


BMJ Open Efficacy of perioperative intravenous lidocaine infusion on postoperative pulmonary complications in patients undergoing video-assisted thoracoscopic lung resection surgery: protocol for a randomised controlled trial

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ABSTRACT

Introduction Postoperative pulmonary complications (PPCs) are the most common complications following thoracoscopic surgery, resulting in increased hospital costs and perioperative mortality. Studies have shown that intravenous lidocaine infusion can exert its anti-inflammatory properties by reducing the release of proinflammatory cytokines. This study is designed to investigate whether intraoperative intravenous lidocaine infusion can reduce the incidence of PPCs in adult patients undergoing video-assisted thoracoscopic lung resection surgery.

Methods and analysis This single-centre, double-blinded study will enrol 366 patients scheduled for video-assisted thoracoscopic lung resection surgery. Patients will be randomly assigned to the lidocaine or placebo infusion group in a 1:1 ratio. The lidocaine group will receive lidocaine intravenously during the intraoperative period, while the placebo group will be administered normal saline at an equal volume, infusion rate and timing. The primary outcome is the incidence of PPCs within 7 days following surgery. The secondary outcomes are quality of postoperative recovery 40 scores; length of hospital stay (determined by the number of days from admission to discharge); incidence of moderate to severe pain within 24 and 48 hours at rest and when coughing; incidence of additional rescue analgesics use and incidence of adverse events.

Ethics and dissemination The study was reviewed and approved by the Ethics Committee of Sichuan Provincial People's Hospital (approval no. 20222241). Written informed consent will be obtained from all patients before randomisation. The results of this trial will be disseminated in a peer-reviewed journal.

Trial registration number ChiCTR2200061979.

INTRODUCTION

Postoperative pulmonary complications (PPCs) are common, especially in patients undergoing thoracic surgery,¹ and are often

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The study includes an appropriate sample size, randomisation and a double-blind, placebo-controlled design, to provide reliable data for the effect of lidocaine on postoperative pulmonary complications in patients undergoing thoracoscopic lung resection surgery.
- ⇒ The full analysis set consists of all randomised patients according to the intention-to-treat principle; a per-protocol analysis set will be used for the sensitivity analyses.
- ⇒ Use of the quality of postoperative recovery 40 scores will increase measurement precision for the core quality of recovery domains.
- ⇒ An important limitation of the study is the single-centre setting.

associated with delayed recovery, perioperative mortality, increased hospital costs, prolonged hospital stays, increased chances of rehospitalisation and decreased long-term survival.^{2,3} The incidence of PPCs after video-assisted thoracoscopic (VATS) lung resection surgery is still high owing to one-lung ventilation, nerve injury, inherent lung disease of patients, higher intraoperative inhaled oxygen concentration, inflammatory response to trauma and acute or chronic pain.^{3,4} Currently, some interventions, such as prophylactic respiratory physiotherapy, prophylactic mucolytics, enhanced recovery pathways, lung-protective intraoperative ventilation, goal-directed haemodynamic therapy and other strategies have contributed to a possible reduction in PPCs. However, the evidence for these interventions is predominantly of low quality.⁵

Surgery has a significant impact on the body's proinflammatory and anti-inflammatory pathways. The anti-inflammatory component could induce infections, while the proinflammatory component could cause postoperative complications (eg, pain, lung injury and ileus). Previous studies have shown that perioperative intravenous lidocaine infusion could reduce some of these proinflammatory responses.⁶ Some benefits of perioperative lidocaine infusion have been demonstrated, including reductions in pain, nausea, ileus duration, opioid requirement and length of hospital stay.⁷ During thoroscopic surgery, lung atrophy on the affected side, imbalance of ventilation and blood flow ratio, mechanical ventilation and surgical operations can cause damage to alveolar epithelial cells, release inflammatory substances and lead to lung injury. Therefore, it is unclear whether perioperative lidocaine infusion can reduce PPCs.^{8,9} We hypothesise that perioperative intravenous lidocaine infusion compared with placebo can reduce the incidence of PPCs and improve the quality of postoperative recovery in adult patients undergoing VATS lung resection surgery.

METHODS AND ANALYSIS

Study design, approval and registration

The present study is a single-centre, double-blind, randomised controlled trial. The protocol is designed in accordance with the Standard Protocol Items for Clinical trials: Recommendations for Interventional Trials 2013 statement.¹⁰ All procedures were performed in accordance with the Declaration of Helsinki. The study was reviewed and approved by Sichuan Provincial People's Hospital Institutional Review Board (approval no. 20222241), and has been registered at chictr.org.cn (ChiCTR2200061979). The study flow chart and the study schedule are detailed in [figures 1 and 2](#), respectively.

Participants and informed consent

All participants scheduled for VATS lung resection surgery at Sichuan Provincial People's Hospital will be screened. All study participants or legal guardians will sign the informed written consent form (online supplemental file 1) before enrolment. Patients who participate in the study will have the right to obtain all relevant information and be allowed to withdraw their consent or discontinue participation at any time during the study.

Inclusion criteria

The inclusion criteria are as follows: participants scheduled for VATS lung resection surgery (wedge, segment and lobe) at Sichuan Provincial People's Hospital, aged between 18 and 80 years, American Society of Anaesthesiologists (ASA) status I–III, with signed informed consent forms and willingness to cooperate with clinical health-care practitioners.

Exclusion criteria

The exclusion criteria are as follows: patients with severe mental illness, such as schizophrenia, depression, dementia, etc; severe hepatic insufficiency (aspartate aminotransferase or alanine transaminase or bilirubin >2.5 times the upper limit of normal), renal impairment (creatinine clearance <60 mL/min); participants who are allergic to amide local anaesthetics or have a history of seizures; patients with Ass syndrome, pre-excitation syndrome and severe heart block (including sinus, atrio-ventricular and intraventricular block); history of chronic pain or opioid dependence.

Randomisation, allocation and concealment

Participants will be randomised into the lidocaine and saline (control) groups in a 1:1 ratio. Randomisation will be performed with a random number list generated by a computer. Opaque sealed envelopes containing the patient's order on the outside and the participant's group on the inside will be used to ensure that the group allocation is not disclosed. Before surgery, the opaque sealed envelope with the patient's distribution information will be opened by the research investigator. According to the group allocation, a 50 mL syringe labelled 'research solution' consisting of lidocaine or normal saline will be prepared by a research investigator not in the operating room. The participants, surgeons, anaesthesiologists and physicians performing the follow-up will be blinded to the group assignment.

Intervention

In the lidocaine group, at the end of the induction of general anaesthesia, an intravenous lidocaine bolus of 1.5 mg/kg will be administered, followed by a continuous infusion of intravenous lidocaine at 2 mg/kg/hour until the end of surgery. The control group will receive the same volume of normal saline intravenously during anaesthesia.

Anaesthesia management

Preoperative visit and education

The day before surgery, we will instruct patients about the quality of postoperative recovery 40 (QoR-40) scores.¹¹ The QoR-40 scores comprise 40 items on the following five dimensions: physical comfort (12 items), physical independence (5 items), emotional state (9 items), psychological support (7 items) and pain (7 items). All included patients will be asked to complete the QoR-40 scores preoperatively (online supplemental file 2).

Induction and maintenance of anaesthesia

All anaesthetic procedures will be implemented in a standardised manner. Without premedication, the upper limb vein access of patients will be established, and the patients will be routinely monitored using electrocardiography, pulse oximetry, invasive arterial blood pressure and cerebral state index (CSI) in the operating room. After preoxygenation, general anaesthesia will be induced by intravenous propofol 1.5–2.5 mg/

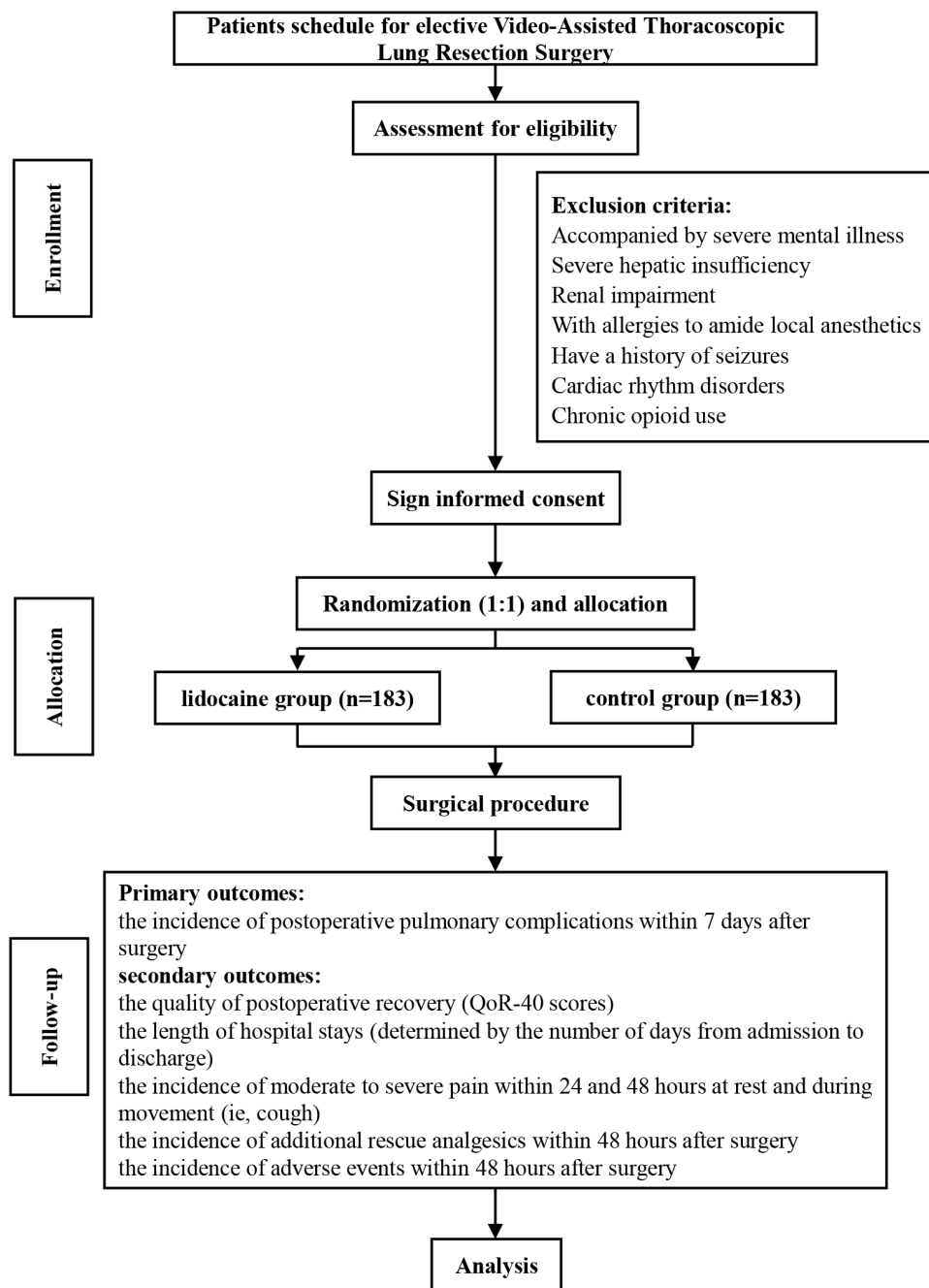


Figure 1 Study flow chart.

kg, sufentanil 0.3 µg/kg and cisatracurium 0.2 mg/kg. Anaesthesia will be maintained using remifentanyl 0.1–0.2 µg/kg/min and sevoflurane inhalation to stabilise CSI within 40–60. Sufentanil 0.1 µg/kg will be given before the skin incision, while dezocine 5 mg will be administered 15 min before the anticipated end of surgery. Intraoperatively, if the ECG detects arrhythmias or ventricular fibrillation, or if the patient has extremely low blood pressure, we will first rule out the surgical intervention (eg, pulling on the tracheal bulge) or anaesthetic drugs as the cause (eg, hypotension after induction). Next, we will investigate any issues induced by equipment signal interference or equipment error.

Lidocaine will be stopped only after excluding the above reasons. Moreover, we will take a blood sample to measure the lidocaine concentration.

At the end of VATS lung resection, 15 mL 0.5% ropivacaine will be administered by the thoracic surgeon via thoracoscopic visualisation to achieve intercostal nerve block. On skin closure, desflurane and remifentanyl will be stopped, and a patient-controlled anaesthesia consisting of sufentanil (0.03 µg/kg), dezocine (10 mg) and tropisetron (5 mg) will be allocated to patients for postoperative analgesia. Patients will then be extubated in the operating room and shifted to the postanesthesia care unit (PACU).

TIMEPOINTS	STUDY PERIOD						
	Enrolment	Allocation		Postallocation			
	Preoperative	0d	Surgery	1d	2d	Discharge from the hospital	Within 7d
ENROLMENT:							
Eligibility screen	X						
Inform consent	X						
Allocation		X					
INTERVENTIONS							
Lidocaine group			X				
Saline group			X				
ASSESSMENTS							
Baseline variables	X						
Intraoperative data			X				
QoR-40 scores	X			X			
Moderate to severe pain				X	X		
Additional rescue analgesics				X	X		
Adverse events				X	X		
Length of hospital stay						X	
Postoperative pulmonary complications				X	X	X	X

Figure 2 Schedule of enrolment, interventions and assessments. QoR-40, quality of postoperative recovery 40.

Postoperative management

Patients will be monitored and the modified Aldrete score will be recorded in the PACU. The severity of pain will be evaluated using the Numerical Rating Scale (NRS, 0=no pain, 1–3=mild pain, 4–6=moderate pain, 6–10=severe pain). Sufentanil will be administered at a dose of 0.1 µg/kg once the patient's NRS score reaches ≥4. Patients will be discharged from the PACU after achieving a modified Aldrete score ≥9.

Follow-up

All participants will be followed up from the day before surgery to 7 days after the intervention. The QoR-40 scores will be assessed on postoperative day 1. The follow-up includes a record of the following: PPCs, the QoR-40 scores, NRS scores, the use of additional rescue analgesics and adverse events. The follow-up will be completed by trained interviewers blinded to the group allocation. Patients will be excluded from the study if any of the following situations occur: the patient has an allergic reaction, severe cardiovascular events that cannot be managed with symptomatic treatment and the patient is unwilling to continue the study.

Data collection

Baseline and intraoperative data

The following preoperative data were recorded: age, sex, height, weight, ASA status and comorbidities. The

intraoperative data collected will be as follows: type of surgery, intraoperative bleeding, duration of surgery and anaesthesia.

Postoperative data

Every morning for the first 7 days after surgery, patients will be followed up closely and evaluated in the hospital wards and if the patients are discharged, telephone follow-up will be used instead. The quality of recovery will be assessed using the QoR-40 scores 24 hours after surgery. Pain at rest and during motion will be evaluated using an 11-point NRS scale (0=no pain, 10=worst pain imaginable) 24 and 48 hours after surgery. Adverse events will be recorded within 48 hours after surgery. The length of hospital stay will be collected from each patient. PPCs will be recorded up to 7 days after surgery.

Outcomes

Primary outcome

The primary outcome is the incidence of PPCs within 7 days following surgery.

Secondary outcomes

The secondary outcomes are: (1) the quality of postoperative recovery (QoR-40 scores); (2) the length of hospital stay (determined by the number of days from admission to discharge); (3) the incidence of moderate to severe

pain within 24 and 48 hours at rest and when coughing; (4) the incidence of additional rescue analgesics use; (5) the incidence of opioid-related adverse events. The definitions of all outcomes are described in online supplemental file 3.

Assessment of safety

The interventional treatment will be implemented in patients with standard haemodynamic monitoring in the setting of a fully equipped operation room, which can ensure immediate detection and treatment of adverse events. Administration of lidocaine will be immediately stopped if the participant shows any relevant adverse events, such as ECG irregularities, drowsiness, light-headedness, metallic taste, peri-oral numbness and tinnitus. Twenty per cent fat emulsion will be prepared routinely in the operating room to manage severe local anaesthetic poisoning. In addition, after leaving the operating room, all patients will be closely monitored for adverse events, first in the PACU and later in the surgical ward. All study-related adverse event details, such as the nature, severity, and treatment received, will be recorded on the case report forms until they are resolved, and the patient is stable. Whenever an adverse event occurs, it will be reported to the principal investigator immediately, and the severity, cause and consequences will be determined. The principal investigator will report suspected or unexpected serious adverse reactions to the national health authorities.

Sample size calculation

Our unpublished pilot investigative data showed that the incidence of PPCs after VATS lung resection surgery was approximately 40%. We assumed a relative 35% difference in the primary outcome would be appropriate and clinically relevant. Assuming a rounded 40% rate of PPCs, we calculated that a total sample size of 366 patients (183 in each group) would have an 80% power to detect a relative risk reduction of 35% in PPCs between groups at a two-sided alpha level of 0.05 and an additional dropout rate of 5%. We plan to recalculate the sample size using only the incidence of PPCs in the control group after half of the originally planned sample size is recruited and to use the new sample size as the final sample size.¹² The investigators will be blinded to all data on the principal exposures during the sample size re-estimation.

Statistical analysis

A biomedical statistician will perform the study's statistical review before the peer-review submission. Multiple imputation will be used for missing data.¹³ After checking for normality with the Kolmogorov-Smirnov test, continuous variables will be presented as mean±SD or medians (IQR). Qualitative data will be presented as counts and percentages. Baseline data will be compared using Student's t-test or non-parametric test, χ^2 test or Fisher's exact test as appropriate. The QoR-40 scores and the length of stay will be compared between the two groups

using the Student's t-test or Mann-Whitney U-test. The incidence of PPCs, the incidence of moderate to severe pain within 24 and 48 hours at rest and when coughing, the incidence of additional rescue analgesics use and the incidence of adverse events will be compared between the two groups using the χ^2 test or Fisher's exact test. P values will be two-tailed, and those <0.05 will be considered statistically significant. Effect sizes with a 95% CI will be calculated if necessary. The full analysis set consists of all randomised patients according to the intention-to-treat principle and per-protocol set, the secondary analysis set, is used for the sensitivity analyses.

Data management and quality control

All data collected in accordance with the study protocol will be manually transferred from the case report forms to an electronic database sheet by two separate trained researchers and proofread to ensure correct data. Electronic data will be stored in a folder with restricted access on a protected server of Sichuan Provincial People's Hospital. Paper-based data are stored in a locked office at the Department of Anesthesiology, Sichuan Provincial People's Hospital. Moreover, patient information will be anonymous, including identity document number, inpatient number, name and telephone number, to protect privacy. After the trial is completed, the folder will be locked and the researchers can no longer modify the data. The data will be deleted as soon as they are no longer used for research. However, paper-based data will be sealed in hospital for 10 years.

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.

Ethics and dissemination

This trial follows the principle of the Declaration of Helsinki. The study protocol and informed consent form were approved by the Ethics Committee of Sichuan Provincial People's Hospital (approval no. 20222241). Written informed consent will be obtained from all patients before randomisation. We expect to publish the findings in a peer-reviewed journal and share it at academic conferences.

DISCUSSION

The present study is designed to explore the effects of lidocaine on the incidence of PPCs in patients undergoing VATS lung resection surgery. Patients will receive an intravenous bolus of 1.5 mg/kg lidocaine, followed by a continuous infusion of intravenous lidocaine at 2 mg/kg/hour until the end of surgery.

PPCs are associated with poor short-term and long-term outcomes following VATS lung resection.^{3 14 15} Its occurrence may be related to extensive tissue destruction, one lung ventilation and proinflammatory cytokines.¹⁶

Surgery triggers inflammation and subsequent reductions in pulmonary compliance and ventilation function, and secretion retention leads to pulmonary complications.^{17,18} Perioperative lidocaine infusion can attenuate some proinflammatory effects by acting on the molecular targets of the inflammatory signalling pathway.^{6,7} A previous study by Lv *et al*¹⁹ demonstrated that lidocaine administration could significantly reduce the release of interleukin (IL)-6, IL-10 and tumour necrosis factor- α , consistent with the results of studies by Song *et al* and Yardeni *et al*.^{20,21}

Safety is an important aspect that cannot be ignored. To date, there have only been a few reported adverse events related to continuous intraoperative lidocaine infusion at 1.5–3 mg/kg/hour.^{6,22,23} The lidocaine dosage of the present study has been repeatedly demonstrated to be safe and did not induce relevant clinical side effects.²⁴ In the present study, patients with hepatic or renal impairment will be excluded to ensure the safety of lidocaine infusion. To identify and manage potential adverse events timely, all patients will be closely monitored after drug administration. Lidocaine will be discontinued immediately if any related adverse events arise, such as ECG irregularities, light-headedness, metallic taste, peri-oral numbness and tinnitus. Furthermore, 20% fat emulsion will be prepared to counteract any local anesthetic-related toxicity.

There are some limitations to our study. First, this trial is a single-centre study, which may result in biased findings that cannot be generalised to other regions or ethnicities. After the publication of the results of this study, we plan to conduct another multicentre randomised controlled trial. Second, the surgical skill of surgeons is associated with the occurrence of postoperative complications²⁵; however, we cannot accurately assess the surgeons' skill levels. Finally, the dose of intravenous lidocaine infusion was chosen at our discretion, and we did not set up a different dose group, which may lead to poor results if the selected dose is inadequate.

In summary, this randomised, placebo-controlled, double-blinded study is designed to evaluate the efficacy of perioperative intravenous lidocaine infusion in reducing PPCs in patients undergoing VATS lung resection surgery. If the present study's hypothesis is validated, perioperative lidocaine infusion may have a role in the enhanced recovery after surgery (ERAS) protocol, serving as a new strategy to reduce the incidence of PPCs and accelerate patient recovery.

Trial status

Recruitment started on the 10 August 2022 and is expected to end in June 2023. Data collection and analysis will be completed within 1 month of trial completion and we expect to complete the submission of the research manuscript to a peer-reviewed journal before 30 September 2023.

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Contributors FW conceived of the study. YH and FW designed the study protocol. FW drew up the statistical plan and drafted the initial manuscript. MZ, QLU, ZZ and LL helped with its implementation. SZ and QLe critically revised the manuscript. SZ and QLe sought funding. All authors approved the final manuscript.

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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.

Data availability statement Data are available on reasonable request. The raw data are available from the corresponding author with applicable reason.

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REFERENCES

- Colquhoun DA, Leis AM, Shanks AM, *et al*. A lower tidal volume regimen during one-lung ventilation for lung resection surgery is not associated with reduced postoperative pulmonary complications. *Anesthesiology* 2021;134:562–76.
- Mathis MR, Duggal NM, Likosky DS, *et al*. Intraoperative mechanical ventilation and postoperative pulmonary complications after cardiac surgery. *Anesthesiology* 2019;131:1046–62.
- Yan T, Liang X-Q, Wang G-J, *et al*. Prophylactic penehyclidine inhalation for prevention of postoperative pulmonary complications in high-risk patients: a double-blind randomized trial. *Anesthesiology* 2022;136:551–66.
- Wang B, Chen Z, Zhao R, *et al*. Development and validation of a nomogram to predict postoperative pulmonary complications following thoracoscopic surgery. *PeerJ* 2021;9:e12366.
- Odor PM, Bampoe S, Gilhooly D, *et al*. Perioperative interventions for prevention of postoperative pulmonary complications: systematic review and meta-analysis. *BMJ* 2020;368:m540.
- Hollmann MW, Durieux ME. Local anesthetics and the inflammatory response: a new therapeutic indication? *Anesthesiology* 2000;93:858–75.

- 7 Dunn LK, Durieux ME. Perioperative use of intravenous lidocaine. *Anesthesiology* 2017;126:729–37.
- 8 Lugg ST, Agostini PJ, Tikka T, *et al.* Long-term impact of developing a postoperative pulmonary complication after lung surgery. *Thorax* 2016;71:171–6.
- 9 Meng J, Lv Q, Yao J, *et al.* Effect of dexmedetomidine on postoperative lung injury during one-lung ventilation in thoracoscopic surgery. *Biomed Res Int* 2020;2020:1–8.
- 10 Chan A-W, Tetzlaff JM, Gøtzsche PC, *et al.* SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346:e7586.
- 11 Myles PS, Weitekamp B, Jones K, *et al.* Validity and reliability of a postoperative quality of recovery score: the QoR-40. *Br J Anaesth* 2000;84:11–15.
- 12 Wijesundera DN, Pearse RM, Shulman MA, *et al.* Assessment of functional capacity before major non-cardiac surgery: an international, prospective cohort study. *Lancet* 2018;391:2631–40.
- 13 Li P, Stuart EA, Allison DB. Multiple imputation: a flexible tool for handling missing data. *JAMA* 2015;314:1966–7.
- 14 Shi Y, Yu H, Huang L, *et al.* Postoperative pulmonary complications and hospital stay after lung resection surgery: a meta-analysis comparing nonintubated and intubated anesthesia. *Medicine* 2018;97:e10596.
- 15 Agostini PJ, Lugg ST, Adams K, *et al.* Risk factors and short-term outcomes of postoperative pulmonary complications after VATS lobectomy. *J Cardiothorac Surg* 2018;13:1–8.
- 16 Yan G, Chen J, Yang G, *et al.* Effects of patient-controlled analgesia with hydromorphone or sufentanil on postoperative pulmonary complications in patients undergoing thoracic surgery: a quasi-experimental study. *BMC Anesthesiol* 2018;18:1–8.
- 17 Duggan M, Kavanagh BP. Pulmonary atelectasis: a pathogenic perioperative entity. *Anesthesiology* 2005;102:838–54.
- 18 Rock P, Freed AN, Nyhan DP, *et al.* Thoracotomy increases peripheral airway tone and reactivity. *Am J Respir Crit Care Med* 1995;151:1047–52.
- 19 Lv X, Li X, Guo K, *et al.* Effects of systemic lidocaine on postoperative recovery quality and immune function in patients undergoing laparoscopic radical gastrectomy. *Drug Des Devel Ther* 2021;15:1861–72.
- 20 Song X, Sun Y, Zhang X, *et al.* Effect of perioperative intravenous lidocaine infusion on postoperative recovery following laparoscopic cholecystectomy—a randomized controlled trial. *Int J Surg* 2017;45:8–13.
- 21 Yardeni IZ, Beilin B, Mayburd E, *et al.* The effect of perioperative intravenous lidocaine on postoperative pain and immune function. *Anesth Analg* 2009;109:1464–9.
- 22 Sun Y, Li T, Wang N, *et al.* Perioperative systemic lidocaine for postoperative analgesia and recovery after abdominal surgery: a meta-analysis of randomized controlled trials. *Dis Colon Rectum* 2012;55:1183–94.
- 23 Gianelly R, von der Groeben JO, Spivack AP, *et al.* Effect of lidocaine on ventricular arrhythmias in patients with coronary heart disease. *N Engl J Med* 1967;277:1215–9.
- 24 Weibel S, Jelting Y, Pace NL, *et al.* Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery in adults. *Cochrane Database Syst Rev* 2018;6:CD009642.
- 25 Stulberg JJ, Huang R, Kreutzer L, *et al.* Association between surgeon technical skills and patient outcomes. *JAMA Surg* 2020;155:960–8.