

BMJ Open Sufentanil target controlled infusion (TCI) versus remifentanil TCI for monitored anaesthesia care for patients with severe tracheal stenosis undergoing fiberoptic bronchoscopy: protocol for a prospective, randomised, controlled study

Wei Wu ¹, Yi Zhou,^{2,3} Yuanjie Zhu,¹ Jianming Liu¹

To cite: Wu W, Zhou Y, Zhu Y, *et al.* Sufentanil target controlled infusion (TCI) versus remifentanil TCI for monitored anaesthesia care for patients with severe tracheal stenosis undergoing fiberoptic bronchoscopy: protocol for a prospective, randomised, controlled study. *BMJ Open* 2022;**12**:e058662. doi:10.1136/bmjopen-2021-058662

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2021-058662>).

WW and YZ contributed equally.

WW and YZ are joint first authors.

Received 31 October 2021
Accepted 09 August 2022



© Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to

Dr Jianming Liu;
drlujianming@163.com

ABSTRACT

Introduction The use of monitored anaesthesia care (MAC) is necessary and ubiquitous for fiberoptic bronchoscopy. Anaesthetic management of patients with severe tracheal stenosis has always been a challenge. 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, randomised 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 hypoxaemia (an oxygen saturation of <90%). The secondary outcome investigates the severity of hypoxaemia, cough severity, haemodynamic variables, sedation scores and satisfaction scores. **Ethics and dissemination** The study has been approved by the Medical Ethics Committee of Shanghai Pulmonary Hospital (approval No. K19-122). The results will be submitted for publication in peer-reviewed journals. **Trial registration number** ChiCTR2100043380.

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 USA annually.¹ Sedation is now generally recommended for all patients undergoing fiberoptic bronchoscopy unless a specific contraindication to sedation exists.²⁻⁴ Sedation during fiberoptic bronchoscopy improves patient comfort and tolerance and

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study is an investigator-initiated, randomised, controlled trial, comparing two monitored anaesthesia care (MAC) strategies.
- ⇒ This is the first prospective study of anaesthetic management of patients with severe tracheal stenosis during fiberoptic bronchoscopy.
- ⇒ A homogeneous patient population with severe tracheal stenosis is included.
- ⇒ The main limitation of our study is that considering the characteristics of the two MAC strategies, the overall trial is not double-blind.
- ⇒ The analysis of the secondary objectives is explorative, due to sample size restrictions.

enhances the willingness to repeat the procedure, without increasing complications.^{3 5 6}

Bronchoscopy has been an integral part of the diagnosis and treatment of patients with severe tracheal stenosis.⁷ Patients affected by severe tracheal stenosis develop symptoms such as stridor, dyspnoea, voice changes, increased mucus production and persistent cough.⁸ Most patients require sedation and analgesia to tolerate fiberoptic bronchoscopy. Anaesthetic management for patients with severe tracheal stenosis during fiberoptic bronchoscopy procedures has always been challenging, and there is no standardised practice currently.^{3 9}

Remifentanil has a rapid onset of action and elimination half-life and a predictable duration of action with no accumulation of effect on repeated dosing or with continuous infusion, which making it suitable for anaesthesia management of diagnostic

and therapeutic bronchoscopy.^{10–15} The degree of the noxious stimulation caused by the insertion and manipulation of a bronchoscope is often similar to a surgical incision. Remifentanyl might cause respiratory depression or haemodynamic instability when effectively inhibiting operational stress, which is often very dangerous for patients with severe tracheal stenosis.^{14 16 17} Sufentanil is a more potent opioid than remifentanyl, its analgesic effect lasts longer and it is superior in terms of haemodynamic stability. Sufentanil has a longer half-time as compared with remifentanyl, but target controlled infusion (TCI) will prevent long-acting opioid-induced accumulation and allow rapid recovery from anaesthesia.¹⁸ There have been no detailed investigations on the efficacy and safety of monitored anaesthesia care (MAC) using sufentanil or remifentanyl TCI in patients with severe tracheal stenosis undergoing fiberoptic bronchoscopy. The aim of our study is to compare sufentanil TCI with remifentanyl TCI in patients with severe tracheal stenosis undergoing fiberoptic bronchoscopy.

Objectives

We aim to conduct a prospective randomised controlled trial comparing sufentanil TCI with remifentanyl TCI and assume that sufentanil TCI would decrease the incidence of hypoxaemia.

Primary objective

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

METHODS AND ANALYSIS

Study design

This is a single-centre, randomised, investigator-initiated clinical trial of 270 patients with severe tracheal stenosis that requires fiberoptic bronchoscopy. The Consolidated Standards of Reporting Trials flow chart is presented in [figure 1](#). A Standard Protocol Items: Recommendations for Interventional Trials figure is included in [figure 2](#) with a checklist included as an additional document (online supplemental 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 remifentanyl 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 physical status classifications I–III and Cotton-Myer grades II–III (the narrow of the endotracheal lumen is

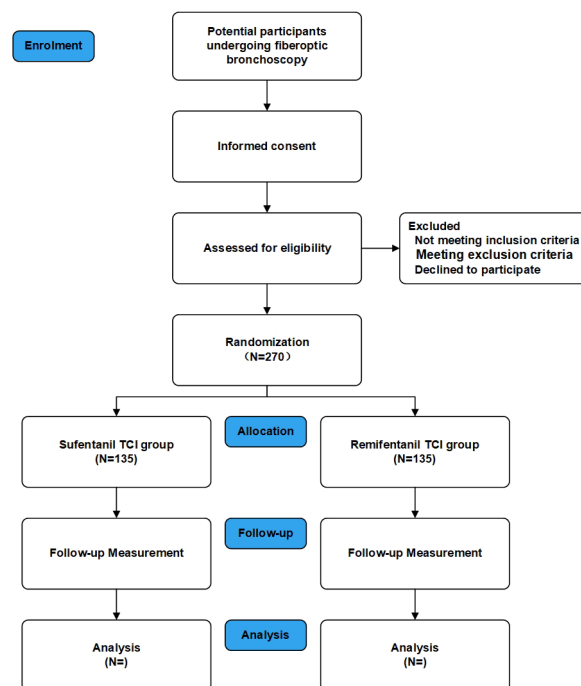


Figure 1 CONSORT flow diagram for the study. CONSORT, Consolidated Standards of Reporting Trials; TCI, target controlled infusion.

more than 50%). The exclusion criteria are shown in [box 1](#).

Recruitment

Consecutive patients who present to respiratory clinics at Shanghai Pulmonary Hospital with a diagnosis of tracheal

STUDY PERIOD					
	Enrolment	Allocation	Post-allocation		Close-out
TIMEPOINT	t ₋₁	t ₀	t ₁	t ₂	t ₃
	Feb 2021–Jun 2023		During the procedure	PACU	
ENROLMENT:					
Eligibility screen	X				
Informed consent	X				
Allocation		X			
INTERVENTIONS:					
Sufentanil TCI			X		
Remifentanyl TCI			X		
ASSESSMENTS:					
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. PACU, postanesthesia care unit; SPIRIT, Standard Protocol Items: Recommendations for Interventional Trials; TCI, target controlled infusion.

Box 1 Summary of exclusion criteria of the trial

Exclusion criteria

1. Body mass index >30 or <18.5 kg/m².
2. Baseline oxygen desaturation (resting SpO₂<90%).
3. Chronic opioid treatment, substance abuse or drug use.
4. Pregnancy.
5. History of allergy to related drugs.
6. Severe coagulation dysfunction.
7. Severe hepatic and renal dysfunction.
8. Gastro-oesophageal reflux disease.
9. History of abnormal recovery from anaesthesia.
10. No informed consent.
11. Patients with acute exacerbation of chronic obstructive pulmonary disease.

stenosis and meet the inclusion criteria will be offered the opportunity to enrol 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 authorised representative (LAR) prior to enrolment 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. A copy of the letter of information and consent is provided in online supplemental file 2.

Randomisation 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. Randomisation will be performed by sealed envelopes available at the Shanghai Pulmonary Hospital. A masked researcher will generate treatment assignments using a computer-generated random number list of variable block sizes (block size 4-6-8) by Stata V.16.0 (StataCorp). Randomisation envelopes to be opened will be created by the research assistant (RA) just prior to when they are ready to randomise a patient. The integrity and presence of the envelopes will be checked at each monitoring visit.

The RA who will be blinded to the randomised assignment of patients will conduct all baseline interviews. The patients will be blinded to their intervention as will the research staff completing the postprocedural follow-up questionnaire. It is not possible to blind anaesthesiologists involved in a patient's care, but bronchoscopists will be blinded.

Study treatment

Patients will fast prior to the procedure. After premedication with intravenous midazolam 0.02 mg/kg in the

reception area, patients will be transferred to the operating theatre. Patients will be monitored with ECG, pulse oximetry and non-invasive arterial pressure during the procedure and recovery period (until postanaesthesia care unit discharge). All patients will receive oxygen application via a nasal tube with 2 L of O₂/min initially. Once the plasma-site concentration (C_p) and effect-site concentration (C_e) has achieved equilibrium, a soft rubber type nasopharyngeal airway (No.6/7, Medis Medical, UK) will be inserted. The oxygen supply will be changed from nasal cannula to nasopharyngeal airway connected to an anaesthetic machine with 6 liters of O₂/min and an adjustable pressure-limiting valve setting of 30 cmH₂O. Both groups will be intravenously administered an initial loading dose of 0.8mcg/kg dexmedetomidine, followed by a maintenance dose of 0.5 mcg/(kg·h) during the procedure. A 4mL of 1% lignocaine solution will be administered by nasopharyngeal airway to throat, then three aliquots of 4mL of 1% lignocaine solution will be administered by endoscopist, one each to supraglottic, subglottic and carina through bronchoscope using the 'spray as-you-go' technique.¹⁹ A BF-260 electronic bronchoscope (BF-1T260/6C260, Olympus, Japan) will be used. The airway will be fully assessed and the appropriate interventional procedure will be performed to relieve the obstruction and stabilise the airway. If biopsies are required, these specimens will be taken and sent for appropriate investigations. Procedures performed will involve debridement or coring out of the endoluminal lesion, balloon dilation, serial mechanical dilation with tapering, cryotherapy, variously sized dilators, laser disobliteration or airway stenting.

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

Management of hypoxaemia

Definition of hypoxaemia: SpO₂<90% at any time.²⁰ The severity of hypoxaemia is classified as follows: subclinical hypoxaemia (SPO₂ of 90%–95%), moderate hypoxaemia (SPO₂ of 75%–89%, ≤60s) and severe hypoxaemia (SpO₂<90% for >60s or SpO₂<75% at any time).²¹

Once hypoxaemia develops, it will be corrected using the following sequence: (1) patient stimulation, (2) increasing the volume of supplementary oxygen from 6 to 10 L of O₂/min, (3) opening the airway using a jaw-thrust manoeuvre, (4) removing the bronchoscope tube

and mask ventilation, and (5) laryngeal mask or tracheal intubation for mechanical ventilation.

Trial outcomes

Primary outcome

The primary outcome is the incidence of hypoxaemia.

Secondary outcomes

Secondary outcome variables include the following:

1. The severity of hypoxaemia.
2. Cough severity rated on a 4-point scale (no cough=1, slight coughing=2, moderate coughing=3, severe coughing=4). Coughing is considered slight if no more than two coughs in sequence occurred, moderate if 3–5 coughs in sequence occurred and severe if more than five coughs in sequence occurred.
3. Haemodynamic variables (blood pressure and heart rate).
4. Modified Ramsay sedation scores during procedure.
5. Patient's comfort and tolerance to fiberoptic assessed by Puchner comfort scale.²²
6. Recovery time.
7. Arterial blood gases (PO₂, PCO₂ and PH) before and after the operation.
8. The incidence of postoperative nausea and vomiting.
9. Satisfaction scores of the patient, bronchoscopist and anaesthesiologist.
10. The willingness of the patient to undergo repeat bronchoscopy.
11. Visual Analogue Scale (0–100 mm) scores of sore throat at 30 min after the end of the operation.
12. Complications related to the procedure and anaesthesia.

Statistical methods

The analysis will be performed on an intention-to-treat basis, such that each patient is analysed in the group to which he or she is randomised, regardless of actual compliance with the intended intervention. All the analyses will be conducted using Stata V.16.0 (StataCorp). A two-tailed p value equal or less than 0.05 will be considered as statistically significant. All tests, except for the primary outcome, will be exploratory. When individual items are missing from a scale, we will calculate the percent of missing items. If less than 10%, we will impute values using the mean of the remaining items. If more than 10%, the scale score will be missing, and unavailable for analysis.

Sample size calculation

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

Descriptive statistics

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

Planned outcome analysis

Primary outcome

The incidences of hypoxia will be compared between the two groups using a χ^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 χ^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.²³ MAC is useful in patients who require repeated fiberoptic bronchoscopy as well as safe in respiratory depression when performed by experienced anaesthesiologists.²⁴ We will use 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, haemodynamic stability, recovery and discharge may also be improved by using TCI. The Ce of sufentanil and remifentanil used in the study are based on our previous unpublished research.

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

ETHICS AND DISSEMINATION

Ethics approval and consent to participate

This clinical study will be conducted following the Declaration of Helsinki. It will be conducted in compliance with the protocol, Good Clinical Practice, designated standard operating procedures, and local laws and regulations

relevant to the country of conduct. The study protocol was approved by the Ethics Committee of Shanghai Pulmonary Hospital of China (approval No. K19-122). Informed consent must be obtained from all patients.

Dissemination policy

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

Data collection, monitoring and management

Preoperative, intraoperative and postoperative follow-up data will be collected from electronic medical records, monitoring machines and relevant manual records by the research staff (YuZ). All electronic and handwriting data will be stored on a password-protected computer. Data will be recorded on a standardised paper form (online supplemental file 3) and subsequently double-entered using Epidata software V.3.1 by two trained RAs. Data and safety monitoring will be the responsibility of the principle investigator (JL).

Trial status

The recruitment commenced in February 2021. It is anticipated that recruitment will end by June 2023. The version number of the protocol are V.3.0.

Patient and public involvement

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

Author affiliations

¹Department of Anaesthesiology, Shanghai Pulmonary Hospital, School of Medicine, Tongji University, Shanghai, China

²School of Life Sciences and Technology, Tongji University, Shanghai, China

³Department of Anaesthesiology, Changhai Hospital, Naval Medical University, Shanghai, China

Contributors WW and YiZ designed the study, they are joint first author. WW and YuZ wrote the manuscript together. YiZ provided substantial contributions to the conception and design of the study, wrote the statistical analysis plan and estimated the sample size. JL 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.

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

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability

of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Wei Wu <http://orcid.org/0000-0002-8001-153X>

REFERENCES

- Ernst A, Silvestri GA, Johnstone D, *et al*. Interventional pulmonary procedures: guidelines from the American College of chest physicians. *Chest* 2003;123:1693–717.
- José RJ, Shaefi S, Navani N. Anesthesia for bronchoscopy. *Curr Opin Anaesthesiol* 2014;27:453–7.
- McCambridge AJ, Boesch RP, Mullon JJ. Sedation in bronchoscopy: a review. *Clin Chest Med* 2018;39:65–77.
- British Thoracic Society Bronchoscopy Guidelines Committee, a Subcommittee of Standards of Care Committee of British Thoracic Society. British thoracic Society guidelines on diagnostic flexible bronchoscopy. *Thorax* 2001;56 Suppl 1:i1–21.
- Maguire GP, Rubinfeld AR, Trembath PW, *et al*. Patients prefer sedation for fibreoptic bronchoscopy. *Respirology* 1998;3:81–5.
- Putinati S, Ballerin L, Corbetta L, *et al*. Patient satisfaction with conscious sedation for bronchoscopy. *Chest* 1999;115:1437–40.
- Emam W, Mostafa Y, Madkour A, *et al*. Bronchoscopic management as an alternative treatment in non-operable benign tracheal stenosis. *Int J Clin Pract* 2021;75:e14058.
- McGrath EE, Warriner D, Anderson P. The insertion of self expanding metal stents with flexible bronchoscopy under sedation for malignant tracheobronchial stenosis: a single-center retrospective analysis. *Arch Bronconeumol* 2012;48:43–8.
- Medford ARL, Bennett JA, Free CM, *et al*. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA): applications in chest disease. *Respirology* 2010;15:71–9.
- Scott LJ, Perry CM. Remifentanyl. *Drugs* 2005;65:1793–823.
- Berkenbosch JW, Graff GR, Stark JM, *et al*. Use of a remifentanyl-propofol mixture for pediatric flexible fiberoptic bronchoscopy sedation. *Paediatr Anaesth* 2004;14:941–6.
- Natalini G, Fassini P, Seramondi V. Remifentanyl vs. fentanyl during interventional rigid bronchoscopy under general anaesthesia and spontaneous assisted ventilation. *European Journal of Anaesthesiology | EJA* 1999;16.
- Lee H, Choe YH, Park S. Analgosedation during flexible fiberoptic bronchoscopy: comparing the clinical effectiveness and safety of remifentanyl versus midazolam/propofol. *BMC Pulm Med* 2019;19:240.
- Ryu JH, Lee SW, Lee JH, *et al*. Randomized double-blind study of remifentanyl and dexmedetomidine for flexible bronchoscopy. *Br J Anaesth* 2012;108:503–11.
- Rezaiguia-Delclaux S, Laverdure F, Kortchinsky T, *et al*. Fiber optic bronchoscopy and remifentanyl target-controlled infusion in critically ill patients with acute hypoxaemic respiratory failure: a descriptive study. *Anaesth Crit Care Pain Med* 2017;36:273–7.
- Caron M, Parrot A, Elabbadi A, *et al*. Pain and dyspnea control during awake fiberoptic bronchoscopy in critically ill patients: safety and efficacy of remifentanyl target-controlled infusion. *Ann Intensive Care* 2021;11:1–9.
- Zha B, Wu Z, Xie P, *et al*. Supraglottic jet oxygenation and ventilation reduces desaturation during bronchoscopy under moderate to deep sedation with propofol and remifentanyl: a randomised controlled clinical trial. *Eur J Anaesthesiol* 2021;38:294–301.
- Derronde N, Lebrun F, Levron J-C, *et al*. Influence of preoperative opioid on postoperative pain after major abdominal surgery: sufentanyl TCI versus remifentanyl TCI. A randomized, controlled study. *Br J Anaesth* 2003;91:842–9.
- Kaur H, Dhooira S, Aggarwal AN, *et al*. A Randomized Trial of 1% vs 2% Lignocaine by the Spray-as-You-Go Technique for Topical Anesthesia During Flexible Bronchoscopy. *Chest* 2015;148:739–45.
- Ryu JH, Lee SW, Lee JH, *et al*. Randomized double-blind study of remifentanyl and dexmedetomidine for flexible bronchoscopy. *Br J Anaesth* 2012;108:503–11.



- 21 Qin Y, Li LZ, Zhang XQ, *et al.* Supraglottic jet oxygenation and ventilation enhances oxygenation during upper gastrointestinal endoscopy in patients sedated with propofol: a randomized multicentre clinical trial. *Br J Anaesth* 2017;119:158–66.
- 22 Puchner W, Egger P, Pühringer F, *et al.* Evaluation of remifentanyl as single drug for awake fiberoptic intubation. *Acta Anaesthesiol Scand* 2002;46:350–4.
- 23 ASA. Position on monitored anesthesia care 2018.
- 24 Hong KS, Choi EY, Park D-A, *et al.* Safety and efficacy of the moderate sedation during flexible bronchoscopic procedure: a systematic review and meta-analysis of randomized controlled trials. *Medicine* 2015;94:e1459–e59.