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Validity of transcutaneous PCO_2 in monitoring chronic hypoventilation treated with non-invasive ventilation

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ABSTRACT

Background: Non-invasive ventilation (NIV) is an efficient treatment for patients with chronic hypercapnic respiratory failure (CRF), but requires regular monitoring to detect both diurnal and nocturnal residual hypercapnia.
The present study was designed to determine 1) whether transcutaneous PCO_2 ($PtcCO_2$) is a valid tool for monitoring $PaCO_2$ in this group of patients, and 2) if overnight instrumental drift of the $PtcCO_2$ sensor is clinically significant.
Methods: Sixty-seven patients with CRF on long term NIV were included. Arterial blood gases (ABG) were sampled from the radial artery during $PtcCO_2$ measurement. $PtcCO_2$ was recorded 2 min after ABG sampling. Instrumental drift was tested by measuring a gas of known CO_2 concentration after auto-calibration of the sensor in the evening, and on the following morning.
Findings: $PaCO_2$ values ranged from 3·97 kPa to 9.0 kPa. Thirty-six (53%) patients were hypercapnic. Correlation between $PaCO_2$ and $PtcCO_2$ was highly significant ($r^2 = 0.9$, $p < 0.0001$), Bias (d) and SD of bias (s) were 0.23 kPa and 0.28 kPa respectively, with a minor underestimation of $PaCO_2$. Limits of agreement ($d \pm 2s$) were; −0.32; 0.79 kPa. None of the paired values of $PaCO_2/PtcCO_2$ had a difference exceeding 1 kPa. The mean drift of $PtcCO_2$ was 0.14 ± 0.54 kPa/8 h ($p = 0.04$; 95% CI: 0.01–0.27).
Interpretation: With the device tested, in stable patients under NIV-treatment for CRF, $PtcCO_2$ accurately reflects $PaCO_2$. $PtcCO_2$ can be used to monitor CO_2 overnight during NIV without any clinically significant drift.
Trial registration N°: NCT01845233.

1. Introduction

Non-invasive ventilation (NIV) is an efficient treatment for patients with chronic hypercapnic respiratory failure (CRF) due to neuromuscular diseases, (NMD), restrictive thoracic disorders (RTD), obesity hypoventilation syndrome (OHS), and central hypoventilation syndromes (CHS). Regular assessment of the efficacy of ventilation is recommended, usually including a daytime sampling of arterial blood gases (ABG) and nocturnal pulse oximetry [1,2].

The importance of correcting daytime arterial CO_2 ($PaCO_2$) in patients treated with long term nocturnal NIV has recently been stressed [3–6]. ABG analysis is the gold standard for measuring $PaCO_2$. However, ABG sampling requires expertise, can be painful and difficult to perform in patients with severe deformities or morbid obesity, and carries a risk of complications [7]. Furthermore ABG analysis is rarely available in sleep centres [8] or in patients' homes.

Abbreviations: ABG, Arterial blood gas; CRF, Chronic hypercapnic respiratory failure; NIV, Non-invasive ventilation; NMD, Neuro muscular diseases; OHS, Obesity hypoventilation syndrome; PaCO2, Arterial CO2; PtcCO2, Transcutaneous PCO2; RTD, Restrictive thoracic disorders; CHS, Central hypoventilation syndrome.

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ABG analysis, although necessary, yields limited information. For instance, daytime ABG are poor predictors of nocturnal hypoventilation [9,10]. Sampling of ABG during sleep may detect nocturnal hypoventilation, but will not reflect variations of $PaCO_2$ related to sleep stages, position or mask leaks. Nocturnal pulse oximetry, although useful and easy to perform, may underestimate nocturnal hypoventilation [8,9,11], and it cannot discriminate nocturnal hypoventilation from other causes of hypoxaemia [2].

Transcutaneous monitoring of carbon dioxide ($PtcCO_2$) allows non-invasive and continuous measurements of $PaCO_2$. Although the accuracy of $PtcCO_2$ has been a subject of debate, $PtcCO_2$ monitors have become easier to use in clinical practice [12] and have shown acceptable agreement with $PaCO_2$ in a geriatric population [13], in patients with acute dyspnoea [14], patients with ALS [15], patients with severe obesity [16] and during cardiopulmonary exercise testing [17]. Conversely, studies conducted at emergency departments [18,19], during surgery [20,21] and in ICUs [20] report conflicting or poorer results, indicating that validity of $PtcCO_2$ may depend on the population studied and the clinical setting in which it is used. The small number of studies conducted in patients with CRF treated with NIV have either used older $PtcCO_2$ devices [22,23] or included a limited number of patients [24–26].

Although continuous $PtcCO_2$ measurement for 5–8 h is well tolerated, without causing cutaneous lesions, one concern is the overnight drift of the $PtcCO_2$ signal. Most studies addressing this issue include a limited number of patients, and both the methods used to measure the instrumental drift and the results differ considerably [22,23,25–30]. The uncertainty regarding $PtcCO_2$ drift is reflected in the conflicting recommendations regarding drift correction after nocturnal $PtcCO_2$ recordings [8,31,32]. This cumbersome procedure implies *in vivo* calibration with arterial or capillary blood gas sampling, adding discomfort for the patient and limiting its use in sleep centres and in patients' homes.

The present study was designed to determine 1) whether $PtcCO_2$ is a sufficiently accurate and precise tool for monitoring PaCO2 during routine follow-up visits in a large group of patients with CRF treated with long term NIV, and 2) if, in this setting, overnight drift of the $PtcCO_2$ sensor is clinically significant.

2. Materials and methods

The study protocol was approved by the Regional Committee for Medical and Health Research Ethics, NO = 2012/1142. Written informed consent was obtained from all participants.

2.1. Patients

Patients with CRF due to NMD, RTD, OHS or CHS on long term NIV for a minimum of 3 months and scheduled for a regular follow-up visit were included. Exclusion criteria were: age below 18 years, inability to co-operate, hospitalization due to an acute exacerbation or change of NIV-treatment <3 months before inclusion.

2.2. Measurements

Daytime ABG sampling from the radial artery was performed after the patients had been seated and were breathing room air for at least 30 min and then immediately analysed (COBAS B 221, Roche, Germany). Daytime and overnight $PtcCO_2$ was measured with a TCM Tosca® with the Sensor 92 (Radiometer, Denmark) attached via a single-use ear clip to the patients' earlobe and probe temperature set at 43 °C [33]. Auto-calibration, membrane replacement, temperature and metabolic correction were performed according to manufacturer's recommendations. Overnight $PtcCO_2$ signal was integrated to an online sleep recording system (Embletta Gold, Embla, Broomfield, USA). The $PtcCO_2$ sensor measures changes in pH produced by CO_2 diffusing through the skin to a buffer solution in the electrode. In order to measure the instrumental drift of the TCM Tosca capnograph, repeated ex vivo measurements of a calibration gas with a known CO_2 concentration were performed. The sensor was attached to a test unit containing the calibration gas and the PCO_2 was recorded. (Calibration Gas mixture for Blood Gas Analyzers, 11·2% CO_2, balanced N_2, Radiometer, Denmark).

2.3. Study design

Patients were hospitalized for their regular NIV follow-up. Prior to daytime ABG sampling, performed between 12:00 and 2:00 PM, $PtcCO_2$ was monitored continuously for at least 22 min to allow stabilisation of $PtcCO_2$ readings, as recommended by the manufacturer. Daytime $PtcCO_2$ was defined as the $PtcCO_2$ value recorded 2 min after ABG sampling [28,34]. The same sensor membrane was used during the night-time measurements. During overnight $PtcCO_2$ recordings, the signal quality was checked at least hourly. The instrumental drift was assessed by a repeated ex vivo calibration test. PCO_2 was measured using a gas mixture with a known CO_2 concentration. This procedure was performed at 11:00 PM after auto-calibration of the sensor, before attaching the sensor to the patient, and repeated at 7:00 AM before recalibration of the sensor.

2.4. Statistics

Correlation between $PtcCO_2$ and $PaCO_2$ was assessed by calculating Pearson's coefficient of correlation. Comparison between $PtcCO_2$ and $PaCO_2$ was performed according to Bland and Altman: mean difference between $PtcCO_2$ and $PaCO_2$ (d: bias), standard deviation of d (s: precision) and limits of agreement (LA = d ± 2s) were reported. A maximum bias of 1 kPa was considered as acceptable based on previous studies [20,25–27]. Paired sample t-tests were used to determine if the instrumental drift was significantly different from zero. P-values below 0.05 were considered significant. SPSS Software for Windows and MedCalc version 14.10.2 were used for statistical analysis.

2.5. Role of the funding source

The study was funded by the Norwegian National Advisory Unit on Long Term Mechanical Ventilation, Haukeland University Hospital and the Norwegian Neuro Muscular Diseases Foundation. The funders had no involvement in study design, in collection, analysis and interpretation of data, in writing of the report, or in the decision to submit the paper for publication.

3. Results

All patients with long term NIV scheduled for a regular follow-up visit at the Department of Pulmonary Medicine of Oslo University Hospital Ullevål between April 2013 and May 2014 were evaluated: 95 patients met the inclusion criteria. Twenty-eight patients were not included (Fig. 1). The remaining 67 patients were treated with NIV for OHS (n = 16), NMD (n = 36), CHS (n = 5) or RTD (n = 10). Main characteristics of patients are given in Table 1.

3.1. Comparison between transcutaneous and arterial PCO_2

Paired samples of ABG and $PtcCO_2$ were analysed in all 67 patients. $PaCO_2$ values ranged from 3.97 kPa to 9.0 kPa. Correlation between $PaCO_2$ and $PtcCO_2$ was highly significant ($r = 0.95$ $p < 0.0001$). Ninety percent of the variability of $PtcCO_2$ was

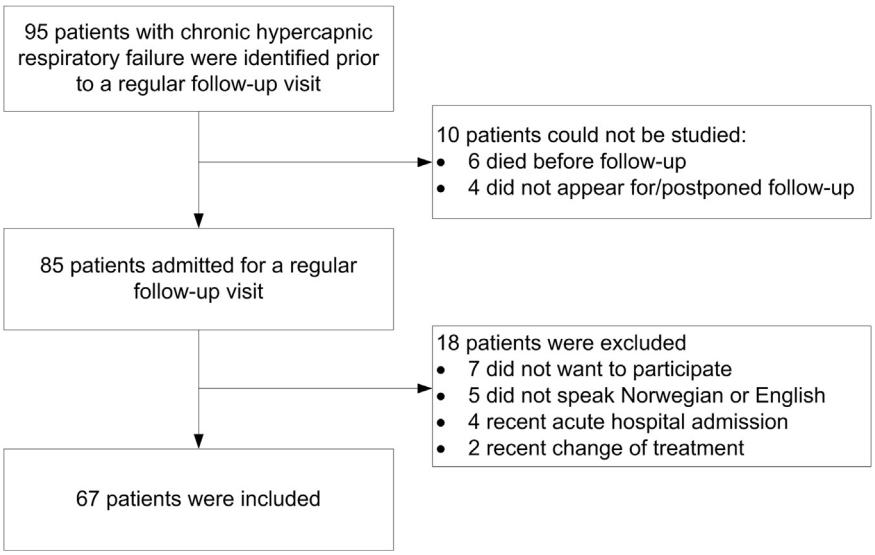

Fig. 1. Flow chart showing numbers of identified patients and reasons for not participating.

explained by changes in $PaCO_2$ ($r^2 = 0.9$, $p < 0.0001$). Bias (d) and SD of bias (s) were 0.23 kPa and 0.28 kPa, respectively, with $PtcCO_2$ on average slightly underestimating $PaCO_2$. Limits of agreement (d ± 2s) were; −0.32; 0.79 kPa (Fig. 2). None of the paired values of $PaCO_2$/$PtcCO_2$ differed by more than 1 kPa.

Mean $PaCO_2$ was 6·1 kPa (SD 0.9). Thirty-six (53%) of the patients were hypercapnic ($PaCO_2$ > 6.0 kPa), while none of the patients had a respiratory acidemia (pH < 7.3) and only 2 had a pH < 7.34. Agreement between $PaCO_2$ and $PtcCO_2$ in the sub-group of patients with a $PaCO_2$ > 6.0 kPa did not differ from that of the entire group; bias was 0.3 kPa, and limits of agreement were: −0.28; 0.84 kPa.

3.2. Instrumental drift of $PtcCO_2$

One patient disconnected the sensor prior to the morning measurement, and one recording showed an obvious technical error (morning $PtcCO_2$: 15 kPa). Thus, 65 paired measurements were analysed.

In six patients there was an intermittent loss of $PtcCO_2$ signal during the night: in two patients the sensor fell off and had to be reconnected (one needed a new ear clip), and in four patients there was probably a temporary displacement of the sensor, which corrected itself without interference from the staff. None of these incidents required recalibration of sensor or change of membrane.

The mean drift of $PtcCO_2$ (difference between morning and evening $PtcCO_2$ readings of 11.2% CO_2 gas sample) was 0.14 ± 0.54 kPa/8 h ($p = 0.04$; 95% CI: 0.01–0.27) (Fig. 3). Of the 3 measurements showing a difference >1 kPa/8 h, 2 had a temporary loss of $PtcCO_2$ signal.

Table 1
Main characteristics of study population (N = 67).

Age, years	57.7 ± 19.2
Male/female, n	35/32
Duration of NIV, months (range)	54.4 (3–324)
BMI, kg/m^2	28.1 ± 7.7
$PaCO_2$, kPa[a]	6.1 ± 0.9
PaO_2, kpa[a]	9·4 ± 1.5
pH	7.38 ± 0.04
FEV_1, % of predicted value	47 ± 24
FVC, % of predicted value	51 ± 26

Values presented as Mean ± SD, unless specified otherwise.
[a] Values reported were sampled in patients seated and breathing room air for at least 30 min.

4. Discussion

To our knowledge, this is the first study to compare arterial with transcutaneous values of PCO_2 and to measure overnight instrumental drift of $PtcCO_2$ in a large group of patients treated with NIV for CRF. Our results show that daytime $PaCO_2$ values were strongly correlated with $PtcCO_2$, over a wide range of $PaCO_2$ values, with a low bias and clinically acceptable limits of agreement. Importantly, none of the paired values of $PaCO_2$ − $PtcCO_2$ had a difference exceeding 1 kPa. Our data also show that $PtcCO_2$ can be used for overnight monitoring of NIV, most often without any clinically significant drift: overnight drift exceeded 1 kPa in 3 cases only. Finally, few problems related to the measurements occurred: one recording showed an obvious technical error, and 2 patients required reconnection of the sensor, without recalibration.

Bias (the mean of differences between $PaCO_2$ and $PtcCO_2$) was

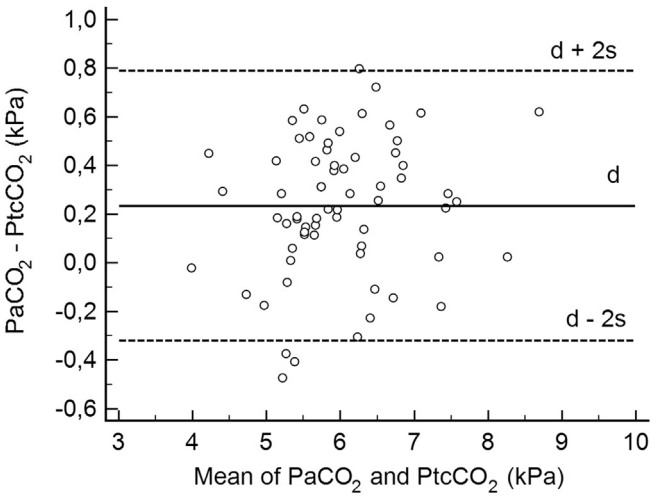

Fig. 2. Bias and limits of agreement of $PtcCO_2$ compared with $PaCO_2$ (n = 65).

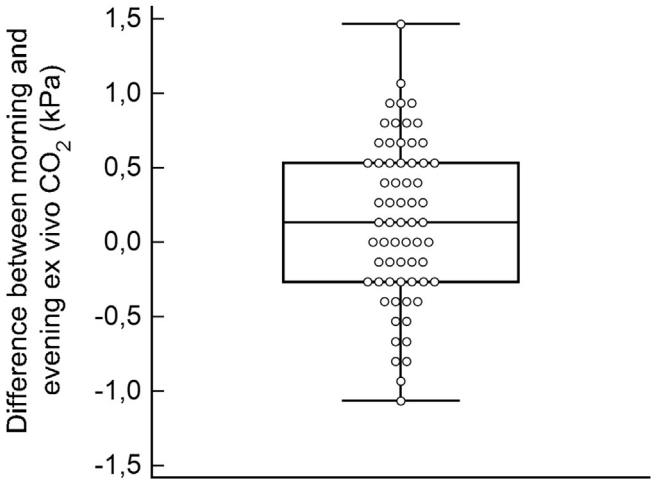

Fig. 3. Box-and-whisker plot of the difference between each paired measurement of ex vivo CO_2 testing. (n = 65). The central box represents median and 25 to 75 percentile values; 0.13 kPa and −0.27–0.53 kPa. The horizontal line extends from the minimum to the maximum value.

low (0.26 kPa), and Δ($PaCO_2$-$PtcCO_2$) never exceeded the previously defined clinically acceptable range of ±1 kPa [26,27]. Limits of agreement were also within values reported as acceptable: ±1.33 kPa [18], ±1.0 kPa [26] and ±0.67 kPa [14]. This is comparable with studies performed on other patient groups [13,15–17,35]. Patients included in the current study were in a stable clinical condition, without severe respiratory acidemia, hemodynamic instability, hypothermia, profound skin vasoconstriction or vasopressor treatment, factors which have all been associated with higher bias values and/or wider limits of agreement [18,20,36]. Indeed, in a study of 53 critically ill ICU patients, Bendjelid et al. compared more than 400 paired measurements of $PaCO_2$ and $PtcCO_2$ [27]: 19% of all paired measurements were defined as discordant, i.e. with a Δ($PtcCO_2$-$PaCO_2$) exceeding 1 kPa. The temperature of the sensor has also been shown to influence the accuracy of $PtcCO_2$ measurements. Nishiyama et al. suggested that sensor temperature should be at least 43 °C [33] as in the current study. Higher probe temperatures may indeed increase local hyperaemia in the capillary bed and thus have a positive impact on bias and limits of agreement of $PtcCO_2$; conversely, the poorer results found in previous studies may have been influenced by the use of lower sensor temperatures [20,27,36]. However, several studies using a probe T° of 42 °C showed similar results to ours [15–17,25], suggesting that other factors such as technical improvements in devices may also play an important role. Since our study did not compare different temperature settings and different sensors, we cannot quantify the importance of these factors.

Previous studies of $PtcCO_2$ in patients with chronic hypoventilation most often included a limited number of patients, few non-COPD patients, and were conducted with older devices or during NIV. The only study of stable patients with chronic hypoventilation breathing spontaneously included 12 patients (6 non-COPD), and showed both a low bias and low limits of agreement [24]. However, accuracy decreased and limits of agreement increased with higher CO_2-values (>7.3 kPa), a finding also described in other studies [22,23]. In our data, accuracy and limits of agreements were unaffected by increasing levels of $PaCO_2$. This discrepancy could be due to the low number of patients included or the devices assessed in the studies mentioned above [22–24]. Another study compared overnight $PtcCO_2$ with repeated ABG from an indwelling catheter in 15 patients: bias was low, but with wide limits of agreement [26], probably caused by “outliers” amongst a low number of measurements. Our results are in agreement with an overnight study of 24 patients with CRF (9 non-COPD patients) by Storre et al., reporting a good agreement between capillary ABG and $PtcCO_2$ during NIV. In two of the three devices tested (Sentec DM and Tosca 500), discrepancies exceeding the clinically acceptable threshold of 1 kPa were rare (1–2% of the recordings). Bias was low and limits of agreement were unchanged in the sub-group of measurements with a $PaCO_2$ > 6.7 kPa [25]. A compilation of studies reporting on $PtcCO_2$ performance is summarized in Table 2 [37–53] (For details see Supplementary data).

ABG remain the gold standard for detecting daytime hypercapnia. However, our data suggest that PtcCO2 can be a valid substitute in hemodynamically stable patients, and prove to be particularly useful in settings were ABG sampling is difficult to perform, such as sleep clinics or home monitoring of long term mechanical ventilation. A critical requirement for obtaining reliable $PtcCO_2$ measurements is appropriate handling and knowledge of the equipment and procedure. Our team has long term experience with use of the $PtcCO_2$ device, probably contributing to the low number of technical problems encountered.

The second aim of the investigation was to study the instrumental drift of the $PtcCO_2$ sensor during overnight NIV-treatment. Mean drift was 0.02 kPa/hrs. Only one of the paired measurements showed an overnight drift exceeding 1.33 kPa, while three exceeded 1 kPa [27]. Thus, our study confirms that the vast majority of overnight $PtcCO_2$ recordings were performed without any clinically significant drift.

Instrumental drift during $PtcCO_2$ measurements has been evaluated using various methods (Table 2). In an 8 h sleep study of 6 stable ICU patients, change in bias over time was used as a measurement of drift [30]. $PaCO_2$-$PtcCO_2$ difference increased linearly from 0.22 kPa to 0.72 kPa, suggesting an instrumental drift. Using the same methodology on a limited number of patients, 4 studies found lower levels of drift [16,22,23,26]. Another study performed on 29 healthy individuals found no significant drift during continuous 4 h $PtcCO_2$ recordings [45].

Two studies evaluated instrumental drift with a method similar to ours. Storre et al. calculated the total drift as the difference between 2 in vitro calibration measurements performed at the beginning of $PtcCO_2$ monitoring and after 4 h in 10 patients [28], showing a significant drift of 0.17 kPa/h. Conversely, in an 8 h-overnight study of 24 patients using three different devices (SenTec DM, Tosca 500 and TCM4 TINA), a low drift of $PtcCO_2$ was observed [25]. The results of this study, using modern devices, are in concordance with ours. Recent developments of $PtcCO_2$ devices may have contributed to improved results when compared to studies using older devices. Although newer devices still measure CO_2 by determining changes in pH of an electrolyte solution in the sensor separated from the skin by a permeable membrane, developments have been made both in the algorithm of the devices and the sensor [12]. For instance, modern algorithms allow automatic correction for the anaerobic factor and for the metabolic constant, and sensors are smaller and better protected. Overall, results of the current and other recent studies show good agreement between $PtcCO_2$ and $PaCO_2$ in patients with chronic hypoventilation, questioning the need for an initial *in vivo* calibration (i.e.: by ABG). In addition, the low instrumental drift diminishes the need for an *in vivo* or an ex vivo calibration at the end of an overnight monitoring. Thus, overnight monitoring of $PtcCO_2$ can be performed reliably in settings where ABG are not readily available, with a low percentage of erroneous readings.

A few problems related to the overnight measurements of PtcCO2 were observed. In one patient, an obvious technical error occurred. We did not observe any conflict between the interface banding (mask) and the PtcCO2 sensor connected to the earlobe.

Table 2
Compilation of clinical data from 2005 to 2014 reporting on sensor temperature, bias, limits of agreement and drift of transcutaneous CO_2.[e]

Author	Year	No. of patients	Capnograph	Temperature of sensor °C	Patient group/clinical setting	Bias kPa[a,b]	Limits of agreement kPa[a,b]	Drift methods/hr	Drift/hrs kPa[c]
Chronic respiratory failure treated with long term mechanical ventilation									
Aarrestad	2015	67	TCM Tosca	43	Breathing spontaneously/ NIV	0·2	−0.3–0.8	Ex vivo/8 h	0·02
Storre [25]	2011	24	TCM4 Tina	42	NIV/sleep study	−0·2	−2.1–1.7	Ex vivo/8 h	−0·05
		24	SenTec	42	NIV/sleep study	0·1	−0.6–0.9	Ex vivo/8 h	0·01
		24	Tosca 500	42	NIV/sleep study	0·1	−0.9–1.1	Ex vivo/8 h	−0·07
Hazenberg [26]	2011	15	Tosca	42	NIV/ICU	−0·4	−1.3–0.5	Change in bias/8 h	n.s
Cuvelier [24]	2005	12	TCM3 Tina	44	Breathing spontaneously	0·1	−0.7–0.9	n.a.	
Acute medical illness/emergency department									
Delemere [14]	2012	48	Tosca 500	42	Acute dyspnea/ED	0·1	−0.5–0.7	n.a.	
Gancel [48]	2011	21	Tosca 500	42	ARF/ED	0	−0.8–0.8	n.a.	
Kelly [18]	2011	46	TCM4	n.a	ARF/NIV/ED	0·8	−1.3–3.0	n.a.	
Nicolini [35]	2011	80	Tosca	n.a	ARF/NIV/IRCU	0·1	−0.5–0.7	n.a.	
Perrin [19]	2011	24	Tosca 500	n.a	ARF/ED	0	−0.5–0.5	n.a.	
MCVicar [49]	2009	49	Tosca 500	42	Acutely ill/ED	0	−0.9–0.9	n.a.	
Storre [28]	2007	10	SenTec	42	ARF on CRF/NIV/Ward	0·6	−0.5–1.8	Ex vivo/4 h	0·17
Cox [51]	2005	22	Tosca	42	ARF/NIV/IRCU	0·1	−0.6–0.9	n.a	
Surgery/intra and postoperative care									
Liu [21]	2014	21	TCM4	44	Laparoscopic/bariatric	0·1	−0.2–0.5	n.a.	
Nishiyama [37]	2011	10	Sentec	42	Abdominal	0·2	−1.0–1.5	n.a.	
		10	TCM4	43		0·2	−0.6–0.9	n.a.	
De Oliveira [38]	2010	40	Tosca 500	42	Hysteroscopy	−0·2	−1.3–0.8	n.a.	
Xue [39]	2010	16	SenTec	n.a	Prolonged laparoscopic	−0·1	−1.0–0.7	n.a.	
Chakravathy [40]	2010	32	TCM4	43	Cardiac	−0·2	−1.2–0.9	n.a.	
Hirabayashi [41]	2009	15	TCM3	44	Abdominal/ventilated	0	−0.7–0.6	n.a.	
		24	TCM3	44	Abdominal/postoperative	−0·1	−1.2–1.0	n.a.	
Fanelli [53]	2008	13	SenTec	n.a	Major surgery/ postoperative	0·5	−0.7–1.8	n.a	
Bolliger [20]	2007	122	SenTec	42	Cardiac/thoracic	−0·6	−2.6–1.5	n.a	
		122	Tosca 500	42		−0·3	−1.7–1.1		
Bendjelid [27]	2005	55	Tosca	42	Major surgery/critical ill	−0·2	−1.8–1.4	n.a	
Stein [50]	2006	30	Tosca 500	42	Vascular/abdominal/ thoracic	−0·7	−1.7–0.2	n.a.	
Nishiyama [47]	2006	5	TCM4	43	Abdominal	0·1[d]	−1.2–1.3	n.a.	
Intensive care unit									
Berlowitz [30]	2011	6	TCM3 Tina	43	Stable	−0·2	−0.7–0.2	Change in bias/8 h	−0·06
Hinkelbein [42]	2008	34	TCM4	41–42	Critically ill/transport	0·1	−1.9–2.1	n.a.	
Johnson [43]	2008	38	Sentec	42	Stable/ventilated/LTAC	0·1	−1.0–1.1	n.a.	
Bolliger [20]	2007	50	SenTec	42	Critical ill/surgery	−0·4	−1.9–1.2	n.a	
		50	Tosca	42	Critical ill/surgery	−0·4	−1.5–1.0		
Rodriguez [36]	2006	50	SenTec	42	Critically ill	0	−1.3–1.2	n.a	
Senn [44]	2005	18	Tosca	42	Critically ill	−0·4	−1.3–0.5	n.a.	
Other patients groups/settings									
Rafiq [15]	2012	40	Tosca 500	42	ALS	−0·1	−0.7–0.6	n.a.	
Randerath [45]	2010	29	Tosca 500	42	Healthy subjects/Ward	−0·8	−2.4–0.8	Change in bias/4 h	0·02
Fuke [52]	2009	9	Tosca	42	Healthy/experimental	0·2	−0.5–1.0	n.a.	
Maniscalco [16]	2008	35	Tosca	42	Obese patients/Ward	−0·2	−0.5–0.1	n.a.	
Stege [17]	2009	21	Tosca 500	42	Respiratory diseases/CPET	0	−0.8–0.7	n.a.	
Parker [46]	2007	48	Tosca	42	Respiratory diseases/ Ward	0	−1.4–1.3	n.a.	
Janssens [13]	2005	40	TCM3 Tina	43	Geriatric patients	0	−1.1–1.1	n.a.	

n.a. = Not available from original publication; ED = Emergency department; ARF = Acute respiratory failure; NIV = Non-invasiv ventilation; CPET = Cardiopulmonary exercise test; IRCU = Intermediate respiratory care unit; LTAC = Long term acute care facility; CRF = Chronic respiratory failure; n.s = No significant drift.

[a] Bias = $PaCO_2$-$PtcCO_2$.

[b] In studies including drift measurements, baseline and drift uncorrected values are displayed if available.

[c] Studies with drift measurement ≥4 h.

[d] Data from chest placement.

[e] Based on a systematic Pub Med search for literature published between 2005 and March 2015.

However displacement of the interface banding due to patient movement may have contributed to the intermittent loss of signal seen in 6 patients. If this problem occurs, an alternative location for the sensor could be a solution, preferably the upper chest [47]. An overnight drift of more than 1 kPa was observed in 3 patients. In 2 of these patients an intermittent loss of $PtcCO_2$ signal was observed. Recalibration of the sensor after these incidents would probably have improved the results in these cases. Visual inspection of the overnight graphic display in addition to absolute values of $PtcCO_2$ could help the clinician in detecting these occasional events and in interpreting the results. Figs. 4–5 show examples of graphic displays of overnight $PtcCO_2$.

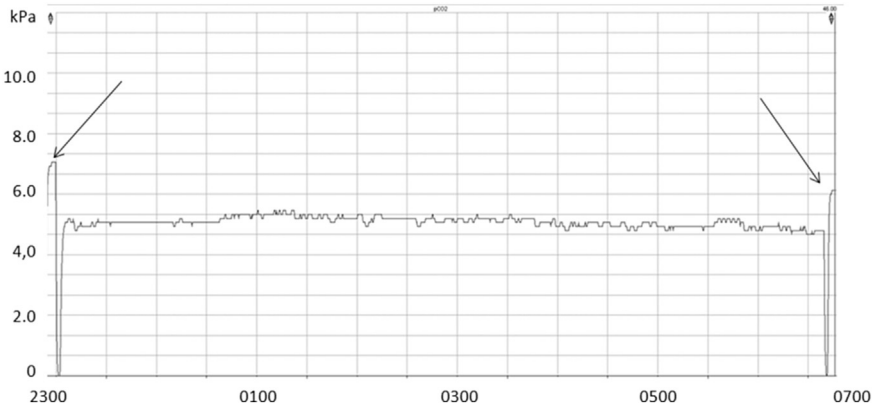

Fig. 4. 8 h overnight normal $PtcCO_2$ tracing. Arrows show ex vivo measurements.

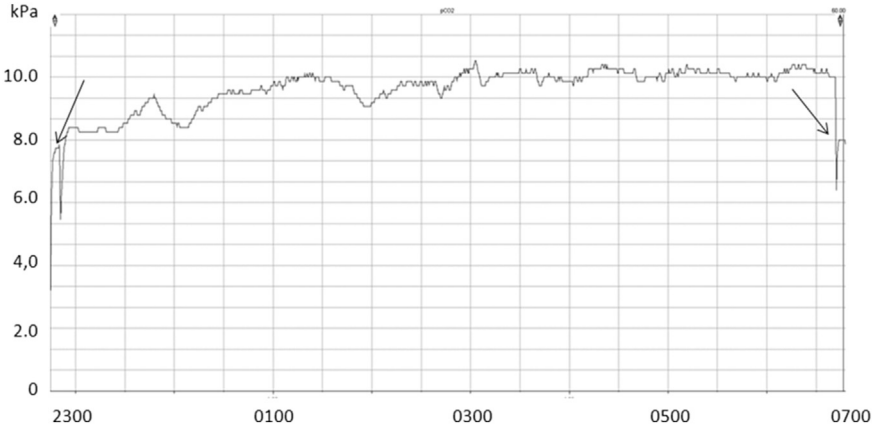

Fig. 5. 8 h overnight $PtcCO_2$ tracing; severe hypercapnia with an increase overnight. Arrows show ex vivo measurements.

There are some limitations to our study. We only evaluated one of the commercially available $PtcCO_2$ devices and only one probe position i.e. the earlobe. Thus, the relevance of our findings is theoretically limited to this equipment and probe position. However, our results are similar to those presented by Storre et al. [25] using the Tosca 500 with a chest probe instead of an earlobe probe. The Tosca 500 uses an identical sensor, algorithm, and CO_2 detection method as the TCM Tosca. These authors also obtained similar results using the SenTec device [25]. The wider limits of agreement found using the TCM4 Tina may be due to the lower sensor temperature used [25]. Finally, Cuvelier et al. using the TCM3 Tina with the sensor temperature set to 44 °C, reported similar bias and limits of agreement as in our study [24].

5. Conclusions

In a large group of patients with a variety of diseases causing chronic hypercapnic respiratory failure, we found that the accuracy of transcutaneous measurement of CO_2 tension was acceptable for estimating $PaCO_2$ over a wide range of CO_2 levels. In addition, the overnight instrumental drift of the $PtcCO_2$ sensor was minor, questioning the necessity of systematic *in vivo* or ex vivo calibration.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.rmed.2016.01.017.

Author contributions

S.A. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. S.A, A.L.K. and M.Q. contributed substantial to acquisition of data. S.A, E.T, A.L.K, M.Q, J.J. and O.H.S. contributed substantial to the study concept and design, data interpretation, critical revision of the manuscript for important intellectual content, and final approval of the manuscript.

Declaration of interests

S.A, E.T, A.L.K, M.Q, J.J. and O.H.S. have no potential conflicts of interest with any companies/organizations whose products or services may be discussed in this article.

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Other contributions

This study was performed at Oslo University Hospital Ullevål, Department of Pulmonary Medicine.

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