study comparing ETCO₂ to vpCO₂ during initial assessment and resuscitation in a single PED, we found that ETCO₂ is highly correlated with vpCO₂. However, there is greater bias between vpCO₂ and ETCO₂ among pediatric patients with hypercarbic respiratory failure. The worsening bias of ETCO₂ and vpCO₂ at higher vpCO₂ values is likely a direct result of inadequate ventilation, leading to alterations in the exhaled CO₂ that is detected by the ETCO₂ detector. Our findings support the emergency clinician using capnometry as a routine adjunctive tool during initial evaluation and resuscitation, but capnometry should be interpreted in the context of the patient's specific ventilatory status. Future studies of capnometry during initial evaluation and resuscitation of critically ill pediatric patients in the PED should focus upon ETCO₂ in patients with respiratory failure requiring ventilatory support.

AUTHOR CONTRIBUTIONS

Michael Stratton, Kevin Overmann, Richard Ruddy, and Yin Zhang conceived and designed the study. Michael Stratton performed data collection, and Michael Stratton and Kevin Overmann supervised data collection. Yin Zhang provided statistical advice and analyzed the data. Michael Stratton, Kevin Overmann, and Richard Ruddy drafted the manuscript, and all authors contributed substantially to its revision. Michael Stratton takes full responsibility for the paper as a whole.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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