Safety and efficacy of fentanyl combined with midazolam in bronchoscopy under bispectral index-guided conscious sedation

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Safety and efficacy of fentanyl combined with midazolam in bronchoscopy under bispectral index-guided conscious sedation

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Abstract

Background: Sedation combined with local anesthesia during bronchoscopy is widely accepted in America and Europe, and receiving great attention in China. This study aimed to investigate the safety and efficacy of fentanyl combined with midazolam for bispectral index (BIS) titrated conscious sedation during bronchoscopy in the Chinese population.

Methods: Data from 436 patients who underwent bronchoscopy under local anesthesia (LA group) or BIS-guided conscious sedation combined with local anesthesia (FM group) were retrospectively analyzed. The analysis included vital signs, adverse events recorded during the procedure, and questionnaire information, such as patient tolerance and satisfaction, operator satisfaction, and the cough score noted after the procedure.

Results: A total of 225 patients in the LA group, and 211 in the FM group were enrolled in the study. The blood pressure and oxygen saturation were significantly higher in the LA group than in the FM group during bronchoscopy ($P<0.001$). The heart rate was significantly faster in the LA group at $T3_{max}$, $T3_{min}$ and T4 than in the FM group. The incidence of hypoxia and bradycardia was higher in the FM group than in the LA group, whereas incidence of hypertension and tachycardia was lower. Patient satisfaction and tolerance of the procedure were significantly better in the FM group. visual analog scale (VAS) scores for cough and operator satisfaction were better in the FM group than in the LA group. Sub-group analysis (inspection, biopsy and transbronchial biopsy guided by radial endobronchial ultrasound (rEBUS-TBB)) indicated that the vital signs, adverse event(hypoxia) and patient satisfaction of the two groups were similar to the previous results. However, the VAS scores for operators' satisfaction was no significant difference between the two groups in patients

undergoing inspection.

Conclusions: The conscious sedation regimen of fentanyl combined with midazolam monitored by BIS during bronchoscopy is safe and effective. Although the incidence of hypoxia and bradycardia was higher, the patient's tolerance and physician's satisfaction were significantly improved, especially during lengthy procedures, such as intrabronchial biopsy and transbronchial biopsy guided by radial endobronchial ultrasound.

Trial registration: The study was approved by the ethics committee of Changzhou first people's Hospital (2019-020).

Key words: bronchoscopy, bispectral index, conscious sedation, midazolam, fentanyl.

Background

Bronchoscopy is one of the most commonly used methods for the diagnosis and treatment of lung diseases. The procedure related discomfort, such as cough, shortness of breath, nausea, sore throat, sore nose,[1] caused by repeated bronchoalveolar lavage (BAL), endobronchial ultrasound and complicated treatment of bronchoscopy are increasing in frequency compared to simple diagnosis.[2] Sedation and analgesia during bronchoscopy have gained popularity,[3] as they alleviate anxiety and pain, and diminish patient movement and respiratory response. The American College of Chest Physicians recommends a combination of benzodiazepines and opiates because its synergistic effect results in good patient tolerance.[4] Midazolam is the most commonly used benzodiazepine with anxiolytic, amnestic, and hypnotic effects. Fentanyl, as an opioid, is ideal for bronchoscopy because of its fast onset and short duration.

Sedation depth is often monitored throughout the operation. Bispectral index (BIS) is a non-invasive method used to monitor the depth of sedation, which is based on the patients'

electroencephalographic and electromyographic analysis. BIS can quantify the depth of sedation from 0 to 100 (fully awake). Previous studies have suggested that BIS can be used safely without anesthesiologists in endoscopy.[5,6]

Hence, in our study, we aimed to analyze the safety and efficacy of bronchoscopy under conscious sedation from the perspective of the patients and operators.

Methods

Study Patients

Patients who underwent bronchoscopy in the Respiratory and Critical Care Medicine department of the Third Affiliated Hospital of Soochow University (Changzhou first people's Hospital) between September 2018 and July 2019 were included in this study. The local anesthesia group (LA group) included patients who underwent bronchoscopy under local anesthesia, and the conscious sedation group (FM group) included patients who underwent bronchoscopy under BIS-guided conscious sedation with fentanyl and midazolam, in addition to local anesthesia.

The exclusion criteria were as follows: age <18 or >85 years, American Society of Anesthesiologists(ASA) physical status classification IV or V, hepatic and renal dysfunction, blood platelet count of $<50.0\times10^9$ /L, history of neuropsychosis and the need to take psychotropic drugs for a long time, history of bronchoscopy through an artificial airway, bronchoscopist experience not more than 3 years, incomplete information, and failure to explore the lesion with radial ultrasonography.

Procedure and sedation

Preoperative preparation included: taking the patient's complete medical history before starting bronchoscopy; complete routine examination, including blood tests, coagulation function, infectious

disease markers, electrocardiogram, chest computed tomography, blood gas analysis, if necessary, and cardiac ultrasound; patients fasting for 6 hours before undergoing procedure; and an intravenous catheter placed into the forearm for drug administration.

Before conducting the procedure, all the patients were nebulized with 5 mL of 2% lignocaine for 15 minutes in the preparation room and administered 3 L/min oxygen through nasal catheter. The blood pressure was monitored using an automated pressure cuff, and the heart rate and rhythm were monitored electrocardiographically. A peripheral pulse oximeter was used to monitor oxygen saturation (SpO2).

In the FM group, the subjects were administered IV fentanyl (10 ml: 0.5 mg, Yichang Renfu Pharmaceutical Co. Ltd; 1 ug/Kg; maximum 50 ug) and midazolam (2 ml: 10 mg, Jiangsu Enhua Pharmaceutical Co. Ltd.; 0.05 mg/Kg; the initial dose for patients aged >70 years not exceeding 3 mg) by a nurse, as directed by the bronchoscopist. A disposable BIS Quatro Sensor (Covidien IIc, 186-0106, USA) was connected to the forehead of patients in the study group for monitoring the BIS value. Bronchoscopy was started when the BIS value was <80. If the BIS value was >80, or if persistent patient movement interfered with the procedure, then additional midazolam 1 mg was administered. If the bronchoscopist deemed that persistent cough interfered with the procedure, oral secretions were suctioned and/or 2 mL 2% lidocaine was administered through the bronchoscope. If the BIS value was not <60, then it was up to the bronchoscopist to decide whether to add midazolam 1 mg or not. The total dose of midazolam did not exceed 10 mg.

Bronchoscopy Procedure

Bronchoscopy was carried out according to the “Guidelines for the Clinical Application of Fiberoptic bronchoscopy (draft bronchoscopy)” formulated by the Bronchoscopy Group of the

88 Respiratory Diseases Branch of the Chinese Medical Association. The bronchoscopy procedures
89 were performed by a bronchoscopist with more than 3 years of bronchoscopy experience. All the
90 medical staff were familiar with the rescue process for hemoptysis and respiratory failure,
91 cardiopulmonary resuscitation, and the drugs and antagonists used for sedation. The bronchoscopy
92 room was equipped with rescue and resuscitation drugs and equipment. The types of
93 bronchoscopes used included BF-Q290, BF-P290, BF-1T260, and BF-UC260FW (Olympus,
94 Japan). 2% lidocaine 5 ml was injected through the bronchoscope when entering the trachea, left
95 and right main bronchus, and before lavage.
96 Types of operation: These included basic inspection: bronchial observation, with or without
97 brushing, and BAL; biopsy: biopsy of intrabronchial lesions, with or without brushing, and BAL;
98 rEBUS-TBB: Transbronchial biopsy guided by radial endobronchial ultrasound with or without
99 brushing/BAL; EBUS-TBNA: endobronchial ultrasound-guided transbronchial needle aspiration;
100 interventional therapy: argon plasma coagulation(APC), cryotherapy, electrocoagulation, metal
101 stent placement, foreign body removal; two or more procedures: more than two procedures.
102 During the procedure, vital parameters, including SpO2, systolic blood pressure (SBP), diastolic
103 blood pressure (DBP), and heart rate were recorded before sedation (T1), before bronchoscopy (T2),
104 during bronchoscopy (T3), and at the end of bronchoscopy (T4). The blood pressure was recorded
105 every 5 minutes. SpO2 and heart rate were recorded at the lowest ($T3_{min}$) and the highest points
106 ($T3_{max}$).
107 **Observation index**
108 Adverse events were recorded and defined as follows: hypertension (SBP >180 mmHg or DBP >100
109 mmHg), hypotension (SBP <90 mmHg or mean arterial pressure <60 mmHg), tachycardia (heart

rate >100 beats/min; if high before the procedure, an increase of >20%), bradycardia (heart rate <60 beats/min; if low before the operation, a decrease of >20%), hypoxia (SpO2 <90%,); bleeding, which was further classified as medium (needed an intravenous hemostat), and massive (the procedure should be stopped); airway spasm; manual ventilation, if respiratory arrest or failure occurred, needing artificial ventilation through a laryngeal mask, simple respirator or tracheal intubation if hypoxia showed no improvement in spite of increased oxygen flow, pushing the head back, mandibular support and other measures; need to stop bronchoscopy; and death.

Bronchoscopy operator evaluation: The cough scores used a 10-point visual analog scale (VAS), wherein 0 represented no cough and 10 represented incessant coughing; Operator satisfaction score, wherein, bronchoscopists were asked to record their perception of the procedure, using the same 10-point VAS at the end of the procedure (0 indicated very unsatisfied and 10 indicated very satisfied); Procedure time was defined as the time between bronchoscope insertion into and removal from the nasal cavity. The general condition of the patients was followed up by telephone 4-8 hours post-operation. The patients were asked to use the 10-point VAS to rate their discomfort (tolerance) associated with the procedure, wherein 0 represented no discomfort and 10 represented the greatest possible discomfort. VAS scores were also used to ask for patient satisfaction (0 indicated very unsatisfied and 10 indicated very satisfied). Willingness to undergo repeat bronchoscopy was also recorded. Patients were also asked if they were conscious throughout the process.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation or medians and interquartile ranges, according to distribution. Categorical variables were expressed as proportions. For counting data and categorical variables, we used the $\chi 2$ or Fisher exact tests. For quantitative variables, we

used the Student's t-test or Mann-Whitney test, depending on whether or not data distribution was normal, as evaluated by the Kolmogorov-Smirnov test. All data were analyzed by the SPSS 19.0 software (Chicago, IL). A p value <0.05 was taken to indicate statistical significance.

Results

From September 2018 to July 2019, among the patients who underwent bronchoscopy, 317 patients received LA, out of which, 92 were excluded. Thus, 225 cases were included in the LA group. On the other hand, 240 patients received BIS-guided FM (fentanyl and midazolam), out of which, 29 were excluded. Thus, 211 patients were included in the FM group (Figure 1).

The characteristics of study population are shown in Table 1. There were no differences between the two groups in terms of age, gender, weight, and height (P >0.05). However, there were significant differences in baseline SpO2 between the two groups (P <0.001).

Table 1. Demographic characteristic of the Study Population

Group		**LA**	**FM**	***P value***
N		225	211	
Gender (n,%)male		148(65.8%)	126(59.7%)	0.19
Year（Mean ± SD）		59.99±9.60	60.23±11.56	0.83
Weight (Kg)		63.37±10.19	61.76±9.72	0.79
Height(cm)		164.96±8.03	165.15±7.18	0.09
Bronchoscope Types	Inspection	92	84	0.20
	Biopsy	47	36	
	REBUS-TB	69	64	
	EBUS-TBNA	3	3	
	Intervention	2	7	
	Two types	12	17	

Of the total participants(436 patients), 176 underwent simple bronchoscopy inspection with or without BAL (92 patients in the LA group, 84 patients in the FM group). Endobronchial biopsy was done for 83 patients (47 patients in the LA group, 36 patients in the FM group), and 133 patients underwent r-EBUS (69 patients in the LA group, 64 patients in the FM group). Six patients underwent EBUS-TBNA (3 patients in the LA group, 3 patients in the FM group), 29 underwent two or more procedures (12 patients in the LA group, 17 patients in the FM group), and the remaining patients underwent interventional procedures. There was no significant difference in the constituent ratio of bronchoscopy procedures between the two groups ($P>0.05$) (Table 1). The procedure time in the FM group was longer than that in the LA group (24.40 ±12.37 vs. 20.29 ± 10.96 minutes; $P < 0.001$).

Blood pressure: There was no significant difference in basic blood pressure (SBP and DBP) between the two groups. The SBP and DBP in the two groups increased gradually during bronchoscopy (T3-1, T3-2, T3-3, T3-4). However, at the end of the bronchoscopy (T4), the blood pressure (SBP and DBP) in the locally anesthetized group showed a decrease. The blood pressure was significantly lower in the FM group than in the LA group at all times (Figure 1).

Heart rate: The basic heart rate revealed no significant difference between the two groups. During bronchoscopy, the heart rates of the LA group in T2, $T3_{max}$, $T3_{min}$ and T4 were significantly faster than those of the FM group ($P<0.001$). No serious arrhythmias occurred in either group (Figure 1).

SpO2: The SpO2 of the FM group from T1 to T4 was lower than that of the LA group ($P<0.05$). The median SpO2in both the groups was >90% at all times (Figure 1).

Adverse event: There were no significant differences in the incidence of bronchospasm,

respiratory failure, and moderate and severe bleeding between the two groups. The number of cases of hypertension and tachycardia were significantly less in the FM group than in the LA group. However, hypoxemia and bradycardia were more common in the FM group than in the LA group (Table 2).

Table2: Adverse events of the two groups

		Hypoxia	Hypertension	Hypotension	Tachycardia	Bradycardia	Spasm	Bleeding		Assisted ventilation
								medium	massive	
LA	All	4	90	0	57	6	3	15	5	0
	Inspection	1	29	0	24	2	1	0	0	0
	Biopsy	2	23	0	9	2	0	4	2	0
	REBUS	1	30	0	22	1	2	5	3	0
FM	All	31	59	0	34	17	6	13	0	0
	Inspection	12	24	0	13	6	2	0	0	0
	Biopsy	8	11	0	7	4	2	3	0	0
	REBUS	8	11	0	5	3	2	8	0	0
P	P1	<0.001	0.008	1	0.02	0.01	0.33	0.83	0.06	1
value	P2	<0.001	0.67	1	0.08	0.15	0.61	1	1	1
	P3	0.02	0.11	1	0.97	0.39	0.19	1	0.5	1
	P4	0.01	<0.001	1	<0.001	0.35	1	0.31	0.25	1

P1: Comparison of all patients in the two groups

P2: Comparison of patients receiving only Inspection in the two groups

P3: Comparison of patients receiving Biopsy in the two groups

P4: Comparison of patients receiving rEBUS-TBB in the two groups

Evaluation by patients and operators: The VAS scores for coughing, operator and patient satisfaction, and patient discomfort were significantly better in the FM group than in the LA group.

177 The proportion of patients who were conscious during bronchoscopy was higher in the LA group

178 than in the FM group. A majority of patients in the FM group were willing to undergo a repeat

179 bronchoscopy as compared to those in the LA group (Table 3).

180 Table 3: Evaluation of patients and operators

		Procedure time (minute)	**Patient evaluation**				**Operators evaluation**	
			Discomfort (VAS)	Satisfaction (VAS)	Awareness (yes)	Reexamination (yes)	Cough (VAS)	Satisfaction (VAS)
LA	All	16.93±11.07	3.72±1.91	5.84±1.97	212	33	3.69±1.62	7.54±1.76
	Inspection	11.76±9.16	3.78±1.85	5.89±1.94	89	16	3.03±1.35	8.10±1.27
	Biopsy	18.55±8.84	3.72±2.22	5.74±2.15	47	7	4.06±1.67	7.06±2.08
	rEBUS	20.93±9.94	3.71±1.89	5.78±2.04	68	6	4.12±1.51	7.28±1.79
FM	All	20.29±10.96	0.14±0.45	9.65±0.63	17	209	3.04±1.62	7.91±1.58
	Inspection	11.42±4.95	0.04±0.24	9.87±0.46	9	84	2.54±1.56	8.14±1.58
	Biopsy	17.92±5.53	0.11±0.32	9.69±0.47	2	34	3.08±1.48	8.08±1.18
	rEBUS	27.84±8.95	0.29±0.63	9.45±0.75	5	63	3.55±1.63	9.45±0.75
P *value*	P1	0.002	<0.001	<0.001	<0.001	<0.001	<0.001	0.021
	P2	0.76	<0.001	<0.001	<0.001	<0.001	0.02	0.84
	P3	0.71	<0.001	<0.001	<0.001	<0.001	0.007	0.006
	P4	<0.001	<0.001	<0.001	<0.001	<0.001	0.04	<0.001

181 P1: Comparison of all patients in the two groups

182 P2: Comparison of patients receiving only Inspection in the two groups

183 P3: Comparison of patients receiving Biopsy in the two groups

184 P4: Comparison of patients receiving rEBUS-TBB in the two groups

185 **Different types of bronchoscopy**

186 We performed a sub-group analysis of patients who underwent different types of bronchoscopy,

including inspection, biopsy and rEBUS-TB. Amongst patients undergoing inspection and biopsy, there was no significant difference in the procedure time between the LA group and the FM group. However, among patients who received r-EBUS, the operation time was significantly longer in the FM group than in the LA group.

Blood pressure: The SBP and DBP were lower in the FM group than in the LA group at all times, and most of them were statistically significant. However, amongst patients undergoing biopsy, the DBP values during the procedure at T2, T3-2, T3-3, and T3-4 were not significantly different between the two groups (Figures 2, 3, and 4).

Heart rate: In Patients undergoing bronchoscopy inspection, the heart rate was significantly slower in the FM group than in the LA group at $T3_{min}$, $T3_{max}$, T4. In patients undergoing biopsy, the heart rate at T4 was slower in the FM group than in the LA group. However, there were no differences in maximum and minimum heart rate between the two groups. In patients who received rEBUS-TBB, the minimum heart rate was higher in the LA group than in the FM group, and there was no group difference in maximum and T4 heart rate (Figures 2, 3, and 4).

SpO2: The SpO2 in the FM group was significantly lower than that in the LA group, during bronchoscopy inspection. However, the SpO2 of patients undergoing biopsy did not differ between the two groups during bronchoscopy. In patients who received rEBUS-TB, the minimum and maximum SpO2 significantly differed between the LA and FM groups. At the end of bronchoscopy (T4), the difference in SpO2 between the two groups did not reach statistical significance (Figures 2, 3, and 4).

Adverse event: The difference of adverse events (hypotension, bradycardia, bleeding, bronchospasm or respiratory failure) between the two groups for the three different types of

bronchoscopy procedures (bronchoscopy inspection, biopsy, and rEBUS-TB) was not significantly different. However, hypoxemia was more common in the FM group than in the LA group. In patients receiving rEBUS-TB, the incidence of hypertension and tachycardia was significantly less in the FM group than in the LA group (Table 2).

Evaluation by patients and operators: Patients in the conscious sedation group had better scores for patients' discomfort and satisfaction. They also showed significantly better tolerance with bronchoscopy procedures, VAS score of coughing, as well as global tolerance for the whole procedure. In patients undergoing biopsy and rEBUS-TB, the VAS scores for operators' satisfaction was significantly better in the FM group than in the LA group. However, there was no significant difference between the two groups in patients undergoing inspection (Table 3).

Discussion

In this study, we retrospectively analyzed the related indicators for BIS-monitored conscious sedation during bronchoscopy. The results indicated that BIS-monitored conscious sedation was safe and effective for different types of bronchoscopy procedures.

Painless bronchoscopy was generally performed under intravenous anesthesia conducted by an anesthesiologist. Due to the relative shortage of anesthesiologists in China, fewer hospitals can appoint full-time anesthesiologists in the bronchoscopy room, which in turn affects the execution of sedation and analgesia in patients undergoing bronchoscopy. With the emergence of BIS monitoring, bronchoscopy procedures were performed under moderate sedation, without the participation of anesthesiologists [7]. Midazolam has been the major drug of choice for bronchoscopy owing to its fast acting and amnestic properties.[8] Fentanyl, an opioid sedative hypnotic agent, is also used during bronchoscopy because of its lipophilic properties, which result in a rapid onset and short

half-life[9].

In the present study, a greater increase in heart rate and blood pressure during bronchoscopy were observed among patients who were given local anesthesia compared with those who were given fentanyl and midazolam. However, in comparison with the placebo group[10], there was no significant difference in blood pressure and heart rate between patients in the fentanyl-midazolam group during bronchoscopy in Prabhudev's study. This could be due to the small percentage of biopsy (12/76, 15.8% in the Placebo group; 18/88, 20.5% in the fentanyl-midazolam group). In our study, 58.2% patients in the local anesthesia group (131/225), and 56.9% in the sedation group (120/211) received biopsy. Biopsy often takes a longer time and is more likely to cause circulatory problems in the LA group. Our findings show that a combination of midazolam and fentanyl is superior to local anesthesia in attenuating hemodynamic responses during bronchoscopy. In our study, there were statistically significant differences in basal blood SpO2 between the two groups. However, the median SpO2 in the two groups was 98%. The SpO2 of all patients receiving bronchoscopy were ≥90%. This is in line with previous findings[11].

Amongst patients who received conscious sedation, the incidence of hypertension and tachycardia was less, but that of hypoxemia and bradycardia was higher. None of the patients needed manual ventilation or died due to bronchoscopy in either group. In the analysis of the different types of bronchoscopy, the number of cases of hypertension and tachycardia in patients who received rEBUS-TB was significantly higher in the LA group. We considered that since rEBUS-TB takes a relatively longer time than only inspection or biopsy, the LA group was prone to hemodynamic changes. In all three types of bronchoscopy, the conscious sedation group was prone to hypoxemia. The reported frequency of desaturation (SpO2<90%) during bronchoscopy with midazolam

253 sedation ranged from 14.4% to approximately 35%[11]. In Ogawa's study[12], about 75.4% of the
254 patients received supplemental oxygen. Some studies suggest that fentanyl could cause mild
255 respiratory depression.[13,14] However, a randomized study comparing the midazolam group and
256 fentanyl-midazolam groups found no significant difference in blood SpO2 during bronchoscopy.[10]
257 Therefore, we considered that hypoxemia was mainly attributable to the use of midazolam in the
258 FM group. Other potential causes of hypoxemia, common to both groups, include obstruction of the
259 tracheal lumen by the endoscope, and cough. However, no intubation was performed, and no
260 procedure was suspended due to desaturation, as these events were considered to be transitory; the
261 patients improved as a result of the actions carried out, particularly in terms of elevation of the jaw,
262 and increased nasal catheter oxygen flow.

263 Patient satisfaction and tolerance of the procedure are an important part of the assessment[15,16].
264 In the present study, both of these were significantly better in the fentanyl-midazolam group, than
265 in the LA group. Many studies have the same results as ours. In other words, patients receiving
266 sedation during bronchoscopy were more satisfied than patients who were not sedated. In the
267 fentanyl-midazolam group, among the patients who answered the questionnaire, 190/211 were
268 willing to undergo a repeat bronchoscopy in the future, if required. In Lorenzo's study,[17] 95.9%
269 of sedated patients would "definitely return" for EBUS-TBNA. In addition to patient satisfaction,
270 operator satisfaction is equally important.[18] In our study, VAS scores for coughing and operator
271 discomfort were better in the FM group than in the LA group, as recorded by bronchoscopists. This
272 is in agreement with the results of a study by Daisuke et al.[19] Some studies suggest that the
273 advantage of opioids compared to benzodiazepines is the suppression of cough and pain.[17,20,21]
274 Our results allude to the fact that patient cooperation and physician's comfort level were

275 significantly better in the fentanyl-midazolam group.

276 Sub-group analysis (different bronchoscopy types) indicated that a longer procedure time in the
277 FM group than in the LA group was mainly due to the obvious long time in the r-EBUS group. We
278 analyzed that this was because after sedation, the patients were quiet and cooperated well, and radial
279 ultrasonography was performed by the bronchoscopist unhurriedly. Further, the success rate of
280 ultrasound exploration in the sedation group was 99.6% (239/240) a significantly higher rate than
281 the success rate of 95.9% in the LA group (304/317) (P=0.006).

282 This study had some limitations. First, the sample size was small for both operations (EBUS-
283 TBNA and Interventional therapy), and we need to expand it in further studies. Second, the pulse
284 rate and SpO2 were recorded at only two points ($T3_{max}$, and $T3_{min}$) during flexible bronchoscopy,
285 which may have influenced the results. Furthermore, this research may be biased because it was a
286 retrospective, single-center study.

287 Conclusions

288 In conclusion, bronchoscopy under conscious sedation using fentanyl and midazolam prescribed
289 by the pulmonologist with BIS assistance is a safe and efficient procedure. The patient's cooperation
290 and physician's comfort are enhanced due to sedation, especially during lengthy procedures, such
291 as intrabronchial biopsy and rEBUS-TBB, and the risks involved, such as hypoxia, are small and
292 manageable.

293 Abbreviations

294 BIS: bispectral index; LA: local anesthesia; FM: fentanyl-midazolam; BAL: bronchoalveolar lavage;
295 ASA: American Society of Anesthesiologists; SpO2: oxygen saturation; rEBUS-TBB:
296 Transbronchial biopsy guided by radial endobronchial ultrasound. EBUS-TBNA: endobronchial

ultrasound-guided transbronchial needle aspiration; APC: argon plasma coagulation; SBP: systolic blood pressure; DBP: diastolic blood pressure; VAS: visual analog scale.

Declarations

Ethics approval and consent to participate: Informed consent was obtained from all patients before the procedures. The Institutional Review Board of Changzhou first people's Hospital approved this study, and the requirement for informed consent was waived because of the retrospective nature of the study (No.2019-020).

Consent for publication: Not applicable.

Availability of data and materials: The data used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Competing interests: The authors declare that they have no competing interests.

Figure1. flow diagram

Figure2: (All patients) Comparison of the vital signs between the two groups *:P <0.05; **:P <0.01; ***:P <0.001

Figure3: (Inspection) Comparison of the vital signs between the two groups *:P <0.05; **:P <0.01; ***:P <0.001

Figure4: (Biopsy) Comparison of the vital signs between the two groups *:P <0.05; **:P <0.01; ***:P <0.001

Figure5: (REBUS-TB) Comparison of the vital signs between the two groups *:P <0.05; **:P <0.01; ***:P <0.001

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Figures

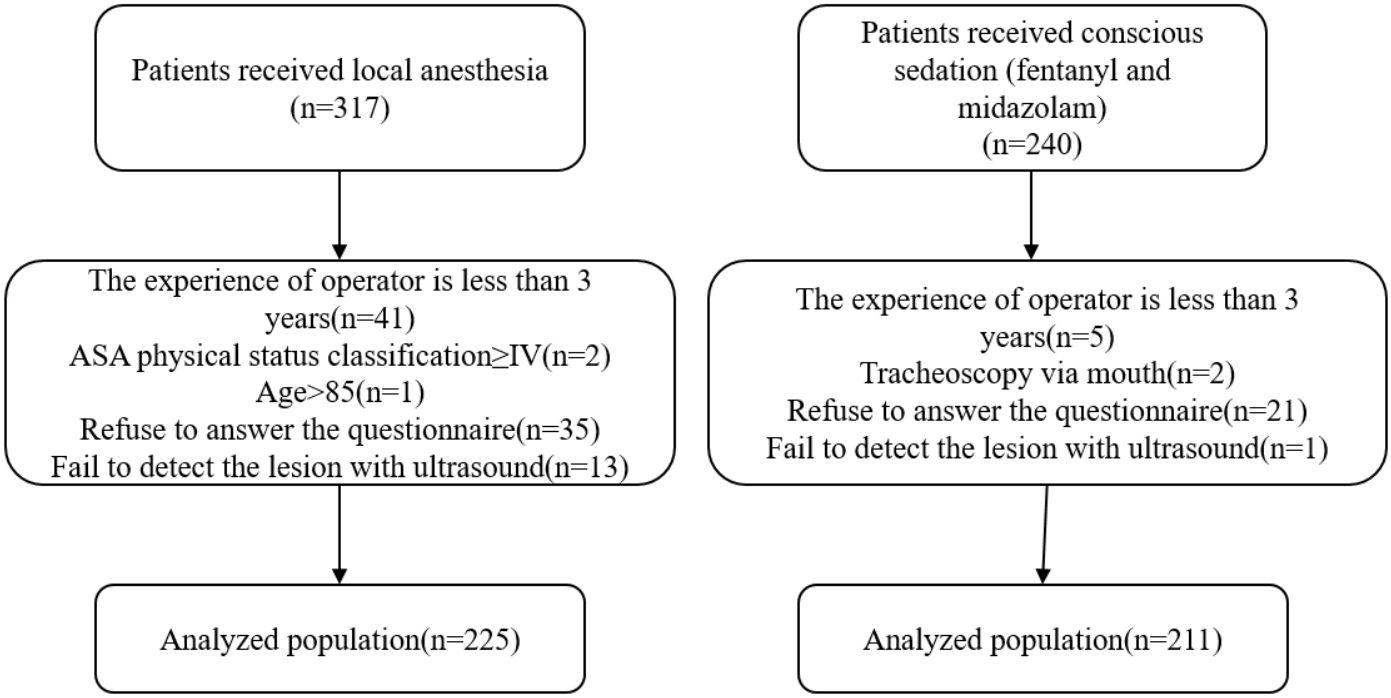

Figure 1

flow diagram

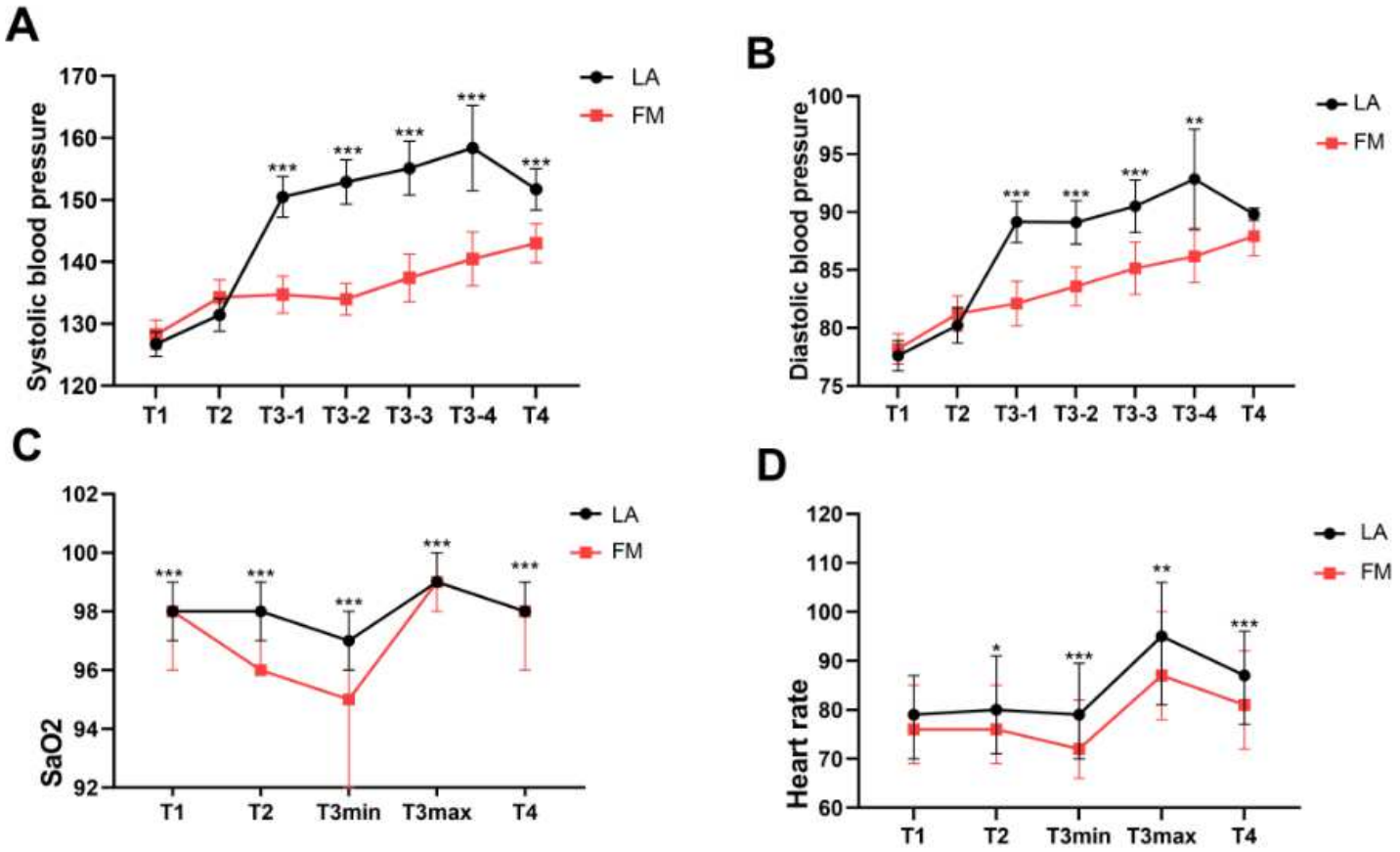

Figure 2

(All patients) Comparison of the vital signs between the two groups *:P <0.05; **:P <0.01; ***:P <0.001

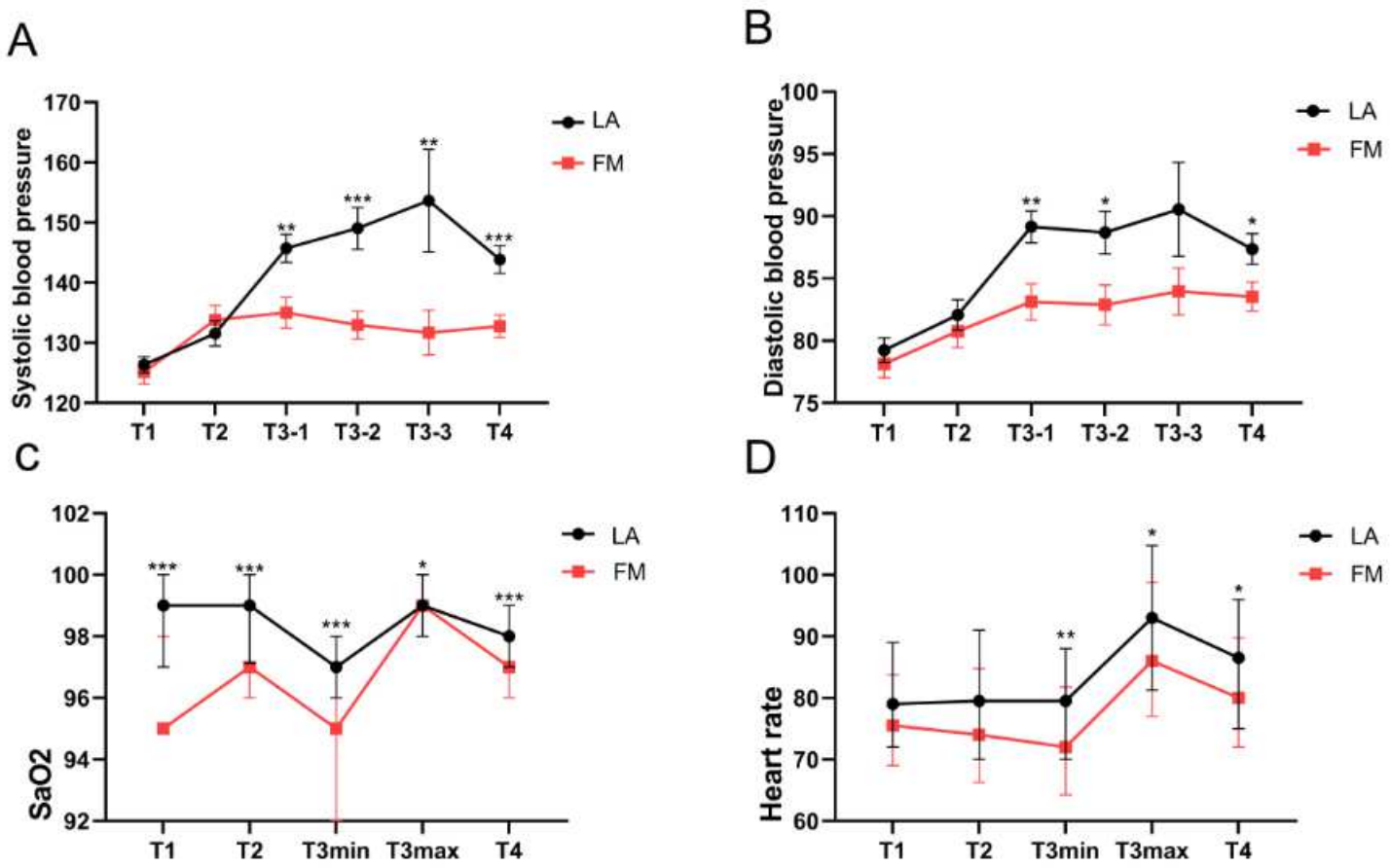

Figure 3

(Inspection) Comparison of the vital signs between the two groups *:P <0.05; **:P <0.01; ***:P <0.001

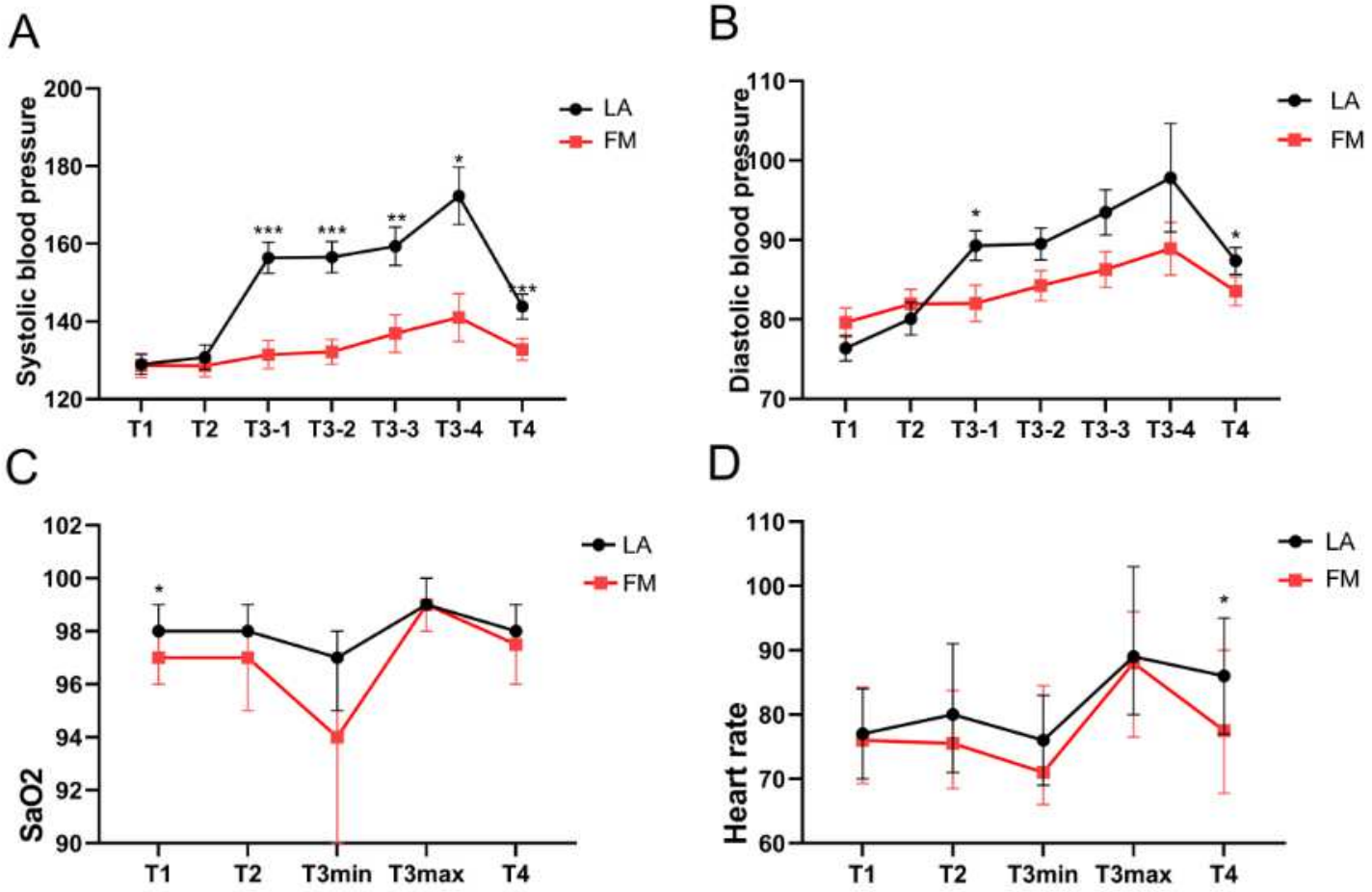

Figure 4

(Biopsy) Comparison of the vital signs between the two groups *:P <0.05; **:P <0.01; ***:P <0.001

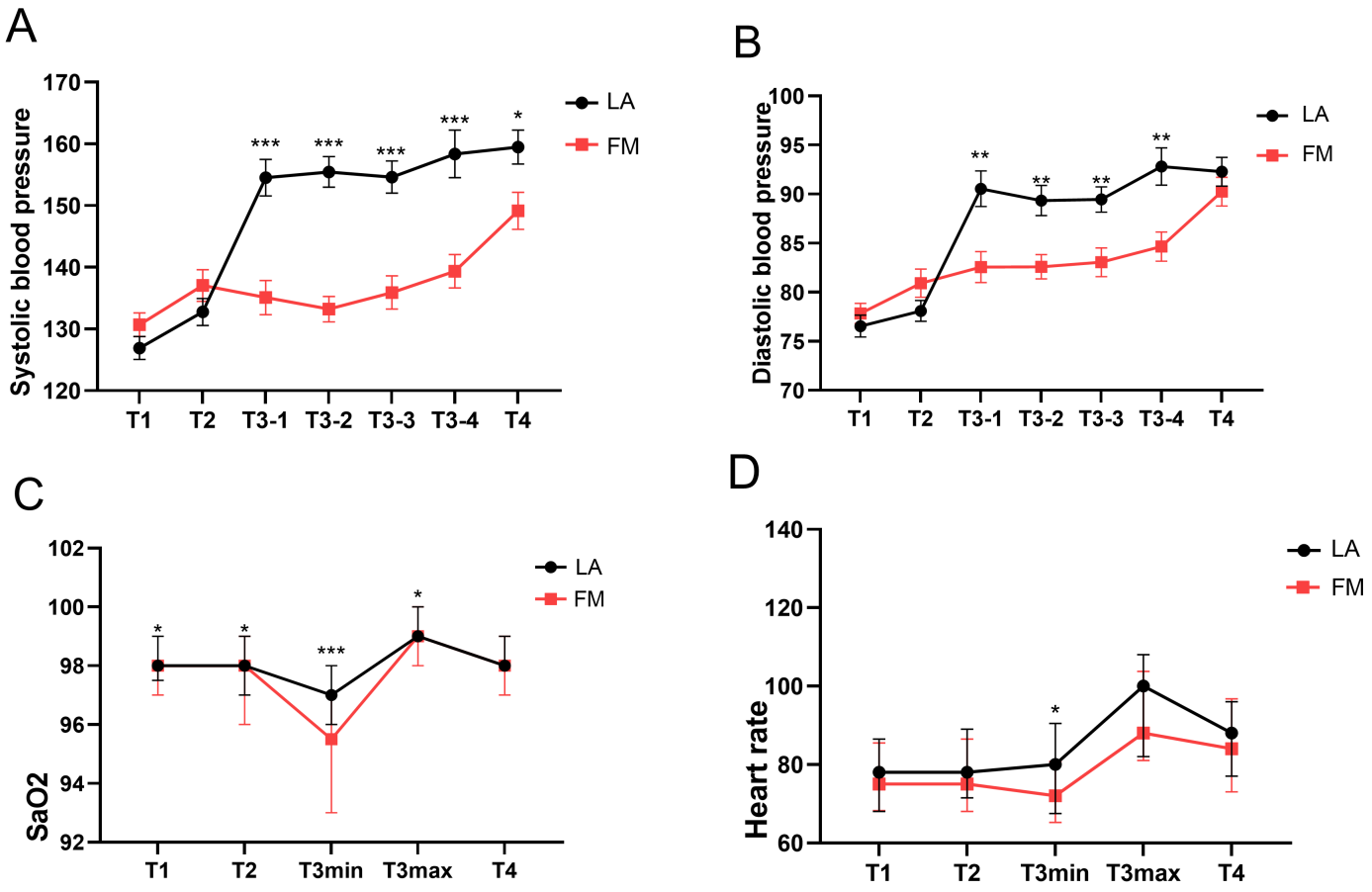

Figure 5

(REBUS-TB) Comparison of the vital signs between the two groups *:P <0.05; **:P <0.01; ***:P <0.001