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A prospective observation study of the dynamic monitoring of transcutaneous arterial blood oxygen saturation and carbon dioxide during bronchoscopy

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Abstract

Background and Aims Because bronchoscopy is an invasive procedure, sedatives and analgesics are commonly administered, which may suppress the patient's spontaneous breathing and can lead to hypoventilation and hypoxemia. Few reports exist on the dynamic monitoring of oxygenation and ventilation during bronchoscopy. This study aimed to prospectively monitor and evaluate oxygenation and ventilation during bronchoscopy using transcutaneous arterial blood oxygen saturation and carbon dioxide.

Methods We included patients who required pathological diagnosis using fluoroscopic bronchoscopy at our hospital between March 2021 and April 2022. Midazolam was intravenously administered to all patients as a sedative during bronchoscopy, and fentanyl was administered in addition to midazolam when necessary. A transcutaneous blood gas monitor was used to measure dynamic changes, including arterial blood partial pressure of carbon dioxide (tcPCO₂), transcutaneous arterial blood oxygen saturation (SpO₂), pulse rate, and perfusion index during bronchoscopy. Quantitative data of tcPCO₂ and SpO₂ were presented as mean ± standard deviation (SD) (min–max), while the quantitative data of midazolam plus fentanyl and midazolam alone were compared. Similarly, data on sex, smoking history, and body mass index were compared. Subgroup comparisons of the difference (Δ value) between baseline tcPCO₂ at the beginning of bronchoscopy and the maximum value of tcPCO₂ during the examination were performed.

Results Of the 117 included cases, consecutive measurements were performed in 113 cases, with a success rate of 96.6%. Transbronchial lung biopsy was performed in 100 cases, whereas transbronchial lung cryobiopsy was performed in 17 cases. Midazolam and fentanyl were used as anesthetics during bronchoscopy in 46 cases, whereas midazolam alone was used in 67 cases. The median Δ value in the midazolam plus fentanyl and midazolam alone groups was 8.10 and 4.00 mmHg, respectively, indicating a significant difference of $p < 0.005$. The mean ± standard deviation of tcPCO₂ in the midazolam plus fentanyl and midazolam alone groups was 44.8 ± 7.83 and 40.6 ± 4.10 mmHg, respectively. The SpO₂ in the midazolam plus fentanyl and midazolam alone groups was 94.4 ± 3.37 and $96.2 \pm 2.61\%$, respectively, with a larger SD and greater variability in the midazolam plus fentanyl group.

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Conclusion A transcutaneous blood gas monitor is non-invasive and can easily measure the dynamic transition of CO_2 . Furthermore, tcPCO_2 can be used to evaluate the ventilatory status during bronchoscopy easily. A transcutaneous blood gas monitor may be useful to observe regarding respiratory depression during bronchoscopy, particularly when analgesics are used.

Keywords Bronchoscopy, Dynamic monitoring, Saturation of percutaneous oxygen (SpO_2), Transcutaneous carbon dioxide partial pressure (tcPCO_2)

Introduction

Bronchoscopy is an invasive procedure, and sedatives and analgesics are usually given during the procedure to reduce a patient's discomfort and pain. Respiratory depression is expected to occur during the examination, and patients should be monitored to improve safety during bronchoscopy. [1]

Recently, highly invasive bronchoscopic procedures, such as cryobiopsy for diagnosing lung cancer and interstitial pneumonia, thermoplasty for bronchial asthma, and bronchial occlusion for pneumothorax, have been performed more frequently. These procedures are usually performed under endotracheal intubation and are accompanied by sedatives and analgesics [2]. Notably, on using sedatives and analgesics during bronchoscopy, respiratory depression often induces decreased oxygen saturation in patients and delayed arousal after the examination [3].

Carbon dioxide (CO_2) partial pressure (pCO_2) is generally measured using arterial blood gas analysis. However, repeated analysis during bronchoscopy measurements requires the insertion of a catheter for arterial pressure measurement, which is an unsuitable procedure in actual clinical practice. In previous studies, the partial pressure of exhaled terminal CO_2 (PetCO_2) and transcutaneous CO_2 (tcPCO_2) have been identified as biomarkers of ventilatory status [4]. The value of PetCO_2 fluctuates in patients with other diseases such as heart failure, chronic obstructive pulmonary disease (COPD), and asthma [5]. Furthermore, air leakage around the mask or from the mouth makes accurate measurement difficult [6–8]. Notably, smaller errors are observed in tcPCO_2 measurement regardless of the patient's situation and air leaks, and more reliable data are obtained for tcPCO_2 measurement than for PetCO_2 measurement under various conditions [9–11]. The measurement of tcPCO_2 is non-invasive, simple, and highly correlates with that of PCO_2 [12]. Notably, few reports exist on the dynamic monitoring of oxygenation and ventilation during bronchoscopy. Therefore, this study aimed to prospectively collect and analyze the dynamic data of transcutaneous arterial blood oxygen saturation (SpO_2) and CO_2 during bronchoscopy.

Materials and methods

This open-label, prospective observational study was conducted in accordance with the ethical principles of the 2013 Revision of the Declaration of Helsinki.

This study was approved by the Ethics Committee of St. Marianna University Hospital (HREC No. 5129). All subjects were informed about the non-invasive monitoring to be used in this study, which constituted consent for bronchoscopic examination and participation in this study.

Study patients

Patients who required fluoroscopic bronchoscopy for diagnosis of lung cancer or interstitial pneumonia between March 2021 and April 2022 at our hospital were enrolled in this study.

Study procedure

The Sentec Digital Monitoring System (TOKIBO Co., Ltd, Tokyo, Japan.) was used as the monitoring device. After the patient was placed on the examination bed in a supine position, the sensor of the Sentec Digital Monitoring System was attached to the auricle, and recording was initiated. Bronchoscopy was initiated with oxygen at 2L/min using a nasal cannula. All patients received intravenous midazolam as anesthesia during the examination. Fentanyl was used during endotracheal intubation or when midazolam alone did not provide sufficient anesthesia. Additional midazolam or fentanyl was administered when more adequate sedation was needed during the examination. The time at which the bronchoscope passed through the vocal cords was used as the base point for monitoring. Oxygen administration was gradually increased according to SpO_2 during the examination. Endotracheal intubation was used in cases with a high risk of bleeding, such as cryobiopsy, and those requiring insertion and removal of a bronchoscope during the examination. SACETT™ Endotracheal Tube (8.0 mm; Smiths Medical Japan, Inc, Tokyo, Japan.) was used as the intubation tube. During endotracheal intubation, a 1574 Hudson RCI—Teleflex Hch Assy, Aqua+, 30/CS (Teleflex Medical Japan K.K, Tokyo, Japan.) was attached to the endotracheal tube, and an oxygen supply tube was

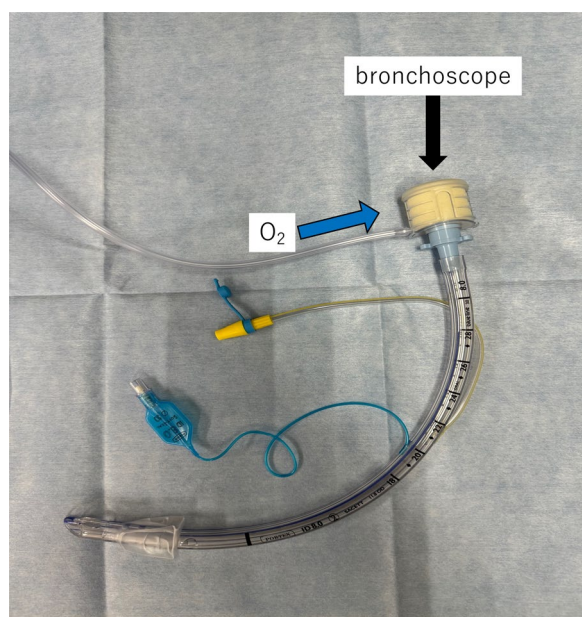


Fig. 1 Oxygen administration tools under intubation during bronchoscopy

connected to the port for oxygen administration (Fig. 1). After the examination, the monitor was removed, and the recording was stopped. Recorded data of all cases were collected and statistically analyzed. The measured data were dynamic changes in the measured parameters, including $tcPCO_2$, SpO_2 , pulse rate, and perfusion index. These parameters were compared based on analgesic agent, sex, smoking history, and body mass index (BMI).

Study statistics

For each parameter, graphs showing the changes in $tcPCO_2$ and SpO_2 over time during bronchoscopy were drawn. The vertical axis of the graph showed $tcPCO_2$ (mmHg) or SpO_2 (%), whereas the horizontal axis showed the time (min) at which the bronchoscope passed through the vocal cords. The oxygen flow rates were presented in different colors on the graphs (blue, 2–3 L/min; yellow, 4–6 L/min; red, ≥ 7 L/min). During the examination, each parameter was measured every minute. Quantitative data of $tcPCO_2$ and SpO_2 were presented as mean \pm standard deviation (min–max). For each parameter, we analyzed significant differences in $tcPCO_2$ and SpO_2 . The smokers were compared using the Brinkman index and grouped as heavy smokers (≥ 800) and non-smokers or light smokers (< 800). Furthermore, patients with a BMI of ≥ 25 were defined as obese by the Japan Society for the Study of Obesity, whereas those with a BMI of < 25 were defined as non-obese.

Table 1 Patients' clinical characteristics

Age, (mean \pm SD) (years, range)	71.26 \pm 9.96 (35–91)
Gender, <i>n</i> (%)	
Male	65(57.5)
Female	48(42.5)
Smoking history, <i>n</i> (%)	
Never smoked	33(29.2)
B.I. < 800	31(27.4)
B.I. ≥ 800	49(43.4)
BMI	
≥ 25	28(24.8)
< 25	85(75.2)
Intravenous anesthetics	
Fentanyl + Midazolam	46(40.7)
Midazolam	67(59.3)

B.I. Brinkman index, BMI body mass index, SD standard deviation

The patient groups were compared using the Mann–Whitney *U* test, performed with Excel Statistics (version 8.0 for Windows). Subgroup comparisons of the difference (Δ value) between baseline $tcPCO_2$ at the beginning of bronchoscopy and the maximum value of $tcPCO_2$ during the examination were performed using Mann–Whitney's *U* test. Statistical significance was set at $p < 0.05$. We performed a Cox's proportional hazard model based on univariate and multivariate analysis of $tcPCO_2$ and SpO_2 .

Results

Bronchoscopy was performed in 117 cases during the study period, with transbronchial lung biopsy performed in 100 cases and transbronchial lung cryobiopsy performed in 17 cases. There were four cases of measurement failure, including poor auricular placement ($n = 2$), prolonged dropout due to patient movement during the examination ($n = 1$), and poor calibration of the measurement device ($n = 1$). Therefore, only 113 cases could be measured continuously and were successfully analyzed.

The measurement success rate was 96.6%. Patients' clinical and demographic data are presented in Table 1. Midazolam and fentanyl were administered as anesthesia during bronchoscopy in 46 cases, whereas midazolam alone was administered in 67 cases. Midazolam was additionally administered during the examination in 14 cases and fentanyl in 8 cases. Univariate and multivariate analysis for $tcPCO_2$ and SpO_2 on these parameters are presented in Table 2A, B.

Figure 2 show the dynamic trends of $tcPCO_2$ and SpO_2 , respectively, in all cases. The mean bronchoscopy time was 38.5 min. The mean $tcPCO_2$ and SpO_2 were 42.7 ± 6.52 mmHg and $95.3 \pm 3.11\%$, respectively.

Table 2 Univariate and multivariate analysis for tcPCO₂ and SpO₂

Independent variable	Univariate			Multivariate		
	HR	95% CI	p value	HR	95% CI	p value
(A) COX proportional hazard model for tcPCO₂						
Age, <75 vs. ≥75	0.75	0.52–1.10	0.34	0.83	0.58–1.36	0.41
Gender, male, vs. female	0.95	0.66–1.40	0.78	0.86	0.58–1.30	0.86
B.I., never smoked and <800 vs. ≥800	0.9	0.62–1.31	0.43	0.9	0.59–1.40	0.59
BMI, <25 vs. ≥25	0.72	0.47–0.96	0.05*	0.71	0.45–1.13	0.05*
I.A, fentanyl and midazolam, vs midazolam	0.47	0.32–0.71	0.01**	0.48	0.31–0.76	0.01**
Additional midazolam administration, without versus with	0.9	0.85–1.12	0.41	0.94	0.88–1.20	0.45
Additional fentanyl administration, without versus with	1.12	0.93–1.37	0.23	1.09	0.89–1.43	0.26
(B) COX proportional hazard model for SpO₂						
Age, <75 vs. ≥75	1.32	0.91–1.94	0.15	1.26	0.79–1.84	0.21
Gender, male, vs. female	1.09	0.75–1.59	0.6	1.02	0.65–1.59	0.58
B.I., never smoked and <800 vs. ≥800	0.97	0.67–1.42	0.58	0.93	0.63–1.51	0.57
BMI, <25 vs. ≥25	0.98	0.63–1.50	0.52	0.98	0.63–1.51	0.5
I.A, fentanyl and midazolam, vs midazolam	0.42	0.29–0.63	0.03*	0.43	0.29–0.66	0.01**
Additional midazolam administration, without versus with	0.98	0.55–1.72	0.61	0.99	0.50–1.76	0.63
Additional fentanyl administration, without versus with	0.83	0.32–2.07	0.2	0.85	0.35–2.10	0.21

HR hazard ratio, B.I. Brinkman index, BMI body mass index, I.A. intravenous anesthetics

*p < 0.01 ≤ 0.05, **p ≤ 0.01

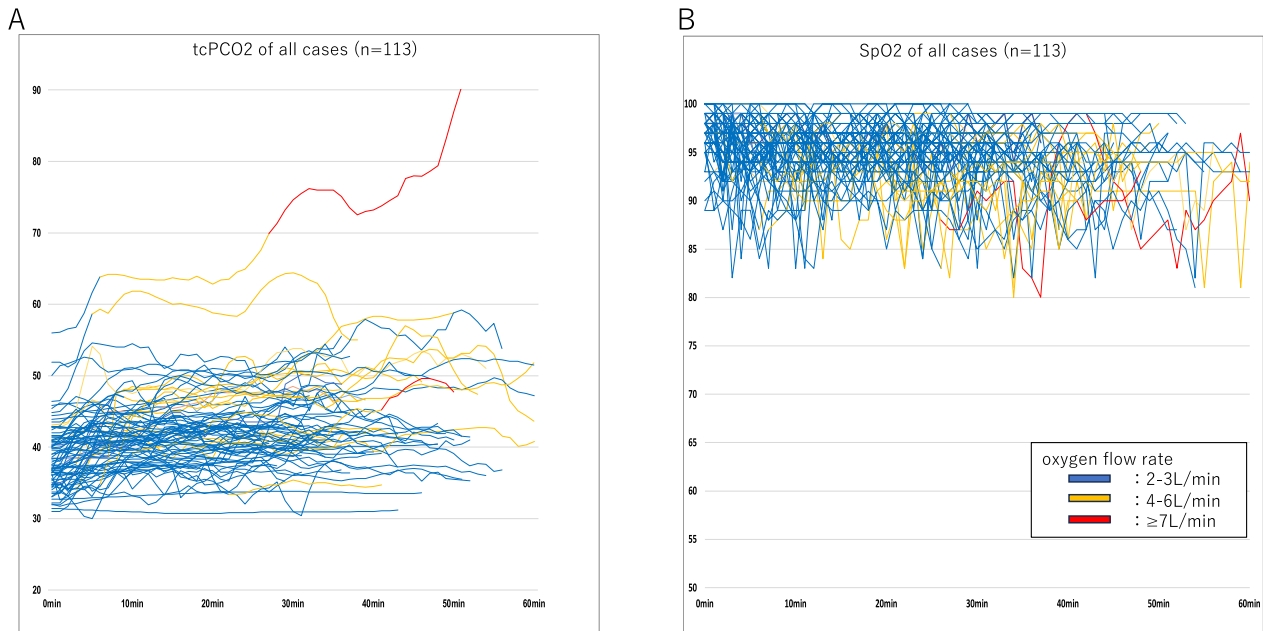


Fig. 2 Dynamic trend of tcPCO₂/SpO₂ of all cases during bronchoscopy. SpO₂ saturation of percutaneous oxygen, tcPCO₂ transcutaneous carbon dioxide partial pressure

The tcPCO₂ (mmHg) trends in the midazolam plus fentanyl and midazolam alone groups are shown in Fig. 3A, B. The tcPCO₂ in the midazolam plus fentanyl and midazolam alone groups was 44.8 ± 7.83 and 40.6 ± 4.10 mmHg, respectively. The tcPCO₂ was

significantly higher in the midazolam plus fentanyl group (p = 0.01). In most cases, tcPCO₂ remained between 40 and 50 mmHg, and gradual CO₂ sequestration during the examination was observed in many cases. Patients with high tcPCO₂ before the

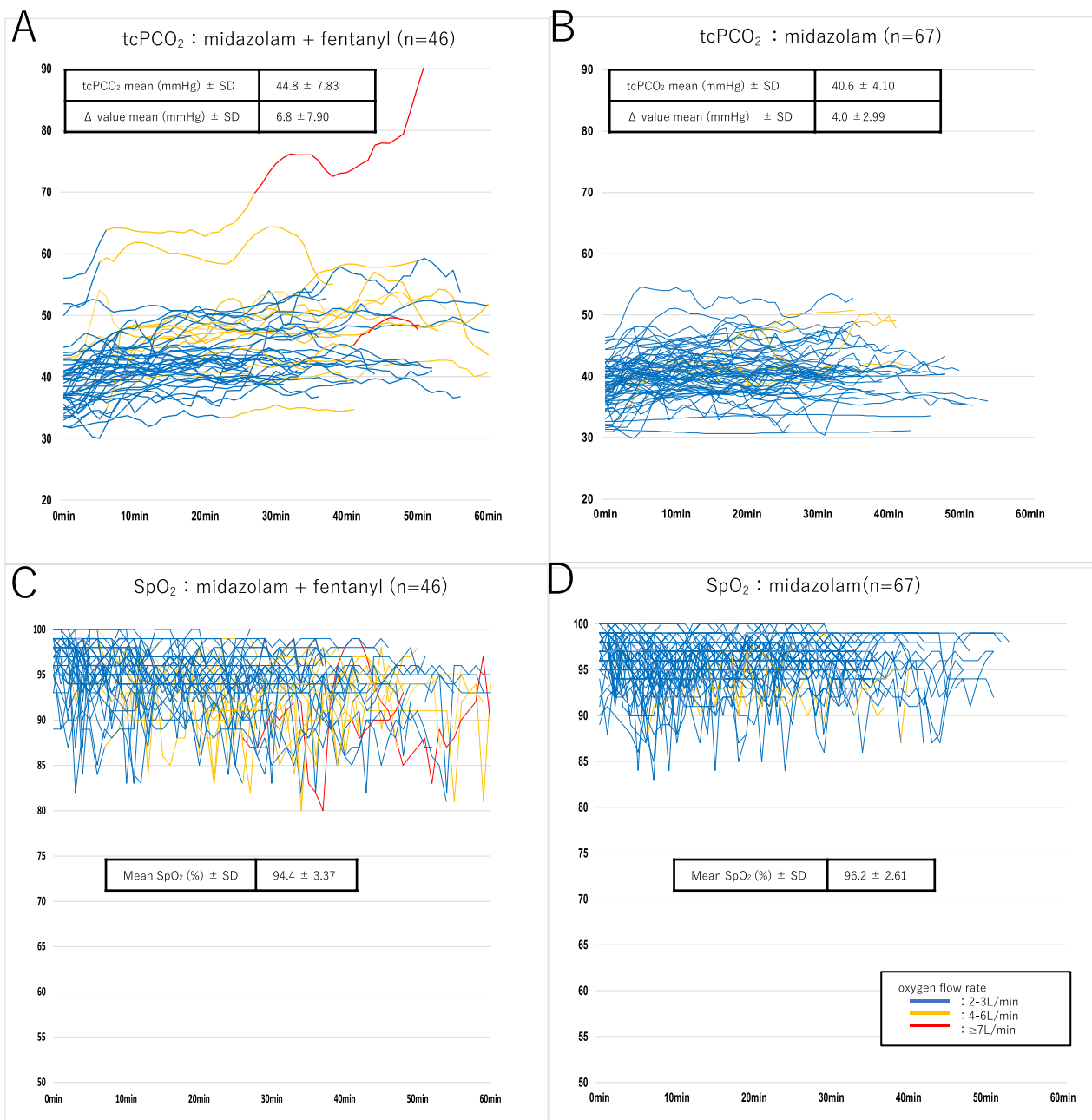


Fig. 3 tcPCO₂/SpO₂ over time in the midazolam + fentanyl group and the midazolam group. SpO₂ saturation of percutaneous oxygen, tcPCO₂ transcutaneous carbon dioxide partial pressure

examination exhibited high CO₂ retention during the examination. Compared with the midazolam plus fentanyl group, the midazolam alone group showed no rapid increase in tcPCO₂; however, CO₂ slowly accumulated in many cases. The median Δ value was 8.10 and 4.00 mmHg in the midazolam plus fentanyl and midazolam alone groups, respectively, with the midazolam plus fentanyl group having a significantly larger

value ($p=0.005$). The tcPCO₂ in the groups with and without additional midazolam was 40.5 ± 3.34 and 40.6 ± 4.02 mmHg, respectively, with no statistically significant difference ($p=0.45$) (Table 2A). The median Δ value was 3.85 and 4.15 mmHg in the groups with and without additional midazolam, respectively, with no statistically significant difference ($p=0.32$). The tcPCO₂ in the groups with and without additional fentanyl was

46.8 ± 8.23 and 42.9 ± 5.54 mmHg, respectively, with no statistically significant difference ($p=0.26$) (Table 2A). The median Δ value was 8.35 and 7.85 mmHg in the groups with and without additional fentanyl, respectively, with no statistically significant difference ($p=0.12$).

The SpO₂ (%) trends in the midazolam plus fentanyl and midazolam alone groups are shown in Fig. 3C, D. SpO₂ fluctuation was greater in the midazolam plus fentanyl group, and SpO₂ imbalance was observed even with oxygen administration at a high flow rate. SpO₂ in the midazolam plus fentanyl and midazolam alone groups was 94.4 ± 3.37 and 96.2 ± 2.61%, respectively, with the midazolam alone group showing a significantly larger value ($p=0.01$). The SpO₂ in the groups with and without additional midazolam was 96.6 ± 3.02 and 95.8 ± 3.22%, respectively, with no statistically significant difference ($p=0.63$) (Table 2B). The SpO₂ in the groups with and without additional fentanyl was 93.7 ± 3.46% and 95.1 ± 3.08%, respectively, with no statistically significant difference ($p=0.21$) (Table 2B).

Subgroup analysis according to smoking history and graphs over time are shown in Fig. 4. Among the patients, 49 (43.4%) were heavy smokers, whereas 64 (56.6%) were nonsmokers or light smokers. The tcPCO₂ trends over time in the heavy smoker and nonsmoker or light smoker groups are shown in Fig. 4A, B. The tcPCO₂ in the heavy smoker and nonsmoker or light smoker groups was 43.3 ± 7.87 and 42.1 ± 5.34 mmHg, respectively, with no statistically significant difference ($p=0.59$). The median Δ value was 6.80 and 5.30 mmHg in the heavy smoker and nonsmoker or light smoker groups, respectively, with no statistically significant difference ($p=0.063$).

The SpO₂ trends over time in the heavy smoker and nonsmoker or light smoker groups are shown in Fig. 4C, D. In both groups, SpO₂ fluctuated significantly during bronchoscopy. SpO₂ in the heavy smoker and nonsmoker or light smoker groups was 95.3 ± 3.10 and 95.3 ± 3.14%, respectively, with no statistically significant difference ($p=0.57$).

Subgroup analysis according to BMI and graphs over time are shown in Fig. 5. Among the patients, 28 (24.8%) had a BMI of ≥ 25 , whereas 85 (75.2%) had a BMI of <25 . The tcPCO₂ trends over time in the BMI ≥ 25 and BMI <25 groups are shown in Fig. 5A, B. The tcPCO₂ in the BMI ≥ 25 and BMI <25 groups was 44.2 ± 8.97 and 41.2 ± 5.23 mmHg, respectively, with the BMI ≥ 25 group having a significantly higher tcPCO₂ ($p=0.05$). The median Δ value was 7.40 and 4.70 mmHg in the BMI ≥ 25 and BMI <25 groups, respectively, with no statistically significant difference ($p=0.19$).

The SpO₂ trends over time in the BMI ≥ 25 and BMI <25 groups are shown in Fig. 5C, D. SpO₂ in the

BMI ≥ 25 and BMI <25 groups was 95.4 ± 2.94 and 95.3 ± 3.17%, respectively, with no statistically significant difference ($p=0.5$).

Subgroup analysis according to sex and graphs over time are shown in Fig. 6. Among the patients, 65 (57.5%) were men, whereas 48 (42.5%) were women. The tcPCO₂ trends over time in the male and female groups are shown in Fig. 6A, B. The tcPCO₂ in the male and female groups was 42.8 ± 7.07 and 42.6 ± 5.43 mmHg, respectively, with no statistically significant difference ($p=0.86$).

The median Δ value was 6.60 and 5.50 mmHg in the male and female groups, respectively, with no statistically significant difference ($p=0.08$).

The SpO₂ trends over time in the male and female groups are shown in Fig. 6C, D. SpO₂ in the male and female groups was 95.1 ± 3.20 and 95.5 ± 2.99%, respectively, with no statistically significant difference ($p=0.58$).

Discussion

In the present study, the dynamic changes in ventilation and oxygenation during bronchoscopy were successfully observed using a transcutaneous blood gas monitor. Few reports have described changes in ventilation and oxygenation over time during bronchoscopy; however, percutaneous CO₂ monitoring had a high measurement success rate and was less invasive.

In the subgroup analysis, mean tcPCO₂ and median Δ value were significantly higher in the midazolam plus fentanyl group than in the midazolam alone group ($p=0.01$ and 0.005, respectively). Therefore, the use of analgesics as anesthesia during bronchoscopy increased the patient's PCO₂. Hypoventilation during bronchoscopy was presumably caused by excessive sedation due to the use of fentanyl as an analgesic. Sedatives are administered in small additional doses to avoid excessive sedation because the effect varies among patients. Notably, apnea during bronchoscopy with fentanyl and midazolam administration is inevitable, and the duration of apnea is longer with higher total doses of anesthetic agents [13].

Benzodiazepines are recommended as sedatives because they have anterograde amnesic effects, reduce patient discomfort, increase tolerance to the procedure, and make the procedure easier and more satisfying for the examiner. Notably, midazolam is widely used due to its immediate effect and short duration of action [14, 15] and is recommended in British Thoracic Society (BTS) guidelines and American College of Chest Physicians (ACCP) statements [16, 17]. Because opioids decrease the cough reflex and improve patient tolerance to the procedure when added to midazolam [18], the BTS guidelines and ACCP statements also recommend that concomitant use should be considered or recommended; therefore, short-acting opioids such as fentanyl are recommended

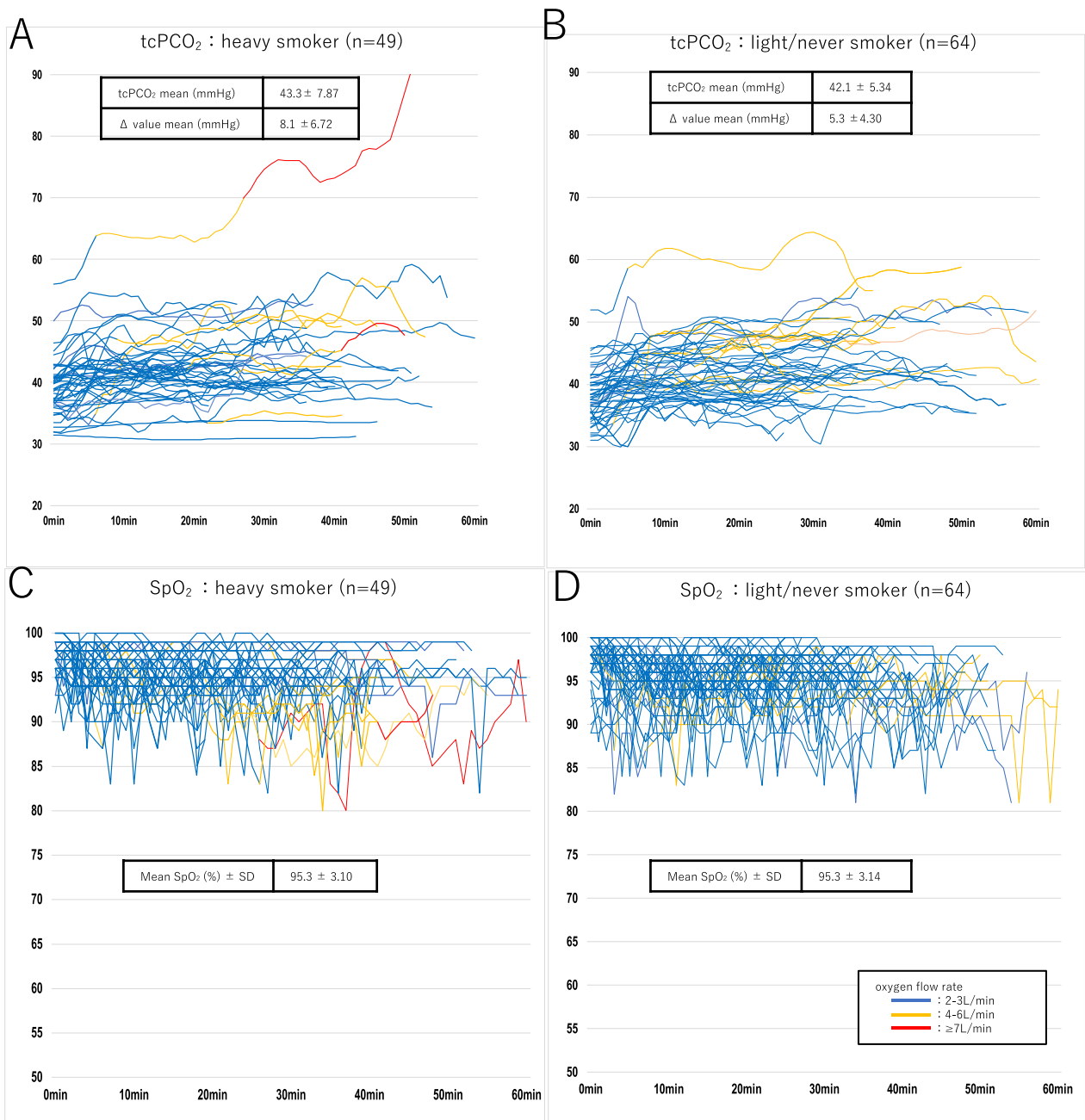


Fig. 4 tcPCO₂/SpO₂ over time in the heavy smoker group and the light/never smoker group. SpO₂ saturation of percutaneous oxygen, tcPCO₂ transcutaneous carbon dioxide partial pressure

[16, 17]. When administered with other sedatives, an initial dose of 25–50 μg of fentanyl is recommended [16]. The routine administration of fentanyl during bronchoscopy at our hospital is 15 μg intravenously before bronchoscope insertion and 5 μg/h continuously until the end of the examination. The total dose of fentanyl was approximately 19 μg, calculated from the mean examination time, and bronchoscopy could be performed using

a dose lower than that recommended in the BTS guidelines. This indicates that the combination of midazolam and fentanyl or continuous fentanyl administration may reduce the total dose of fentanyl during bronchoscopy. In the present study, despite the use of fentanyl dose less than the standard dose, respiratory depression may have occurred due to the small BMI of the Japanese population.

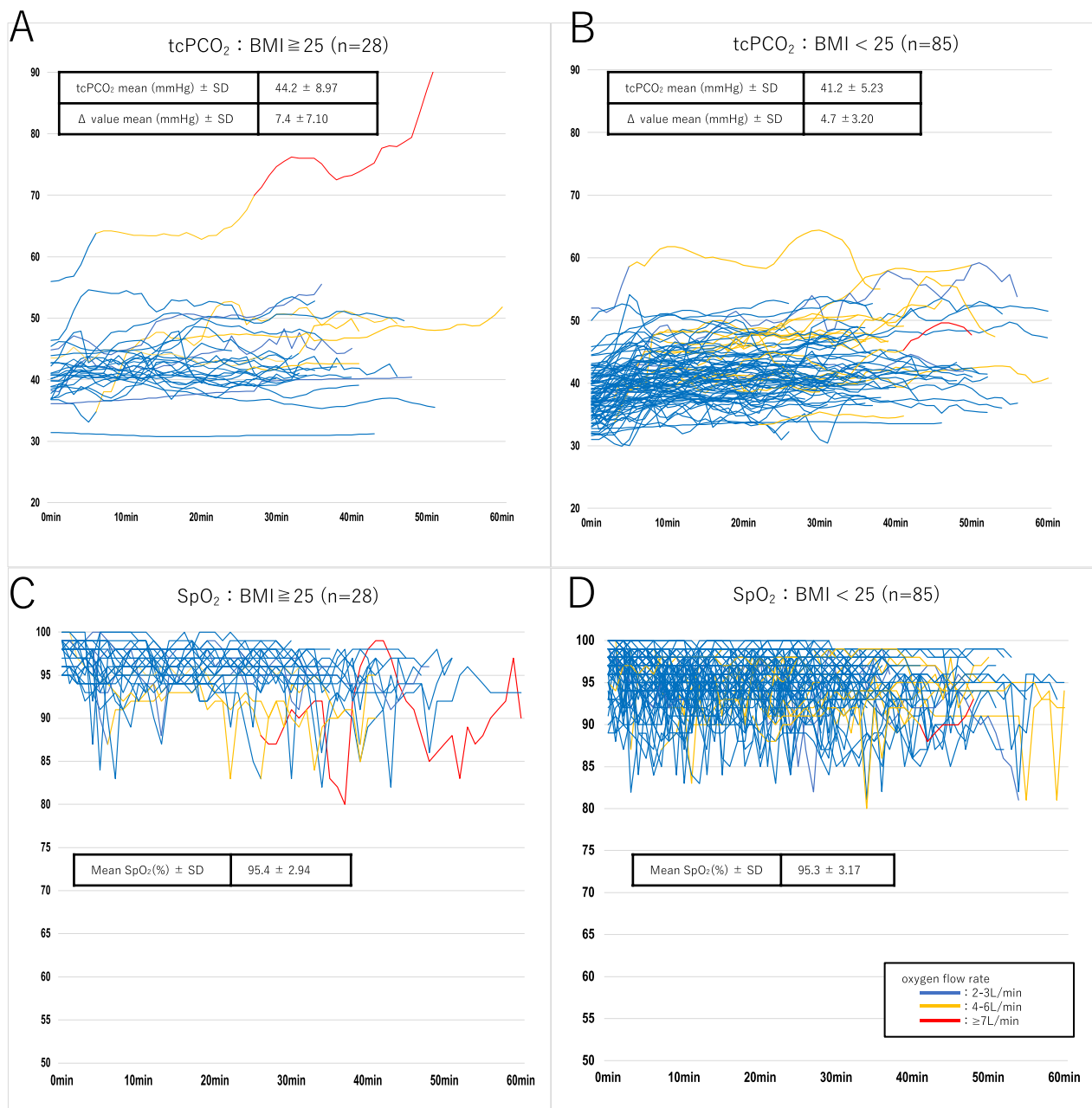


Fig. 5 tcPCO₂/SpO₂ over time in the BMI ≥ 25 group and the BMI < 25 group. *BMI* body mass index, *SpO₂* saturation of percutaneous oxygen, *tcPCO₂* transcutaneous carbon dioxide partial pressure

The SpO₂ was significantly lower in the midazolam plus fentanyl group ($p=0.01$). The group included patients who were endotracheally intubated, suggesting that the oxygen delivery route of the intubation tube was not established and that respiratory depression induced hypoxia. In Japan, bronchoscopy is not performed under general anesthesia due to the issue of medical insurance, which does not cover the examination cost and the number of patients. Therefore, the

respiratory status is managed under local anesthesia, which is equivalent to a closed-circuit oxygen administration method under general anesthesia. In our hospital, the oxygen administration method is used for intubated bronchoscopy, as shown in Fig. 1; however, this system is not actually a closed circuit and does not provide sufficient oxygen to the patient. Currently, the oxygen administration method for intubated bronchoscopy has not been completely established, and

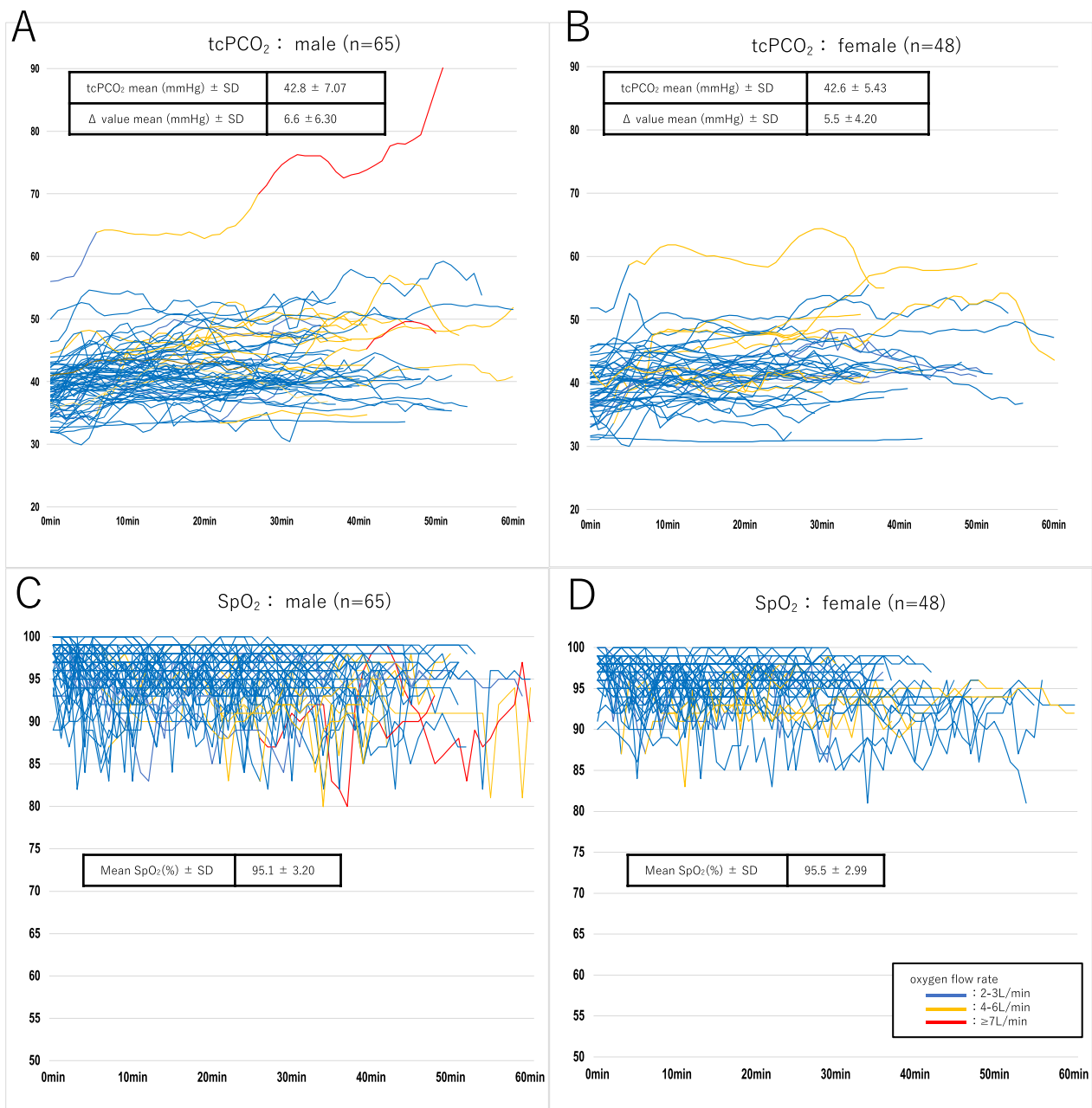


Fig. 6 tcPCO₂/SpO₂ (%) over time in male and female group. SpO₂ saturation of percutaneous oxygen, tcPCO₂ transcutaneous carbon dioxide partial pressure

developing better examination tools and techniques in the future is necessary.

Hypoventilation during bronchoscopy may also be caused by upper airway obstruction or ventilation-perfusion mismatch associated with bronchoscopy procedures [19]. In the present study, mean tcPCO₂ was significantly higher in the BMI ≥ 25 group than in the

BMI < 25 group ($p=0.05$), suggesting that obesity may be one of the causes of hypoventilation during bronchoscopy. Owing to anesthesia induction during bronchoscopy, obese patients were considered to have upper airway obstruction during the examination. However, no significant difference was observed in the median Δ value, indicating the degree of increase in tcPCO₂ during bronchoscopy ($p=0.19$).

The BTS guidelines warn that patients with severe COPD may experience hypoventilation due to oversedation during bronchoscopy and that examiners should be alert for signs of respiratory failure [20]. In the present study, we compared changes in ventilation and oxygenation over time with smoking history using the Brinkman index. No significant difference in $tcPCO_2$ and SpO_2 was observed between the heavy smoker and nonsmoker or light smoker groups ($p=0.59$ and 0.57 , respectively). We believe that some of the heavy smokers were not patients with COPD because respiratory function tests were not routinely performed in all patients before bronchoscopy in our institution.

This study has certain limitations. First, although it was a single-center prospective study, the sample size was small because the number of laboratories that could provide equipment was limited; therefore, we could not measure all the tests performed at our institution. Second, the doses of analgesics and sedatives varied among studies, and statistics for each dose were unavailable. Third, this study included only five patients with a BMI ≥ 30 and no patients with a BMI > 35 . This may reflect the Japanese population but is different from the BMI distribution in western populations. Finally, the authors could not attempt to assess respiratory function before bronchoscopy.

Conclusion

Percutaneous CO_2 monitoring is non-invasive and easy to use. The ventilatory status during bronchoscopy can be evaluated using $tcPCO_2$. Continuous monitoring of oxygenation and ventilation is important during bronchoscopy with endotracheal intubation and analgesics.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12931-024-02990-0>.

Additional file 1: Patients' clinical characteristics in all cases. Patients' clinical characteristics in all case are described.

Additional file 2: Changes in $tcPCO_2$ measured in all cases. The $tcPCO_2$ over time in all cases is shown.

Additional file 3: Changes in SpO_2 measured in all cases. The SpO_2 over time in all cases is shown.

Author contributions

Conception and design: YS, KM. Data collection: YS, KM, HK, KN, ST, HT, SM, HH, HN, MM. Statistical analysis: YS, KM. Interpretation: YS, KM, MM. Drafting the first version of the manuscript: YS, KM, HH, HN. Review and editing of the manuscript: YS, KM, MM.

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Availability of data and materials

Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate

This study was performed at the Department of Respiratory Medicine at St. Marianna University School of Medicine Hospital, with ethics approval (human research and ethics committee approval reference number 5129). All subjects were informed about the non-invasive monitoring to be used in this study, which constituted consent for bronchoscopic examination and participation in this study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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