

## ORIGINAL INVESTIGATION

# Overnight Transcutaneous Carbon Dioxide Monitoring in Eucapnic Patients with Obstructive Sleep Apnea Syndrome

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## Abstract

**OBJECTIVES:** We monitored increases in CO<sub>2</sub> levels during sleep by measuring transcutaneous pCO<sub>2</sub> (PtcCO<sub>2</sub>) to determine its relationship with polysomnographic data in normocapnic patients with obstructive sleep apnea syndrome (OSAS).

**MATERIAL AND METHODS:** Between October 2011 and December 2012, 139 patients underwent PtcCO<sub>2</sub> monitoring with polysomnography. All patients were evaluated with arterial blood gas (ABG) measurements and pulmonary function tests (PFTs). We excluded 13 patients with COPD and/or daytime hypercapnia and 29 patients whose PtcCO<sub>2</sub> records could not be evaluated.

**RESULTS:** The patients' mean age was 46.8±10.3 years. Fifty-nine patients (60.8%) were male, and 38 (39.2%) patients were female. The mean overnight PtcCO<sub>2</sub> was ≤45 mm Hg in 84 (86.6%) patients and >45 mm Hg in 13 (13.4%) patients. In the group with PtcCO<sub>2</sub>>45 mm Hg, 10 patients had an apnea-hypopnea index (AHI) >15, and 3 patients had an AHI<15, without a statistically significant difference (p=0.078). The mean apnea and apnea/interapnea periods were similar. The mean PtcCO<sub>2</sub> values correlated with time spent when the SpO<sub>2</sub> was <90% (r=0.220, p<0.031). When we grouped the patients by AHI, 60 (61.8%) patients had an AHI>15 (moderate to severe OSAS), and 37 (37.2%) had an AHI<15 (mild OSAS). Of the former group, 16.7% had a mean PtcCO<sub>2</sub>>45 mm Hg, whereas this ratio was 8.1% in the latter group. The difference was not statistically significant (p=0.359). In the group with an AHI>15, the highest PtcCO<sub>2</sub> levels were significantly higher (p<0.05).

**CONCLUSION:** We conclude that seemingly eucapnic OSAS patients may experience hypercapnia when sleeping, and PtcCO<sub>2</sub> monitoring may be useful in the early diagnosis of hypercapnia.

**KEY WORDS:** Obstructive sleep apnea syndrome, transcutaneous PCO<sub>2</sub>, nocturnal hypercapnia

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## INTRODUCTION

In healthy adults, the hypercapnic ventilatory response is depressed during sleep. This ventilatory response is lower in NREM sleep than in wakefulness and is lowest in REM sleep. Generally, arousal develops before the partial pressure of carbon dioxide in arterial blood (PaCO<sub>2</sub>) rises more than 10 mm Hg over the PaCO<sub>2</sub> values of wakefulness to prevent further increases in PaCO<sub>2</sub> [1]. Berthon-Jones and Sullivan defined the threshold of increase in PaCO<sub>2</sub> that causes arousal as 6 mm Hg in healthy adults [2].

Mechanisms that prevent hypercapnia during sleep may be damaged in patients with sleep breathing disorders. Chronic hypercapnia in association with obesity has been termed 'obesity hypoventilation syndrome.' Patients suffering from this syndrome can exhibit nocturnal hypoventilation unrelated to upper airway obstruction [3]. On the other hand, obstructive sleep apnea syndrome (OSAS) is characterized by intermittent closure of the pharyngeal airway during sleep, resulting in episodic hypoxemia and sleep disruption. Maintenance of eucapnia during sleep in OSAS requires a balance between CO<sub>2</sub> loading during apnea and CO<sub>2</sub> elimination. However, some patients with OSAS may exhibit daytime hypercapnia. The prevalence of daytime hypercapnia in these patients varies from 11%-43%, according to previous reports [4-11]. In these studies, lower forced expiratory volume in 1 second (FEV<sub>1</sub>), vital capacity (VC), total lung capacity (TLC), minimum overnight saturation level of oxygen by pulse oximetry (SpO<sub>2</sub>), higher body mass index (BMI), and apnea-hypopnea index (AHI) have been found to be related to hypercapnia. On the other hand, some studies have reported an association between AHI and daytime hypercapnia in patients with OSAS, even after excluding chronic obstructive pulmonary disease (COPD) patients [9,10]. Labaan's study detected daytime hypercapnia in OSAS patients without COPD or obesity [10]. These results point out that there might be other mechanisms causing chronic daytime hypercapnia in patients with OSAS. Berger et al. [12] found that acute hypercapnia during periodic breathing while



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sleeping may occur when ventilation/perfusion (V/Q) is mismatched. They also found that compensation for  $\text{CO}_2$  accumulation during 'apnoea/hypopnoea may be limited by the duration of the inter-event interval, as well as by the magnitude of the inter-event ventilation.'

With these findings in mind, we investigated whether  $\text{PCO}_2$  monitoring should be practiced routinely in patients with OSAS during a polysomnography. Further, we investigated which method should be used for monitoring. Routine transcutaneous  $\text{PCO}_2$  ( $\text{PtcCO}_2$ ) monitoring has minimal clinical use in adult polysomnographies; its slow response time makes it unsuitable for monitoring blood gas pressures during sleep, in which rapid and short-lasting changes can occur.  $\text{PtcCO}_2$  monitoring may be of some use in adults with waking hypercapnia or suspected sleep-related alveolar hypoventilation [13,14]; however, many studies have shown that continuous  $\text{PtcCO}_2$  monitoring is useful in monitoring and diagnosing sleep-related breathing disorders, especially in children, intensive care patients, patients with non-invasive mechanical ventilation support, and perioperative patients [15-21]. The American Academy of Sleep Medicine (AASM) manual for scoring sleep mentioned both end-tidal  $\text{PCO}_2$  and  $\text{PtcCO}_2$  measurements as being optional for hypoventilation scoring [22].

Regarding these findings, we aimed to examine  $\text{PtcCO}_2$  increases and the relation between increased  $\text{PtcCO}_2$  and polysomnographic findings prospectively by monitoring  $\text{PtcCO}_2$  during polysomnographies in eucapnic OSAS patients, as only a few studies have been done with such patients.

## MATERIAL AND METHODS

We performed polysomnographies and  $\text{PtcCO}_2$  monitoring on 139 patients admitted to our clinic between October 2011 and December 2012 who complained of witnessed sleep apnea, snoring, and daytime sleepiness. All patients signed an informed consent form before entering the study. Before the polysomnography, we measured arterial blood gases (ABGs) while patients were in the supine position during wakefulness. The day after the polysomnography, we performed pulmonary function tests (PFTs). Twenty-nine patients were excluded, because their  $\text{PtcCO}_2$  records were unreliable. Out of the remaining 110 patients with reliable records, we excluded 9, because they had COPD, and we excluded 4 because they had daytime hypercapnia without COPD, according to the PFT and ABG procedures we performed. We diagnosed COPD according to GOLD criteria in patients with a post-bronchodilator  $\text{FEV}_1/\text{FVC} < 0.7$  [23].

The standard overnight polysomnography (PSG) included electroencephalography (EEG) recordings, electrooculography (EOG) recordings, submental and bilateral leg electromyographs, and an electrocardiography (ECG). We measured air flow with a nasal pressure transducer and an oro-nasal thermistor; respiratory effort via respiratory inductance plethysmography; and arterial oxyhemoglobin saturation via a finger pulse oximeter ( $\text{SpO}_2$ ). All signals were collected and digitalized by computerized PSG systems (Comet Grass, Astro-Med, Inc., West Warwick, RI, USA and Viasys Cephalo Pro, SomnoStar, Viasys Healthcare, Hoechberg, Germany)

by experienced technicians. We scored sleep stages in 30-second epochs using the Rechtachaffen-Kales and 2007 AASM scoring systems [22,24]. We analyzed each epoch for the number of episodes of apnea and hypopnea. We defined apnea as a cessation of air flow for more than 10 seconds and hypopnea as a reduction of air flow  $>50\%$  for  $>10$  seconds plus oxygen desaturation of  $>3\%$  or arousal [22,25]. We calculated the apnea/interapnea duration ratio using the average apnea and interapnea times. Certified specialists who were experienced in sleep medicine conducted this scoring. We determined the disease classifications according to the AASM's 2005 guide [26]. We graded patients according to the AASM's 1999 criteria as follows: an  $\text{AHI} < 5$  as normal, an  $\text{AHI} \geq 5$  and  $\leq 15$  as mild, an  $\text{AHI} > 15$  and  $\leq 30$  as moderate, and an  $\text{AHI}$  above 30 as severe [25].

We monitored  $\text{PtcCO}_2$  with a V-Sign Sensor attached to the patients' earlobes using the SenTec digital monitoring system and VSTATS PC-based software (Switzerland), which previous sleep studies have proven to be reliable [13-15]. We identified the average, maximum, and minimum  $\text{PtcCO}_2$  values by downloading the overnight records. We excluded unreliable records (20) (inexplicable, abrupt, and excessive increases in  $\text{PtcCO}_2$  or sustained  $\text{PtcCO}_2 < 30$  mm Hg). We classified mean  $\text{PtcCO}_2$  levels of more than 45 mm Hg as overnight hypercapnia.

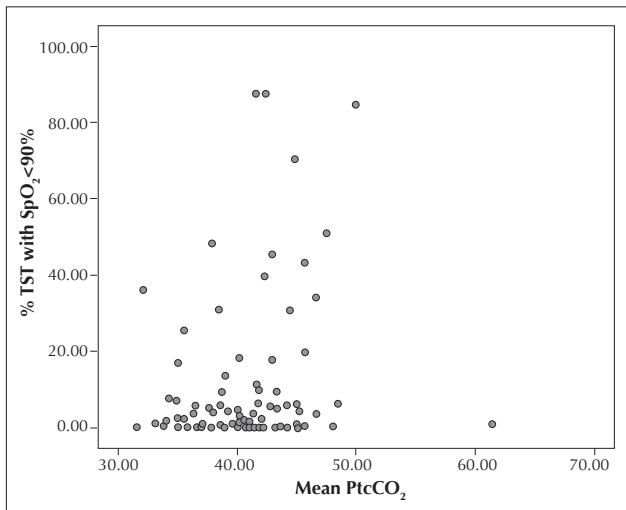
## Statistical Analysis

We entered all of the data into the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) 17.0 package program. We analyzed the categorical variables using chi-square and Fisher's exact tests. We presented the results as the mean  $\pm$  SD. We assessed group differences with the Mann-Whitney U-test and the student's t-test. We determined correlations between  $\text{PtcCO}_2$  and anthropometric, respiratory, and polysomnographic variables using Pearson's correlation coefficient.

## RESULTS

The mean age of all 97 patients included in the study was  $46.8 \pm 10.3$ . Fifty-nine (60.8%) patients were male, and 38 (39.2%) were female. Eighty-six (86.6%) patients had a  $\text{PtcCO}_2 < 45$  mm Hg, and 13 (13.4%) patients had a  $\text{PtcCO}_2 > 45$  mm Hg. All of the patients in the second group had an  $\text{AHI} > 5$ . Even though  $\text{AHI}$  scores were higher in the second group, the difference was not statistically significant ( $p=0.078$ ). There was no significant difference between the two groups in terms of mean apnea duration, the apnea/interapnea duration ratio, or sleep  $\text{SpO}_2$  measurements. When we made comparisons according to sleep architecture, there was a significant increase ( $p=0.018$ ) in the N2 ratio in the second group; the N3 ratio was lower, but the difference was not statistically significant ( $p=0.066$ ). The demographic properties and PFT, ABG, and polysomnography findings are illustrated in Table 1.

In 14 (14.5%) patients, the percentage of total sleep time (TST%) with  $\text{SpO}_2 < 90\%$  was above 30%. The mean  $\text{PtcCO}_2$  value during sleep correlated with the percentage of TST with  $\text{SpO}_2 < 90\%$  (Figure 1) and ABG measurement results. There was no correlation in terms of other polysomnography findings (Table 2).



**Figure 1.** The correlation between mean PtcCO<sub>2</sub> and %TST with SpO<sub>2</sub><90%

PtcCO<sub>2</sub>: transcutaneous PCO<sub>2</sub>; SpO<sub>2</sub>: pulse oxygen saturation; TST%: the percentage of total sleep time

When we categorized the patients according to their AHI scores, 60 (61.8%) had an AHI>15 (moderate to severe OSAS), and 37 (38.2%) had an AHI <15 (mild OSAS or normal). Eleven patients in the second group had an AHI<5 (normal), and all of these patients had a PtcCO<sub>2</sub><45 mm Hg. Ten (16.7%) patients from the first group had a PtcCO<sub>2</sub>>45 mm Hg, and 3 (8.1%) patients from the second group had a PtcCO<sub>2</sub>>45 mm Hg, but the difference was not statistically significant ( $p=0.359$ ). On the other hand, the maximum PtcCO<sub>2</sub> was significantly higher in the AHI >15 group ( $p<0.05$ ). Also, the mean age, BMI, apnea index (AI), oxygen desaturation index (ODI), apnea duration, and N2% were significantly higher, whereas the N3%, the mean SpO<sub>2</sub>%, and the minimum SpO<sub>2</sub>% were significantly lower ( $p<0.05$  for all). All of these measurements can be seen in Table 3.

## DISCUSSION

In our study, 13 (13.4%) patients had a PtcCO<sub>2</sub>>45 mm Hg during the night of the polysomnography. Even though the difference was not statistically significant, AHI levels were higher in this group, suggesting a possible relationship between OSAS severity and hypercapnia during sleep. In 14.5% of all patients, %TST with SpO<sub>2</sub><90% was above 30%. Average PtcCO<sub>2</sub> during sleep and %TST with SpO<sub>2</sub><90% showed a correlation, which was not a surprising finding, considering the close relation between SpO<sub>2</sub> and PtcCO<sub>2</sub>. When patients were divided according to their AHI levels, the maximum PtcCO<sub>2</sub> values were significantly higher in the AHI >15 group. This finding further supports the previous claim that OSAS severity and hypercapnia during sleep are related. The most important point is that these patients' wakefulness ABCG parameters were within normal limits.

The prevalence of daytime hypercapnia in OSAS patients varies between 11%-43%, according to previous reports [4-11]. These patients are at a higher risk of developing serious cardiovascular disease, leading to early mortality [9,27]. Keeping this risk in mind, our findings may point to a similar

**Table 1.** Demographic properties, PFT, ABG and polysomnography findings of the cases with PtcCO<sub>2</sub>>45 mm Hg and <45 mm Hg

	PtcCO <sub>2</sub> <45 (n=84)	PtcCO <sub>2</sub> >45 (n=13)	p value
	Mean and SD	Mean and SD	
Age (year)	46.3±10.4	49.6±9.7	0.385
Gender (%) M/F	63/37	46.1/53.9	0.244
BMI (kg/m <sup>2</sup> )	30.9±5.7	33.1±5.2	0.176
PaO <sub>2</sub> (mm Hg)	92±16	85.7±12.3	0.369
PaCO <sub>2</sub> (mm Hg)	37±4.1	39.3±2.8	0.082
SaO <sub>2</sub> (%)	96.2±3.9	96.4±1.5	0.665
FEV <sub>1</sub> (%)	97.4±12.3	95±23.3	0.848
FVC (%)	100.7±13.4	97.5±25.7	0.689
FEV <sub>1</sub> /FVC	80.5±5.6	81±7.5	0.921
AHI	30.6±28.1	44.7±30.8	0.078
AI	17.8±25.9	25.8±31.1	0.307
ODI	22.9±24.4	37±34.6	0.131
Minimum SpO <sub>2</sub> (%)	80.8±10.1	76.1±12.1	0.162
Mean SpO <sub>2</sub> (%)	93.6±3.1	92.8±2.7	0.223
TST% with SpO <sub>2</sub> <90%	9.7±18.3	19±26.5	0.197
NREM apnea time (sec)	19.8±8.6	21.8±6.7	0.287
NREM hypopnea time (sec)	25.6±6.6	25.7±4.3	0.767
REM apnea time (sec)	21.3±14.9	22.7±9.6	0.520
REM hypopnea time (sec)	26.8±16.1	24.7±12.4	0.577
Mean apnea time (sec)	21.6±10.2	23±5.6	0.282
Apnea time/interapnea time	0.54±1.31	0.47±0.75	0.298
Sleep efficiency (%)	82.1±9.4	77.8±14.1	0.327
REM (%)	15.4±5.2	14±5	0.322
N1 (%)	7.6 ±4.6	7.4±4	0.781
N2 (%)	62.1±9.3	67±6.2	0.018
N3 (%)	14.7±7.4	11.4±6.1	0.066
Basal PtcCO <sub>2</sub> (mm Hg)	38.3±3.3	39.9±2.6	0.074
Max PtcCO <sub>2</sub> (mm Hg)	44.6±4	50.9±3.7	<0.001
Min PtcCO <sub>2</sub> (mm Hg)	35.4±2.9	39.9±2.2	<0.001
Mean PtcCO <sub>2</sub> (mm Hg)	39.4±3.2	47.8±4.3	<0.001
Mean heart rate	68±9.2	71.5±12.3	0.174

PtcCO<sub>2</sub>: transcutaneous PCO<sub>2</sub>; M: male; F: female; BMI: body mass index; PaO<sub>2</sub>: partial oxygen pressure; PaCO<sub>2</sub>: partial carbon dioxide pressure; SaO<sub>2</sub>: arterial oxygen saturation; FEV<sub>1</sub>: forced expiratory volume in the first second; FVC: forced vital capacity; AHI: apnea-hypopnea index; AI: apnea index; ODI: oxygen desaturation index; SpO<sub>2</sub>: pulse oxygen saturation; TST%: the percentage of total sleep time; NREM: non-rapid eye movement; REM: rapid eye movement; Max: maximum; Min: minimum

risk increase in patients who do not have daytime hypercapnia but who do have sleep hypercapnia.

Previous studies have found that chronic airway obstruction, obesity, gender, nocturnal respiratory abnormalities, abnor-

**Table 2.** The correlation between mean PtcCO<sub>2</sub> with the other parameters

	Correlation (r)	p value
Age	0.058	0.574
BMI (kg/m <sup>2</sup> )	0.133	0.205
PaO <sub>2</sub> (mm Hg)	-0.261	0.037
PaCO <sub>2</sub> (mm Hg)	0.332	0.007
SaO <sub>2</sub> (%)	0.058	0.644
FEV <sub>1</sub> (%)	-0.124	0.241
FVC (%)	-0.151	0.152
FEV <sub>1</sub> /FVC	0.095	0.369
AHI	0.125	0.224
AI	0.087	0.397
ODI	0.163	0.113
Minimum SpO <sub>2</sub> (%)	-0.199	0.052
Mean SpO <sub>2</sub> (%)	-0.164	0.110
TST% with SpO <sub>2</sub> <90%	0.220	0.031
NREM apnea time	0.122	0.236
NREM hypopnea time	-0.016	0.879
REM apnea time	0.059	0.567
REM hypopnea time	-0.090	0.383
Mean apnea time	0.133	0.195
Apnea time/interapnea time	0.025	0.805
Sleep efficiency (%)	-0.056	0.590
REM (%)	0.006	0.955
N1 (%)	0.064	0.534
N2 (%)	0.035	0.737
N3 (%)	-0.085	0.408
Basal PtcCO <sub>2</sub> (mm Hg)	0.437	0.000
max PtcCO <sub>2</sub> (mm Hg)	0.687	0.000
min PtcCO <sub>2</sub> (mm Hg)	0.778	0.000
Mean heart rate	0.097	0.347

PtcCO<sub>2</sub>: transcutaneous PCO<sub>2</sub>; BMI: body mass index; PaO<sub>2</sub>: partial oxygen pressure; PaCO<sub>2</sub>: partial carbon dioxide pressure; SaO<sub>2</sub>: arterial oxygen saturation; FEV<sub>1</sub>: forced expiratory volume in the first second; FVC: forced vital capacity; AHI: apnea-hypopnea index; AI: apnea index; ODI: oxygen desaturation index; SpO<sub>2</sub>: pulse oxygen saturation; TST%: the percentage of total sleep time; NREM: non-rapid eye movement; REM: rapid eye movement; Max: maximum; Min: minimum

mal ventilator responses, and alcohol intake contribute to daytime hypercapnia in patients with OSAS [4-11,28]. Many studies specified AHI as an independent risk factor for daytime hypercapnia [9,11,29,30]. Our findings suggest that AHI might also be an independent risk factor for sleep hypercapnia.

A study based on male Japanese OSAS patients found that 38% of OSAS patients had daytime hypercapnia; it also found that the average SpO<sub>2</sub>% during sleep was significantly lower for hypercapnic patients [29]. Other studies found that %TST with SpO<sub>2</sub><90% was significantly higher in patients with daytime hypercapnia [28,30]. Our finding regarding the

**Table 3.** Demographic properties and PFT, ABG, and polysomnography findings of the cases with AHI>15 and AHI<15

	AHI>15 (n=60)	AHI<15 (n=37)	p value
Age (year)	50±9.3	41.5±9.7	<0.001
Gender (%) M/F	63.3/36.7	56.8/43.2	0.519
BMI (kg/m <sup>2</sup> )	32.5±5.8	29.2±4.7	0.007
PaO <sub>2</sub> (mm Hg)	92.3±16.5	88.9±13.7	0.424
PaCO <sub>2</sub> (mm Hg)	37.3±3.8	37.3±4.6	0.976
SaO <sub>2</sub> (%)	96.4±3.7	95.8±3.6	0.529
FEV <sub>1</sub> (%)	97.3±15.5	96.6±11.8	0.816
FVC (%)	100.6±17.6	99.8±11.5	0.823
FEV <sub>1</sub> /FVC	80.3±6.4	80.9±4.7	0.656
AHI	47.5±27	8.1±4.5	<0.001
AI	29.5±29.2	1.6±1.8	<0.001
ODI	37.2±26.5	4.6±3.3	<0.001
Minimum SpO <sub>2</sub> (%)	75.3±10.3	88±4	<0.001
Mean SpO <sub>2</sub> (%)	92.4±3.3	95.2±1.2	<0.001
%TST with SpO <sub>2</sub> <90 (%)	16.2±22.4	2.3±9.4	0.001
NREM apnea time	23.3±7.1	14.8±7.7	<0.001
NREM hypopnea time	25.6±5.4	25.5±7.7	0.961
REM apnea time	27.4±12.9	11.9±11	0.000
REM hypopnea time	27±17	25.6±13.2	0.658
Mean apnea time	25.8±8.8	15.2±7.2	<0.001
Apnea time/interapnea time	0.86±1.50	0.01±0.01	0.001
Sleep efficiency (%)	80.7±9.5	83±11.3	0.289
REM (%)	15.6±5.4	14.7±4.7	0.415
N1 (%)	8.2 ±5.2	6.5±2.7	0.079
N2 (%)	64.5±10.2	59.7±5.5	0.010
N3 (%)	11.4±7.2	18.9±4.9	<0.001
Basal PtcCO <sub>2</sub> (mm Hg)	38.9±3.5	37.9±2.8	0.168
Max PtcCO <sub>2</sub> (mm Hg)	46.4±4.7	43.8±3.7	0.007
Min PtcCO <sub>2</sub> (mm Hg)	36.3±3.2	35.4±3.2	0.169
Mean PtcCO <sub>2</sub> (mm Hg)	40.9±4	40±4.9	0.359
Mean heart rate	69±10.2	67.5±8.7	0.466

PtcCO<sub>2</sub>: transcutaneous PCO<sub>2</sub>; BMI: body mass index; PaO<sub>2</sub>: partial oxygen pressure; PaCO<sub>2</sub>: partial carbon dioxide pressure; SaO<sub>2</sub>: arterial oxygen saturation; FEV<sub>1</sub>: forced expiratory volume in the first second; FVC: forced vital capacity; AHI: apnea-hypopnea index; AI: apnea index; ODI: oxygen desaturation index; SpO<sub>2</sub>: pulse oxygen saturation; TST%: the percentage of total sleep time; NREM: non-rapid eye movement; REM: rapid eye movement; Max: maximum; Min: minimum

correlation between %TST with SpO<sub>2</sub><90% and hypercapnia during sleep is consistent with those studies, which highlight the presence of nighttime hypercapnia in seemingly eucapnic patients during the daytime.

There was no difference in mean age, gender, BMI, ODI, mean and minimum SpO<sub>2</sub> %, or % TST with SpO<sub>2</sub><90% between the PtcCO<sub>2</sub> groups. In patients with a PtcCO<sub>2</sub>>45 mm Hg, N3% was lower and N2% was higher than in the PtcCO<sub>2</sub>

<45 mm Hg group. We believe that the occurrence of higher N3% and lower N2% is associated with increased AHI scores and not directly related to CO<sub>2</sub> levels.

Berger's studies detected a lower post-event minute ventilation and a higher apnea/interapnea duration ratio in hypercapnic patients compared to eucapnic patients by evaluating post-event minute ventilation and interapnea time following every apnea [31,32]. Even though we did not use breath-by-breath analysis in our study, by calculating average apnea and interapnea times, we could not detect a relation between the apnea/interapnea duration ratio and average PtcCO<sub>2</sub> or hypercapnia during sleep.

Although some studies suggest that PtcCO<sub>2</sub> monitoring during sleep is not reliable because of the occurrence of sharp changes caused by the patients' movements during sleep [13,14], other studies comparing PtcCO<sub>2</sub> monitoring to ABG measurements in children during polysomnographies, in intensive care patients, in patients with non-invasive mechanical ventilation support, and in perioperative patients have proven this method's reliability [15-21]. The AASM recommends PtcCO<sub>2</sub> monitoring for patients suspected to have obesity hypoventilation syndrome. Taking these facts into consideration, although not taking ABG measurements during sleep might be a limitation of our study, we think that our results are reliable, because we used a method that has been proven to be reliable by previous studies. We also discarded any unreliable records.

In conclusion, hypercapnia develops during sleep in seemingly eucapnic OSAS patients. We believe PtcCO<sub>2</sub> monitoring to be useful in the early diagnosis of hypercapnia, taking into account the relation of hypercapnia with increased morbidity and mortality in OSAS patients. Further studies with higher patient numbers are needed on this topic.

**Ethics Committee Approval:** Because PtcCO<sub>2</sub> monitoring during polysomnography is recommended by AASM, ethic committee approval was not considered necessary.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - B.S.; Design - B.S.; Supervision - B.Ç., B.S.; Funding - B.Ç., B.S.; Materials - N.K., G.S.; Data Collection and/or Processing - E.P., Ü.A.; Analysis and/or Interpretation - A.F., B.S.; Literature Review - Ü.A., S.Ş.C.; Writer - E.P., B.S., E.S.; Critical Review - B.Ç.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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## REFERENCES

1. Douglas NJ. Respiratory Physiology: Control of Ventilation. In: Kryger MH, Roth T, Dement WC, eds. Principles and Practise of Sleep Medicine. 4<sup>th</sup> ed. Philadelphia: Elsevier Saunders; 2005.p.224-31. [\[CrossRef\]](#)
2. Berthon-Jones M, Sullivan CE. Ventilation and arousal responses to hypercapnia in normal sleeping adults. *J Appl Physiol* 1984;57:59-67.
3. Burwell CS, Robin ED, Whaley RD, Bickelmann AG. Extreme obesity associated with alveolar hypoventilation: a Pickwickian syndrome. *Am J Med* 1956;21:811-8. [\[CrossRef\]](#)
4. Rapoport DM, Garay SM, Epstein H, Goldring RM. Hypercapnia in the obstructive sleep apnea syndrome. A reevaluation of the "Pickwickian syndrome". *Chest* 1986;89:627-35. [\[CrossRef\]](#)
5. Krieger J, Sforza E, Apprill M, et al. Pulmonary hypertension, hypoxemia, and hypercapnia in obstructive sleep apnea cases. *Chest* 1989;96:729-37. [\[CrossRef\]](#)
6. Weitzenblum E, Chaouat A, Kessler R, et al. Daytime hypoventilation in obstructive sleep apnoea syndrome. *Sleep Med Rev* 1999;3:79-93. [\[CrossRef\]](#)
7. Resta O, Barbaro MPF, Brindicci C, et al. Hypercapnia in overlap syndrome: possible determinant factors. *Sleep Breath* 2002;6:11-7. [\[CrossRef\]](#)
8. Golpe R, Jimenez A, Carpizo R. Diurnal hypercapnia in cases with obstructive sleep apnea syndrome. *Chest* 2002;122:1100-1. [\[CrossRef\]](#)
9. Kaw R, Hernandez AV, Walker E, et al. Determinants of Hypercapnia in Obese Cases with Obstructive Sleep Apnea: A systematic review and meta-analysis of cohort studies. *Chest* 2009;136:787-96. [\[CrossRef\]](#)
10. Laaban JP, Chailleux E. Daytime hypercapnia in adult cases with obstructive sleep apnea syndrome in France, before initiating nocturnal nasal continuous positive airway pressure therapy. *Chest* 2005;127:710-5. [\[CrossRef\]](#)
11. Kawata N, Tatsumi K, Terada J, et al. Daytime hypercapnia in obstructive Sleep Apnea Syndrome. *Chest* 2007;132:1832-8. [\[CrossRef\]](#)
12. Berger KI, Ayappa I, Sorkin IB, et al. CO<sub>2</sub> homeostasis during periodic breathing in obstructive sleep apnea. *J Appl Physiol* 2000;88:257-64.
13. Lee-Chiong TL, Magalang U. Monitoring respiration during sleep. *Respir Care Clin N Am* 2005;11:663-78.
14. Cuvelier A, Grigoriu B, Molano LC, Muir JF. Limitations of transcutaneous carbon dioxide measurements for assessing long-term mechanical ventilation. *Chest* 2005;127:1744-8. [\[CrossRef\]](#)
15. Storre JH, Magnet FS, Dreher M, Windisch W. Transcutaneous monitoring as a replacement for arterial PCO<sub>2</sub> monitoring during nocturnal non-invasive ventilation. *Respir Med* 2011;105:143-50. [\[CrossRef\]](#)
16. Paiva R, Krivec U, Aubertin G, et al. Carbondioxide monitoring during long-term noninvasive respiratory support in children. *Intensive Care Med* 2009;35:1068-74. [\[CrossRef\]](#)
17. Ramirez A, Khirani S, Delord V, et al. Assessment of sleep quality by pulse wave amplitude and actigraphy in children with sleep-disordered breathing: evaluation at diagnosis and under noninvasive ventilation. *Sleep Breath* 2013;17:827-35. [\[CrossRef\]](#)
18. Tobias JD. Transcutaneous carbon dioxide monitoring in infants and children. *Paediatr Anaesth* 2009;19:434-44. [\[CrossRef\]](#)
19. Kirk VG, Batuyong ED, Bohn SG. Transcutaneous carbon dioxide monitoring and capnography during pediatric polysomnography. *Sleep* 2006;29:1601-8.
20. Nakamura A, Kanai M, Mizushima A, et al. The accuracy of transcutaneous carbon dioxide monitoring during laparoscopic surgery. *Masui. The Japanese Journal of Anesthesiology* 2003;52:846-51.
21. Janssens JP, Perrin E, Bennani I, et al. Is continuous transcutaneous monitoring of PCO<sub>2</sub> (TcPCO<sub>2</sub>) over 8 h reliable in adults? *Respir Med* 2001;95:331-5. [\[CrossRef\]](#)
22. Iber C, Ancoli-Israel S, Chesson AL, Quan SF. The AASM Manual for the Scoring of Sleep and Associated Events. Rules, Terminology and Technical Specifications. Westchester, IL: American Academy of Sleep Medicine; 2007.
23. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management and prevention of chronic

ic obstructive pulmonary disease. Revised 2011. [http://www.goldcopd.org/uploads/users/files/GOLD\\_Report\\_2011\\_Jan21.pdf](http://www.goldcopd.org/uploads/users/files/GOLD_Report_2011_Jan21.pdf)

24. Rechtachaffen A, Kales A. A Manuel of Standardized Terminology, Techniques and Scoring System For Sleep Stages of Human Subjects. Washington DC: US. Government Printing Office 1968.
25. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. *Sleep* 1999;22:667-89.
26. American Academy of Sleep Medicine. International classification of sleep disorders, 2<sup>nd</sup> Edition: Diagnostic and Coding Manual. Westchester, IL: American Academy of Sleep Medicine; 2005.
27. Mokhlesi B, Kryger MH, Grunstein RR. Assessment and management of cases with obesity hypoventilation syndrome. *Proc Am Thoracic Soc* 2008;5:218-25. [\[CrossRef\]](#)
28. Resta O, Foschino-Barbaro MP, Bonfitto P, et al. Prevalence and mechanisms of diurnal hypercapnia in a sample of morbidly obese subjects with obstructive sleep apnoea. *Respir Med* 2000;94:240-6. [\[CrossRef\]](#)
29. Akashiba T, Kawahara S, Kosaka N, et al. Determinants of chronic hypercapnia in Japanese men with obstructive sleep apnea syndrome. *Chest* 2002;121:415-21. [\[CrossRef\]](#)
30. Resta O, Foschino Barbaro MP, Bonfitto P, et al. Hypercapnia in obstructive sleep apnoea syndrome. *Neth J Med* 2000;56:215-22. [\[CrossRef\]](#)
31. Ayappa I, Berger KI, Norman RG, et al. Hypercapnia and ventilatory periodicity in obstructive sleep apnea syndrome. *Am J Respir Crit Care Med* 2002;166:1112-5. [\[CrossRef\]](#)
32. Berger KI, Ayappa I, Sorkin IB, et al. Postevent ventilation as a function of CO<sub>2</sub> load during respiratory events in obstructive sleep apnea. *J Appl Physiol* 2002;93:917-24.