# What Is the Potential Role of Transcutaneous Carbon Dioxide in Guiding Acute Noninvasive Ventilation?

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**BACKGROUND: Transcutaneous carbon dioxide ($P_{tcCO_2}$) monitoring is rarely used in the acute hospital setting, where serial samples of arterial blood are instead taken to measure carbon dioxide tension ($P_{aCO_2}$). In this pilot observational study, we assessed the potential of $P_{tcCO_2}$ monitoring to calculate pH and guide management of acute noninvasive ventilation (NIV). METHODS: Ten subjects with acute hypercapnic respiratory failure were recruited. All had arterial lines placed to guide acute NIV. $P_{tcCO_2}$ was monitored for 12 h (TOSCA TCM4) and compared with $P_{aCO_2}$. Noninvasive transcutaneous pH was determined from $P_{tcCO_2}$ and calculated bicarbonate and then compared with true arterial pH. Agreements between $P_{CO_2}$ and pH methods were assessed using Bland-Altman analysis of limits of agreement and Pearson correlation coefficients. Hypothetical adjustments to acute NIV settings were based on transcutaneous data alone and evaluated in comparison with true management. Pain scores for each method were compared using the Wilcoxon signed-rank test. RESULTS: $P_{CO_2}$ time trends were concordant. Mean $P_{CO_2}$ bias was −2.33 (95% limits of agreement of −9.60 to 5.03) mm Hg, and r = 0.89 ($P < .001$). Mean pH bias was 0.012 (95% limits of agreement of −0.070 to 0.094), and r = 0.84 ($P < .001$). Hypothetical clinical decisions based on transcutaneous data alone matched true management on 85% of 34 occasions. Initiation of transcutaneous monitoring was less painful than the arterial equivalent ($P = .008$). CONCLUSIONS: This pilot study demonstrates that $P_{tcCO_2}$ monitoring provides a continuous and reliable trend and also allows pH prediction. This patient-friendly approach is a promising alternative to repeated arterial blood gas sampling in patients requiring NIV for acute hypercapnic respiratory failure.** *Key words: transcutaneous carbon dioxide; acute hypercapnic respiratory failure; type 2 respiratory failure; noninvasive ventilation; NIV.* [Respir Care 2015;60(4):484–491. © 2015 Daedalus Enterprises]

## Introduction

Noninvasive ventilation (NIV) is standard treatment for acute hypercapnic respiratory failure caused by COPD, obesity hypoventilation syndrome, and neuromuscular disorders, and it avoids the trauma and infection risks associated with intubation. The accepted standard for monitoring NIV is still arterial blood gas sampling, an invasive and often time-consuming technique that measures $P_{aCO_2}$, $P_{aO_2}$, bicarbonate, and pH. A transcutaneous technique using a Stow-Severinghaus electrochemical sensor[1] provides an alternative to arterial blood gas sampling and avoids the potential complications of aneurysms and limb ischemia.[2]

Transcutaneous $P_{CO_2}$ ($P_{tcCO_2}$) monitoring is an accepted test in the homes of chronic users of nocturnal NIV,[3,4] but

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The authors have disclosed a relationship with Radiometer, who provided the instrument used in this study.

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is still rarely used in the acute hospital setting. Studies have reported $P_{tcCO_2}$ monitoring to be reliable over short time periods during acute NIV[5-11] and over 8 h during chronic NIV.[4,8,12] To date, no studies have assessed its use over longer periods in acute NIV. The clinical value of

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transcutaneous data are still questionable, with only one reported trial assessing subject management based on $P_{tcCO_2}$ readings alone.[13] A key limitation is that during COPD exacerbation (the most common NIV indication[14]), arterial blood samples must still be taken to measure pH.

We aimed to determine whether reliable calculations of pH can be obtained during continuous $P_{tcCO_2}$ monitoring and whether reducing the frequency of invasive testing improves patient experience.

**QUICK LOOK**

**Current knowledge**

Mechanical ventilation adjustments are commonly guided by blood gas analysis and pulse oximetry. In adult patients, end-tidal carbon dioxide can be a surrogate for arterial carbon dioxide. Transcutaneous carbon dioxide ($P_{tcCO_2}$) has been used in infants, but neither is routinely used in the ICU.

**What this paper contributes to our knowledge**

In a small group of subjects undergoing noninvasive ventilation, $P_{tcCO_2}$ monitoring trended with $P_{aCO_2}$ and arterial pH. Bias of the transcutaneous sensor is greater at elevated $P_{aCO_2}$. Transcutaneous monitoring was preferred over arterial blood sampling by the subjects.

## Methods

### Study Design, Setting, and Population

A prospective observational cohort study was carried out over 4 months in the Medical High Dependence Unit at Queen's Medical Centre in Nottingham, United Kingdom. Subjects were approached for recruitment (Fig. 1) if they were receiving NIV for acute hypercapnic respiratory failure, were 18–85 y old, and had an arterial line already inserted. Subjects unable to give informed consent, including those with reduced consciousness from hypercapnia, were excluded.

### Protocol and Measurements

The study was approved by the Leicester Research Ethics Committee (12/EM/0354). Informed consent was obtained from all study participants. Age, gender, diagnosis, and auricular capillary refill time were recorded. Routine clinical observations and arterial blood gas results were recorded both at the time of NIV initiation and at study recruitment.

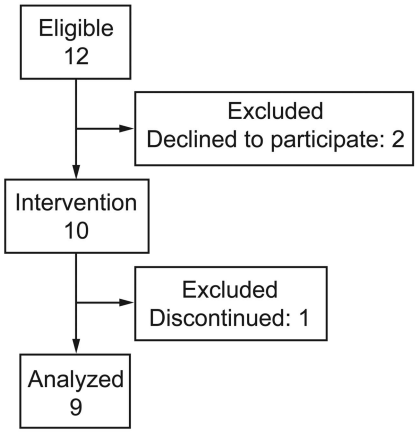


Fig. 1. Flow diagram.

A new probe membrane, adhesive clip, and contact gel were used to attach a $P_{tcCO_2}$ probe (TOSCA TCM4, Radiometer, Brønshøj, Denmark) to each subject's cleaned earlobe. The trace was observed, and time 0 was noted when the plateau phase appeared. At this point, blood was sampled from the arterial line, and values for $P_{aCO_2}$, arterial pH, and bicarbonate were measured using a Radiometer ABL90 blood gas analyzer. $P_{tcCO_2}$ was recorded 2 min later to account for sensor lag time.[11] Subjects were asked to rate the pain experienced during the establishment of each $P_{CO_2}$ monitoring method on the Numerical Rating Scale[15] from 1 to 10.

Noninvasive transcutaneous pH was determined from $P_{tcCO_2}$ using the Henderson-Hasselbalch equation and a bicarbonate calculation algorithm (Table 1), which used a reference value for arterial bicarbonate concentration obtained by arterial blood gas at NIV initiation or 24 h before recruitment (whichever was more recent). Values for mean rate of change were calculated from preliminary data relating to 15 subjects during their first 24 h of NIV treatment (Table 2). If the reference arterial bicarbonate concentration was $< 32.0$ mmol/L, subsequent values were calculated by applying a mean rate of change of 0.225 mmol/L/h. If the reference arterial bicarbonate concentration exceeded 32.0 mmol/L, a slower mean rate of change of 0.120 mmol/L/h was applied. Of note, this prediction rule was derived solely from subjects with pure respiratory acidosis.

$P_{tcCO_2}$ and transcutaneous pH were recorded continuously for 12 h from time 0 and compared with arterial

Table 1. pH Calculation Algorithm

| $P_{CO_2}$ (mm Hg) | pH Calculated at Bicarbonate Concentrations (mmol/L) of: | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 |
| 30.0 | 7.45 | 7.47 | 7.49 | 7.51 | 7.52 | 7.54 | 7.56 | 7.58 | 7.59 | 7.61 | 7.62 | 7.64 | 7.65 | 7.66 | 7.68 | 7.69 | 7.70 |
| 31.5 | 7.42 | 7.45 | 7.47 | 7.48 | 7.50 | 7.52 | 7.54 | 7.55 | 7.57 | 7.59 | 7.60 | 7.61 | 7.63 | 7.64 | 7.65 | 7.67 | 7.68 |
| 33.0 | 7.40 | 7.43 | 7.45 | 7.46 | 7.48 | 7.50 | 7.52 | 7.53 | 7.55 | 7.57 | 7.58 | 7.59 | 7.61 | 7.62 | 7.63 | 7.65 | 7.66 |
| 34.5 | 7.38 | 7.41 | 7.43 | 7.45 | 7.46 | 7.48 | 7.50 | 7.51 | 7.53 | 7.55 | 7.56 | 7.57 | 7.59 | 7.60 | 7.62 | 7.63 | 7.64 |
| 36.0 | 7.37 | 7.39 | 7.41 | 7.43 | 7.45 | 7.46 | 7.48 | 7.50 | 7.51 | 7.53 | 7.54 | 7.56 | 7.57 | 7.58 | 7.60 | 7.61 | 7.62 |
| 37.5 | 7.35 | 7.37 | 7.39 | 7.41 | 7.43 | 7.45 | 7.46 | 7.48 | 7.49 | 7.51 | 7.52 | 7.54 | 7.55 | 7.57 | 7.58 | 7.59 | 7.60 |
| 39.0 | 7.33 | 7.35 | 7.37 | 7.39 | 7.41 | 7.43 | 7.45 | 7.46 | 7.48 | 7.49 | 7.51 | 7.52 | 7.54 | 7.55 | 7.56 | 7.57 | 7.59 |
| 40.5 | 7.31 | 7.34 | 7.36 | 7.38 | 7.39 | 7.41 | 7.43 | 7.45 | 7.46 | 7.48 | 7.49 | 7.51 | 7.52 | 7.53 | 7.55 | 7.56 | 7.57 |
| 42.0 | 7.30 | 7.32 | 7.34 | 7.36 | 7.38 | 7.40 | 7.41 | 7.43 | 7.45 | 7.46 | 7.48 | 7.49 | 7.50 | 7.52 | 7.53 | 7.54 | 7.55 |
| 43.5 | 7.28 | 7.31 | 7.33 | 7.34 | 7.36 | 7.38 | 7.40 | 7.41 | 7.43 | 7.45 | 7.46 | 7.47 | 7.49 | 7.50 | 7.51 | 7.53 | 7.54 |
| 45.0 | 7.27 | 7.29 | 7.31 | 7.33 | 7.35 | 7.37 | 7.38 | 7.40 | 7.42 | 7.43 | 7.45 | 7.46 | 7.47 | 7.49 | 7.50 | 7.51 | 7.52 |
| 46.5 | 7.25 | 7.28 | 7.30 | 7.32 | 7.33 | 7.35 | 7.37 | 7.39 | 7.40 | 7.42 | 7.43 | 7.45 | 7.46 | 7.47 | 7.49 | 7.50 | 7.51 |
| 48.0 | 7.24 | 7.26 | 7.28 | 7.30 | 7.32 | 7.34 | 7.36 | 7.37 | 7.39 | 7.40 | 7.42 | 7.43 | 7.45 | 7.46 | 7.47 | 7.48 | 7.50 |
| 49.5 | 7.23 | 7.25 | 7.27 | 7.29 | 7.31 | 7.32 | 7.34 | 7.36 | 7.37 | 7.39 | 7.40 | 7.42 | 7.43 | 7.45 | 7.46 | 7.47 | 7.48 |
| 51.0 | 7.21 | 7.24 | 7.26 | 7.28 | 7.29 | 7.31 | 7.33 | 7.35 | 7.36 | 7.38 | 7.39 | 7.41 | 7.42 | 7.43 | 7.45 | 7.46 | 7.47 |
| 52.5 | 7.20 | 7.22 | 7.24 | 7.26 | 7.28 | 7.30 | 7.32 | 7.33 | 7.35 | 7.36 | 7.38 | 7.39 | 7.41 | 7.42 | 7.43 | 7.45 | 7.46 |
| 54.0 | 7.19 | 7.21 | 7.23 | 7.25 | 7.27 | 7.29 | 7.30 | 7.32 | 7.34 | 7.35 | 7.37 | 7.38 | 7.39 | 7.41 | 7.42 | 7.43 | 7.45 |
| 55.5 | 7.18 | 7.20 | 7.22 | 7.24 | 7.26 | 7.28 | 7.29 | 7.31 | 7.32 | 7.34 | 7.35 | 7.37 | 7.38 | 7.40 | 7.41 | 7.42 | 7.43 |
| 57.0 | 7.17 | 7.19 | 7.21 | 7.23 | 7.25 | 7.26 | 7.28 | 7.30 | 7.31 | 7.33 | 7.34 | 7.36 | 7.37 | 7.38 | 7.40 | 7.41 | 7.42 |
| 58.5 | 7.16 | 7.18 | 7.20 | 7.22 | 7.23 | 7.25 | 7.27 | 7.29 | 7.30 | 7.32 | 7.33 | 7.35 | 7.36 | 7.37 | 7.39 | 7.40 | 7.41 |
| 60.0 | 7.14 | 7.17 | 7.19 | 7.20 | 7.22 | 7.24 | 7.26 | 7.27 | 7.29 | 7.31 | 7.32 | 7.33 | 7.35 | 7.36 | 7.37 | 7.39 | 7.40 |
| 61.5 | 7.13 | 7.15 | 7.17 | 7.19 | 7.21 | 7.23 | 7.25 | 7.26 | 7.28 | 7.29 | 7.31 | 7.32 | 7.34 | 7.35 | 7.36 | 7.38 | 7.39 |
| 63.0 | 7.12 | 7.14 | 7.16 | 7.18 | 7.20 | 7.22 | 7.24 | 7.25 | 7.27 | 7.28 | 7.30 | 7.31 | 7.33 | 7.34 | 7.35 | 7.37 | 7.38 |
| 64.5 | 7.11 | 7.13 | 7.15 | 7.17 | 7.19 | 7.21 | 7.23 | 7.24 | 7.26 | 7.27 | 7.29 | 7.30 | 7.32 | 7.33 | 7.34 | 7.36 | 7.37 |
| 66.0 | 7.10 | 7.12 | 7.14 | 7.16 | 7.18 | 7.20 | 7.22 | 7.23 | 7.25 | 7.26 | 7.28 | 7.29 | 7.31 | 7.32 | 7.33 | 7.35 | 7.36 |
| 67.5 | 7.09 | 7.11 | 7.13 | 7.15 | 7.17 | 7.19 | 7.21 | 7.22 | 7.24 | 7.25 | 7.27 | 7.28 | 7.30 | 7.31 | 7.32 | 7.34 | 7.35 |
| 69.0 | 7.08 | 7.10 | 7.12 | 7.14 | 7.16 | 7.18 | 7.20 | 7.21 | 7.23 | 7.24 | 7.26 | 7.27 | 7.29 | 7.30 | 7.31 | 7.33 | 7.34 |
| 70.5 | 7.07 | 7.10 | 7.12 | 7.13 | 7.15 | 7.17 | 7.19 | 7.20 | 7.22 | 7.24 | 7.25 | 7.26 | 7.28 | 7.29 | 7.30 | 7.32 | 7.33 |
| 72.0 | 7.07 | 7.09 | 7.11 | 7.13 | 7.14 | 7.16 | 7.18 | 7.20 | 7.21 | 7.23 | 7.24 | 7.26 | 7.27 | 7.28 | 7.30 | 7.31 | 7.32 |
| 73.5 | 7.06 | 7.08 | 7.10 | 7.12 | 7.14 | 7.15 | 7.17 | 7.19 | 7.20 | 7.22 | 7.23 | 7.25 | 7.26 | 7.27 | 7.29 | 7.30 | 7.31 |
| 75.0 | 7.05 | 7.07 | 7.09 | 7.11 | 7.13 | 7.14 | 7.16 | 7.18 | 7.19 | 7.21 | 7.22 | 7.24 | 7.25 | 7.26 | 7.28 | 7.29 | 7.30 |
| 76.5 | 7.04 | 7.06 | 7.08 | 7.10 | 7.12 | 7.14 | 7.15 | 7.17 | 7.18 | 7.20 | 7.21 | 7.23 | 7.24 | 7.26 | 7.27 | 7.28 | 7.29 |
| 78.0 | 7.03 | 7.05 | 7.07 | 7.09 | 7.11 | 7.13 | 7.14 | 7.16 | 7.18 | 7.19 | 7.21 | 7.22 | 7.23 | 7.25 | 7.26 | 7.27 | 7.29 |
| 79.5 | 7.02 | 7.04 | 7.06 | 7.08 | 7.10 | 7.12 | 7.14 | 7.15 | 7.17 | 7.18 | 7.20 | 7.21 | 7.23 | 7.24 | 7.25 | 7.27 | 7.28 |
| 81.0 | 7.01 | 7.04 | 7.06 | 7.07 | 7.09 | 7.11 | 7.13 | 7.14 | 7.16 | 7.18 | 7.19 | 7.20 | 7.22 | 7.23 | 7.24 | 7.26 | 7.27 |
| 82.5 | 7.01 | 7.03 | 7.05 | 7.07 | 7.09 | 7.10 | 7.12 | 7.14 | 7.15 | 7.17 | 7.18 | 7.20 | 7.21 | 7.22 | 7.24 | 7.25 | 7.26 |
| 84.0 | 7.00 | 7.02 | 7.04 | 7.06 | 7.08 | 7.10 | 7.11 | 7.13 | 7.14 | 7.16 | 7.17 | 7.19 | 7.20 | 7.22 | 7.23 | 7.24 | 7.25 |
| 85.5 | 6.99 | 7.01 | 7.03 | 7.05 | 7.07 | 7.09 | 7.10 | 7.12 | 7.14 | 7.15 | 7.17 | 7.18 | 7.19 | 7.21 | 7.22 | 7.23 | 7.25 |
| 87.0 | 6.98 | 7.00 | 7.02 | 7.04 | 7.06 | 7.08 | 7.10 | 7.11 | 7.13 | 7.14 | 7.16 | 7.17 | 7.19 | 7.20 | 7.21 | 7.23 | 7.24 |
| 88.5 | 6.98 | 7.00 | 7.02 | 7.04 | 7.05 | 7.07 | 7.09 | 7.11 | 7.12 | 7.14 | 7.15 | 7.17 | 7.18 | 7.19 | 7.21 | 7.22 | 7.23 |
| 90.0 | 6.97 | 6.99 | 7.01 | 7.03 | 7.05 | 7.07 | 7.08 | 7.10 | 7.11 | 7.13 | 7.14 | 7.16 | 7.17 | 7.19 | 7.20 | 7.21 | 7.22 |
| 91.5 | 6.96 | 6.98 | 7.00 | 7.02 | 7.04 | 7.06 | 7.07 | 7.09 | 7.11 | 7.12 | 7.14 | 7.15 | 7.17 | 7.18 | 7.19 | 7.20 | 7.22 |
| 93.0 | 6.95 | 6.98 | 7.00 | 7.01 | 7.03 | 7.05 | 7.07 | 7.08 | 7.10 | 7.12 | 7.13 | 7.14 | 7.16 | 7.17 | 7.18 | 7.20 | 7.21 |
| 94.5 | 6.95 | 6.97 | 6.99 | 7.01 | 7.03 | 7.04 | 7.06 | 7.08 | 7.09 | 7.11 | 7.12 | 7.14 | 7.15 | 7.16 | 7.18 | 7.19 | 7.20 |
| 96.0 | 6.94 | 6.96 | 6.98 | 7.00 | 7.02 | 7.04 | 7.05 | 7.07 | 7.09 | 7.10 | 7.12 | 7.13 | 7.14 | 7.16 | 7.17 | 7.18 | 7.20 |
| 97.5 | 6.93 | 6.95 | 6.97 | 6.99 | 7.01 | 7.03 | 7.05 | 7.06 | 7.08 | 7.09 | 7.11 | 7.12 | 7.14 | 7.15 | 7.16 | 7.18 | 7.19 |
| 99.0 | 6.93 | 6.95 | 6.97 | 6.99 | 7.01 | 7.02 | 7.04 | 7.06 | 7.07 | 7.09 | 7.10 | 7.12 | 7.13 | 7.14 | 7.16 | 7.17 | 7.18 |

blood gas samples at 0, 4, 8, and 12 h. To assess the clinical value of this transcutaneous data, the doctor responsible for the subject's care was shown blinded values for $P_{tcCO_2}$, transcutaneous pH, $P_{aCO_2}$, and arterial pH and to indicate whether the same management decision would be made based on each data set.

Table 2. Bicarbonate Prediction Algorithm

| Initial Bicarbonate (mmol/L) | Bicarbonate (mmol/L) Calculated at: | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0.5 h | 1 h | 2 h | 3 h | 4 h | 5 h | 6 h | 7 h | 8 h | 9 h | 10 h | 12 h | 14 h | 16 h | 18 h | 20 h | 22 h |
| 15.0 | 15.11 | 15.23 | 15.45 | 15.68 | 15.90 | 16.13 | 16.35 | 16.58 | 16.80 | 17.03 | 17.25 | 17.70 | 18.15 | 18.60 | 19.05 | 19.50 | 19.95 |
| 15.5 | 15.61 | 15.73 | 15.95 | 16.18 | 16.40 | 16.63 | 16.85 | 17.08 | 17.30 | 17.53 | 17.75 | 18.20 | 18.65 | 19.10 | 19.55 | 20.00 | 20.45 |
| 16.0 | 16.11 | 16.23 | 16.45 | 16.68 | 16.90 | 17.13 | 17.35 | 17.58 | 17.80 | 18.03 | 18.25 | 18.70 | 19.15 | 19.60 | 20.05 | 20.50 | 20.95 |
| 16.5 | 16.61 | 16.73 | 16.95 | 17.18 | 17.40 | 17.63 | 17.85 | 18.08 | 18.30 | 18.53 | 18.75 | 19.20 | 19.65 | 20.10 | 20.55 | 21.00 | 21.45 |
| 17.0 | 17.11 | 17.23 | 17.45 | 17.68 | 17.90 | 18.13 | 18.35 | 18.58 | 18.80 | 19.03 | 19.25 | 19.70 | 20.15 | 20.60 | 21.05 | 21.50 | 21.95 |
| 17.5 | 17.61 | 17.73 | 17.95 | 18.18 | 18.40 | 18.63 | 18.85 | 19.08 | 19.30 | 19.53 | 19.75 | 20.20 | 20.65 | 21.10 | 21.55 | 22.00 | 22.45 |
| 18.0 | 18.11 | 18.23 | 18.45 | 18.68 | 18.90 | 19.13 | 19.35 | 19.58 | 19.80 | 20.03 | 20.25 | 20.70 | 21.15 | 21.60 | 22.05 | 22.50 | 22.95 |
| 18.5 | 18.61 | 18.73 | 18.95 | 19.18 | 19.40 | 19.63 | 19.85 | 20.08 | 20.30 | 20.53 | 20.75 | 21.20 | 21.65 | 22.10 | 22.55 | 23.00 | 23.45 |
| 19.0 | 19.11 | 19.23 | 19.45 | 19.68 | 19.90 | 20.13 | 20.35 | 20.58 | 20.80 | 21.03 | 21.25 | 21.70 | 22.15 | 22.60 | 23.05 | 23.50 | 23.95 |
| 19.5 | 19.61 | 19.73 | 19.95 | 20.18 | 20.40 | 20.63 | 20.85 | 21.08 | 21.30 | 21.53 | 21.75 | 22.20 | 22.65 | 23.10 | 23.55 | 24.00 | 24.45 |
| 20.0 | 20.11 | 20.23 | 20.45 | 20.68 | 20.90 | 21.13 | 21.35 | 21.58 | 21.80 | 22.03 | 22.25 | 22.70 | 23.15 | 23.60 | 24.05 | 24.50 | 24.95 |
| 20.5 | 20.61 | 20.73 | 20.95 | 21.18 | 21.40 | 21.63 | 21.85 | 22.08 | 22.30 | 22.53 | 22.75 | 23.20 | 23.65 | 24.10 | 24.55 | 25.00 | 25.45 |
| 21.0 | 21.11 | 21.23 | 21.45 | 21.68 | 21.90 | 22.13 | 22.35 | 22.58 | 22.80 | 23.03 | 23.25 | 23.70 | 24.15 | 24.60 | 25.05 | 25.50 | 25.95 |
| 21.5 | 21.61 | 21.73 | 21.95 | 22.18 | 22.40 | 22.63 | 22.85 | 23.08 | 23.30 | 23.53 | 23.75 | 24.20 | 24.65 | 25.10 | 25.55 | 26.00 | 26.45 |
| 22.0 | 22.11 | 22.23 | 22.45 | 22.68 | 22.90 | 23.13 | 23.35 | 23.58 | 23.80 | 24.03 | 24.25 | 24.70 | 25.15 | 25.60 | 26.05 | 26.50 | 26.95 |
| 22.5 | 22.61 | 22.73 | 22.95 | 23.18 | 23.40 | 23.63 | 23.85 | 24.08 | 24.30 | 24.53 | 24.75 | 25.20 | 25.65 | 26.10 | 26.55 | 27.00 | 27.45 |
| 23.0 | 23.11 | 23.23 | 23.45 | 23.68 | 23.90 | 24.13 | 24.35 | 24.58 | 24.80 | 25.03 | 25.25 | 25.70 | 26.15 | 26.60 | 27.05 | 27.50 | 27.95 |
| 23.5 | 23.61 | 23.73 | 23.95 | 24.18 | 24.40 | 24.63 | 24.85 | 25.08 | 25.30 | 25.53 | 25.75 | 26.20 | 26.65 | 27.10 | 27.55 | 28.00 | 28.45 |
| 24.0 | 24.11 | 24.23 | 24.45 | 24.68 | 24.90 | 25.13 | 25.35 | 25.58 | 25.80 | 26.03 | 26.25 | 26.70 | 27.15 | 27.60 | 28.05 | 28.50 | 28.95 |
| 24.5 | 24.61 | 24.73 | 24.95 | 25.18 | 25.40 | 25.63 | 25.85 | 26.08 | 26.30 | 26.53 | 26.75 | 27.20 | 27.65 | 28.10 | 28.55 | 29.00 | 29.45 |
| 25.0 | 25.11 | 25.23 | 25.45 | 25.68 | 25.90 | 26.13 | 26.35 | 26.58 | 26.80 | 27.03 | 27.25 | 27.70 | 28.15 | 28.60 | 29.05 | 29.50 | 29.95 |
| 25.5 | 25.61 | 25.73 | 25.95 | 26.18 | 26.40 | 26.63 | 26.85 | 27.08 | 27.30 | 27.53 | 27.75 | 28.20 | 28.65 | 29.10 | 29.55 | 30.00 | 30.45 |
| 26.0 | 26.11 | 26.23 | 26.45 | 26.68 | 26.90 | 27.13 | 27.35 | 27.58 | 27.80 | 28.03 | 28.25 | 28.70 | 29.15 | 29.60 | 30.05 | 30.50 | 30.95 |
| 26.5 | 26.61 | 26.73 | 26.95 | 27.18 | 27.40 | 27.63 | 27.85 | 28.08 | 28.30 | 28.53 | 28.75 | 29.20 | 29.65 | 30.10 | 30.55 | 31.00 | 31.45 |
| 27.0 | 27.11 | 27.23 | 27.45 | 27.68 | 27.90 | 28.13 | 28.35 | 28.58 | 28.80 | 29.03 | 29.25 | 29.70 | 30.15 | 30.60 | 31.05 | 31.50 | 31.95 |
| 27.5 | 27.61 | 27.73 | 27.95 | 28.18 | 28.40 | 28.63 | 28.85 | 29.08 | 29.30 | 29.53 | 29.75 | 30.20 | 30.65 | 31.10 | 31.55 | 32.00 | 32.45 |
| 28.0 | 28.11 | 28.23 | 28.45 | 28.68 | 28.90 | 29.13 | 29.35 | 29.58 | 29.80 | 30.03 | 30.25 | 30.70 | 31.15 | 31.60 | 32.05 | 32.50 | 32.95 |
| 28.5 | 28.61 | 28.73 | 28.95 | 29.18 | 29.40 | 29.63 | 29.85 | 30.08 | 30.30 | 30.53 | 30.75 | 31.20 | 31.65 | 32.10 | 32.55 | 33.00 | 33.45 |
| 29.0 | 29.11 | 29.23 | 29.45 | 29.68 | 29.90 | 30.13 | 30.35 | 30.58 | 30.80 | 31.03 | 31.25 | 31.70 | 32.15 | 32.60 | 33.05 | 33.50 | 33.95 |
| 29.5 | 29.61 | 29.73 | 29.95 | 30.18 | 30.40 | 30.63 | 30.85 | 31.08 | 31.30 | 31.53 | 31.75 | 32.20 | 32.65 | 33.10 | 33.55 | 34.00 | 34.45 |
| 30.0 | 30.11 | 30.23 | 30.45 | 30.68 | 30.90 | 31.13 | 31.35 | 31.58 | 31.80 | 32.03 | 32.25 | 32.70 | 33.15 | 33.60 | 34.05 | 34.50 | 34.95 |
| 30.5 | 30.61 | 30.73 | 30.95 | 31.18 | 31.40 | 31.63 | 31.85 | 32.08 | 32.30 | 32.53 | 32.75 | 33.20 | 33.65 | 34.10 | 34.55 | 35.00 | 35.45 |
| 31.0 | 31.11 | 31.23 | 31.45 | 31.68 | 31.90 | 32.13 | 32.35 | 32.58 | 32.80 | 33.03 | 33.25 | 33.70 | 34.15 | 34.60 | 35.05 | 35.50 | 35.95 |
| 31.5 | 31.61 | 31.73 | 31.95 | 32.18 | 32.40 | 32.63 | 32.85 | 33.08 | 33.30 | 33.53 | 33.75 | 34.20 | 34.65 | 35.10 | 35.55 | 36.00 | 36.45 |
| 32.0 | 32.06 | 32.12 | 32.24 | 32.36 | 32.48 | 32.60 | 32.72 | 32.84 | 32.96 | 33.08 | 33.20 | 33.44 | 33.68 | 33.92 | 34.16 | 34.40 | 34.64 |
| 32.5 | 32.56 | 32.62 | 32.74 | 32.86 | 32.98 | 33.10 | 33.22 | 33.34 | 33.46 | 33.58 | 33.70 | 33.94 | 34.18 | 34.42 | 34.66 | 34.90 | 35.14 |
| 33.0 | 33.06 | 33.12 | 33.24 | 33.36 | 33.48 | 33.60 | 33.72 | 33.84 | 33.96 | 34.08 | 34.20 | 34.44 | 34.68 | 34.92 | 35.16 | 35.40 | 35.64 |
| 33.5 | 33.56 | 33.62 | 33.74 | 33.86 | 33.98 | 34.10 | 34.22 | 34.34 | 34.46 | 34.58 | 34.70 | 34.94 | 35.18 | 35.42 | 35.66 | 35.90 | 36.14 |
| 34.0 | 34.06 | 34.12 | 34.24 | 34.36 | 34.48 | 34.60 | 34.72 | 34.84 | 34.96 | 35.08 | 35.20 | 35.44 | 35.68 | 35.92 | 36.16 | 36.40 | 36.64 |
| 34.5 | 34.56 | 34.62 | 34.74 | 34.86 | 34.98 | 35.10 | 35.22 | 35.34 | 35.46 | 35.58 | 35.70 | 35.94 | 36.18 | 36.42 | 36.66 | 36.90 | 37.14 |
| 35.0 | 35.06 | 35.12 | 35.24 | 35.36 | 35.48 | 35.60 | 35.72 | 35.84 | 35.96 | 36.08 | 36.20 | 36.44 | 36.68 | 36.92 | 37.16 | 37.40 | 37.64 |
| 35.5 | 35.56 | 35.62 | 35.74 | 35.86 | 35.98 | 36.10 | 36.22 | 36.34 | 36.46 | 36.58 | 36.70 | 36.94 | 37.18 | 37.42 | 37.66 | 37.90 | 38.14 |
| 36.0 | 36.06 | 36.12 | 36.24 | 36.36 | 36.48 | 36.60 | 36.72 | 36.84 | 36.96 | 37.08 | 37.20 | 37.44 | 37.68 | 37.92 | 38.16 | 38.40 | 38.64 |
| 36.5 | 36.56 | 36.62 | 36.74 | 36.86 | 36.98 | 37.10 | 37.22 | 37.34 | 37.46 | 37.58 | 37.70 | 37.94 | 38.18 | 38.42 | 38.66 | 38.90 | 39.14 |
| 37.0 | 37.06 | 37.12 | 37.24 | 37.36 | 37.48 | 37.60 | 37.72 | 37.84 | 37.96 | 38.08 | 38.20 | 38.44 | 38.68 | 38.92 | 39.16 | 39.40 | 39.64 |
| 37.5 | 37.56 | 37.62 | 37.74 | 37.86 | 37.98 | 38.10 | 38.22 | 38.34 | 38.46 | 38.58 | 38.70 | 38.94 | 39.18 | 39.42 | 39.66 | 39.90 | 40.14 |
| 38.0 | 38.06 | 38.12 | 38.24 | 38.36 | 38.48 | 38.60 | 38.72 | 38.84 | 38.96 | 39.08 | 39.20 | 39.44 | 39.68 | 39.92 | 40.16 | 40.40 | 40.64 |
| 38.5 | 38.56 | 38.62 | 38.74 | 38.86 | 38.98 | 39.10 | 39.22 | 39.34 | 39.46 | 39.58 | 39.70 | 39.94 | 40.18 | 40.42 | 40.66 | 40.90 | 41.14 |
| 39.0 | 39.06 | 39.12 | 39.24 | 39.36 | 39.48 | 39.60 | 39.72 | 39.84 | 39.96 | 40.08 | 40.20 | 40.44 | 40.68 | 40.92 | 41.16 | 41.40 | 41.64 |

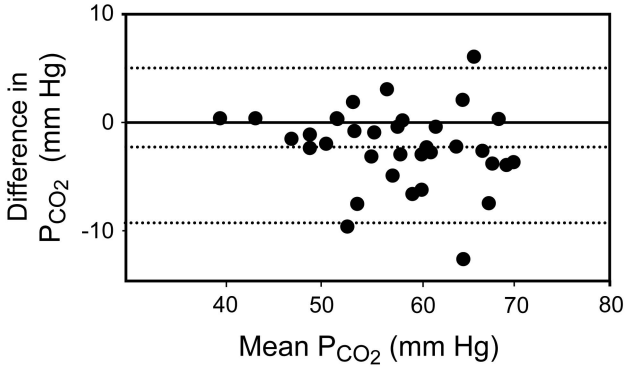


Fig. 2. Bland-Altman analysis of agreement between $P_{CO_2}$ methods. The center horizontal dotted line represents the mean bias, with the upper and lower horizontal dotted lines showing +2 SD and −2 SD, respectively.

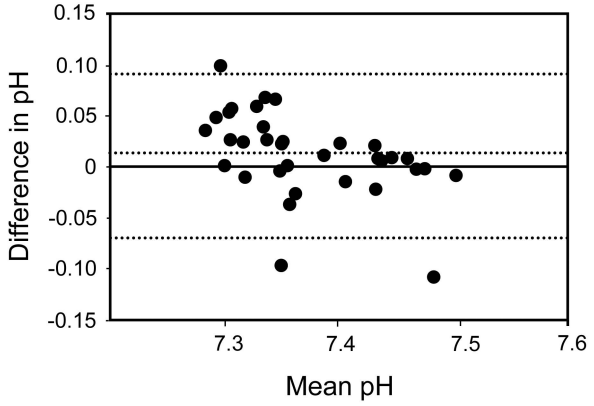


Fig. 3. Bland-Altman analysis of agreement between pH methods. The center horizontal dotted line represents the mean bias, with the upper and lower horizontal dotted lines showing +2 SD and −2 SD, respectively.

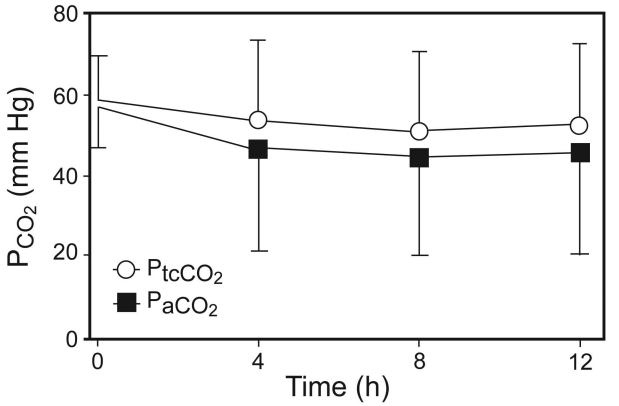


Fig. 4. Time trends for $P_{CO_2}$ methods. Data are shown as mean ± SD. $P_{tcCO_2}$ = transcutaneously measured partial pressure of carbon dioxide.

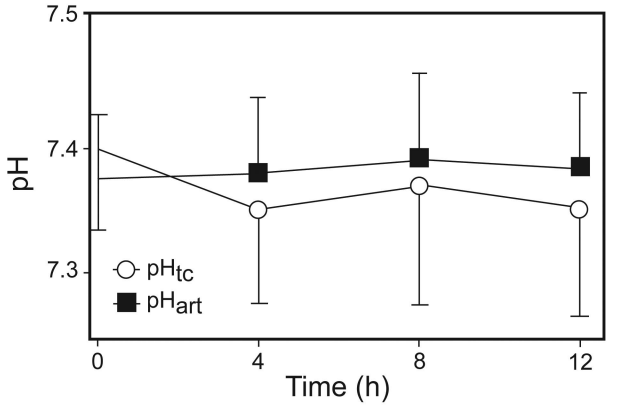


Fig. 5. Time trends for pH methods. Data are shown as mean ± SD. $pH_{tc}$ = transcutaneous pH; $pH_{art}$ = arterial pH.

### Outcome Measures

The primary outcome measures were to assess agreement between $P_{tcCO_2}$ and $P_{aCO_2}$ and also between arterial pH and calculated transcutaneous pH. Secondary objectives assessed reported pain scores for each method, as well as the clinical value of isolated transcutaneous data.

### Data Analysis

A Bland-Altman scatterplot[16] was constructed by plotting the difference between $P_{tcCO_2}$ and $P_{aCO_2}$ against the mean of these 2 measurements (Fig. 2). The same method was used to analyze transcutaneous pH and arterial pH (Fig. 3). Reference lines were added for mean bias and 95% limits of agreement (± 1.96 SD). Pearson correlation coefficients were determined for $P_{CO_2}$ and pH paired data to quantify any relationship. The mean time trends for $P_{CO_2}$ (Fig. 4) and pH (Fig. 5) methods were plotted, and the trends for individual subjects were reviewed. Mean $P_{CO_2}$ biases at 0 and 12 h were compared using the Wilcoxon signed-rank test to assess sensor drift.

The clinical management decisions based on blinded pH and $P_{CO_2}$ data were analyzed qualitatively. The statistical difference between pain scores for each procedure (paired non-parametric data[17]) was assessed using the Wilcoxon signed-rank test.

Values are presented as mean point estimates with 2 SD or median with interquartile range (IQR). Data analysis and presentation were carried out using SPSS 21 (SPSS, Chicago, Illinois), and Prism 5.04 (GraphPad Software, San Diego, California).

## Results

Of 12 eligible subjects, 10 provided consent and were recruited, with one later withdrawing from the study. Diagnoses were exacerbation of COPD (6 subjects), obesity

hypoventilation syndrome (2 subjects), motor neuron disease (one subject), and myasthenia gravis (one subject). The median age was 68.4 (IQR 62.5–72.3) y. Mean arterial blood gas values of $P_{aCO_2}$, pH, and bicarbonate on admission were 75.53 (2 SD 48.15) mm Hg, 7.26 (2 SD 0.20), and 29.67 (2 SD 10.76) mmol/L, respectively. The median time between NIV initiation and study recruitment was 21.9 (IQR 10.5–29.8) h, which varied due to high-dependency unit admission via other wards and initially reduced consciousness impairing ability to consent. The median time for the device plateau phase to appear was 8 (IQR 6–8) min.

No serious adverse events occurred due to the TCM4 probe, and the sensor was tolerated well by most subjects. Technical problems were limited to blown fuses on 2 occasions. One subject found the probe uncomfortable to lie on and withdrew from the study. The $P_{tcCO_2}$ trace was lost twice and required correction by replacing the adhesive ear clip. On 2 occasions, arterial lines became obstructed and precluded further blood sampling. For one of these subjects, it was deemed clinically unnecessary to resume invasive monitoring at that time, and therefore, data collection from that volunteer was discontinued. No other arterial line complications occurred.

In every subject, $P_{tcCO_2}$ and $P_{aCO_2}$ followed a concordant trend over 12 h. Mean $P_{CO_2}$ bias was −2.33 (2 SD 7.35, 95% limits of agreement of 9.60–4.95) mm Hg. Bland-Altman analysis (see Fig. 2) revealed weaker agreement at severe hypercapnia above 65 mm Hg. The Pearson correlation coefficient, $r = 0.89$ ($P < .001$), indicated a positive, statistically significant relationship between $P_{CO_2}$ data. Mean $P_{CO_2}$ bias weakened from −1.95 (2 SD 4.58) mm Hg at time 0 to −2.63 (2 SD 12.30) mm Hg after 12 h, although this drift was statistically insignificant ($P = .58$). Analysis of mean (see Fig. 4) and individual subject time trends revealed a concordant pattern, where $P_{tcCO_2}$ generally overestimated $P_{aCO_2}$, with agreement strongest at 8 h. Establishing transcutaneous monitoring was significantly less painful ($P = .008$) than setting up a line for arterial sampling (Fig. 6).

Mean pH bias was 0.012 (2 SD 0.084, 95% limits of agreement of −0.070 to 0.094). Bland-Altman analysis (see Fig. 3) showed that transcutaneous pH generally agreed with arterial pH, with weaker agreement in severe acidosis below 7.30. A positive, statistically significant relationship ($r = 0.84$, $P < .001$) existed between the pH methods. Mean transcutaneous pH (see Fig. 5) initially overestimated arterial pH by 0.022 (2 SD 0.108) and, after 12 h, underestimated by 0.031 (2 SD 0.109), mirroring the trend in $P_{CO_2}$.

Analysis of blinded data revealed that if clinical decisions had been based on transcutaneous monitoring alone, NIV management would have been identical on 85% of 34 occasions. Inconsistencies in hypothetical management decisions were due to inaccurate calculation of bicarbonate rather than disparity between $P_{CO_2}$ methods.

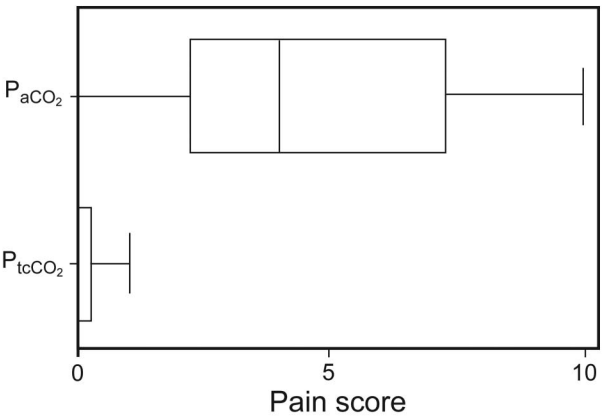


Fig. 6. Numerical Rating Scale pain scores for $P_{CO_2}$ methods. Box plots show the 25th and 75th percentiles, the vertical line shows the median, and whiskers denote maximum range. $P_{tcCO_2}$ = transcutaneously measured partial pressure of carbon dioxide.

## Discussion

This pilot study found that subjects requiring NIV for acute hypercapnic respiratory failure preferred transcutaneous monitoring to arterial blood gas measurement. $P_{tcCO_2}$ monitoring provided a reliable time trend. Moreover, $P_{tcCO_2}$ in conjunction with calculated bicarbonate enabled the construction of a pH prediction algorithm that could be used (particularly with COPD subjects) to guide NIV therapy and had the potential to minimize arterial $P_{CO_2}$ measurements.

Eight studies have compared arterial to $P_{tcCO_2}$ values in subjects requiring NIV. Of these, only 2 studies have assessed the time trend over 4 h[11] and 8 h[8] in subjects requiring NIV for acute on chronic hypercapnic respiratory failure. Our study evaluated sustained $P_{tcCO_2}$ monitoring over a 12-h period in subjects receiving NIV for a broad etiology of acute hypercapnic respiratory failure. Our study population was representative of those patients who usually receive NIV, and therefore, our results are likely to be generalizable. This is the first study to demonstrate that patients prefer $P_{tcCO_2}$ to arterial blood gas measurement in acute settings. Our use of a pH prediction algorithm is another novelty and has the potential to transform the monitoring of patients receiving NIV, enabling noninvasive monitoring for NIV.

In our study, the mean $P_{CO_2}$ bias of −2.33 (2 SD 7.35) mm Hg is similar to that reported previously.[6] Bland-Altman analysis showed $P_{CO_2}$ bias to be more divergent at higher mean $P_{CO_2}$, suggesting that sustained severe

hypercapnia was monitored with less precision by the transcutaneous method. Previous authors have suggested 7.50 mm Hg as the clinically acceptable limit for the maximum mean bias between $P_{CO_2}$ methods.[4,10,18,19] Ninety-five percent of $P_{tcCO_2}$ values in this study were within 7.35 mm Hg of $P_{aCO_2}$, which we feel would be acceptable in the clinical environment for $P_{CO_2}$ monitoring. Agreement was unacceptably weak for 2 subjects ($P_{tcCO_2}$ overestimated by up to 12.68 mm Hg); however, the time trend was recorded correctly. The consistent transcutaneous overestimation of $P_{aCO_2}$ rouses suspicion that a systematic error may exist in the device calibration algorithm.

The reliability of transcutaneous pH monitoring was assessed over the range 7.30–7.50. Bland-Altman analysis revealed that calculated transcutaneous pH generally agreed well with arterial pH. The broad 95% limits of agreement (−0.070 to 0.094) were caused by data from one subject who was unable to give consent for recruitment until 106 h after NIV initiation; our algorithm for bicarbonate prediction may therefore be applicable in the first 24–48 h after admission and is perhaps invalid once the acute phase of therapy has stabilized. Bicarbonate prediction was also poor when the initial arterial bicarbonate reading was very high: when initial bicarbonate was above 34.0 mmol/L, the concentration was observed to decrease more rapidly during NIV treatment. This may be correctable with an improved prediction algorithm based on a wider review of patients. Moreover, all subjects in our study had pure respiratory acidosis, and our pH prediction is unlikely to work in patients with a mixed or metabolic acidosis.

Subjects could have received similar NIV treatment based on 85% of 34 paired measurements if transcutaneous data for $P_{CO_2}$ and pH were considered alone. Of the remainder, the differences would have led to altered management for 2 subjects. On one occasion the pH algorithm failed due to an initially high bicarbonate concentration of 39 mmol/L that resolved faster than predicted. On an additional 2 occasions, the error was due to significant transcutaneous overestimation of $P_{aCO_2}$.

Our study was limited by the small sample size, and subjects were recruited > 24 h after admission. This meant that the majority of subjects only had a mild acidosis. We plan a future study to investigate subjects within 24 h of admission, allowing better representation of those with more severe acidosis and also informing a pH prediction algorithm that takes into account those with high bicarbonate concentrations at admission.

## Conclusions

Arterial blood gas analysis can be time-consuming and painful for patients. Furthermore, blood samples are taken intermittently, potentially delaying the recognition of clinically important changes in patients. Although further work is required to validate pH calculation in this cohort, this study demonstrates that continuous $P_{tcCO_2}$ monitoring provides a promising alternative to repeated blood sampling in subjects requiring NIV for acute hypercapnic respiratory failure.


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