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# BMJ Open

## Sufentanil target controlled infusion (TCI) vs remifentanil TCI for monitored anaesthesia care for patients with severe tracheal stenosis undergoing fiberoptic bronchoscopy: protocol for a prospective, randomized, controlled study

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Manuscripts

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4 **Sufentanil target controlled infusion (TCI) vs remifentanil TCI for monitored**  
5 **anaesthesia care for patients with severe tracheal stenosis undergoing**  
6 **fiberoptic bronchoscopy: protocol for a prospective, randomized, controlled**  
7 **study**  
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## ABSTRACT

### Introduction

The use of monitored anaesthesia care (MAC) is necessary and ubiquitous for fiberoptic bronchoscopy. The efficacy and safety of the MAC with sufentanil target controlled infusion (TCI) and remifentanil TCI in patients with severe tracheal stenosis are still unknown.

### Methods analysis

This study is a prospective, investigator-initiated, two-arm, randomized control trial to compare the efficacy and safety of sufentanil TCI with remifentanil TCI in patients with severe tracheal stenosis undergoing fiberoptic bronchoscopy. 270 patients will be randomly assigned to the sufentanil TCI group or remifentanil TCI group, with a 1:1 ratio in two groups. The primary outcome is the incidence of hypoxemia (an oxygen saturation of <90%).

### Ethics and dissemination

The study has been approved by the Medical Ethics Committee of Shanghai Pulmonary Hospital. The results will be submitted for publication in peer-reviewed journals.

**Trial registration number** ChiCTR2100043380

### Strengths and limitations of this study

- This study is an investigator-initiated, randomized, controlled trial, comparing two MAC strategies.
- This study includes only subjects with severe tracheal stenosis.
- The main limitation of our study is that considering the characteristics of the two MAC strategies, the overall trial is not double-blind.

## INTRODUCTION

Since the introduction of the flexible fiberoptic bronchoscope, bronchoscopy has been widely used as a diagnostic tool in the field of clinical respiratory medicine. Approximately 500,000 fiberoptic bronchoscopy are performed in the United States

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4 annually<sup>1</sup>. Sedation is now generally recommended for all patients undergoing  
5 fiberoptic bronchoscopy unless a specific contraindication to sedation exists<sup>2-4</sup>.  
6 Sedation during fiberoptic bronchoscopy improves patient comfort and tolerance, and  
7 enhances the willingness to repeat the procedure, without increasing complications<sup>3 5</sup>  
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14 Bronchoscopy has been an integral part of the diagnosis and treatment of patients  
15 with severe tracheal stenosis<sup>7</sup>. Patients affected by severe tracheal stenosis develop  
16 symptoms such as stridor, dyspnea, voice changes, mucus production increasing, and  
17 persistent cough<sup>8</sup>. Most patients require sedation and analgesia to tolerate fiberoptic  
18 bronchoscopy. Anaesthetic management for patients with severe tracheal stenosis  
19 during fiberoptic bronchoscopy procedures has always been challenging, and there is  
20 no standardized practice currently<sup>3 9</sup>.  
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28 Remifentanil has a rapid onset of action and elimination half-life and a predictable  
29 duration of action with no accumulation of effect on repeated dosing or with continuous  
30 infusion, which making it suitable for anaesthesia management of diagnostic and  
31 therapeutic bronchoscopy<sup>10-15</sup>. The degree of the noxious stimulation caused by the  
32 insertion and manipulation of a bronchoscope is often similar to a surgical incision.  
33 Remifentanil might cause respiratory depression or hemodynamic instability when  
34 effectively inhibiting operational stress, which is often very dangerous for patients with  
35 severe tracheal stenosis<sup>14 16 17</sup>. Sufentanil is a more potent opioid than remifentanil, its  
36 analgesic effect lasts longer and it is superior in terms of hemodynamic stability.  
37 Sufentanil has a longer half-time as compared with remifentanil, but TCI will prevent  
38 long-acting opioid-induced accumulation and allow rapid recovery from anaesthesia<sup>18</sup>.  
39 There have been no detailed investigations on the efficacy and safety of monitored  
40 anesthesia care (MAC) using sufentanil or remifentanil TCI in patients with severe  
41 tracheal stenosis undergoing fiberoptic bronchoscopy. The aim of our study is to  
42 compare sufentanil TCI with remifentanil TCI in patients with severe tracheal stenosis  
43 undergoing fiberoptic bronchoscopy.  
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## 58 **Objectives**

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We aim to conduct a prospective randomized controlled trial comparing sufentanil TCI with remifentanil TCI and assume that sufentanil TCI would decrease the incidence of hypoxemia.

### **Primary objective**

Determine the incidence of hypoxemia of MAC with sufentanil TCI versus MAC with remifentanil TCI in patients with severe tracheal stenosis undergoing bronchoscopy.

## **METHODS AND ANALYSIS**

### **Study design**

This is a single-center, randomized, investigator-initiated clinical trial of 270 patients with severe tracheal stenosis that requires fiberoptic bronchoscopy. The CONSORT flow chart is presented in Figure 1. A SPIRIT figure is included in Figure 2 with a checklist included as an additional document (Supplementary file 1). Patients will be randomly assigned to one of two groups. Group S will be received sufentanil TCI and Group R will be received remifentanil TCI.

### **Inclusion criteria**

All patients treated with fiberoptic bronchoscopy in Shanghai Pulmonary Hospital will be screened for eligibility in strict accordance with the inclusion and exclusion criteria. Tracheal stenosis is defined as narrowing of the endotracheal lumen. The diagnosis will be determined by the same respiratory physician together with the same endoscopist. The inclusion criteria are patients aged 18–65 years, with the American Society of Anesthesiologists (ASA) physical status classifications I–III and Cotton-Myer grades II-III (the narrow of the endotracheal lumen is more than 50%). The exclusion criteria are shown in Table 1.

Table 1. Summary of exclusion criteria of the trial.

Exclusion criteria
BMI > 30 or < 18.5
Baseline oxygen desaturation (resting SpO <sub>2</sub> < 90%)
Chronic opioid treatment, substance abuse or drug use

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Pregnancy

History of allergy to related drugs

Severe coagulation dysfunction

Severe hepatic and renal dysfunction

Gastroesophageal reflux disease

History of abnormal recovery from anaesthesia

No informed consent

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### **Recruitment**

Consecutive patients who present to respiratory clinics at Shanghai Pulmonary Hospital with a diagnosis of tracheal stenosis and meet the inclusion criteria will be offered the opportunity to enroll in our study. We will inform them of details about our study. All patients will be provided with full information of their part in our study and assure that their information will be kept strictly confidential.

### **Information consent**

Informed consent will be obtained from each patient or legally authorized representative (LAR) prior to enrollment in our study. This will provide a clear understanding that their participation is entirely voluntary, and they have a right to withdraw at any time during the study. Refusal to sign or participate will not affect the patient's right to receive medical care. No study procedures will be done prior to obtaining informed consent.

### **Randomization and blinding**

After obtaining a signed informed consent from the patient or the LAR, the patient will be randomly allocated 1:1 to Group S or Group R. Randomization will be performed by sealed envelopes available at the Shanghai Pulmonary Hospital. A researcher who will be masked will generate treatment assignments using a computer-generated random number list of variable block sizes (block size 4-6-8) by Stata 16.0 (STATACORP LLC.4905 Lake Way Drive). Randomization envelopes to be opened will be created by the research assistant just prior to when they are ready to randomize

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4 a patient. The integrity and presence of the envelopes will be checked at each  
5 monitoring visit.  
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7 The research assistant (RA) who will be blinded to the randomized assignment of  
8 patients will conduct all baseline interviews. The patients will be blinded to their  
9 intervention as will the research staff completing the post-procedural follow-up  
10 questionnaire. It is not possible to blind anaesthesiologists involved in a patient's care,  
11 but bronchoscopists will be blinded.  
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### 17 **Study treatment**

18 Patients will fast prior to the procedure. After premedication with i.v. midazolam 0.02  
19 mg/kg in the reception area, patients will be transferred to the operating theatre.  
20 Patients will be monitored with ECG, pulse oximetry, and non-invasive arterial pressure  
21 during the procedure and recovery period [until post-anaesthesia care unit (PACU)  
22 discharge]. All patients will receive oxygen application via a nasal tube with 2 liters of  
23 O<sub>2</sub>/min initially. Once the plasma-site concentration (C<sub>p</sub>) and effect-site concentration  
24 (C<sub>e</sub>) has achieved equilibrium, a soft rubber type nasopharyngeal airway (No.6/7,  
25 Medis Medical, UK) will be inserted. The oxygen supply will be changed from nasal  
26 cannula to nasopharyngeal airway connected to an anaesthetic machine with 6  
27 liters of O<sub>2</sub>/min and an adjustable pressure-limiting (APL) valve setting of 30  
28 cmH<sub>2</sub>O. Both groups will be intravenously administered an initial loading dose of  
29 0.8mcg/kg dexmedetomidine, followed by a maintenance dose of 0.5mcg/(kg·h) during  
30 the procedure. 4 mL of 1% lignocaine solution will be administered by  
31 nasopharyngeal airway to throat, then three aliquots of 4 mL of 1% lignocaine solution  
32 will be administered by endoscopist, one each to supraglottic, subglottic and carina  
33 through bronchoscope using the "spray as-you-go" technique<sup>19</sup>. A BF-260 electronic  
34 bronchoscope (BF-1T260/6C260, Olympus Corporation, Japan) will be used.  
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52 TCI plasma-site concentration (C<sub>p</sub>) for sufentanil or remifentanil will be achieved  
53 using the Fresenius DPS workstation using the Gepts or Minto pharmacokinetic  
54 model respectively. The EC<sub>95</sub> of sufentanil or remifentanil is set as the plasma target  
55 concentration and which is 0.212 ng/ml or 2.710 ng/ml respectively. Intravenous  
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4 injection of 10-20 mg propofol will be used as a remedy and repeatedly as  
5 necessary. The effective concentration (Ce) of sufentanil and remifentanil are based  
6 on our previous research using the biased coin up-and-down design sequential  
7 method. A MAP < 80% of baseline or 60 mmHg is regarded as hypotension. In the  
8 event hypotension happens, an intravenous injection of phenylephrine (25~100 mcg)  
9 will be administered as a rescue vasopressor.  
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### 15 **Management of hypoxemia**

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17 Definition of hypoxemia: SpO<sub>2</sub> < 90% at any time<sup>20</sup>. The severity of hypoxemia is  
18 classified as follows: subclinical hypoxemia (SPO<sub>2</sub> of 90-95%), moderate hypoxemia  
19 (SPO<sub>2</sub> of 75-89%, ≤60 s), and severe hypoxemia (SpO<sub>2</sub> < 90% for >60 s or SpO<sub>2</sub> < 75%  
20 at any time)<sup>21</sup>.  
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25 Once hypoxemia develops, it will be corrected using the following sequence: (1)  
26 patient stimulation, (2) increasing the volume of supplementary oxygen from 6 to 10  
27 liters of O<sub>2</sub>/min, (3) opening the airway using a jaw-thrust maneuver, (4) removing the  
28 bronchoscope tube and mask ventilation, and (5) laryngeal mask or tracheal intubation  
29 for mechanical ventilation.  
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### 35 **Trial outcomes**

#### 36 **Primary outcome**

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38 The primary outcome is the incidence of hypoxemia.  
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#### 41 **Secondary outcomes**

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43 1. Secondary outcome variables include the following :
- 44 2. The severity of hypoxemia.
  - 45 3. Cough severity rated on a 4-point scale (no cough=1, slight coughing=2, moderate  
46 coughing = 3, severe coughing = 4). Coughing is considered slight if no more than  
47 2 coughs in sequence occurred, moderate if 3-5 coughs in sequence occurred and  
48 severe if more than 5 coughs in sequence occurred.
  - 49 4. Hemodynamic variables (blood pressure and heart rate).
  - 50 5. Ramsay sedation scores during procedure.
  - 51 6. Patient's comfort and tolerance to fiberscope assessed by Puchner comfort scale<sup>22</sup>.
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- 4 7. Recovery time.
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- 6 8. Arterial blood gases (PO<sub>2</sub>, PCO<sub>2</sub> and PH) before and after the operation.
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- 8 9. The incidence of postoperative nausea and vomiting .
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- 10 10. Satisfaction scores of the patient, bronchoscopist and anaesthesiologist.
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- 12 11. The willingness of the patient to undergo repeat bronchoscopy.
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- 14 12. Visual analog scale (VAS, 0-100mm) scores of sore throat at 30 min after the end
- 15 of the operation.
- 16
- 17 13. Complications related to the procedure and anaesthesia.
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### 19 **Statistical methods**

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21 The analysis will be performed on an intention-to-treat basis, such that each patient is  
22 analyzed in the group to which he or she is randomized, regardless of actual  
23 compliance with the intended intervention. All the analyses will be conducted using  
24 Stata 16.0 (STACORP LLC.4905 Lake Way Drive). A two-tailed p value equal or  
25 less than 0.05 will be considered as statistically significant. All tests, except for the  
26 primary outcome, will be exploratory. When individual items are missing from a scale,  
27 we will calculate the percent of missing items. If less than 10%, we will impute values  
28 using the mean of the remaining items. If more than 10%, the scale score will be  
29 missing, and unavailable for analysis.  
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### 38 **Sample size calculation**

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40 Our previous study (unpublished) shows that the incidences of hypoxemia in the two  
41 groups are 10% (1/10) in sufentanil group and 27.27% (3/11) in remifentanil group. We  
42 determined that enrolment of 270 patients would provide a power of 90% to show a  
43 reduction in the rate of incidences of hypoxia between two groups at a two-sided alpha  
44 level of 0.05, accounting for 20% lost to follow-up.  
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### 50 **Descriptive statistics**

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52 Continuous variables will be described using means and SD for normally distributed  
53 data. For continuous variables with non-normally distributed data, medians and ranges  
54 will be used. Categorical data will be described using counts, proportions, and risk  
55 ratios with 95% CIs.  
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## Planned outcome analysis

### Primary outcome

The incidences of hypoxia will be compared between the two groups using a  $\chi^2$  test or an exact Fisher's exact test if required. The incidences of hypoxia will then be modelled (secondary analysis) using a multivariate logistic regression.

### Secondary outcomes

Secondary endpoints will be compared between the two treatment groups by means of Student's t-test (or the Mann-Whitney U test, if necessary) for continuous quantitative variables and by means of the  $\chi^2$  test (or Fisher's exact test) for qualitative variables. Linear models and logistics models will be used to compare the two groups in multivariate analyses. Time-to-event analyses will involve the Kaplan-Meier method and the Cox proportional hazards model.

## DISCUSSION

MAC is a specific anaesthesia service performed by a qualified anaesthesia provider for a diagnostic or therapeutic procedure<sup>23</sup>. MAC is useful in patients who require repeated fiberoptic bronchoscopy as well as safe in respiratory depression when performed by experienced anaesthesiologists<sup>24</sup>. We will utilize MAC for patients with severe tracheal stenosis that requires fiberoptic bronchoscopy in this study.

TCI allows an accurate adaptation of the anaesthesia level and fewer overdose-linked adverse effects. As a decreased cumulative dose of sufentanil or remifentanil, hemodynamic stability, recovery and discharge may also be improved by using TCI. The  $C_e$  of sufentanil and remifentanil used in the study are based on our previous unpublished research.

This trial is the first randomized controlled study powered to test the hypothesis that sufentanil TCI compared with remifentanil TCI for MAC can reduce the incidence of hypoxemia and related adverse events in patients with severe tracheal stenosis undergoing fiberoptic bronchoscopy. We believe that the findings of this study will have

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4 significant clinical implications. This might mean that more studies are needed to  
5 determine the optimal strategies for anaesthesia management to prevent hypoxemia.  
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### 8 9 **Data collection, monitoring and management**

10 Preoperative, intraoperative and postoperative follow-up data will be collected from  
11 electronic medical records, monitoring machines and relevant manual records by the  
12 research staff (YJZ). All electronic and handwriting data will be stored on a password-  
13 protected computer. Data and safety monitoring will be the responsibility of the  
14 principle investigator (JML).  
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### 20 21 **Trial status**

22 The recruitment commenced in February 2021. It is anticipated that recruitment will  
23 end by June 2022. The version number of the protocol are v2.0.  
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### 27 28 **Patient and public involvement**

29 Patients or the public were not involved in the design of our research and will not be  
30 involved in conduct, reporting or dissemination of our research.  
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### 33 34 **Dissemination policy**

35 The results of this study will be disseminated regardless of the effect of the intervention  
36 on study outcomes. The manuscript describing the effect of the intervention will be  
37 submitted to a peer-reviewed journal when data collection and analyses are complete.  
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### 40 41 **Contributors**

42 WW and YZ designed the study, they are joint first author. WW and YJZ wrote the  
43 manuscript together. YZ provided substantial contributions to the conception and  
44 design of the study, wrote the statistical analysis plan and estimated the sample size.  
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JML was responsible for designing the study and drafting the work, revising it critically  
for important intellectual content and approved the final version of the manuscript. All  
authors gave their agreement to be accountable for all aspects of the work, and ensure  
the accuracy and integrity of any part of the work.

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4 NO.201940366).

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6 **Ethics approval and consent to participate**

7 The study protocol was approved by the Ethics Committee of Shanghai Pulmonary  
8 Hospital of China (approval No. K19-122). Informed consent must be obtained from  
9  
10 all patients.  
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13 **Patient consent for publication**

14  
15 Not required.  
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17 **Competing interests**

18  
19 The authors declare that they have no competing interests.  
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4 Figure 1  
5 CONSORT flow diagram for the study. CONSORT, Consolidated Standards of  
6 Reporting Trials.  
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14 Figure 2  
15 SPIRIT Figure-Schedule of enrolment, interventions, and assessments. SPIRIT,  
16 Standard Protocol Items: Recommendations for Interventional Trials.  
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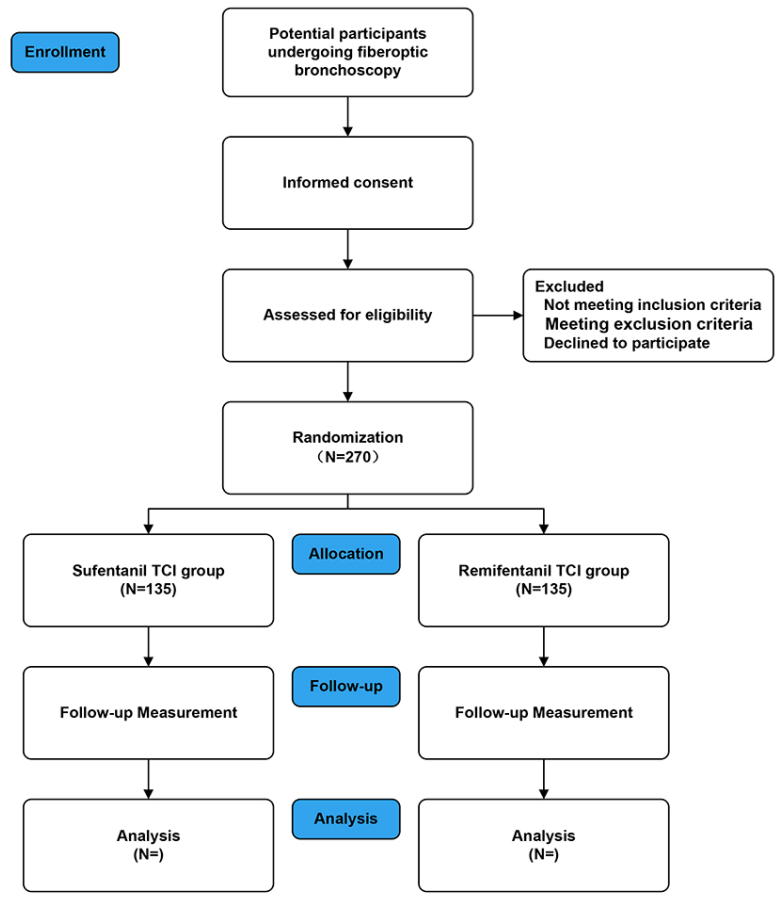


Figure 1. CONSORT flow diagram for the study. CONSORT, Consolidated Standards of Reporting Trials

STUDY PERIOD					
	Enrolment	Allocation	Post-allocation		Close-out
TIMEPOINT	t <sub>1</sub>	t <sub>0</sub>	t <sub>1</sub>	t <sub>2</sub>	t <sub>3</sub>
	Feb 2021- Jun 2022		During the procedure	PACU	
<b>ENROLMENT:</b>					
Eligibility screen	X				
Informed consent	X				
Allocation		X			
<b>INTERVENTIONS:</b>					
Sufentanil TCI			X		
Remifentanil TCI			X		
<b>ASSESSMENTS:</b>					
Baseline variables	X	X			
Hypoxemia			X		
Cough severity			X		
Hemodynamic variables			X		
Sedation scores			X		
Patient's comfort			X		
Recovery time				X	
Postoperative nausea and vomiting				X	
Satisfaction				X	
Visual analog scale				X	

Figure 2. SPIRIT Figure-Schedule of enrolment, interventions, and assessments. SPIRIT, Standard Protocol Items: Recommendations for Interventional Trials



STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

## SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents\*

Section/item	Item No	Description	Addressed on page number
<b>Administrative information</b>			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	___ 1 ___
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	___ 2 ___
	2b	All items from the World Health Organization Trial Registration Data Set	___ YES ___
Protocol version	3	Date and version identifier	___ 10 ___
Funding	4	Sources and types of financial, material, and other support	___ 11 ___
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	___ 1,10 ___
	5b	Name and contact information for the trial sponsor	___ 1,10 ___
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	___ 10 ___
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	___ 10 ___

**Introduction**

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	1-3
	6b	Explanation for choice of comparators	1-2
Objectives	7	Specific objectives or hypotheses	4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	4

**Methods: Participants, interventions, and outcomes**

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	4-5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	4-5
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	6-7
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	N/A
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	7-8
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Fig2

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 August 2022  
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1	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	_____8_____
2				
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4	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	_____5_____
5				

## 6 **Methods: Assignment of interventions (for controlled trials)**

### 7 Allocation:

10	Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	_____5-6_____
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16	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	_____5-6_____
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20	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	_____5-6_____
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24	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	_____5-6_____
25				
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27		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	_____N/A_____
28				
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## 31 **Methods: Data collection, management, and analysis**

33	Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	_____9-10_____
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39		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	_____9-10_____
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1	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	_____ 9-10 _____
2				
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4				
5	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	_____ 8-9 _____
6				
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8		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	_____ 8-9 _____
9				
10		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	_____ 8-9 _____
11				
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13				
14	<b>Methods: Monitoring</b>			
15				
16	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	_____ 9-10 _____
17				
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22		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	_____ N/A _____
23				
24				
25	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	_____ 9-10 _____
26				
27				
28	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	_____ N/A _____
29				
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31				
32	<b>Ethics and dissemination</b>			
33				
34	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	_____ 2,10 _____
35				
36				
37	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	_____ 9-10 _____
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1	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	_____5_____
2				
3				
4		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	_____N/A_____
5				
6				
7	Confidentiality	27	How personal information about potential and enrolled participants will be collected, stored, and maintained in order to protect confidentiality before, during, and after the trial	_____10_____
8				
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10	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	_____10_____
11				
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13	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	_____10_____
14				
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16	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	_____10_____
17				
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20	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	_____10_____
21				
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24		31b	Authorship eligibility guidelines and any intended use of professional writers	_____10_____
25				
26		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	_____10_____
27				
28				
29	<b>Appendices</b>			
30				
31	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	__Translated ICFs can be provided on request_____
32				
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36	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	_____N/A_____
37				
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1 \*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items.  
2 Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons  
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# BMJ Open

## Sufentanil target controlled infusion (TCI) vs remifentanil TCI for monitored anaesthesia care for patients with severe tracheal stenosis undergoing fiberoptic bronchoscopy: protocol for a prospective, randomized, controlled study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-058662.R1
Article Type:	Protocol
Date Submitted by the Author:	26-May-2022
Complete List of Authors:	wu, wei; Tongji University Affiliated Shanghai Pulmonary Hospital, Department of Anaesthesiology Zhou, Yi; Tongji University, School of Life Sciences and Technology; Naval Medical University, Department of Anaesthesiology Zhu, Yuanjie; Tongji University Affiliated Shanghai Pulmonary Hospital, Department of Anaesthesiology Liu, Jianming; Tongji University Affiliated Shanghai Pulmonary Hospital, Department of Anaesthesiology
<b>Primary Subject Heading</b>:	Anaesthesia
Secondary Subject Heading:	Anaesthesia, Surgery, Respiratory medicine
Keywords:	Adult anaesthesia < ANAESTHETICS, Endoscopic surgery < OTOLARYNGOLOGY, Bronchoscopy < THORACIC MEDICINE, Chronic airways disease < THORACIC MEDICINE, Respiratory tract tumours < THORACIC MEDICINE

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Manuscripts

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4 1 **Sufentanil target controlled infusion (TCI) vs remifentanil TCI for monitored**  
5 2 **anaesthesia care for patients with severe tracheal stenosis undergoing**  
6 3 **fiberoptic bronchoscopy: protocol for a prospective, randomized, controlled**  
7 4 **study**  
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13 6 **Wei Wu<sup>1\*</sup>, Yi Zhou<sup>2,3\*</sup>, Yuanjie Zhu<sup>1</sup>, Jianming Liu<sup>1#</sup>**  
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49 26 **Keywords: Adult anaesthesia, Endoscopic surgery, Bronchoscopy, Chronic airways**  
50 27 **disease, Respiratory tract tumours**  
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## 1 **ABSTRACT**

### 2 **Introduction**

3 The use of monitored anaesthesia care (MAC) is necessary and ubiquitous for  
4 fiberoptic bronchoscopy. Anesthetic management of patients with severe tracheal  
5 stenosis has always been a challenge. The efficacy and safety of the MAC with  
6 sufentanil target controlled infusion (TCI) and remifentanil TCI in patients with severe  
7 tracheal stenosis are still unknown.

### 8 **Methods analysis**

9 This study is a prospective, investigator-initiated, two-arm, randomized control trial to  
10 compare the efficacy and safety of sufentanil TCI with remifentanil TCI in patients with  
11 severe tracheal stenosis undergoing fiberoptic bronchoscopy. 270 patients will be  
12 randomly assigned to the sufentanil TCI group or remifentanil TCI group, with a 1:1  
13 ratio in two groups. The primary outcome is the incidence of hypoxemia (an oxygen  
14 saturation of <90%). The secondary outcome investigates the severity of hypoxemia,  
15 cough severity, hemodynamic variables, sedation scores and satisfaction scores.

### 16 **Ethics and dissemination**

17 The study has been approved by the Medical Ethics Committee of Shanghai  
18 Pulmonary Hospital. The results will be submitted for publication in peer-reviewed  
19 journals.

20 **Trial registration number** ChiCTR2100043380

### 21 **Strengths and limitations of this study**

- 22 ● This study is an investigator-initiated, randomized, controlled trial, comparing two  
23 MAC strategies.
- 24 ● This is the first prospective study of Anesthetic management of patients with  
25 severe tracheal stenosis during fiberoptic bronchoscopy.
- 26 ● A homogeneous patient population with severe tracheal stenosis is included.
- 27 ● The main limitation of our study is that considering the characteristics of the two  
28 MAC strategies, the overall trial is not double-blind.
- 29 ● The analysis of the secondary objectives is explorative, due to sample size

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## 1 INTRODUCTION

2 Since the introduction of the flexible fiberoptic bronchoscope, bronchoscopy has been  
3 widely used as a diagnostic tool in the field of clinical respiratory medicine.  
4 Approximately 500,000 fiberoptic bronchoscopy are performed in the United States  
5 annually<sup>1</sup>. Sedation is now generally recommended for all patients undergoing  
6 fiberoptic bronchoscopy unless a specific contraindication to sedation exists<sup>2-4</sup>.  
7 Sedation during fiberoptic bronchoscopy improves patient comfort and tolerance, and  
8 enhances the willingness to repeat the procedure, without increasing complications<sup>3 5</sup>  
9 <sup>6</sup>.

10 Bronchoscopy has been an integral part of the diagnosis and treatment of patients  
11 with severe tracheal stenosis<sup>7</sup>. Patients affected by severe tracheal stenosis develop  
12 symptoms such as stridor, dyspnea, voice changes, mucus production increasing, and  
13 persistent cough<sup>8</sup>. Most patients require sedation and analgesia to tolerate fiberoptic  
14 bronchoscopy. Anaesthetic management for patients with severe tracheal stenosis  
15 during fiberoptic bronchoscopy procedures has always been challenging, and there is  
16 no standardized practice currently<sup>3 9</sup>.

17 Remifentanil has a rapid onset of action and elimination half-life and a predictable  
18 duration of action with no accumulation of effect on repeated dosing or with continuous  
19 infusion, which making it suitable for anaesthesia management of diagnostic and  
20 therapeutic bronchoscopy<sup>10-15</sup>. The degree of the noxious stimulation caused by the  
21 insertion and manipulation of a bronchoscope is often similar to a surgical incision.  
22 Remifentanil might cause respiratory depression or hemodynamic instability when  
23 effectively inhibiting operational stress, which is often very dangerous for patients with  
24 severe tracheal stenosis<sup>14 16 17</sup>. Sufentanil is a more potent opioid than remifentanil, its  
25 analgesic effect lasts longer and it is superior in terms of hemodynamic stability.  
26 Sufentanil has a longer half-time as compared with remifentanil, but TCI will prevent  
27 long-acting opioid-induced accumulation and allow rapid recovery from anaesthesia<sup>18</sup>.  
28 There have been no detailed investigations on the efficacy and safety of monitored  
29 anesthesia care (MAC) using sufentanil or remifentanil TCI in patients with severe

1 tracheal stenosis undergoing fiberoptic bronchoscopy. The aim of our study is to  
2 compare sufentanil TCI with remifentanil TCI in patients with severe tracheal stenosis  
3 undergoing fiberoptic bronchoscopy.

#### 4 **Objectives**

5 We aim to conduct a prospective randomized controlled trial comparing sufentanil TCI  
6 with remifentanil TCI and assume that sufentanil TCI would decrease the incidence of  
7 hypoxemia.

#### 8 **Primary objective**

9 Determine the incidence of hypoxemia of MAC with sufentanil TCI versus MAC with  
10 remifentanil TCI in patients with severe tracheal stenosis undergoing bronchoscopy.

### 12 **METHODS AND ANALYSIS**

#### 13 **Study design**

14 This is a single-center, randomized, investigator-initiated clinical trial of 270 patients  
15 with severe tracheal stenosis that requires fiberoptic bronchoscopy. The CONSORT  
16 flow chart is presented in Figure 1. A SPIRIT figure is included in Figure 2 with a  
17 checklist included as an additional document (Supplementary file 1). Patients will be  
18 randomly assigned to one of two groups. Group S will be received sufentanil TCI and  
19 Group R will be received remifentanil TCI.

#### 20 **Inclusion criteria**

21 All patients treated with fiberoptic bronchoscopy in Shanghai Pulmonary Hospital will  
22 be screened for eligibility in strict accordance with the inclusion and exclusion criteria.  
23 Tracheal stenosis is defined as narrowing of the endotracheal lumen. The diagnosis  
24 will be determined by the same respiratory physician together with the same  
25 endoscopist. The inclusion criteria are patients aged 18–65 years, with the American  
26 Society of Anesthesiologists (ASA) physical status classifications I–III and Cotton-Myer  
27 grades II–III (the narrow of the endotracheal lumen is more than 50%). The exclusion  
28 criteria are shown in Table 1.

29 Table 1. Summary of exclusion criteria of the trial.

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## Exclusion criteria

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BMI>30 or < 18.5

Baseline oxygen desaturation (resting SpO<sub>2</sub> <90%)

Chronic opioid treatment, substance abuse or drug use

Pregnancy

History of allergy to related drugs

Severe coagulation dysfunction

Severe hepatic and renal dysfunction

Gastroesophageal reflux disease

History of abnormal recovery from anaesthesia

No informed consent

Patients with acute exacerbation of chronic obstructive pulmonary disease (COPD)

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## 2 **Recruitment**

3 Consecutive patients who present to respiratory clinics at Shanghai Pulmonary  
4 Hospital with a diagnosis of tracheal stenosis and meet the inclusion criteria will be  
5 offered the opportunity to enroll in our study. We will inform them of details about our  
6 study. All patients will be provided with full information of their part in our study and  
7 assure that their information will be kept strictly confidential.

## 8 **Information consent**

9 Informed consent will be obtained from each patient or legally authorized  
10 representative (LAR) prior to enrollment in our study. This will provide a clear  
11 understanding that their participation is entirely voluntary, and they have a right to  
12 withdraw at any time during the study. Refusal to sign or participate will not affect the  
13 patient's right to receive medical care. No study procedures will be done prior to  
14 obtaining informed consent. A copy of the letter of information and consent is provided  
15 in Supplementary file 2.

## 16 **Randomization and blinding**

17 After obtaining a signed informed consent from the patient or the LAR, the patient will

1 be randomly allocated 1:1 to Group S or Group R. Randomization will be performed  
2 by sealed envelopes available at the Shanghai Pulmonary Hospital. A researcher who  
3 will be masked will generate treatment assignments using a computer-generated  
4 random number list of variable block sizes (block size 4-6-8) by Stata 16.0  
5 (STATA CORP LLC.4905 Lake Way Drive). Randomization envelopes to be opened  
6 will be created by the research assistant just prior to when they are ready to randomize  
7 a patient. The integrity and presence of the envelopes will be checked at each  
8 monitoring visit.

9 The research assistant (RA) who will be blinded to the randomized assignment of  
10 patients will conduct all baseline interviews. The patients will be blinded to their  
11 intervention as will the research staff completing the post-procedural follow-up  
12 questionnaire. It is not possible to blind anaesthesiologists involved in a patient's care,  
13 but bronchoscopists will be blinded.

#### 14 **Study treatment**

15 Patients will fast prior to the procedure. After premedication with i.v. midazolam 0.02  
16 mg/kg in the reception area, patients will be transferred to the operating theatre.  
17 Patients will be monitored with ECG, pulse oximetry, and non-invasive arterial pressure  
18 during the procedure and recovery period [until post-anaesthesia care unit (PACU)  
19 discharge]. All patients will receive oxygen application via a nasal tube with 2 liters of  
20 O<sub>2</sub>/min initially. Once the plasma-site concentration (C<sub>p</sub>) and effect-site concentration  
21 (C<sub>e</sub>) has achieved equilibrium, a soft rubber type nasopharyngeal airway (No.6/7,  
22 Medis Medical, UK) will be inserted. The oxygen supply will be changed from nasal  
23 cannula to nasopharyngeal airway connected to an anaesthetic machine with 6  
24 liters of O<sub>2</sub>/min and an adjustable pressure-limiting (APL) valve setting of 30  
25 cmH<sub>2</sub>O. Both groups will be intravenously administered an initial loading dose of  
26 0.8mcg/kg dexmedetomidine, followed by a maintenance dose of 0.5mcg/(kg·h) during  
27 the procedure. 4 mL of 1% lignocaine solution will be administered by  
28 nasopharyngeal airway to throat, then three aliquots of 4 mL of 1% lignocaine solution  
29 will be administered by endoscopist, one each to supraglottic, subglottic and carina



1 through bronchoscope using the “spray as-you-go” technique<sup>19</sup>. A BF-260 electronic  
2 bronchoscope (BF-1T260/6C260, Olympus Corporation, Japan) will be used. The  
3 airway will be fully assessed and the appropriate interventional procedure will be  
4 performed to relieve the obstruction and stabilize the airway. If biopsies are required,  
5 these specimens will be taken and sent for appropriate investigations. Procedures  
6 performed will involve debridement or coring out of the endoluminal lesion, balloon  
7 dilation, serial mechanical dilation with tapering, cryotherapy, variously sized dilators,  
8 laser disobliteration, or airway stenting.

9 TCI plasma-site concentration ( $C_p$ ) for sufentanil or remifentanil will be achieved  
10 using the Fresenius DPS workstation using the Gepts or Minto pharmacokinetic  
11 model respectively. The EC<sub>95</sub> of sufentanil or remifentanil is set as the plasma target  
12 concentration and which is 0.212 ng/ml or 2.710 ng/ml respectively. Intravenous  
13 injection of 10-20 mg propofol will be used as a remedy and repeatedly as  
14 necessary. The effective concentration ( $C_e$ ) of sufentanil and remifentanil are based  
15 on our previous research using the biased coin up-and-down design sequential  
16 method. A MAP < 80% of baseline or 60 mmHg is regarded as hypotension. In the  
17 event hypotension happens, an intravenous injection of phenylephrine (25~100 mcg)  
18 will be administered as a rescue vasopressor.

### 19 **Management of hypoxemia**

20 Definition of hypoxemia:  $SpO_2 < 90\%$  at any time<sup>20</sup>. The severity of hypoxemia is  
21 classified as follows: subclinical hypoxemia ( $SPO_2$  of 90-95%), moderate hypoxemia  
22 ( $SPO_2$  of 75-89%,  $\leq 60$  s), and severe hypoxemia ( $SpO_2 < 90\%$  for >60 s or  $SpO_2 < 75\%$   
23 at any time)<sup>21</sup>.

24 Once hypoxemia develops, it will be corrected using the following sequence: (1)  
25 patient stimulation, (2) increasing the volume of supplementary oxygen from 6 to 10  
26 liters of  $O_2$ /min, (3) opening the airway using a jaw-thrust maneuver, (4) removing the  
27 bronchoscope tube and mask ventilation, and (5) laryngeal mask or tracheal intubation  
28 for mechanical ventilation.

### 29 **Trial outcomes**

## 1 **Primary outcome**

2 The primary outcome is the incidence of hypoxemia.

## 3 **Secondary outcomes**

4 Secondary outcome variables include the following :

- 5 1. The severity of hypoxemia.
- 6 2. Cough severity rated on a 4-point scale (no cough=1, slight coughing=2, moderate  
7 coughing = 3, severe coughing = 4). Coughing is considered slight if no more than  
8 2 coughs in sequence occurred, moderate if 3-5 coughs in sequence occurred and  
9 severe if more than 5 coughs in sequence occurred.
- 10 3. Hemodynamic variables (blood pressure and heart rate).
- 11 4. Modified Ramsay sedation scores during procedure.
- 12 5. Patient's comfort and tolerance to fiberscope assessed by Puchner comfort scale<sup>22</sup>.
- 13 6. Recovery time.
- 14 7. Arterial blood gases (PO<sub>2</sub>, PCO<sub>2</sub> and PH) before and after the operation.
- 15 8. The incidence of postoperative nausea and vomiting .
- 16 9. Satisfaction scores of the patient, bronchoscopist and anaesthesiologist.
- 17 10. The willingness of the patient to undergo repeat bronchoscopy.
- 18 11. Visual analog scale (VAS, 0-100mm) scores of sore throat at 30 min after the end  
19 of the operation.
- 20 12. Complications related to the procedure and anaesthesia.

## 21 **Statistical methods**

22 The analysis will be performed on an intention-to-treat basis, such that each patient is  
23 analyzed in the group to which he or she is randomized, regardless of actual  
24 compliance with the intended intervention. All the analyses will be conducted using  
25 Stata 16.0 (STACORP LLC.4905 Lake Way Drive). A two-tailed p value equal or  
26 less than 0.05 will be considered as statistically significant. All tests, except for the  
27 primary outcome, will be exploratory. When individual items are missing from a scale,  
28 we will calculate the percent of missing items. If less than 10%, we will impute values

1 using the mean of the remaining items. If more than 10%, the scale score will be  
2 missing, and unavailable for analysis.

### 3 **Sample size calculation**

4 Our previous study (unpublished) shows that the incidences of hypoxemia in the two  
5 groups are 10% (1/10) in sufentanil group and 27.27% (3/11) in remifentanil group. We  
6 determined that enrolment of 270 patients would provide a power of 90% to show a  
7 reduction in the rate of incidences of hypoxia between two groups at a two-sided alpha  
8 level of 0.05, accounting for 20% lost to follow-up.

### 9 **Descriptive statistics**

10 Continuous variables will be described using means and SD for normally distributed  
11 data. For continuous variables with non-normally distributed data, medians and ranges  
12 will be used. Categorical data will be described using counts, proportions, and risk  
13 ratios with 95% CIs.

### 14 **Planned outcome analysis**

#### 15 **Primary outcome**

16 The incidences of hypoxia will be compared between the two groups using a  $\chi^2$  test or  
17 an exact Fisher's exact test if required. The incidences of hypoxia will then be modelled  
18 (secondary analysis) using a multivariate logistic regression.

#### 19 **Secondary outcomes**

20 Secondary endpoints will be compared between the two treatment groups by means  
21 of Student's t-test (or the Mann-Whitney U test, if necessary) for continuous  
22 quantitative variables and by means of the  $\chi^2$  test (or Fisher's exact test) for  
23 qualitative variables. Linear models and logistics models will be used to compare the  
24 two groups in multivariate analyses. Time-to-event analyses will involve the Kaplan-  
25 Meier method and the Cox proportional hazards model.

## 27 **DISCUSSION**

28 MAC is a specific anaesthesia service performed by a qualified anaesthesia provider  
29 for a diagnostic or therapeutic procedure<sup>23</sup>. MAC is useful in patients who require

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2  
3  
4 1 repeated fiberoptic bronchoscopy as well as safe in respiratory depression when  
5 2 performed by experienced anaesthesiologists<sup>24</sup>. We will utilize MAC for patients with  
6 3 severe tracheal stenosis that requires fiberoptic bronchoscopy in this study.  
7  
8

9 4 TCI allows an accurate adaptation of the anaesthesia level and fewer overdose-  
10 5 linked adverse effects. As a decreased cumulative dose of sufentanil or remifentanil,  
11 6 hemodynamic stability, recovery and discharge may also be improved by using TCI.  
12 7 The Ce of sufentanil and remifentanil used in the study are based on our previous  
13 8 unpublished research.  
14  
15

16 9 This trial is the first randomized controlled study powered to test the hypothesis that  
17 10 sufentanil TCI compared with remifentanil TCI for MAC can reduce the incidence of  
18 11 hypoxemia and related adverse events in patients with severe tracheal stenosis  
19 12 undergoing fiberoptic bronchoscopy. We believe that the findings of this study will have  
20 13 significant clinical implications. This might mean that more studies are needed to  
21 14 determine the optimal strategies for anaesthesia management to prevent hypoxemia.  
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### 33 16 **Data collection, monitoring and management**

34 17 Preoperative, intraoperative and postoperative follow-up data will be collected from  
35 18 electronic medical records, monitoring machines and relevant manual records by the  
36 19 research staff (YJZ). All electronic and handwriting data will be stored on a password-  
37 20 protected computer. Data will be recorded on a standardised paper form  
38 21 (Supplementary file 3) and subsequently double-entered using Epidata software v3.1  
39 22 by two trained research assistants. Data and safety monitoring will be the responsibility  
40 23 of the principle investigator (JML).  
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### 48 24 **Trial status**

49 25 The recruitment commenced in February 2021. It is anticipated that recruitment will  
50 26 end by June 2023. The version number of the protocol are v3.0.  
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53

### 54 27 **Patient and public involvement**

55 28 Patients or the public were not involved in the design of our research and will not be  
56 29 involved in conduct, reporting or dissemination of our research.  
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4 **1 Dissemination policy**

5  
6 2 The results of this study will be disseminated regardless of the effect of the intervention  
7  
8 3 on study outcomes. The manuscript describing the effect of the intervention will be  
9  
10 4 submitted to a peer-reviewed journal when data collection and analyses are complete.

11 **5 Contributors**

12  
13 6 WW and YZ designed the study, they are joint first author. WW and YJZ wrote the  
14  
15 7 manuscript together. YZ provided substantial contributions to the conception and  
16  
17 8 design of the study, wrote the statistical analysis plan and estimated the sample size.  
18  
19 9 JML was responsible for designing the study and drafting the work, revising it critically  
20  
21 10 for important intellectual content and approved the final version of the manuscript. All  
22  
23 11 authors gave their agreement to be accountable for all aspects of the work, and ensure  
24  
25 12 the accuracy and integrity of any part of the work.

26  
27 **13 Funding**

28  
29 14 The study is funded by Shanghai Municipal Health Commission (Project  
30  
31 15 NO.201940366).

32  
33 **16 Ethics approval and consent to participate**

34  
35 17 The study protocol was approved by the Ethics Committee of Shanghai Pulmonary  
36  
37 18 Hospital of China (approval No. K19-122). Informed consent must be obtained from  
38  
39 19 all patients.

40 **20 Patient consent for publication**

41  
42 21 Not required.

43  
44 **22 Competing interests**

45  
46 23 The authors declare that they have no competing interests.  
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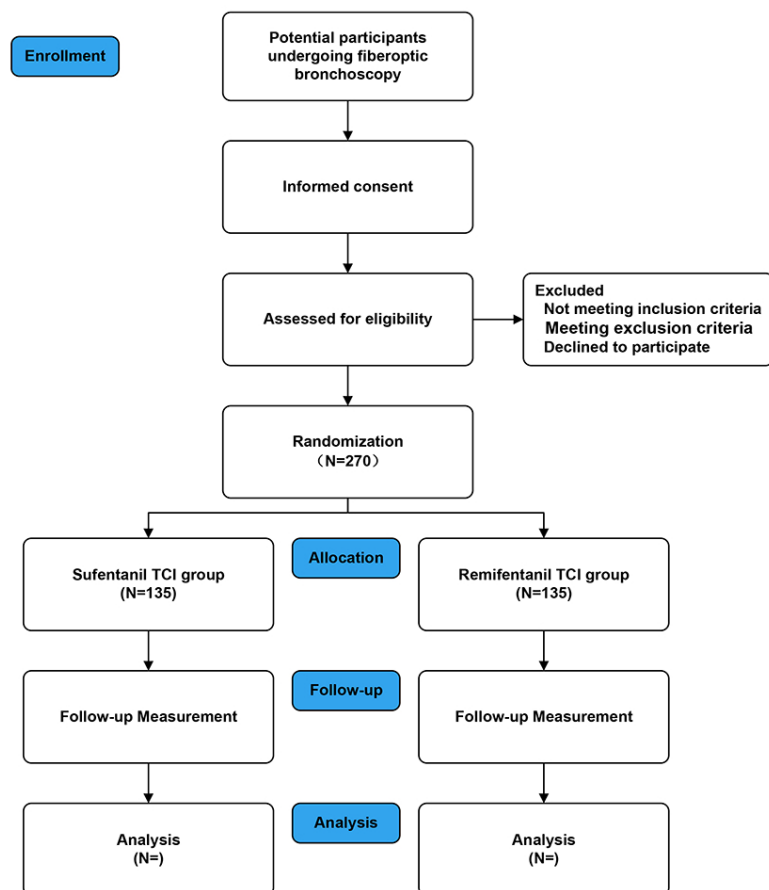
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1 Figure 1  
2 CONSORT flow diagram for the study. CONSORT, Consolidated Standards of  
3 Reporting Trials.

9 Figure 2  
10 SPIRIT Figure-Schedule of enrolment, interventions, and assessments. SPIRIT,  
11 Standard Protocol Items: Recommendations for Interventional Trials.

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CONSORT flow diagram for the study. CONSORT, Consolidated Standards of Reporting Trials.

STUDY PERIOD					
	Enrolment	Allocation	Post-allocation		Close-out
TIMEPOINT	t <sub>1</sub>	t <sub>0</sub>	t <sub>1</sub>	t <sub>2</sub>	t <sub>3</sub>
	Feb 2021- Jun 2022		During the procedure	PACU	
<b>ENROLMENT:</b>					
Eligibility screen	X				
Informed consent	X				
Allocation		X			
<b>INTERVENTIONS:</b>					
Sufentanil TCI			X		
Remifentanil TCI			X		
<b>ASSESSMENTS:</b>					
Baseline variables	X	X			
Hypoxemia			X		
Cough severity			X		
Hemodynamic variables			X		
Sedation scores			X		
Patient's comfort			X		
Recovery time				X	
Postoperative nausea and vomiting				X	
Satisfaction				X	
Visual analog scale				X	

SPIRIT Figure-Schedule of enrolment, interventions, and assessments. SPIRIT, Standard Protocol Items: Recommendations for Interventional Trials.



STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents\*

Section/item	Item No	Description	Addressed on page number
<b>Administrative information</b>			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	___ 1 ___
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	___ 2 ___
	2b	All items from the World Health Organization Trial Registration Data Set	___ YES ___
Protocol version	3	Date and version identifier	___ 10 ___
Funding	4	Sources and types of financial, material, and other support	___ 11 ___
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	___ 1,10 ___
	5b	Name and contact information for the trial sponsor	___ 1,10 ___
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	___ 10 ___
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	___ 10 ___

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1	<b>Introduction</b>			
2				
3	Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	_____ 1-3 _____
4				
5				
6		6b	Explanation for choice of comparators	_____ 1-2 _____
7				
8	Objectives	7	Specific objectives or hypotheses	_____ 4 _____
9				
10	Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	_____ 4 _____
11				
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13				
14	<b>Methods: Participants, interventions, and outcomes</b>			
15				
16	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	_____ 4-5 _____
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19	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	_____ 4-5 _____
20				
21				
22	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	_____ 6-7 _____
23				
24		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	_____ N/A _____
25				
26		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	_____ N/A _____
27				
28		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	_____ N/A _____
29				
30	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	_____ 7-8 _____
31				
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34	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	_____ Fig2 _____
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1	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	_____8_____
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4	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	_____5_____
5				

### 6 **Methods: Assignment of interventions (for controlled trials)**

#### 7 Allocation:

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10	Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	_____5-6_____
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16	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	_____5-6_____
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20	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	_____5-6_____
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24	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	_____5-6_____
25				
26				
27		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	_____N/A_____
28				
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### 31 **Methods: Data collection, management, and analysis**

32				
33	Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	_____9-10_____
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39		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	_____9-10_____
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1	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	_____ 9-10 _____
2				
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5	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	_____ 8-9 _____
6				
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8		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	_____ 8-9 _____
9				
10		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	_____ 8-9 _____
11				
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14	<b>Methods: Monitoring</b>			
15				
16	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	_____ 9-10 _____
17				
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22		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	_____ N/A _____
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25	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	_____ 9-10 _____
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28	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	_____ N/A _____
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32	<b>Ethics and dissemination</b>			
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34	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	_____ 2,10 _____
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37	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	_____ 9-10 _____
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1	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	_____5_____
2				
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4		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	_____N/A_____
5				
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7	Confidentiality	27	How personal information about potential and enrolled participants will be collected, stored, and maintained in order to protect confidentiality before, during, and after the trial	_____10_____
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10	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	_____10_____
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13	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	_____10_____
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16	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	_____10_____
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20	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	_____10_____
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24		31b	Authorship eligibility guidelines and any intended use of professional writers	_____10_____
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26		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	_____10_____
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29	<b>Appendices</b>			
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31	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	__Translated ICFs can be provided on request_____
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36	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	_____N/A_____
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\*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.

For peer review only



1 Practice name:

2 Participant ID:

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## 11 Informed Consent

### 16 Informed Consent form for patient.

17 This Informed Consent Form is for men and women who attend Shanghai Pulmonary  
18 Hospital and who we are inviting to participate in research on anesthesia for  
19 bronchoscopy.

20  
21 The title of our research project is: *Sufentanil target controlled infusion (TCI) vs*  
22 *remifentanil TCI for monitored anaesthesia care for patients with severe tracheal*  
23 *stenosis undergoing fiberoptic bronchoscopy.*

24  
25  
26 **Principal Investigator:** Jianming Liu, MD

27  
28 **Organization:** Department of Anaesthesiology, Shanghai Pulmonary Hospital, Tongji  
29 University School of Medicine

### 31 This Informed Consent Form has two parts:

- 32  
33 1. Information Sheet (to share information about the research with you)  
34 2. Certificate of Consent (for signatures if you agree to take part)

35  
36  
37 **You will be given a copy of the full Informed Consent Form**

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## **PART 1: Information Sheet**

### **Introduction**

I am Jianming Liu, working for department of Anaesthesiology. We are doing research on monitored anaesthesia care for patients with severe tracheal stenosis undergoing fiberoptic bronchoscopy. I am going to give you information and invite you to be part of this research.

You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research. There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me, the study doctor or the staff.)

### **Purpose of the research**

Bronchoscopy has been an integral part of the diagnosis and treatment of patients with tracheal stenosis. The two opioids most commonly used are sufentanil and remifentanil. We aim to conduct a trial comparing sufentanil with remifentanil in patients with severe tracheal stenosis undergoing fiberoptic bronchoscopy.

### **Participant selection**

We are inviting all adults with severe tracheal stenosis attend Shanghai Pulmonary Hospital to participate in the research.

### **Voluntary Participation**

Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. If you choose not to participate in this research project, you will offer the treatment that is routinely offered, and we will tell you more about it later. You may change your mind later and stop participating even if you agreed earlier.

### **Procedures and Protocol**

Participants will be randomly assigned to one of two groups. Participants in one group will be given monitored anaesthesia care (MAC) using sufentanil target controlled infusion. Participants in the other group will be given monitored anaesthesia care (MAC) using remifentanil. We will then compare which of the two has the best results. The healthcare workers will be looking after you and the other participants very carefully during the study. If we are concerned about what the treatment is doing, we will find out which treatment you are getting and make changes. If there is anything you are concerned about or that is bothering you about the research please talk to me or one of the other researchers.

### **For any clinical study (if relevant):**

We will take arterial blood from your arm using a syringe through arterial line. This blood taken is painless. In total, we will take about 2 samples of 1 ml arterial blood. At

1  
2  
3 the end of the research any left-over blood sample will be destroyed).  
4  
5

### 6 **Description of the Process**

7 In the first time, a small amount of blood, equal to about a teaspoon, will be taken from  
8 your arm with a syringe through arterial catheter. This blood will be tested with a blood  
9 analyzer. We will ask you a few questions about your general health.

10 You'll be anesthetized during fiberoptic bronchoscopy. After treatment we'll draw your  
11 blood and also ask you a few questions.  
12  
13  
14

### 15 **Duration**

16 The research takes place over 1/2 days.  
17  
18

### 19 **Risks**

20 Any risk can appear during the process. Mechanical complications of fiberoptic  
21 bronchoscopy include nasopharyngeal, vocal cord, and airway trauma as well as  
22 bronchospasm, laryngospasm, pulmonary derecruitment/atelectasis, pneumothorax,  
23 airway hemorrhage, and introduction or exacerbation of infection. Systemic  
24 complications are primarily related to the procedure itself, medication administration,  
25 or patient comorbidities. The healthcare workers will be looking after you and the other  
26 participants very carefully during the study. If we are concerned about what the  
27 treatment is doing, we will find out which treatment you are getting and make changes.  
28  
29  
30  
31

### 32 **Benefits**

33 If you participate in this research, you will have the following benefits: any interim  
34 illnesses will be treated at no charge to you. The Fresenius DPS workstation for TCI  
35 used for free. Your participation is likely to help us find the answer to the research  
36 question.  
37  
38  
39

### 40 **Reimbursements**

41 Your participation is free. You will not be given any other money or gifts to take part in  
42 this research.  
43  
44

### 45 **Confidentiality**

46 With this research, something out of the ordinary is being done in your community. It  
47 is possible that if others in the community are aware that you are participating, they  
48 may ask you questions. We will not be sharing the identity of those participating in the  
49 research.  
50

51 The information that we collect from this research project will be kept confidential.  
52 Information about you that will be collected during the research will be put away and  
53 no-one but the researchers will be able to see it. Any information about you will have a  
54 number on it instead of your name. Only the researchers will know what your number  
55 is and we will lock that information up with a lock and key. It will not be shared with  
56 or given to anyone except [Yi Zhou and Jianming Liu) who will have access to the  
57 information.  
58  
59  
60

### **Sharing the Results**

The knowledge that we get from doing this research will be shared with you through community meetings before it is made widely available to the public. Confidential information will not be shared. After these meetings, we will publish the results in order that other interested people may learn from our research.

### **Right to Refuse or Withdraw**

You do not have to take part in this research if you do not wish to do so. You may also stop participating in the research at any time you choose. It is your choice and all of your rights will still be respected.

### **Alternatives to Participating**

If you do not wish to take part in the research, you will be provided with the established standard treatment available at our hospital.

### **Who to Contact**

If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following:

DR. Jianming Liu, Phone: 86-18019285297

This proposal has been reviewed and approved by the Ethics Committee of Shanghai Pulmonary Hospital of China (approval No. K19-122) which is a committee whose task it is to make sure that research participants are protected from harm.

**You can ask me any more questions about any part of the research study, if you wish to. Do you have any questions?**

**PART 2: Certificate of Consent**

This section should be written in the first person and have a statement similar to the one in bold below. If the participant is illiterate but gives oral consent, a witness or a legally authorized representative must sign. A researcher or the person going over the informed consent must sign each consent. The understanding should perhaps be better tested through targeted questions during the reading of the information sheet (some examples of questions are given above), or through the questions being asked at the end of the reading of the information sheet, if the potential participant is reading the information sheet him/herself.

**Please  
initial  
each box**

1 I have read the foregoing information, or it has been read to me.

2 I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction.

3 I consent voluntarily to participate as a participant in this research.

**Print Name of Participant**

---

**Signature of Participant**

---

**Date(Day/month/year)**

---

**If illiterate**

Aliterate witness or legally authorized representative must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb-print as well.

Please  
initial  
each box

1 I have witnessed the accurate reading of the consent form to the potential participant

2 I have witnessed the individual has had the opportunity to ask questions.

3 I confirm that the individual has given consent freely.

**Print Name of witness or legally authorized representative**

---

**Signature of witness or legally authorized representative**

---

**Date(Day/month/year)**

---

**Thumb print of participant**

**Statement by the researcher/person taking consent**

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

**A copy of this ICF has been provided to the participant.**

**Print Name of Researcher** \_\_\_\_\_

**Signature of Researcher** \_\_\_\_\_

**Date(Day/month/year)** \_\_\_\_\_

Protocol No:	P20200828V3		
Site	<input type="checkbox"/> <input type="checkbox"/>	Subject ID:	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Randomisation No:	<input type="checkbox"/> <input type="checkbox"/>	Subject Initials:	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Investigator	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
Identifier:			

### Case Report Form

**Sufentanil target controlled infusion (TCI) vs remifentanil TCI  
for monitored anaesthesia care for patients with severe tracheal  
stenosis undergoing fiberoptic bronchoscopy**

By  
**Shanghai Pulmonary Hospital**



**Inclusion Criteria**

Subjects who meet the following criteria may be included in the study. Did the subject meet the following criteria requirements for inclusion? ( ✓ Yes or No)		Yes 1	No* 2
01	Cotton-Myer grades II-III		
02	Aged 18–65 years		
03	ASA I-III		

\* If No, document on Subject Eligibility Page.

**Exclusion Criteria**

The following will exclude potential subjects from the study. Does the subject have any of the following? ( √ Yes or No)		Yes* 1	No 2
01	BMI>30 or < 18.5		
02	Baseline oxygen desaturation (resting SpO <sub>2</sub> <90%)		
03	Pregnancy		
04	History of allergy to related drugs		
05	Severe coagulation dysfunction		
06	Severe hepatic and renal dysfunction		
07	Gastroesophageal reflux disease		
08	History of abnormal recovery from anaesthesia		
09	No informed consent		

\*If Yes, document on Subject Eligibility Page

**Information Session**

Date of Information Session	Did the subject attend the Information Session?	Comments
____ / ____ / ____ DD / MM / YY	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No (explain, if No)	

**Subject Eligibility**

Date the Subject Signed the Informed Consent Form:		____ / ____ / ____ DD / MM / YY		
Did the subject meet all of the inclusion/exclusion criteria?		1 <input type="checkbox"/> Yes		
		2 <input type="checkbox"/> No		
If the subject did not meet all of the Inclusion/Exclusion criteria, provide criterion number and explanation below.				
Category	Inclusion/Exclusion No.	Explanation	Exemption Granted?	If Yes, Date Granted DD/MM/YYYY
1 <input type="checkbox"/> Inclusion			1 <input type="checkbox"/> Yes	____ / ____ / ____
2 <input type="checkbox"/> Exclusion			2 <input type="checkbox"/> No	
1 <input type="checkbox"/> Inclusion			1 <input type="checkbox"/> Yes	____ / ____ / ____
2 <input type="checkbox"/> Exclusion			2 <input type="checkbox"/> No	
1 <input type="checkbox"/> Inclusion			1 <input type="checkbox"/> Yes	____ / ____ / ____
2 <input type="checkbox"/> Exclusion			2 <input type="checkbox"/> No	

**Demographics**

Date DD/MM/YYYY	Date of Birth DD/MM/YYYY	Gender	Ethnicity
<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	1 <input type="checkbox"/> Male	1 <input type="checkbox"/> Han
		2 <input type="checkbox"/> Female	2 <input type="checkbox"/> Non-han
<b>Body Measurements</b>			
Were Body Measurements Collected?		Date DD/MM/YYYY	
1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No		<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Parameter	Unit	Result	
Height	cm	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Weight	Kg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
<b>Vital Signs</b>			
Were Body Measurements Collected?		Date DD/MM/YYYY	
1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No		<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Body Temperature	°C	<input type="checkbox"/> <input type="checkbox"/> . <input type="checkbox"/>	
<b>12-Lead Electrocardiogram Report</b>			
Was ECG performed?		Date DD/MM/YYYY	Actual Time 24-hour clock
1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No		<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> : <input type="checkbox"/> <input type="checkbox"/>
ECG Interpretation:	1 <input type="checkbox"/> Normal	2 <input type="checkbox"/> Abnormal, NCS	3 <input type="checkbox"/> Abnormal
Comments Regarding CS Findings:			

**Medical History**

Does the subject have any relevant medical history?		Date DD/MM/YYYY	
1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No		____/____/____	
Diagnosis/Procedure	Date of Onset DD/MM/YYYY	Date of Resolution DD/MM/YYYY	
1	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
2	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
3	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
4	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
5	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
6	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
7	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
8	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
9	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING

**Laboratory Analysis**

Parameter	Unit	Result
SPO <sub>2</sub>		□ □ □
Arterial blood gas analysis		
PH		□ . □ □
PaCO <sub>2</sub>	mmHg	□ □ □
PaO <sub>2</sub>	mmHg	□ □ □
HCO <sub>3</sub>	mEq/L	□ □

For peer review only

**Intervention Phase**

Date DD/MM/YYYY	____ / ____ / ____			
Group	1 <input type="checkbox"/> Group R		2 <input type="checkbox"/> Group S	
Whether or not hypoxemia occurs				
1 <input type="checkbox"/> subclinical hypoxemia (SPO2 of 90-95%),	2 <input type="checkbox"/> moderate hypoxemia (SPO2 of 75-89%, $\leq 60$ s		3 <input type="checkbox"/> severe hypoxemia (SpO2 < 90% for >60 s or SpO2 < 75% at any time)	
Management of hypoxemia				
1 <input type="checkbox"/> patient stimulation	2 <input type="checkbox"/> increasing the volume of supplementary oxygen	3 <input type="checkbox"/> jaw-thrust maneuver	4 <input type="checkbox"/> mask ventilation	5 <input type="checkbox"/> mechanical ventilation.
Puchner five-point fiber-optic intubation comfort scale				
1 <input type="checkbox"/> No reaction	2 <input type="checkbox"/> Slight grimacing	3 <input type="checkbox"/> Heavy grimacing	4 <input type="checkbox"/> Verbal objection	5 <input type="checkbox"/> Defensive movement

T0	10 minutes after entering the operation room	
Parameter	Unit	Result
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>

T1	Cp and Ce has achieved equilibrium		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>

	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T2	When bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T3	1 minute after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T4	5 minutes after bronchoscope is inserted	
Parameter	Unit	Result
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>



Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T5	10 minutes after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T6	15 minutes after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>

	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T6	20 minutes after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T7	25 minutes after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T8	30 minutes after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	

Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T9	60 minutes after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

Type of fiberoptic bronchoscopy procedure				
1 <input type="checkbox"/> Diagnostic		2 <input type="checkbox"/> Therapeutic		
If it is Therapeutic bronchoscopy				
1 <input type="checkbox"/> Injection of medication	2 <input type="checkbox"/> Endotherm knife	3 <input type="checkbox"/> Cryotherapy		
4 <input type="checkbox"/> Laser	5 <input type="checkbox"/> Stent			
Operation time	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	min	Endoscopist	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Satisfaction scores of bronchoscopist	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	
	4 <input type="checkbox"/>	5 <input type="checkbox"/>		
Satisfaction scores of anaesthesiologist	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	
	4 <input type="checkbox"/>	5 <input type="checkbox"/>		

Vasoactive drugs used			
Whether or not vasoactive drugs are used	1 <input type="checkbox"/> Yes	2 <input type="checkbox"/> No	
Vasoactive drug type	name	dosage	whether it is effective or not
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No

**Post Intervention Phase**

Recovery time	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	min		
Whether nausea and vomiting occur				
1 <input type="checkbox"/> Yes	2 <input type="checkbox"/> No			
Assessment of PONV				
1 <input type="checkbox"/> Mild	2 <input type="checkbox"/> moderate	3 <input type="checkbox"/> severe		
Satisfaction scores of the patient				
1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>
willingness of the patient to undergo repeat bronchoscopy.				
1 <input type="checkbox"/> Not at all likely	2 <input type="checkbox"/> 1-3	3 <input type="checkbox"/> 4-6	4 <input type="checkbox"/> 7-9	5 <input type="checkbox"/> Extremely likely (10)
VAS scores of sore throat				
1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>
6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>	9 <input type="checkbox"/>	10 <input type="checkbox"/>
T10	At PACU			
Parameter	Unit	Result		
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>		
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	
	7 <input type="checkbox"/>	8 <input type="checkbox"/>		
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>
Arterial blood gas analysis				
PH		<input type="checkbox"/> . <input type="checkbox"/> <input type="checkbox"/>		
PaCO <sub>2</sub>	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
PaO <sub>2</sub>	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
HCO <sub>3</sub>	mEq/L	<input type="checkbox"/> <input type="checkbox"/>		

**Adverse Event information**

Whether adverse events occurred		
1 <input type="checkbox"/> Yes	2 <input type="checkbox"/> No	
Whether serious adverse events occurred		
1 <input type="checkbox"/> Yes	2 <input type="checkbox"/> No	
Describe the AE and the connection to project procedures		
AE onset date	□□/□□/□□□□	DD/MM/YYYY
AE stop date	□□/□□/□□□□	DD/MM/YYYY
Date of AE awareness	□□/□□/□□□□	DD/MM/YYYY
Severity		
1 <input type="checkbox"/> mild	2 <input type="checkbox"/> moderate	3 <input type="checkbox"/> severe
Outcome		
1 <input type="checkbox"/> recovered/resolved	2 <input type="checkbox"/> recovered/resolved with sequelae	3 <input type="checkbox"/> study participant died
4 <input type="checkbox"/> continuing	5 <input type="checkbox"/> unknown	6 <input type="checkbox"/> other
SAE causality		
1 <input type="checkbox"/> Not related	2 <input type="checkbox"/> Unlikely	3 <input type="checkbox"/> Possibly
4 <input type="checkbox"/> Probably	5 <input type="checkbox"/> Definitely	
Describe the AE and the connection to project procedures		
AE onset date	□□/□□/□□□□	DD/MM/YYYY
AE stop date	□□/□□/□□□□	DD/MM/YYYY
Date of AE awareness	□□/□□/□□□□	DD/MM/YYYY
Severity		
1 <input type="checkbox"/> mild	2 <input type="checkbox"/> moderate	3 <input type="checkbox"/> severe
Outcome		
1 <input type="checkbox"/> recovered/resolved	2 <input type="checkbox"/> recovered/resolved with sequelae	3 <input type="checkbox"/> study participant died

4 <input type="checkbox"/> continuing	5 <input type="checkbox"/> unknown	6 <input type="checkbox"/> other
SAE causality		
1 <input type="checkbox"/> Not related	2 <input type="checkbox"/> Unlikely	3 <input type="checkbox"/> Possibly
4 <input type="checkbox"/> Probably	5 <input type="checkbox"/> Definitely	
Describe the AE and the connection to project procedures		
AE onset date	□□/□□/□□□□	DD/MM/YYYY
AE stop date	□□/□□/□□□□	DD/MM/YYYY
Date of AE awareness	□□/□□/□□□□	DD/MM/YYYY
Severity		
1 <input type="checkbox"/> mild	2 <input type="checkbox"/> moderate	3 <input type="checkbox"/> severe
Outcome		
1 <input type="checkbox"/> recovered/resolved	2 <input type="checkbox"/> recovered/resolved with sequelae	3 <input type="checkbox"/> study participant died
4 <input type="checkbox"/> continuing	5 <input type="checkbox"/> unknown	6 <input type="checkbox"/> other
SAE causality		
1 <input type="checkbox"/> Not related	2 <input type="checkbox"/> Unlikely	3 <input type="checkbox"/> Possibly
4 <input type="checkbox"/> Probably	5 <input type="checkbox"/> Definitely	

# BMJ Open

## Sufentanil target controlled infusion (TCI) vs remifentanil TCI for monitored anaesthesia care for patients with severe tracheal stenosis undergoing fiberoptic bronchoscopy: protocol for a prospective, randomized, controlled study

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4 1 **Sufentanil target controlled infusion (TCI) vs remifentanil TCI for monitored**  
5 2 **anaesthesia care for patients with severe tracheal stenosis undergoing**  
6 3 **fiberoptic bronchoscopy: protocol for a prospective, randomized, controlled**  
7 4 **study**  
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11 5  
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50 27 **disease, Respiratory tract tumours**  
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55 30 **Word count: 2451**  
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## 1 **ABSTRACT**

### 2 **Introduction**

3 The use of monitored anaesthesia care (MAC) is necessary and ubiquitous for  
4 fiberoptic bronchoscopy. Anesthetic management of patients with severe tracheal  
5 stenosis has always been a challenge. The efficacy and safety of the MAC with  
6 sufentanil target controlled infusion (TCI) and remifentanil TCI in patients with severe  
7 tracheal stenosis are still unknown.

### 8 **Methods analysis**

9 This study is a prospective, investigator-initiated, two-arm, randomized control trial to  
10 compare the efficacy and safety of sufentanil TCI with remifentanil TCI in patients with  
11 severe tracheal stenosis undergoing fiberoptic bronchoscopy. 270 patients will be  
12 randomly assigned to the sufentanil TCI group or remifentanil TCI group, with a 1:1  
13 ratio in two groups. The primary outcome is the incidence of hypoxemia (an oxygen  
14 saturation of <90%). The secondary outcome investigates the severity of hypoxemia,  
15 cough severity, hemodynamic variables, sedation scores and satisfaction scores.

### 16 **Ethics and dissemination**

17 The study has been approved by the Medical Ethics Committee of Shanghai  
18 Pulmonary Hospital (approval No. K19-122). The results will be submitted for  
19 publication in peer-reviewed journals.

20 **Trial registration number** ChiCTR2100043380

### 21 **Strengths and limitations of this study**

- 22 ● This study is an investigator-initiated, randomized, controlled trial, comparing two  
23 MAC strategies.
- 24 ● This is the first prospective study of anesthetic management of patients with  
25 severe tracheal stenosis during fiberoptic bronchoscopy.
- 26 ● A homogeneous patient population with severe tracheal stenosis is included.
- 27 ● The main limitation of our study is that considering the characteristics of the two  
28 MAC strategies, the overall trial is not double-blind.
- 29 ● The analysis of the secondary objectives is explorative, due to sample size

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1        restrictions.  
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For peer review only

## 1 INTRODUCTION

2 Since the introduction of the flexible fiberoptic bronchoscope, bronchoscopy has been  
3 widely used as a diagnostic tool in the field of clinical respiratory medicine.  
4 Approximately 500,000 fiberoptic bronchoscopy are performed in the United States  
5 annually<sup>1</sup>. Sedation is now generally recommended for all patients undergoing  
6 fiberoptic bronchoscopy unless a specific contraindication to sedation exists<sup>2-4</sup>.  
7 Sedation during fiberoptic bronchoscopy improves patient comfort and tolerance and  
8 enhances the willingness to repeat the procedure, without increasing complications<sup>3 5</sup>  
9 <sup>6</sup>.

10 Bronchoscopy has been an integral part of the diagnosis and treatment of patients  
11 with severe tracheal stenosis<sup>7</sup>. Patients affected by severe tracheal stenosis develop  
12 symptoms such as stridor, dyspnea, voice changes, increased mucus production, and  
13 persistent cough<sup>8</sup>. Most patients require sedation and analgesia to tolerate fiberoptic  
14 bronchoscopy. Anaesthetic management for patients with severe tracheal stenosis  
15 during fiberoptic bronchoscopy procedures has always been challenging, and there is  
16 no standardized practice currently<sup>3 9</sup>.

17 Remifentanil has a rapid onset of action and elimination half-life and a predictable  
18 duration of action with no accumulation of effect on repeated dosing or with continuous  
19 infusion, which making it suitable for anaesthesia management of diagnostic and  
20 therapeutic bronchoscopy<sup>10-15</sup>. The degree of the noxious stimulation caused by the  
21 insertion and manipulation of a bronchoscope is often similar to a surgical incision.  
22 Remifentanil might cause respiratory depression or hemodynamic instability when  
23 effectively inhibiting operational stress, which is often very dangerous for patients with  
24 severe tracheal stenosis<sup>14 16 17</sup>. Sufentanil is a more potent opioid than remifentanil, its  
25 analgesic effect lasts longer and it is superior in terms of hemodynamic stability.  
26 Sufentanil has a longer half-time as compared with remifentanil, but TCI will prevent  
27 long-acting opioid-induced accumulation and allow rapid recovery from anaesthesia<sup>18</sup>.  
28 There have been no detailed investigations on the efficacy and safety of monitored  
29 anesthesia care (MAC) using sufentanil or remifentanil TCI in patients with severe

1 tracheal stenosis undergoing fiberoptic bronchoscopy. The aim of our study is to  
2 compare sufentanil TCI with remifentanil TCI in patients with severe tracheal stenosis  
3 undergoing fiberoptic bronchoscopy.

#### 4 **Objectives**

5 We aim to conduct a prospective randomized controlled trial comparing sufentanil TCI  
6 with remifentanil TCI and assume that sufentanil TCI would decrease the incidence of  
7 hypoxemia.

#### 8 **Primary objective**

9 Determine the incidence of hypoxemia of MAC with sufentanil TCI versus MAC with  
10 remifentanil TCI in patients with severe tracheal stenosis undergoing bronchoscopy.

### 12 **METHODS AND ANALYSIS**

#### 13 **Study design**

14 This is a single-center, randomized, investigator-initiated clinical trial of 270 patients  
15 with severe tracheal stenosis that requires fiberoptic bronchoscopy. The CONSORT  
16 flow chart is presented in Figure 1. A SPIRIT figure is included in Figure 2 with a  
17 checklist included as an additional document (Supplementary file 1). Patients will be  
18 randomly assigned to one of two groups. Group S will be received sufentanil TCI and  
19 Group R will be received remifentanil TCI.

#### 20 **Inclusion criteria**

21 All patients treated with fiberoptic bronchoscopy in Shanghai Pulmonary Hospital will  
22 be screened for eligibility in strict accordance with the inclusion and exclusion criteria.  
23 Tracheal stenosis is defined as narrowing of the endotracheal lumen. The diagnosis  
24 will be determined by the same respiratory physician together with the same  
25 endoscopist. The inclusion criteria are patients aged 18–65 years, with the American  
26 Society of Anesthesiologists (ASA) physical status classifications I–III and Cotton-Myer  
27 grades II–III (the narrow of the endotracheal lumen is more than 50%). The exclusion  
28 criteria are shown in Table 1.

29 Table 1. Summary of exclusion criteria of the trial.

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## Exclusion criteria

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BMI>30 or < 18.5

Baseline oxygen desaturation (resting SpO<sub>2</sub> <90%)

Chronic opioid treatment, substance abuse or drug use

Pregnancy

History of allergy to related drugs

Severe coagulation dysfunction

Severe hepatic and renal dysfunction

Gastroesophageal reflux disease

History of abnormal recovery from anaesthesia

No informed consent

Patients with acute exacerbation of chronic obstructive pulmonary disease (COPD)

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## 2 **Recruitment**

3 Consecutive patients who present to respiratory clinics at Shanghai Pulmonary  
4 Hospital with a diagnosis of tracheal stenosis and meet the inclusion criteria will be  
5 offered the opportunity to enroll in our study. We will inform them of details about our  
6 study. All patients will be provided with full information of their part in our study and  
7 assure that their information will be kept strictly confidential.

## 8 **Information consent**

9 Informed consent will be obtained from each patient or legally authorized  
10 representative (LAR) prior to enrollment in our study. This will provide a clear  
11 understanding that their participation is entirely voluntary, and they have a right to  
12 withdraw at any time during the study. Refusal to sign or participate will not affect the  
13 patient's right to receive medical care. No study procedures will be done prior to  
14 obtaining informed consent. A copy of the letter of information and consent is provided  
15 in Supplementary file 2.

## 16 **Randomization and blinding**

17 After obtaining a signed informed consent from the patient or the LAR, the patient will

1 be randomly allocated 1:1 to Group S or Group R. Randomization will be performed  
2 by sealed envelopes available at the Shanghai Pulmonary Hospital. A masked  
3 researcher will generate treatment assignments using a computer-generated random  
4 number list of variable block sizes (block size 4-6-8) by Stata 16.0 (STATACORP  
5 LLC.4905 Lake Way Drive). Randomization envelopes to be opened will be created by  
6 the research assistant just prior to when they are ready to randomize a patient. The  
7 integrity and presence of the envelopes will be checked at each monitoring visit.

8 The research assistant (RA) who will be blinded to the randomized assignment of  
9 patients will conduct all baseline interviews. The patients will be blinded to their  
10 intervention as will the research staff completing the post-procedural follow-up  
11 questionnaire. It is not possible to blind anaesthesiologists involved in a patient's care,  
12 but bronchoscopists will be blinded.

### 13 **Study treatment**

14 Patients will fast prior to the procedure. After premedication with i.v. midazolam 0.02  
15 mg/kg in the reception area, patients will be transferred to the operating theatre.  
16 Patients will be monitored with ECG, pulse oximetry, and non-invasive arterial pressure  
17 during the procedure and recovery period [until post-anaesthesia care unit (PACU)  
18 discharge]. All patients will receive oxygen application via a nasal tube with 2 liters of  
19 O<sub>2</sub>/min initially. Once the plasma-site concentration (C<sub>p</sub>) and effect-site concentration  
20 (C<sub>e</sub>) has achieved equilibrium, a soft rubber type nasopharyngeal airway (No.6/7,  
21 Medis Medical, UK) will be inserted. The oxygen supply will be changed from nasal  
22 cannula to nasopharyngeal airway connected to an anaesthetic machine with 6  
23 liters of O<sub>2</sub>/min and an adjustable pressure-limiting (APL) valve setting of 30  
24 cmH<sub>2</sub>O. Both groups will be intravenously administered an initial loading dose of  
25 0.8mcg/kg dexmedetomidine, followed by a maintenance dose of 0.5mcg/(kg·h) during  
26 the procedure. 4 mL of 1% lignocaine solution will be administered by  
27 nasopharyngeal airway to throat, then three aliquots of 4 mL of 1% lignocaine solution  
28 will be administered by endoscopist, one each to supraglottic, subglottic and carina  
29 through bronchoscope using the "spray as-you-go" technique<sup>19</sup>. A BF-260 electronic

1 bronchoscope (BF-1T260/6C260, Olympus Corporation, Japan) will be used. The  
2 airway will be fully assessed and the appropriate interventional procedure will be  
3 performed to relieve the obstruction and stabilize the airway. If biopsies are required,  
4 these specimens will be taken and sent for appropriate investigations. Procedures  
5 performed will involve debridement or coring out of the endoluminal lesion, balloon  
6 dilation, serial mechanical dilation with tapering, cryotherapy, variously sized dilators,  
7 laser disobliteration, or airway stenting.

8 TCI plasma-site concentration ( $C_p$ ) for sufentanil or remifentanil will be achieved  
9 using the Fresenius DPS workstation using the Gepts or Minto pharmacokinetic  
10 model respectively. The EC95 of sufentanil or remifentanil is set as the plasma target  
11 concentration and which is 0.212 ng/ml or 2.710 ng/ml respectively. Intravenous  
12 injection of 10-20 mg propofol will be used as a remedy and repeatedly as  
13 necessary. The effective concentration ( $C_e$ ) of sufentanil and remifentanil are based  
14 on our previous research using the biased coin up-and-down design sequential  
15 method. A MAP < 80% of baseline or 60 mmHg is regarded as hypotension. In the  
16 event hypotension happens, an intravenous injection of phenylephrine (25~100 mcg)  
17 will be administered as a rescue vasopressor.

### 18 **Management of hypoxemia**

19 Definition of hypoxemia:  $SpO_2 < 90\%$  at any time<sup>20</sup>. The severity of hypoxemia is  
20 classified as follows: subclinical hypoxemia ( $SPO_2$  of 90-95%), moderate hypoxemia  
21 ( $SPO_2$  of 75-89%,  $\leq 60$  s), and severe hypoxemia ( $SpO_2 < 90\%$  for  $>60$  s or  $SpO_2 < 75\%$   
22 at any time)<sup>21</sup>.

23 Once hypoxemia develops, it will be corrected using the following sequence: (1)  
24 patient stimulation, (2) increasing the volume of supplementary oxygen from 6 to 10  
25 liters of  $O_2$ /min, (3) opening the airway using a jaw-thrust maneuver, (4) removing the  
26 bronchoscope tube and mask ventilation, and (5) laryngeal mask or tracheal intubation  
27 for mechanical ventilation.

### 28 **Trial outcomes**

#### 29 **Primary outcome**



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4 1 The primary outcome is the incidence of hypoxemia.

5  
6 2 **Secondary outcomes**

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8 3 Secondary outcome variables include the following :

- 9  
10 4 1. The severity of hypoxemia.  
11  
12 5 2. Cough severity rated on a 4-point scale (no cough=1, slight coughing=2, moderate  
13 coughing = 3, severe coughing = 4). Coughing is considered slight if no more than  
14 2 coughs in sequence occurred, moderate if 3-5 coughs in sequence occurred and  
15 severe if more than 5 coughs in sequence occurred.  
16  
17 3. Hemodynamic variables (blood pressure and heart rate).  
18  
19 4. Modified Ramsay sedation scores during procedure.  
20  
21 5. Patient's comfort and tolerance to fiberoptic assessed by Puchner comfort scale<sup>22</sup>.  
22  
23 6. Recovery time.  
24  
25 7. Arterial blood gases (PO<sub>2</sub>, PCO<sub>2</sub> and PH) before and after the operation.  
26  
27 8. The incidence of postoperative nausea and vomiting .  
28  
29 9. Satisfaction scores of the patient, bronchoscopist and anaesthesiologist.  
30  
31 10. The willingness of the patient to undergo repeat bronchoscopy.  
32  
33 11. Visual analog scale (VAS, 0-100mm) scores of sore throat at 30 min after the end  
34 of the operation.  
35  
36 12. Complications related to the procedure and anaesthesia.  
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41 20 **Statistical methods**

42  
43 21 The analysis will be performed on an intention-to-treat basis, such that each patient is  
44 analyzed in the group to which he or she is randomized, regardless of actual  
45 compliance with the intended intervention. All the analyses will be conducted using  
46 Stata 16.0 (STATA CORP LLC. 4905 Lake Way Drive). A two-tailed p value equal or  
47 less than 0.05 will be considered as statistically significant. All tests, except for the  
48 primary outcome, will be exploratory. When individual items are missing from a scale,  
49 we will calculate the percent of missing items. If less than 10%, we will impute values  
50 using the mean of the remaining items. If more than 10%, the scale score will be  
51 missing, and unavailable for analysis.  
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## 1 **Sample size calculation**

2 Our previous study (unpublished) shows that the incidences of hypoxemia in the two  
3 groups are 10% (1/10) in sufentanil group and 27.27% (3/11) in remifentanil group. We  
4 determined that enrolment of 270 patients would provide a power of 90% to show a  
5 reduction in the rate of incidences of hypoxia between two groups at a two-sided alpha  
6 level of 0.05, accounting for 20% lost to follow-up.

## 7 **Descriptive statistics**

8 Continuous variables will be described using means and SD for normally distributed  
9 data. For continuous variables with non-normally distributed data, medians and ranges  
10 will be used. Categorical data will be described using counts, proportions, and risk  
11 ratios with 95% CIs.

## 12 **Planned outcome analysis**

### 13 **Primary outcome**

14 The incidences of hypoxia will be compared between the two groups using a  $\chi^2$  test or  
15 an exact Fisher's exact test if required. The incidences of hypoxia will then be modelled  
16 (secondary analysis) using a multivariate logistic regression.

### 17 **Secondary outcomes**

18 Secondary endpoints will be compared between the two treatment groups by means  
19 of Student's t-test (or the Mann-Whitney U test, if necessary) for continuous  
20 quantitative variables and by means of the  $\chi^2$  test (or Fisher's exact test) for qualitative  
21 variables. Linear models and logistics models will be used to compare the two groups  
22 in multivariate analyses. Time-to-event analyses will involve the Kaplan-Meier method  
23 and the Cox proportional hazards model.

## 25 **DISCUSSION**

26 MAC is a specific anaesthesia service performed by a qualified anaesthesia provider  
27 for a diagnostic or therapeutic procedure<sup>23</sup>. MAC is useful in patients who require  
28 repeated fiberoptic bronchoscopy as well as safe in respiratory depression when

1 performed by experienced anaesthesiologists<sup>24</sup>. We will utilize MAC for patients with  
2 severe tracheal stenosis that requires fiberoptic bronchoscopy in this study.

3 TCI allows an accurate adaptation of the anaesthesia level and fewer overdose-  
4 linked adverse effects. As a decreased cumulative dose of sufentanil or remifentanil,  
5 hemodynamic stability, recovery and discharge may also be improved by using TCI.  
6 The Ce of sufentanil and remifentanil used in the study are based on our previous  
7 unpublished research.

8 This trial is the first randomized controlled study powered to test the hypothesis that  
9 sufentanil TCI compared with remifentanil TCI for MAC can reduce the incidence of  
10 hypoxemia and related adverse events in patients with severe tracheal stenosis  
11 undergoing fiberoptic bronchoscopy. We believe that the findings of this study will have  
12 significant clinical implications. This might mean that more studies are needed to  
13 determine the optimal strategies for anaesthesia management to prevent hypoxemia.

## 15 **Ethics and dissemination**

### 16 **Ethics approval and consent to participate**

17 This clinical study will be conducted following the Declaration of Helsinki. It will be  
18 conducted in compliance with the protocol, good clinical practice (GCP), designated  
19 standard operating procedures, and local laws and regulations relevant to the country  
20 of conduct. The study protocol was approved by the Ethics Committee of Shanghai  
21 Pulmonary Hospital of China (approval No. K19-122). Informed consent must be  
22 obtained from all patients.

### 23 **Dissemination policy**

24 The results of this study will be disseminated regardless of the effect of the intervention  
25 on study outcomes. The manuscript describing the effect of the intervention will be  
26 submitted to a peer-reviewed journal when data collection and analyses are complete.

### 28 **Data collection, monitoring and management**

1 Preoperative, intraoperative and postoperative follow-up data will be collected from  
2 electronic medical records, monitoring machines and relevant manual records by the  
3 research staff (YJZ). All electronic and handwriting data will be stored on a password-  
4 protected computer. Data will be recorded on a standardised paper form  
5 (Supplementary file 3) and subsequently double-entered using Epidata software v3.1  
6 by two trained research assistants. Data and safety monitoring will be the responsibility  
7 of the principle investigator (JML).

### 8 **Trial status**

9 The recruitment commenced in February 2021. It is anticipated that recruitment will  
10 end by June 2023. The version number of the protocol are v3.0.

### 11 **Patient and public involvement**

12 Patients or the public were not involved in the design of our research and will not be  
13 involved in conduct, reporting or dissemination of our research.

### 14 **Contributors**

15 WW and YZ designed the study, they are joint first author. WW and YJZ wrote the  
16 manuscript together. YZ provided substantial contributions to the conception and  
17 design of the study, wrote the statistical analysis plan and estimated the sample size.  
18 JML was responsible for designing the study and drafting the work, revising it critically  
19 for important intellectual content and approved the final version of the manuscript. All  
20 authors gave their agreement to be accountable for all aspects of the work, and ensure  
21 the accuracy and integrity of any part of the work.

### 22 **Funding**

23 The study is funded by Shanghai Municipal Health Commission (Project  
24 NO.201940366).

### 25 **Patient consent for publication**

26 Not required.

### 27 **Competing interests**

28 The authors declare that they have no competing interests.

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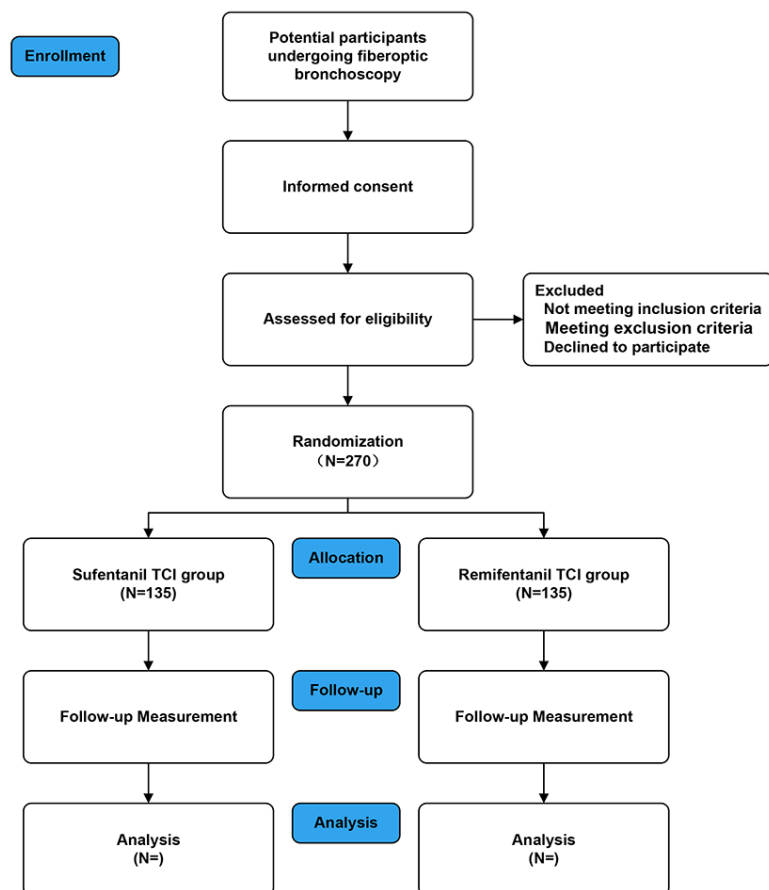
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1 Figure 1  
2 CONSORT flow diagram for the study. CONSORT, Consolidated Standards of  
3 Reporting Trials.

9 Figure 2  
10 SPIRIT Figure-Schedule of enrolment, interventions, and assessments. SPIRIT,  
11 Standard Protocol Items: Recommendations for Interventional Trials.

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CONSORT flow diagram for the study. CONSORT, Consolidated Standards of Reporting Trials.

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STUDY PERIOD					
	Enrolment	Allocation	Post-allocation		Close-out
TIMEPOINT	t <sub>1</sub>	t <sub>0</sub>	t <sub>1</sub>	t <sub>2</sub>	t <sub>3</sub>
	Feb 2021- Jun 2023		During the procedure	PACU	
<b>ENROLMENT:</b>					
Eligibility screen	X				
Informed consent	X				
Allocation		X			
<b>INTERVENTIONS:</b>					
Sufentanil TCI			X		
Remifentanil TCI			X		
<b>ASSESSMENTS:</b>					
Baseline variables	X	X			
Hypoxemia			X		
Cough severity			X		
Hemodynamic variables			X		
Sedation scores			X		
Patient's comfort			X		
Recovery time				X	
Postoperative nausea and vomiting				X	
Satisfaction				X	
Visual analog scale				X	

SPRIT Figure-Schedule of enrolment, interventions, and assessments. SPRIT, Standard Protocol Items: Recommendations for Interventional Trials.



STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents\*

Section/item	Item No	Description	Addressed on page number
<b>Administrative information</b>			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	___ 1 ___
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	___ 2 ___
	2b	All items from the World Health Organization Trial Registration Data Set	___ YES ___
Protocol version	3	Date and version identifier	___ 11 ___
Funding	4	Sources and types of financial, material, and other support	___ 12 ___
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	___ 1,12 ___
	5b	Name and contact information for the trial sponsor	___ 1,12 ___
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	___ 12 ___
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	___ 12 ___

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1	<b>Introduction</b>			
2				
3	Background and	6a	Description of research question and justification for undertaking the trial, including summary of relevant	_____ 2-4 _____
4	rationale		studies (published and unpublished) examining benefits and harms for each intervention	
5				
6		6b	Explanation for choice of comparators	_____ 2-4 _____
7				
8	Objectives	7	Specific objectives or hypotheses	_____ 5 _____
9				
10	Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group),	
11			allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	_____ 2 _____
12				
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14	<b>Methods: Participants, interventions, and outcomes</b>			
15				
16	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will	_____ 5-6 _____
17			be collected. Reference to where list of study sites can be obtained	
18				
19	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and	_____ 5-6 _____
20			individuals who will perform the interventions (eg, surgeons, psychotherapists)	
21				
22	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be	_____ 6-8 _____
23			administered	
24		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose	_____ N/A _____
25			change in response to harms, participant request, or improving/worsening disease)	
26		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence	_____ N/A _____
27			(eg, drug tablet return, laboratory tests)	
28		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	_____ N/A _____
29				
30	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood	_____ 9 _____
31			pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg,	
32			median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen	
33			efficacy and harm outcomes is strongly recommended	
34				
35	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for	_____ Fig2 _____
36			participants. A schematic diagram is highly recommended (see Figure)	
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1	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	_____10_____
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4	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	_____6_____
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### 6 **Methods: Assignment of interventions (for controlled trials)**

#### 7 Allocation:

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10	Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	_____6-7_____
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16	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	_____6-7_____
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20	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	_____6-7_____
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24	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	_____7_____
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27		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	_____N/A_____
28				
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### 31 **Methods: Data collection, management, and analysis**

32				
33	Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	_____10-11_____
34				
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39		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	_____10-11_____
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1	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	_____ 10-11 _____
2				
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5	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	_____ 8-9 _____
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8		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	_____ 9-10 _____
9				
10		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	_____ 9-10 _____
11				
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14	<b>Methods: Monitoring</b>			
15				
16	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	_____ 10-11 _____
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22		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	_____ N/A _____
23				
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25	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	_____ 10-11 _____
26				
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28	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	_____ N/A _____
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32	<b>Ethics and dissemination</b>			
33				
34	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	_____ 2,12 _____
35				
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37	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	_____ 10-11 _____
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1	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	_____6_____
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4		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	_____N/A_____
5				
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7	Confidentiality	27	How personal information about potential and enrolled participants will be collected, stored, and maintained in order to protect confidentiality before, during, and after the trial	_____11-12_____
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10	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	_____11-12_____
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13	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	_____11-12_____
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16	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	_____11-12_____
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20	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	_____11-12_____
21				
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24		31b	Authorship eligibility guidelines and any intended use of professional writers	_____11-12_____
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26		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	_____11-12_____
27				
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29	<b>Appendices</b>			
30				
31	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	__Translated ICFs can be provided on request_____
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36	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	_____N/A_____
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\*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.

For peer review only

1 Practice name:

2 Participant ID:

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## 11 Informed Consent

### 16 Informed Consent form for patient.

17 This Informed Consent Form is for men and women who attend Shanghai Pulmonary  
18 Hospital and who we are inviting to participate in research on anesthesia for  
19 bronchoscopy.

20 The title of our research project is: *Sufentanil target controlled infusion (TCI) vs*  
21 *remifentanil TCI for monitored anaesthesia care for patients with severe tracheal*  
22 *stenosis undergoing fiberoptic bronchoscopy.*

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27 **Principal Investigator:** Jianming Liu, MD

28 **Organization:** Department of Anaesthesiology, Shanghai Pulmonary Hospital, Tongji  
29 University School of Medicine  
30

### 31 This Informed Consent Form has two parts:

- 32 1. Information Sheet (to share information about the research with you)
  - 33 2. Certificate of Consent (for signatures if you agree to take part)
- 34  
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37 **You will be given a copy of the full Informed Consent Form**

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## **PART 1: Information Sheet**

### **Introduction**

I am Jianming Liu, working for department of Anaesthesiology. We are doing research on monitored anaesthesia care for patients with severe tracheal stenosis undergoing fiberoptic bronchoscopy. I am going to give you information and invite you to be part of this research.

You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research. There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me, the study doctor or the staff.)

### **Purpose of the research**

Bronchoscopy has been an integral part of the diagnosis and treatment of patients with tracheal stenosis. The two opioids most commonly used are sufentanil and remifentanil. We aim to conduct a trial comparing sufentanil with remifentanil in patients with severe tracheal stenosis undergoing fiberoptic bronchoscopy.

### **Participant selection**

We are inviting all adults with severe tracheal stenosis attend Shanghai Pulmonary Hospital to participate in the research.

### **Voluntary Participation**

Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. If you choose not to participate in this research project, you will offer the treatment that is routinely offered, and we will tell you more about it later. You may change your mind later and stop participating even if you agreed earlier.

### **Procedures and Protocol**

Participants will be randomly assigned to one of two groups. Participants in one group will be given monitored anaesthesia care (MAC) using sufentanil target controlled infusion. Participants in the other group will be given monitored anaesthesia care (MAC) using remifentanil. We will then compare which of the two has the best results. The healthcare workers will be looking after you and the other participants very carefully during the study. If we are concerned about what the treatment is doing, we will find out which treatment you are getting and make changes. If there is anything you are concerned about or that is bothering you about the research please talk to me or one of the other researchers.

### **For any clinical study (if relevant):**

We will take arterial blood from your arm using a syringe through arterial line. This blood taken is painless. In total, we will take about 2 samples of 1 ml arterial blood. At

1  
2  
3 the end of the research any left-over blood sample will be destroyed).  
4  
5

### 6 **Description of the Process**

7 In the first time, a small amount of blood, equal to about a teaspoon, will be taken from  
8 your arm with a syringe through arterial catheter. This blood will be tested with a blood  
9 analyzer. We will ask you a few questions about your general health.

10 You'll be anesthetized during fiberoptic bronchoscopy. After treatment we'll draw your  
11 blood and also ask you a few questions.  
12  
13  
14

### 15 **Duration**

16 The research takes place over 1/2 days.  
17  
18

### 19 **Risks**

20 Any risk can appear during the process. Mechanical complications of fiberoptic  
21 bronchoscopy include nasopharyngeal, vocal cord, and airway trauma as well as  
22 bronchospasm, laryngospasm, pulmonary derecruitment/atelectasis, pneumothorax,  
23 airway hemorrhage, and introduction or exacerbation of infection. Systemic  
24 complications are primarily related to the procedure itself, medication administration,  
25 or patient comorbidities. The healthcare workers will be looking after you and the other  
26 participants very carefully during the study. If we are concerned about what the  
27 treatment is doing, we will find out which treatment you are getting and make changes.  
28  
29  
30

### 31 **Benefits**

32 If you participate in this research, you will have the following benefits: any interim  
33 illnesses will be treated at no charge to you. The Fresenius DPS workstation for TCI  
34 used for free. Your participation is likely to help us find the answer to the research  
35 question.  
36  
37  
38

### 39 **Reimbursements**

40 Your participation is free. You will not be given any other money or gifts to take part in  
41 this research.  
42  
43  
44

### 45 **Confidentiality**

46 With this research, something out of the ordinary is being done in your community. It  
47 is possible that if others in the community are aware that you are participating, they  
48 may ask you questions. We will not be sharing the identity of those participating in the  
49 research.  
50

51 The information that we collect from this research project will be kept confidential.  
52 Information about you that will be collected during the research will be put away and  
53 no-one but the researchers will be able to see it. Any information about you will have a  
54 number on it instead of your name. Only the researchers will know what your number  
55 is and we will lock that information up with a lock and key. It will not be shared with  
56 or given to anyone except [Yi Zhou and Jianming Liu) who will have access to the  
57 information.  
58  
59  
60

### **Sharing the Results**

The knowledge that we get from doing this research will be shared with you through community meetings before it is made widely available to the public. Confidential information will not be shared. After these meetings, we will publish the results in order that other interested people may learn from our research.

### **Right to Refuse or Withdraw**

You do not have to take part in this research if you do not wish to do so. You may also stop participating in the research at any time you choose. It is your choice and all of your rights will still be respected.

### **Alternatives to Participating**

If you do not wish to take part in the research, you will be provided with the established standard treatment available at our hospital.

### **Who to Contact**

If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following:

DR. Jianming Liu, Phone: 86-18019285297

This proposal has been reviewed and approved by the Ethics Committee of Shanghai Pulmonary Hospital of China (approval No. K19-122) which is a committee whose task it is to make sure that research participants are protected from harm.

**You can ask me any more questions about any part of the research study, if you wish to. Do you have any questions?**

**PART 2: Certificate of Consent**

This section should be written in the first person and have a statement similar to the one in bold below. If the participant is illiterate but gives oral consent, a witness or a legally authorized representative must sign. A researcher or the person going over the informed consent must sign each consent. The understanding should perhaps be better tested through targeted questions during the reading of the information sheet (some examples of questions are given above), or through the questions being asked at the end of the reading of the information sheet, if the potential participant is reading the information sheet him/herself.

**Please  
initial  
each box**

1 I have read the foregoing information, or it has been read to me.

2 I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction.

3 I consent voluntarily to participate as a participant in this research.

**Print Name of Participant**

---

**Signature of Participant**

---

**Date(Day/month/year)**

---

**If illiterate**

Aliterate witness or legally authorized representative must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb-print as well.

**Please  
initial  
each box**

1 I have witnessed the accurate reading of the consent form to the potential participant

2 I have witnessed the individual has had the opportunity to ask questions.

3 I confirm that the individual has given consent freely.

**Print Name of witness or legally  
authorized representative**

---

**Signature of witness or legally  
authorized representative**

---

**Date(Day/month/year)**

---

**Thumb print of participant**

**Statement by the researcher/person taking consent**

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

**A copy of this ICF has been provided to the participant.**

**Print Name of Researcher** \_\_\_\_\_

**Signature of Researcher** \_\_\_\_\_

**Date(Day/month/year)** \_\_\_\_\_

Protocol No:	P20200828V3		
Site	<input type="checkbox"/> <input type="checkbox"/>	Subject ID:	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Randomisation No:	<input type="checkbox"/> <input type="checkbox"/>	Subject Initials:	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Investigator	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
Identifier:			

### Case Report Form

**Sufentanil target controlled infusion (TCI) vs remifentanil TCI  
for monitored anaesthesia care for patients with severe tracheal  
stenosis undergoing fiberoptic bronchoscopy**

By  
**Shanghai Pulmonary Hospital**

**Inclusion Criteria**

Subjects who meet the following criteria may be included in the study. Did the subject meet the following criteria requirements for inclusion? ( ✓ Yes or No)		Yes 1	No* 2
01	Cotton-Myer grades II-III		
02	Aged 18–65 years		
03	ASA I-III		

\* If No, document on Subject Eligibility Page.



**Exclusion Criteria**

The following will exclude potential subjects from the study. Does the subject have any of the following? ( √ Yes or No)		Yes* 1	No 2
01	BMI>30 or < 18.5		
02	Baseline oxygen desaturation (resting SpO <sub>2</sub> <90%)		
03	Pregnancy		
04	History of allergy to related drugs		
05	Severe coagulation dysfunction		
06	Severe hepatic and renal dysfunction		
07	Gastroesophageal reflux disease		
08	History of abnormal recovery from anaesthesia		
09	No informed consent		

\*If Yes, document on Subject Eligibility Page

**Information Session**

Date of Information Session	Did the subject attend the Information Session?	Comments
____ / ____ / ____ DD / MM / YY	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No (explain, if No)	

**Subject Eligibility**

Date the Subject Signed the Informed Consent Form:		____ / ____ / ____ DD / MM / YY		
Did the subject meet all of the inclusion/exclusion criteria?		1 <input type="checkbox"/> Yes		
		2 <input type="checkbox"/> No		
If the subject did not meet all of the Inclusion/Exclusion criteria, provide criterion number and explanation below.				
Category	Inclusion/Exclusion No.	Explanation	Exemption Granted?	If Yes, Date Granted DD/MM/YYYY
1 <input type="checkbox"/> Inclusion			1 <input type="checkbox"/> Yes	____ / ____ / ____
2 <input type="checkbox"/> Exclusion			2 <input type="checkbox"/> No	
1 <input type="checkbox"/> Inclusion			1 <input type="checkbox"/> Yes	____ / ____ / ____
2 <input type="checkbox"/> Exclusion			2 <input type="checkbox"/> No	
1 <input type="checkbox"/> Inclusion			1 <input type="checkbox"/> Yes	____ / ____ / ____
2 <input type="checkbox"/> Exclusion			2 <input type="checkbox"/> No	

**Demographics**

Date DD/MM/YYYY	Date of Birth DD/MM/YYYY	Gender	Ethnicity
<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	1 <input type="checkbox"/> Male	1 <input type="checkbox"/> Han
		2 <input type="checkbox"/> Female	2 <input type="checkbox"/> Non-han
<b>Body Measurements</b>			
Were Body Measurements Collected?		Date DD/MM/YYYY	
1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No		<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Parameter	Unit	Result	
Height	cm	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Weight	Kg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
<b>Vital Signs</b>			
Were Body Measurements Collected?		Date DD/MM/YYYY	
1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No		<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Body Temperature	°C	<input type="checkbox"/> <input type="checkbox"/> . <input type="checkbox"/>	
<b>12-Lead Electrocardiogram Report</b>			
Was ECG performed?		Date DD/MM/YYYY	Actual Time 24-hour clock
1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No		<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> : <input type="checkbox"/> <input type="checkbox"/>
ECG Interpretation:	1 <input type="checkbox"/> Normal	2 <input type="checkbox"/> Abnormal, NCS	3 <input type="checkbox"/> Abnormal
Comments Regarding CS Findings:			

**Medical History**

Does the subject have any relevant medical history?		Date DD/MM/YYYY	
1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No		____/____/____	
Diagnosis/Procedure	Date of Onset DD/MM/YYYY	Date of Resolution DD/MM/YYYY	
1	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
2	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
3	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
4	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
5	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
6	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
7	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
8	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING
9	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	9 <input type="checkbox"/> ONGOING

**Laboratory Analysis**

Parameter	Unit	Result
SPO <sub>2</sub>		□ □ □
Arterial blood gas analysis		
PH		□ . □ □
PaCO <sub>2</sub>	mmHg	□ □ □
PaO <sub>2</sub>	mmHg	□ □ □
HCO <sub>3</sub>	mEq/L	□ □

For peer review only

**Intervention Phase**

Date DD/MM/YYYY	____ / ____ / ____			
Group	1 <input type="checkbox"/> Group R		2 <input type="checkbox"/> Group S	
Whether or not hypoxemia occurs				
1 <input type="checkbox"/> subclinical hypoxemia (SPO2 of 90-95%),	2 <input type="checkbox"/> moderate hypoxemia (SPO2 of 75-89%, $\leq 60$ s		3 <input type="checkbox"/> severe hypoxemia (SpO2 < 90% for >60 s or SpO2 < 75% at any time)	
Management of hypoxemia				
1 <input type="checkbox"/> patient stimulation	2 <input type="checkbox"/> increasing the volume of supplementary oxygen	3 <input type="checkbox"/> jaw-thrust maneuver	4 <input type="checkbox"/> mask ventilation	5 <input type="checkbox"/> mechanical ventilation.
Puchner five-point fiber-optic intubation comfort scale				
1 <input type="checkbox"/> No reaction	2 <input type="checkbox"/> Slight grimacing	3 <input type="checkbox"/> Heavy grimacing	4 <input type="checkbox"/> Verbal objection	5 <input type="checkbox"/> Defensive movement

T0	10 minutes after entering the operation room	
Parameter	Unit	Result
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>

T1	Cp and Ce has achieved equilibrium		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>

	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T2	When bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T3	1 minute after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T4	5 minutes after bronchoscope is inserted	
Parameter	Unit	Result
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>

Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T5	10 minutes after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T6	15 minutes after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>



	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T6	20 minutes after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T7	25 minutes after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T8	30 minutes after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	

Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

T9	60 minutes after bronchoscope is inserted		
Parameter	Unit	Result	
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>	
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
	7 <input type="checkbox"/>	8 <input type="checkbox"/>	
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>
EtCO2	mmHg	<input type="checkbox"/> <input type="checkbox"/>	

Type of fiberoptic bronchoscopy procedure				
1 <input type="checkbox"/> Diagnostic		2 <input type="checkbox"/> Therapeutic		
If it is Therapeutic bronchoscopy				
1 <input type="checkbox"/> Injection of medication	2 <input type="checkbox"/> Endotherm knife	3 <input type="checkbox"/> Cryotherapy		
4 <input type="checkbox"/> Laser	5 <input type="checkbox"/> Stent			
Operation time	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	min	Endoscopist	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Satisfaction scores of bronchoscopist	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	
	4 <input type="checkbox"/>	5 <input type="checkbox"/>		
Satisfaction scores of anaesthesiologist	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	
	4 <input type="checkbox"/>	5 <input type="checkbox"/>		

Vasoactive drugs used			
Whether or not vasoactive drugs are used	1 <input type="checkbox"/> Yes	2 <input type="checkbox"/> No	
Vasoactive drug type	name	dosage	whether it is effective or not
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
1 <input type="checkbox"/> vasoconstrictor 2 <input type="checkbox"/> vasodilator 3 <input type="checkbox"/> Inotropic agents		1 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> $\mu$ g 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> mg	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No

**Post Intervention Phase**

Recovery time	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	min		
Whether nausea and vomiting occur				
1 <input type="checkbox"/> Yes	2 <input type="checkbox"/> No			
Assessment of PONV				
1 <input type="checkbox"/> Mild	2 <input type="checkbox"/> moderate	3 <input type="checkbox"/> severe		
Satisfaction scores of the patient				
1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>
willingness of the patient to undergo repeat bronchoscopy.				
1 <input type="checkbox"/> Not at all likely	2 <input type="checkbox"/> 1-3	3 <input type="checkbox"/> 4-6	4 <input type="checkbox"/> 7-9	5 <input type="checkbox"/> Extremely likely (10)
VAS scores of sore throat				
1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>
6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>	9 <input type="checkbox"/>	10 <input type="checkbox"/>
T10	At PACU			
Parameter	Unit	Result		
Systolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
Diastolic Blood Pressure	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
Heart Rate	beats/minute	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
Respiratory Rate	breaths/minute	<input type="checkbox"/> <input type="checkbox"/>		
Spo2		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
Ramsay Sedation Scale	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	
	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	
	7 <input type="checkbox"/>	8 <input type="checkbox"/>		
Cough	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>
Arterial blood gas analysis				
PH		<input type="checkbox"/> . <input type="checkbox"/> <input type="checkbox"/>		
PaCO <sub>2</sub>	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
PaO <sub>2</sub>	mmHg	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
HCO <sub>3</sub>	mEq/L	<input type="checkbox"/> <input type="checkbox"/>		

**Adverse Event information**

Whether adverse events occurred		
1 <input type="checkbox"/> Yes	2 <input type="checkbox"/> No	
Whether serious adverse events occurred		
1 <input type="checkbox"/> Yes	2 <input type="checkbox"/> No	
Describe the AE and the connection to project procedures		
AE onset date	□□/□□/□□□□	DD/MM/YYYY
AE stop date	□□/□□/□□□□	DD/MM/YYYY
Date of AE awareness	□□/□□/□□□□	DD/MM/YYYY
Severity		
1 <input type="checkbox"/> mild	2 <input type="checkbox"/> moderate	3 <input type="checkbox"/> severe
Outcome		
1 <input type="checkbox"/> recovered/resolved	2 <input type="checkbox"/> recovered/resolved with sequelae	3 <input type="checkbox"/> study participant died
4 <input type="checkbox"/> continuing	5 <input type="checkbox"/> unknown	6 <input type="checkbox"/> other
SAE causality		
1 <input type="checkbox"/> Not related	2 <input type="checkbox"/> Unlikely	3 <input type="checkbox"/> Possibly
4 <input type="checkbox"/> Probably	5 <input type="checkbox"/> Definitely	
Describe the AE and the connection to project procedures		
AE onset date	□□/□□/□□□□	DD/MM/YYYY
AE stop date	□□/□□/□□□□	DD/MM/YYYY
Date of AE awareness	□□/□□/□□□□	DD/MM/YYYY
Severity		
1 <input type="checkbox"/> mild	2 <input type="checkbox"/> moderate	3 <input type="checkbox"/> severe
Outcome		
1 <input type="checkbox"/> recovered/resolved	2 <input type="checkbox"/> recovered/resolved with sequelae	3 <input type="checkbox"/> study participant died

4 <input type="checkbox"/> continuing	5 <input type="checkbox"/> unknown	6 <input type="checkbox"/> other
SAE causality		
1 <input type="checkbox"/> Not related	2 <input type="checkbox"/> Unlikely	3 <input type="checkbox"/> Possibly
4 <input type="checkbox"/> Probably	5 <input type="checkbox"/> Definitely	
Describe the AE and the connection to project procedures		
AE onset date	□□/□□/□□□□	DD/MM/YYYY
AE stop date	□□/□□/□□□□	DD/MM/YYYY
Date of AE awareness	□□/□□/□□□□	DD/MM/YYYY
Severity		
1 <input type="checkbox"/> mild	2 <input type="checkbox"/> moderate	3 <input type="checkbox"/> severe
Outcome		
1 <input type="checkbox"/> recovered/resolved	2 <input type="checkbox"/> recovered/resolved with sequelae	3 <input type="checkbox"/> study participant died
4 <input type="checkbox"/> continuing	5 <input type="checkbox"/> unknown	6 <input type="checkbox"/> other
SAE causality		
1 <input type="checkbox"/> Not related	2 <input type="checkbox"/> Unlikely	3 <input type="checkbox"/> Possibly
4 <input type="checkbox"/> Probably	5 <input type="checkbox"/> Definitely	