

# Transcutaneous carbon dioxide monitoring during flexible bronchoscopy under sedation: A prospective observational study

Sedasyon eşliğinde fleksibl bronkoskopi sırasında transkütanöz karbondioksit monitorizasyonu: Prospektif gözlemsel çalışma

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## Abstract

**Aim:** It is difficult to maintain the necessary depth of sedation during bronchoscopy, and hypoxemia, hypoventilation, and undesirable cardiovascular effects are often encountered. Transcutaneous carbon dioxide monitoring is a reliable means of detecting hypoventilation. The aim of this study was to determine the effects of transcutaneous carbon dioxide (tPCO<sub>2</sub>) monitoring on the amount of propofol required for sedation and examine sedation-induced hypoventilation and other adverse events requiring intervention, such as stopping the procedure to ventilate during flexible bronchoscopy.

**Methods:** This prospective observational study included 60 patients undergoing bronchoscopy who were administered propofol. Of these, 30 patients were observed with transcutaneous carbon dioxide, and 30 were observed without. Propofol was used for sedation in all patients and the amount of propofol was compared between the groups monitored and not monitored transcutaneously for carbon dioxide. The sedation level was determined with the subjective sedation scale of the group that was not monitored.

**Results:** No significant differences were found between the groups in terms of propofol consumption or the number of patients who required airway interventions during the procedure ( $P>0.05$  for both). In this observational study, the partial carbon dioxide pressure in arterial blood was measured with a transcutaneous carbon dioxide monitor, which is a non-invasive method, and the maximum carbon dioxide value measured in prolonged interventions was 85 mmHg. Hypoxia was not observed in patients who developed hypoventilation.

**Conclusions:** Hypoventilation is inevitable during bronchoscopy. Transcutaneous carbon dioxide monitoring may be important for high-risk cardiovascular patients.

**Keywords:** Bronchoscopy, Transcutaneous carbon dioxide, Hypoventilation, Propofol, Moderate sedation

## Öz

**Amaç:** Bronkoskopi sırasında gerekli sedasyon derinliğini korumak zordur, hipoksemi, hypoventilasyon ve sedasyon sırasında sıklıkla istenmeyen kardiyovasküler etkilerle karşılaşılır. Transkütanöz karbondioksit monitorizasyonu, hypoventilasyonun saptanması için güvenilir bir yoldur. Bu çalışmanın amacı, transkütanöz karbondioksit (tPCO<sub>2</sub>) takibinin sedasyon için gereken propofol miktarı üzerindeki etkilerini belirlemek ve Sedasyona bağlı hypoventilasyon ve fleksibl bronkoskopi sırasında ventilasyon için işlemi durdurmayı gerektiren istenmeyen müdahale edilmesini gerektiren diğer olumsuz olayları incelemektir.

**Yöntemler:** Prospektif gözlemsel çalışmaya bronkoskopi yapılan ve propofol titrasyonu uygulanan 60 hasta dahil edildi. 30 hastaya transkütanöz karbondioksit monitorizasyonu uygulandı ve 30 hasta transkütanöz karbondioksit monitorizasyonu olmaksızın gözlemlendi. Tüm hastalarda sedasyon amacıyla propofol kullanıldı ve propofol miktarı transkütanöz karbondioksit ile izlenen ve izlenmeyen gruplar arasında karşılaştırıldı. Sedasyon seviyesi transkütanöz karbondioksit monitorizasyonu ile izlenmeyen grupta subjektif sedasyon skalası ile belirlendi.

**Bulgular:** Gruplar arasında propofol tüketiminde anlamlı fark bulunmadı. Ayrıca işlem sırasında hava yolu müdahalesi gerektiren hasta sayısı arasında anlamlı bir fark bulunmadı ( $P>0.05$ ). Bu gözlemsel çalışmada arterial kan gazındaki parsiyel karbondioksit basıncı invaziv olmayan transkütanöz karbondioksit monitörü ile yapıldı ve maksimum karbondioksit değerinin 85 mmHg olduğu gözlemlendi. Hypoventilasyon gelişen hastalarda hipoksi görülmedi.

**Sonuç:** Bronkoskopi sırasında hypoventilasyon kaçınılmazdır. Transkütanöz karbondioksit monitorizasyonu, yüksek riskli hastalar için önemli olabilir.

**Anahtar kelimeler:** Bronkoskopi, Transkütanöz karbondioksit, Hypoventilasyon, Propofol, Orta düzeyde sedasyon

## Introduction

Flexible bronchoscopy (FB) is a procedure performed by respiratory physicians and has become a gold standard technique to directly visualize and access the airway for diagnostic and therapeutic intervention [1]. Unfortunately, patients frequently suffer from pain, coughing, and the sensation of asphyxiation during the procedure. Thus, this procedure is performed by bronchologists with the patient under sedation to facilitate the examination of the tracheobronchial tree and improve the patient's safety and comfort [2,3].

Sedation during bronchoscopy is frequently recommended. Moderate sedation, also referred to as conscious sedation, maintains the patient's purposeful response to verbal and tactile stimuli and adequate spontaneous breathing, but this target level of sedation is difficult to achieve in practice [4]. Serious complications, including respiratory depression in the form of hypoxia or hypercapnia and cardiovascular instability, may occur during flexible bronchoscopy under moderate sedation. Propofol (2,6-diisopropylphenol) is a moderate sedation drug that is ideal for use in flexible bronchoscopy because it provides rapid recovery due to its pharmacokinetic properties, such as rapid clearance [5].

End tidal carbon dioxide monitoring during bronchoscopy procedure cannot provide accurate measurements. Transcutaneous carbon dioxide (TcCO<sub>2</sub>) monitoring is a non-invasive alternative to arterial blood sampling. Transcutaneous partial carbon dioxide pressure gives results close to those measured by arterial blood gas. We planned this study with the thought that it may be useful to detect patients in cardiovascular risk groups early and prevent over-sedation.

This prospective randomized controlled study was designed to determine the effect of transcutaneous carbon dioxide (tPCO<sub>2</sub>) monitoring on propofol consumption and examine sedation-induced hypoventilation as well as adverse events requiring intervention during flexible bronchoscopy.

## Materials and methods

This study obtained approval (decision number 21.03) from the Kirikkale University Ethical Committee of Clinical Studies. All participants signed the required consent form. Only patients scheduled to undergo flexible bronchoscopy (Karl Storz 11001 BN1) under local anesthesia with sedation were included in the study. Exclusion criteria for the study included patients under 18 years of age, those who refused to participate, those with psychiatric disorders, and those who were allergic to anesthetic drugs such as propofol, midazolam, and fentanyl. Patients with a tracheostomy or endotracheal tube, and peripheral vascular disease were excluded because it may have affected transcutaneous measurement.

### Bronchoscopy procedure

Local anesthesia was provided by applying 2% lidocaine to the patient's oropharynx at the beginning of the procedure. The sedation protocol began with 0.02 mg kg<sup>-1</sup> midazolam and 0.5 mcg kg<sup>-1</sup> fentanyl. Anesthesia was maintained with intermittent boluses of 20–50 mg propofol dependent on clinical judgement and Ramsay Sedation Scale (RSS) scores (Table 1) [6]. The target score was 3–4 to maintain

light or moderate sedation. Standard monitorizations, such as non-invasive blood pressure, electrocardiography, and pulse oximetry, were performed. A computer randomly divided patients into two groups and closed envelopes were prepared by an independent anesthesiologist not associated with the study. The envelopes were subsequently opened by the anesthesiologist who prepared and administered the medicines during the procedure. In the control group (group C, n=30), only standard monitorization was applied. In the transcutaneously monitored group (group TM), continuous tPCO<sub>2</sub> monitoring was performed (TCM4™, Radiometer Copenhagen, Denmark) through a probe placed on the patient's upper left chest using a solution as per the manufacturer's instructions. After applying the transcutaneous probe, the staff anesthesiologist and thoracic surgeon waited to begin the procedure until the sensor completed calibrating. Data collected included the patient's demographics, indication for the bronchoscopy, non-invasive blood pressure measurement values, electrocardiography, pulse oximetry, propofol consumption, transcutaneous carbon dioxide, RSS score, duration of the procedure, and whether interventions were necessary for hypoventilation or respiratory arrest. For this study, we defined hypoventilation as tPCO<sub>2</sub> ≥55 mmHg and hypoxia as SpO<sub>2</sub> <90% (>2 min). All interventions that required stopping the procedure, such as endotracheal intubation or manual mask ventilation, were recorded.

Table 1: Ramsay sedation score system

Score	Definition
1	Patient is anxious and agitated or restless, or both
2	Patient is co-operative, oriented, and tranquil
3	Patient responds to commands only
4	Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
5	Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus
6	Patient exhibits no response

Adapted from Ramsay et al. [6]

### Statistical analysis

Statistical Package for the Social Sciences (SPSS) version 21 (SPSS Inc., Chicago, Illinois, United States) was used for statistical analysis. The demographic data were provided as mean (standard deviation (SD)) or median with minimum (min) and maximum (max), as appropriate. Independent samples *t* tests were used to compare the variables with normal distribution, and the Mann–Whitney test was used to compare the nonparametric variables. Pearson correlation was used to identify the correlation between the independent variables. *P*<0.05 was considered statistically significant.

## Results

Demographic data, propofol consumption, duration of procedure, continuous positive airway pressure (CPAP) and mask-ventilation values of the patients and indication for the procedure are shown in Table 2. Age, gender, indication for the procedure, dose of propofol, mask ventilation, continuous positive airway pressure (CPAP) application, systolic blood pressure (SBP), mean arterial pressure (MAP), and oxygen measurements were not significantly different between the two groups. The distributions of heart rate, mean arterial pressure, pulse oximetry and Ramsay Sedation scores of the patients according to the groups are presented in Table 3.

The patients were divided into two groups as "biopsy" and "lavage" according to the indication, and the two groups were found to significantly differ with respect to the following

parameters: The patients undergoing biopsy were older than those who were undergoing the procedure for lavage, their American Society of Anesthesiologist classification (ASA) scores were higher, the procedure duration was longer, and the diastolic blood pressure (DBP) and MAP values were lower. Among 60 patients, the procedure had to be interrupted for mask ventilation in 15 patients and CPAP ventilation in 5 patients.

Table 2: The demographic data, propofol consumption, duration of procedure, and CPAP and mask-ventilation values of the patients according to the groups

Variable	Control		TM		t / Z	P-value
	Mean (SD) / Median (min-max) / n (%)	Mean (SD) / Median (min-max) / n (%)	Mean (SD) / Median (min-max) / n (%)	Mean (SD) / Median (min-max) / n (%)		
Age (year)	63.50 (23-85)	60.50 (27-84)	-1.176	0.239		
Gender	Female	4 (6.7%)	9 (15.0%)	-1.554	0.120	
	Male	26 (43.3%)	21 (35%)			
Indication	Biopsy	9 (15.0%)	15 (25.0%)	-1.568	0.117	
	Lavage	21 (35.0%)	15 (25.0%)			
ASA	2	13 (21.7%)	12 (20.0%)	-0.260	0.795	
	3	17 (28.3%)	18 (30.0%)			
Weight (kg)	76.50 (60-103)	68 (50-135)	-3.204	0.001		
Height (cm)	170.13(4.68)	168.53(7.62)	0.980	0.331		
BMI (kg/m <sup>2</sup> )	26.38 (20.90-36.49)	22.92 (18.42-41.67)	-2.558	0.011		
Duration (minute)	15	6 (10.0%)	2 (3.3%)	-2.452	0.014	
	20	12 (20.0%)	8 (13.3%)			
	25	9 (15.0%)	11 (18.3%)			
	30	3 (5.0%)	9 (15.0%)			
Propofol (mg)	153.17(36.49)	160.17(57.30)	-0.564	0.575		
CPAP	No	29 (48.3%)	26 (43.3%)	-1.390	0.165	
	Yes	1 (1.7%)	4 (6.7%)			
Mask ventilation	No	25 (41.7%)	20 (33.3%)	-1.478	0.139	
	Yes	5 (8.3%)	10 (16.7%)			

Independent samples t test, Mann-Whitney U test

Table 3: The distribution of heart rate, mean arterial pressure, pulse oximetry and Ramsay Sedation score of the patients according to the groups and indication for the procedure

Variable	Control		TM		P-value
	Mean (SD) / Median (min-max)	Mean (SD) / Median (min-max)	Mean (SD) / Median (min-max)	Mean (SD) / Median (min-max)	
HR0	86.20(11.98)	83.57(13.06)	0.419		
HR5	83.67(11.86)	90.13(15.28)	0.072		
HR10	81.63(12.59)	89.33(13.02)	0.023		
HR15	80.30(11.62)	87.00(12.19)	0.033		
HR20	79.48(11.34)	87.50(13.33)	0.023		
HR25	74.69(12.09)	87.25(12.36)	0.007		
HR30	69.33(16.56)	78.30(10.25)	0.267		
MAP0	95.60(13.65)	91.43(16.68)	0.294		
MAP5	88.67(11.84)	91.93(18.25)	0.414		
MAP10	92.17(14.21)	87.00(14.92)	0.175		
MAP15	85.27(16.22)	84.47(16.20)	0.849		
MAP20	81.44(12.19)	79.32(18.06)	0.623		
MAP25	79.31(14.50)	79.55(20.86)	0.971		
MAP30	76.00(16.09)	74.67(21.31)	0.924		
Oxygen0	96.24(1.62)	95.53(2.97)	0.262		
Oxygen5	93.90(1.84)	94.10(4.83)	0.833		
Oxygen10	92.76(2.71)	91.07(7.06)	0.232		
Oxygen15	93.45(3.48)	93.50(4.31)	0.960		
Oxygen20	93.65(1.55)	92.82(6.96)	0.578		
Oxygen25	94.42(1.73)	95.00(3.81)	0.621		
Oxygen30	94.33(2.08)	96.22(2.86)	0.323		
RSS0	2 (2-2)	2 (2-2)	1.000		
RSS5	3 (3-5)	3 (2-5)	0.312		
RSS10	4 (3-5)	4 (3-6)	0.908		
RSS15	4 (3-5)	4 (2-5)	0.012		
RSS20	4 (3-5)	4 (3-6)	0.105		
RSS25	4 (3-5)	4 (3-6)	0.434		
RSS30	4 (3-4)	4 (3-5)	0.466		

Independent samples t test, Mann-Whitney U test

**Correlation analysis**

No correlation was found between gender, ASA, BMI, required dose of propofol, mask ventilation and CPAP requirement between the groups. The results suggest that older patients who underwent biopsy could have higher ASA scores and the duration of the procedure could be longer. In addition, DBP and MAP should be measured more frequently in patients undergoing lavage. A correlation was found between duration and RSS at the 10<sup>th</sup> (pc=0.300, P=0.020), 15<sup>th</sup> (pc=0.524, P<0.001), and 20<sup>th</sup> minutes (pc=0.463, P=0.001), and the amount of propofol used (pc=0.380, P=0.001). There was a positive correlation between duration and mask ventilation (pc=0.398, P=0.002), as well as the need for CPAP (pc=0.406,

P=0.001). The results suggest that propofol dose, RSS values, mask ventilation rate of these patients, and the need for CPAP increased. The maximum carbon dioxide value measured in prolonged interventions, such as those in which CPAP or mask ventilation was required, was 85 mmHg (Table 4).

Table 4: The maximum levels of transcutaneous carbon dioxide

Group	Variable	n	Minimum	Maximum	Mean	SD
Control	transcutaneous0	-	-	-	-	-
	transcutaneous5	-	-	-	-	-
	transcutaneous10	-	-	-	-	-
	transcutaneous15	-	-	-	-	-
	transcutaneous20	-	-	-	-	-
	transcutaneous25	-	-	-	-	-
	transcutaneous30	-	-	-	-	-
TM	transcutaneous0	30	30.00	47.00	36.57	4.46
	transcutaneous5	30	32.00	57.00	42.73	6.81
	transcutaneous10	30	34.00	68.00	47.53	7.94
	transcutaneous15	30	35.00	77.00	50.97	9.63
	transcutaneous20	27	24.00	85.00	51.67	12.18
	transcutaneous25	20	35.00	74.00	54.00	10.05
	transcutaneous30	9	47.00	63.00	56.44	6.17

**Discussion**

End-tidal CO<sub>2</sub> monitoring during FB can be performed continuously by sampling with a device placed in the mouth of the patient. However, this randomized controlled study used transcutaneous CO<sub>2</sub> measurement to provide more accurate results, since there may be difficulties in end tidal sampling during bronchoscopy.

Previous studies have reported a correlation between end tidal CO<sub>2</sub> and tPCO<sub>2</sub> in volunteers and in spontaneously breathing patients in the intensive care unit [7,8]. A study showed the superiority of tPCO<sub>2</sub> to end tidal CO<sub>2</sub> and suggested that upper airway muscle weakness due to propofol is the reason that end tidal CO<sub>2</sub> monitoring is not useful [9]. Another study reported that false apnea alarms occurred 83 times in 185 patients monitored by end-tidal CO<sub>2</sub> capnography [7]. The current study aimed to reach the optimum sedation level necessary for the bronchoscopist to complete the procedure successfully. Propofol titration during sedation, clinical observation and patient response, and suppression of reflexes were used to keep the sedation score at 4. Deep hypoventilation without hypoxemia was seen in patients with high CO<sub>2</sub> levels when the duration of the bronchoscopy procedure exceeded 15 minutes. Although there was no statistically significant difference between the groups according to the variable parameters, hypoventilation was inevitable. It occurred despite a prolonged treatment time without hypoxemia and although the dose of propofol was well titrated to the appropriate transcutaneous CO<sub>2</sub> values to complete the procedure. Another study showed that propofol-associated complications were more likely to occur during prolonged or complex procedures [10].

Results of the present study suggest that patients monitored by pulse oximetry, which is the standard monitorization in clinical practice, are at cardiovascular risk. This study showed that tPCO<sub>2</sub> monitoring has no effect on propofol dose titration in determining sedation levels. Although acute hypercapnia had no effect on myocardial contractility and relaxation in the physiological system, it led to arrhythmia by causing repolarization abnormalities reflected by an increase in QT dispersion. Hypercapnia also causes pulmonary vasoconstriction in humans [11]. In our study, hypercapnia did not cause arrhythmia, but it is crucial to monitor tPCO<sub>2</sub> in patients with arrhythmia and pulmonary hypertension. Most of the patients

undergoing bronchoscopy are elderly, which increases the likelihood of cardiac arrest due to arrhythmias or cardiac ischemia during bronchoscopy [12]. The heart has rich innervation from the parasympathetic and sympathetic limbs of the autonomic nervous system, and autonomic nervous imbalance is believed to be a crucial factor in these cardiac events [13]. A bronchoscopy can trigger spasms and plaque disruption in the coronary arteries due to an increase in sympathetic activity caused by tension and anxiety. Bronchoscopy under sedation allows for the suppression of anxiety and stress-induced sympathetic activity in patients, while simultaneously allowing the effects of hypoxia and hypercarbia [14]. Monitoring the sedation level becomes important, and titration of the propofol dose is difficult to achieve for the completion of the bronchoscopy procedure, ensuring the comfort of the bronchoscopist and the patient.

Carbon dioxide monitoring during a bronchoscopy under sedation can identify increases in the partial carbon dioxide pressure of the arterial blood early in the procedure, which may occur depending on the central effect of the sedative drugs used or the process itself and cause a ventilation-perfusion mismatch. In a study similar to ours which showed a rise in  $t\text{PCO}_2$  reflecting hypoventilation without hypoxia, sedation was achieved with intermittent boluses of intravenous midazolam and 5 mg of hydrocodone [15]. In our study, propofol administered for sedation with intermittent boluses was monitored using RSS, which is commonly used as a subjective sedation scale.

Another study compared propofol with midazolam + alfentanil used for sedation in bronchoscopies and found that carbon dioxide tension values were significantly higher in the midazolam + alfentanil group than in the propofol group at 5 and 10 minutes following the procedure with transcutaneous carbon dioxide monitoring. They also found that significantly more patients in the midazolam + alfentanil group needed oxygen supplementation or airway support. They concluded that propofol is safer than the combination of midazolam + alfentanil [16]. In our study, sedation protocol was started with 0.02 mg  $\text{kg}^{-1}$  midazolam and 0.5  $\text{mcg kg}^{-1}$  fentanyl, then maintained with intermittent boluses of 20–50 mg of propofol according to clinical judgement and the patient's score on the RSS in the control group. In the  $t\text{PCO}_2$  group, the titration of propofol was determined by monitoring and the response of the patient. The duration of the bronchoscopy and the indication correlated with higher carbon dioxide levels. Transcutaneous carbon dioxide pressure was higher in patients who underwent bronchoscopy for biopsy. Another study determined the maximum value of  $t\text{PCO}_2$  as 59.25 mmHg by examining 22 bronchoscopy patients. The maximum value measured in our study was 85 mmHg, and we found the processing times to be longer. The fact that we did not perform cerebral monitoring, such as bispectral indexing, in our study indicates the lack of objective data on sedation levels. Although it is a short-term intervention, sedation depth measurement with bispectral index monitoring may be more effective in reducing propofol consumption and preventing hypoventilation. One study demonstrated that Bispectral Index (BIS)-guided propofol infusion is feasible, safe, easily tolerated, and provides a fast recovery for patients undergoing FB [17,18].

In their study, carbon dioxide monitorization was not used, and hypoventilation was not assessed.

A previous study showed that bronchoscopists used propofol 50% of the time, capnography was used in 10% of patients, and transcutaneous  $\text{CO}_2$  monitoring was used 1% of the time and only in specialized centers [19]. This suggests that the use of transcutaneous carbon dioxide monitoring is not a cost-effective method for short duration procedures such as bronchoscopy. Although it has the advantage of being a non-invasive method, in clinical practice, calibration takes almost as much time as the procedure itself. However, transcutaneous carbon dioxide monitoring may be appropriate in high-risk cardiovascular patients.

Another undesirable effect during bronchoscopy is the cough reflex. The activation of the cough center results in the contraction of the respiratory muscles. The contraction of the bronchial muscles causes bronchoconstriction, which leads to hypoventilation. The limitation of this study is that patient satisfaction was not evaluated.

Different agents are used for sedation to ensure patient comfort during bronchoscopy. Propofol was the only agent used for sedation in this study. Studies with different sedation drugs, such as dexmedetomidine, are needed.

### Conclusion

Hypoventilation without desaturation is inevitable during bronchoscopy, and transcutaneous carbon dioxide monitoring should be used in patients with arrhythmia, cardiovascular disease, or higher ASA physical status.

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