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# Bilevel positive airway pressure ventilation to prevent hypoxaemia during gastroscopy under sedation in patients at risk of hypoxaemia: study protocol for a prospective randomised controlled trial

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## ABSTRACT

**Introduction** During sedation for gastroscopy, hypoxaemia represents the most common adverse event. The objective of this trial is to assess the efficacy and safety of bilevel positive airway pressure (BPAP) for the prevention of hypoxaemia, in comparison with nasal cannula oxygen therapy, among patients predisposed to hypoxaemia during sedation for gastroscopy.

**Methods and analysis** This randomised controlled trial (RCT) will include 616 patients at risk of hypoxaemia when undergoing gastroscopy, including those with advanced age, frailty, American Society of Anesthesiologists grades III–IV, obesity, obstructive sleep apnoea–hypopnoea syndrome, cardiac disease, respiratory disease and diabetes. The patients will be randomly assigned to either the BPAP or nasal cannula group in a 1:1 ratio. The primary analysis for this study will use the modified intention-to-treat analysis set. The primary outcome is defined as the incidence of hypoxaemia ($SpO_2$ 75%–90%, duration 5–60 s). Outcomes data will be compared using the $\chi^2$ or Fisher's exact tests. Effect sizes will be used to assess the clinical effects of the intervention using absolute risk differences and 95% CIs. To assess the efficacy of BPAP in different patient subgroups, analyses will be performed based on clinical characteristics and risk factors associated with hypoxaemia.

**Ethics and dissemination** The Ethics Committee of the First Affiliated Hospital of Zhengzhou University reviewed and approved this RCT (Scientific Research Ethics Review: 2023-KY-0815-003). Subsequently, the outcome will be published in peer-reviewed journals.

**Trial registration number** ChiCTR2400084596.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The combination of nasal masks and bilevel positive airway pressure for upper gastrointestinal endoscopic anaesthesia enables simultaneous endoscopy and effective airway management.
⇒ Propofol will be titrated according to the modified Observer's Assessment of Alertness/Sedation score and Bispectral Index monitoring to maintain an optimal level of sedation.
⇒ Due to the inherent characteristics of the airway intervention, blinding will not be feasible, which is the main limitation.

## INTRODUCTION

With a high incidence of gastric, oesophageal and colorectal cancers, digestive system tumours account for approximately 50% of the total incidence of malignant tumours.[1–3] Gastrointestinal endoscopy is a standard approach for investigating the digestive tract.[4–6] With the progress of anaesthesia technology and the emergence of anaesthetic drugs such as propofol, the proportion of painless gastrointestinal endoscopies has gradually increased. More than 90% of endoscopic examinations in developed countries are performed under sedation, for example, 98% in the USA,[7] 100% in Australia.[8 9] Propofol, which has a rapid onset, provides an ideal depth of sedation, and has a rapid recovery, is a sedative drug recommended by international guidelines during digestive endoscopy.[8 10 11] However, propofol can increase adverse events such as airway obstruction and respiratory depression.[12 13] Remifentanil is a highly effective and short-acting opioid characterised by rapid onset, quick recovery, precise analgesia, rapid metabolism, minimal impact from liver and kidney function, and strong controllability. These attributes significantly enhance patient comfort and safety during procedural

sedation, making it an ideal analgesic agent.[14 15] However, opioid-induced respiratory depression is one of its most serious adverse reactions, manifesting as reduced respiratory drive, diminished consciousness levels and upper airway obstruction. If not addressed promptly, it may lead to severe complications such as hypoxaemia, hypercapnia and even respiratory arrest.[16 17] Reducing adverse events and ensuring safety in the perioperative period for gastroscopy under sedation are the major problems that need to be solved.

Hypoxaemia is the most prevalent adverse effect during sedation, with an incidence ranging from 4% to 85%.[18–27] Patients over 60 years old,[28–32] and those with frailty,[22 28 33] obstructive sleep apnoea–hypopnoea syndrome,[34 35] obesity,[30 36] diabetes, cardiac disease, hypertension[37] and elevated American Society of Anesthesiologists (ASA) physical status classifications[26 38] are at risk during endoscopy under sedation. Corrective measures for hypoxaemia include oropharyngeal airway placement, mask-positive pressure ventilation and endotracheal intubation. These measures can result in serious adverse events, including operation interruption, prolonged operating time and severe hypoxaemia.[28 39] Severe or prolonged hypoxaemia can cause coronary artery ischaemia, permanent neurological damage and even lead to death.[40] Therefore, for the population at high risk for hypoxaemia, appropriate strategies are important to ensure effective ventilation and minimise the incidence of hypoxaemia during painless gastroscopy.

Improvement in the oxygen administration method is the main measure to prevent hypoxaemia during gastroscopy. New oxygen therapy methods, including nasal masks, high-flow nasal cannulas (NC)[41 42] and supraglottic jet oxygenation ventilation,[43] have been shown to be effective in reducing the incidence of hypoxaemia. However, there is an absence of non-invasive and effective ventilation methods to prevent hypoxaemia in the at-risk population. Bilevel positive airway pressure (BPAP) ventilation improves ventilation, avoids respiratory depression and achieves good results during sleep.[44–46] Studies have shown that BPAP ventilation significantly reduced the incidence of hypoxaemia during sedation in overweight individuals and those with obstructive sleep apnoea syndrome.[36 47] However, the efficacy of BPAP ventilation in preventing hypoxaemia during painless gastroscopy in all populations at risk of hypoxaemia remains uncertain, and large-sample studies are lacking.

Building on our previous research, our team has planned a prospective randomised controlled trial aimed at evaluating the effectiveness and safety of BPAP ventilation in the prevention of hypoxaemia in patients susceptible to this condition during sedation for gastroscopy. We posit that the BPAP ventilation approach will lower the incidence of hypoxaemia in at-risk individuals during painless gastroscopy compared with the conventional NC oxygenation method.

## METHODS AND ANALYSIS

### Design

This single-centre, prospective, randomised controlled study is planned to be conducted at the First Affiliated Hospital of Zhengzhou University in participants undergoing upper gastrointestinal examination under propofol sedation. Written informed consent was obtained from all participants prior to study initiation. Comprehensive details regarding consent procedures, including the complete consent documentation and verification processes, are thoroughly documented in online supplemental material (see: Participant Consent Form). Following informed consent, participants will be randomised into either the intervention group or the control group at a 1:1 ratio for separate intervention implementation. Figure 1 illustrates the flow chart that will guide the study.

### Participants

Inclusion criteria are as follows: (1) individuals aged 18 years or over; (2) gastroscopy performed under propofol sedation; (3) participants at risk of hypoxaemia meeting any of the following: age >60 years, frailty (FRAIL scale score ≥3,[48] ASA classification grades III–IV, body mass index (BMI) ≥30 $kg/m^2$, respiratory sleep apnoea or STOP-Bang score ≥3,[49] combined cardiac disease, combined respiratory diseases and diabetes (the definition of the combined diseases is provided in online supplemental appendix) and (4) signed informed consent form. The exclusion criteria are as follows: (1) individuals with tracheostomy; (2) patients with pneumothorax, pneumomediastinum, cerebrospinal fluid leak, craniocerebral trauma, intracranial trauma or intracranial gas accumulation not suitable for BPAP ventilation; (3) active bleeding or upper gastrointestinal bleeding not effectively controlled; (4) abnormal liver or kidney function; (5) giant vocal cord polyps, acute pharyngitis, tonsillitis or acute asthma attacks; (6) patients who are uncooperative, or allergic to propofol or emulsifier content; (7) the baseline pulse oximeter oxygen saturation is <95% and (8) participation in other clinical studies conducted within the previous 3 months.

### Randomisation and blinding

Preliminary screening of patients aged 18 years and over and secondary screening will be conducted according to the inclusion and exclusion criteria. Following confirmation of inclusion, an independent researcher will use a computer-generated random list to conduct simple randomisation. The researchers will remain unaware of the randomisation outcomes; only coauthors JC and YY will have access to the original randomisation table, while the remaining team members will remain uninformed. Participants will be allocated to either the BPAP group (group B) or the NC group (group N). As patients in this study can

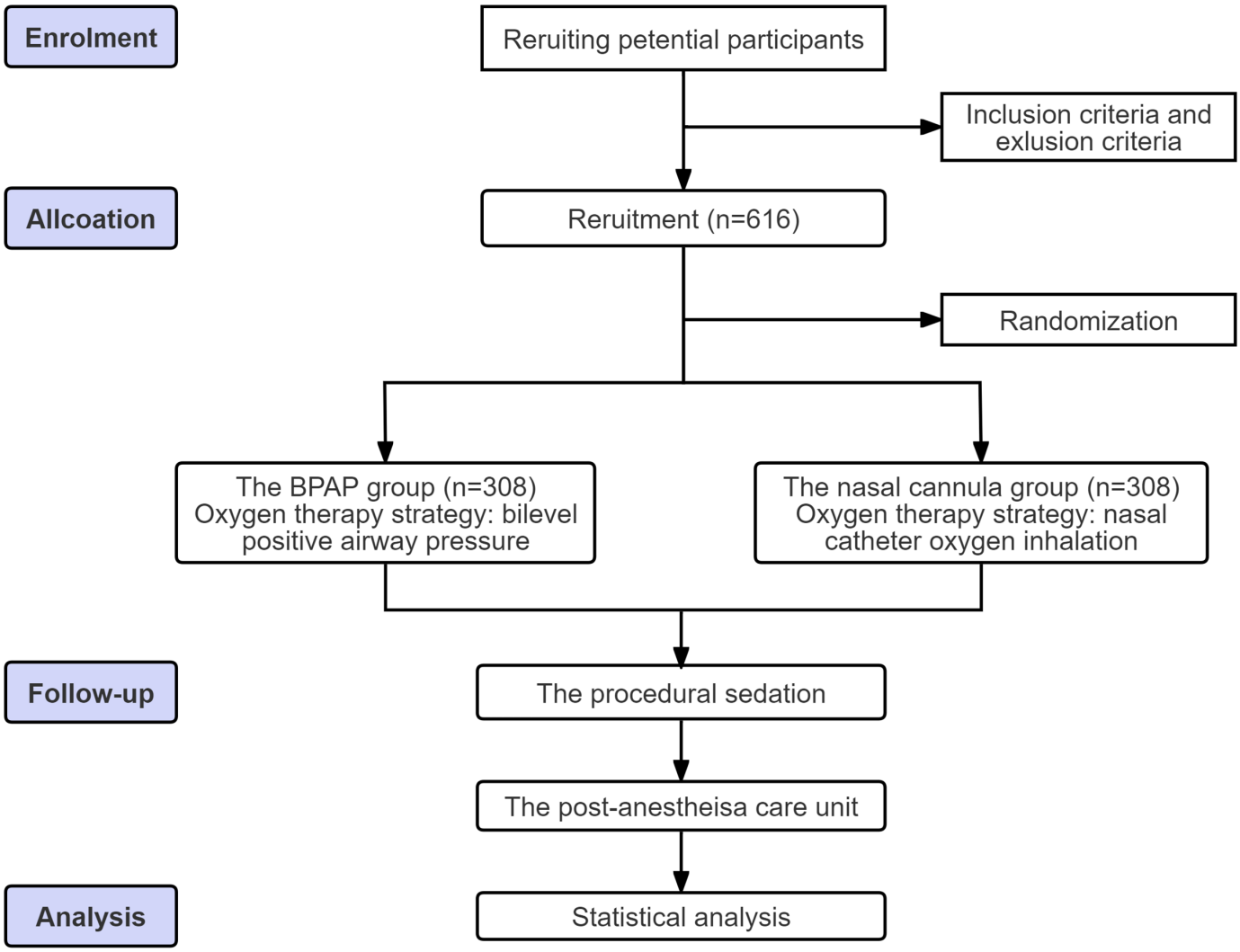


**Figure 1** Flow chart of study process. BPAP, bilevel positive airway pressure.

identify the oxygen therapy device, blinding cannot be implemented. To minimise bias, treatment group information will be hidden in opaque envelopes, to be opened on the day of surgery prior to anaesthesia induction. Preparations before gastroscopy, including the collection of medical record information and screening and group assignment, will be conducted by independent research nurses who are not involved in patient care. Postoperative outcome assessments and statistical analyses will be conducted by independent researchers who are blinded to the group assignments and are not involved in patient screening, sedation or anaesthesia management.

### Anaesthesia and study procedure

After obtaining informed consent signed by the participants, the enrolled patients will be examined by a team of endoscopists, nurses and experienced anaesthetists.

All patients will be fasted for 8 hours before gastroscopy, and lignocaine gel (10 g, containing lignocaine 0.2 g) which will be held in the throat for 1–2 min and then slowly swallowed into the oesophagus 5 min before the examination. For the procedure, the patient will be placed in the left lateral position, where pulse oximetry, measurement of the Bispectral Index (BIS), non-invasive blood pressure assessment, ECG monitoring and measurement of $SpO_2$ will occur following the administration of $O_2$ at 4 L/min through a NC for 3 min. Afterwards, patients in the BPAP group will don a nasal mask (BMC-N5B, Tianjin Jardine Jiaye Medical Technology), instead of a nasal oxygen cannula and will be connected to a non-invasive ventilator (Elisee 350, ResMed Paris SAS, Moissy-Gramayel, France). Patients will then be administered remifentanil (10 µg/mL, Hubei Yichang Renfu Pharmaceutical) at a dose of 0.5 µg/kg over a 10 s period. Subsequently, propofol (10 mg/mL; Jiangsu Enhua Pharmaceutical) will be administered as an intravenous bolus at an infusion rate of 2 mg/s. The initial dose will be 1.0 mg/kg for patients aged 50 years or over and 1.5 mg/kg for those under 50 years. This will be followed by repeated doses of 10–20 mg of propofol, titrated until the patient's Modified Observer's Assessment of Alertness/Sedation (MOAA/S) score is 1 or less.

After induction of anaesthesia, the intervention group will receive BPAP ventilation, whereas the NC group will

continue with inhaled oxygen continuously through the nasal oxygen cannula. BPAP ventilation will use the pressure support mode, with the initial positive end-expiratory pressure set at 4 cm $H_2O$ and inspiratory pressure support set at 8 cm $H_2O$. The apnoea backup ventilation parameters will be: apnoea backup ventilation time, 10 s; respiratory rate, 15 breaths/min; end-tidal volume, 500 mL. The pressure values will be adjusted according to the respiratory movements of the chest wall and tidal volume, with an established maximum inspiratory positive airway pressure (IPAP) of 18 cm $H_2O$ and maximum expiratory positive airway pressure (EPAP) of 6 cm $H_2O$. Endoscopic examination will be initiated by an experienced endoscopist, and insertion of the endoscope into the oral cavity is considered the start of surgery. During the surgery, anaesthesia will be maintained by continuous infusion of propofol at a rate of 4–10 mg/kg/hour. BIS monitoring will be used to assess the level of sedation, aiming to maintain a BIS value between 60 and 80. When the endoscopist has completed the examination, the procedure will be considered complete, and intravenous administration of propofol will be discontinued. Patients will be transferred to the post-anaesthesia care unit after scoring ≥3 on the MOAA/S scale postoperatively. In the procedural sedation process, the induction time refers to the period from the initial administration of the sedative until the MOAA/S score is ≤1. Procedural time is measured from insertion of the gastroscope into the oral cavity until completion of the examination. The recovery time refers to the duration from the cessation of drug injection to the point at which the postoperative MOAA/S score is ≥3. The sedation time is defined as the period from the onset of anaesthesia induction until the postoperative MOAA/S score reaches ≥3.

The protective measures taken during the painless gastroscopy procedure will be as follows: when a patient experiences hypoxaemia ($SpO_2$<90%, lasting>5 s), an airway management protocol is initiated (figure 2). The NC group will receive airway intervention measures, including (1) increasing the oxygen flow rate from 4 to 10 L/min, (2) lifting the patient's chin, (3) performing bag-mask ventilation, (4) inserting an oropharyngeal airway. For the BPAP group, first, the pressure values will be adjusted based on the respiratory movements of the chest wall and the target tidal volume, with the inspiratory airway pressure range set between 12 and 18 cm $H_2O$, and the expiratory airway pressure range between 4 and 6 cm $H_2O$. If hypoxaemia does not improve after adjusting the inspiratory and expiratory airway pressures for 1 min, airway intervention measures will be taken, the same as those for the NC group. All these interventions will be undertaken by experienced anaesthetists, as appropriate. If these measures do not effectively correct the severe hypoxaemia, intubation may be necessary.

## Data collection

The trial schedule is presented in table 1. The demographic and clinical baseline characteristics of all enrolled patients will be documented, including the collection and recording of the following information: age, sex, smoking history, BMI, comorbidities (cardiac, pulmonary, hepatic, renal, psychiatric, sleep apnoea, etc), ASA physical status classification, a history of heavy alcohol consumption, Mallampati score, STOP-Bang score, FRAIL score and use of benzodiazepines. Baseline vital signs (blood pressure, pulse and oxygen saturation) as well as preoperative comorbidities (hypertension, coronary heart disease, diabetes, liver cirrhosis and digestive system tumours) will also be recorded. The definitions of comorbidities are provided in online supplemental material.

During gastroscopy, oxygen saturation, BIS, mean arterial pressure and heart rate will be recorded at patient entry ($T_0$), before induction ($T_1$), at the minimum $SpO_2$ ($T_2$) and at the end of surgery ($T_3$). At the end of the procedure, the doses of propofol, remifentanil and intraoperative vasoactive drugs will be recorded, along with the operation, anaesthesia induction, sedation and awakening times.

Hypoxaemia and apnoea events during the diagnostic and therapeutic procedure will be recorded in a case report form (CRF). All adverse events occurring in the perioperative period will be documented using tools proposed by the International Sedation Task Force of the World Society of Intravenous Anaesthesia (SIVA).[48] Step 1 involves documenting the occurrence of adverse events. Step 2 describes adverse events, including respiratory and sedation-related adverse issues, such as subclinical respiratory depression, hypoxaemia, severe hypoxaemia and other respiratory complications, as well as vomiting/retching, myoclonus, emergence agitation, allergic reactions, bradycardia, tachycardia, hypotension, hypertension, heart failure and other sedation-related adverse events. Step 3 involves recording interventions to correct adverse events, including airway intervention measures, such as increasing the oxygen flow rate, chin lift, mask ventilation, insertion of an oropharyngeal airway, and intubation. Step 4 involves recording patient outcomes. Adverse events related to BPAP ventilation, such as dry eyes, nasal congestion and dryness of the mouth and nose, will also be documented.

## Data management and monitoring

All patient personal information and study data will be securely stored in a separate database, which is protected by passwords and logical validation procedures. This database will be regularly synchronised with backup systems to prevent data loss. The accuracy of data entry will be monitored by an independent supervisor. Any adverse events will be managed appropriately, thoroughly documented and routinely reviewed.

## Outcomes

The primary outcome is the incidence of hypoxaemia, defined as SpO2 levels between 75% and 90% lasting for 5 to 60 s. The secondary outcomes include: (1) duration of hypoxaemia; (2) number of hypoxaemia episodes; (3)

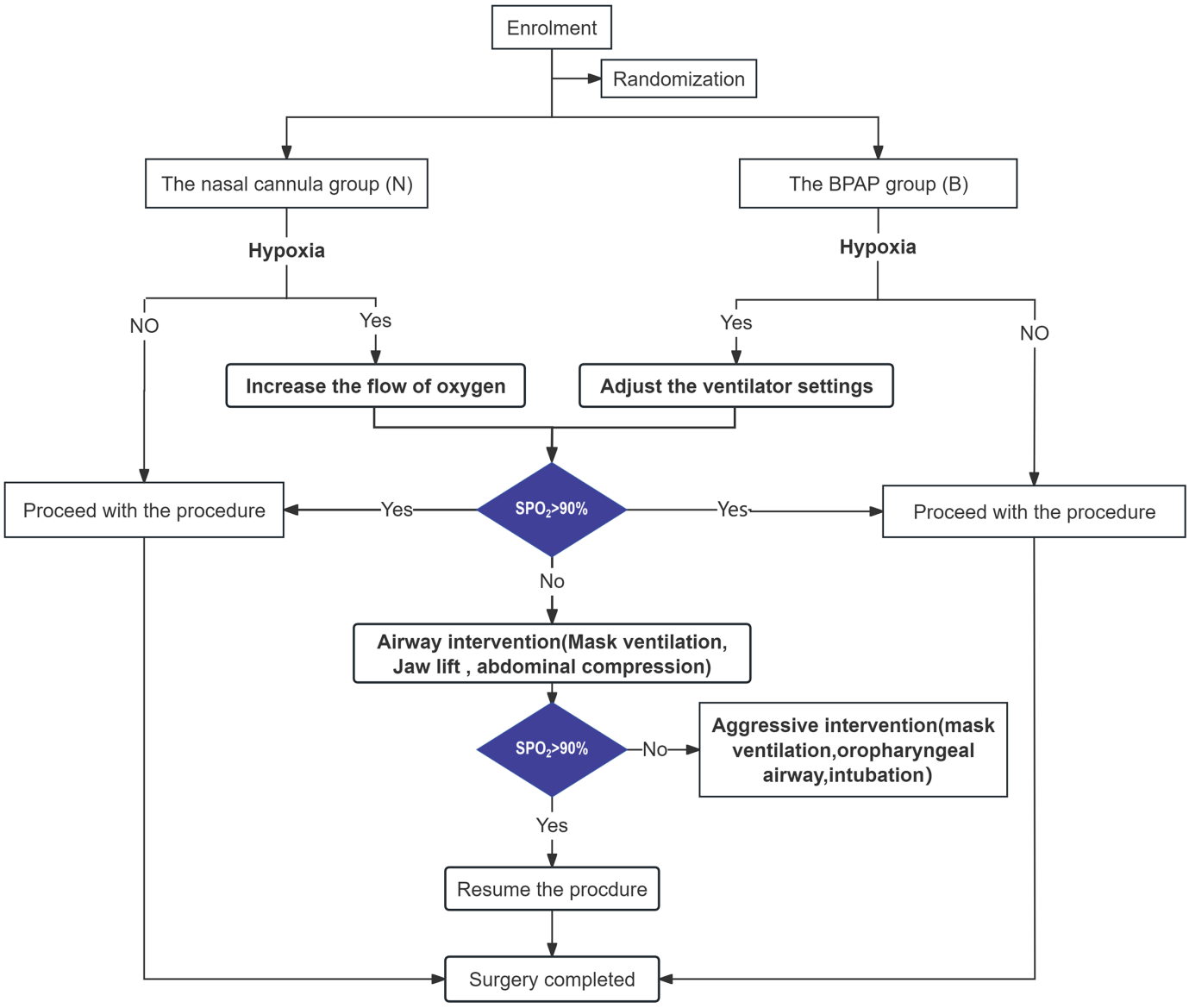


**Figure 2** Flow chart of the hypoxaemia management protocol. BPAP, bilevel positive airway pressure; $SpO_2$, peripheral oxygen saturation.

procedural features, including total dose of propofol, operation time, number of gastroscope intubations, wake time and time of sedation and (4) postoperative satisfaction score of patients, anaesthetists and endoscopists (satisfaction score 0–10, 0 indicating dissatisfaction, 10 indicating complete satisfaction).

Safety evaluations will be as follows: (1) SIVA sedation adverse events; (2) airway interventions, including increased oxygen flow, support of the mandible, mask ventilation, nasopharyngeal ventilation tube and endotracheal intubation and (3) BPAP ventilation-related adverse events, including complications such as dry eyes, pressure ulcers, nasal obstruction and gastric distension.

## Sample size

This is a prospective, two-group, randomised controlled trial, with the BPAP group as the intervention group and the NC group as the control. The primary outcome measure is the incidence of perioperative hypoxaemia. According to previous research, the incidence of perioperative hypoxaemia in the at-risk population is approximately 23%,[20 45 49] and the clinically meaningful absolute risk difference for hypoxaemia is 6%–25%.[18 43 47 49] We hypothesise that BPAP intervention will reduce the incidence of hypoxaemia from 23% to 12%. Controlling for type I error a=0.05 and ensuring a power (test efficacy) of 1–b=90%, according to 1:1 randomisation under a two-sided test, a sample size of 246 patients in each of the two groups was calculated by PASS V.15.0 software (NCSS). Considering a 20% loss to follow-up and refusal rate, a minimum of 308 participants per group, totalling at least 616 participants, will be required for the study.

## Statistical analysis

Statistical analyses will be performed using SPSS software (V.25.0; IBM). The main analysis set of this study will be a

Table 1 Schedule of enrolment, interventions and assessments

| Study period | Screening | Allocation | Examination | PACU |
|---|---|---|---|---|
| Enrolment | | | | |
| Inclusion criteria | × | | | |
| Exclusion criteria | × | | | |
| Informed consent | × | | | |
| Randomisation | × | | | |
| Demographic data | × | | | |
| Interventions | | | | |
| The BPAP group | | | •——• | |
| The nasal catheter group | | | •——• | |
| Assessments | | | | |
| Procedural sedative features | | × | × | |
| Vital sign | | × | × | |
| MOAA/S | | × | × | × |
| Hyoxaemia | | | × | × |
| Airway interventions | | | × | × |
| Adverse event | | | × | × |

BPAP, bilevel positive airway pressure; MOAA/S, Modified Observer's Assessment of Alertness/Sedation; PACU, post-anaesthesia care unit.

modified intention-to-treat dataset, which will include all randomised participants, except for those with revoked informed consent. As this study does not involve long-term follow-up, it is expected that missing data will be less than 5%, and missing values will be filled using multiple interpolations. For quantitative data, normally distributed data will be expressed as mean (SD), non-normally distributed data as median (IQ spacing), and categorical variables as quantity (rate) and standard mean difference.

The incidence of hypoxaemia, airway interventions, and other respiratory and sedation-related adverse events are categorical variables and will be analysed using the $\chi^2$ or Fisher's exact test, and the effect size will be assessed using the absolute risk difference and 95% CI. Quantitative data will be analysed using the t-test or Mann–Whitney U test, based on the data type. The hypothesis tests will be considered statistically significant at $p<0.05$.

To further evaluate the efficacy of the intervention measures in different populations at risk for hypoxaemia, a subgroup analysis will be conducted based on the risk factors for hypoxaemia. The basis for subgroup classification includes: age >60 years, frailty, BMI >25 kg/m$^2$, STOP-Bang score ≥3, the presence of invasive procedures, pulmonary disease, heart disease and diabetes. Because multiple comparisons may lead to type I errors, a $p<0.025$ (Bonferroni correction) will be considered statistically significant.

## 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

The research will be conducted at the First Affiliated Hospital of Zhengzhou University. The study's ethical aspects and communication protocols obtained approval from the hospital's Ethics Committee on 13 September 2023. After providing informed consent, patients will be enrolled in the study, and researchers must ensure rigorous adherence to the research plan and meticulous completion of the CRFs. Participants have the right to withdraw their consent to participate at any time without providing a reason. Paper-based CRF will be used in the research process and regarded as source documents. Two designated members of the research team will perform data collection using a secure spreadsheet application (Excel), while access to the final trial dataset will be restricted to four specific members, including the two first authors, a statistician and the last author. In the event of unexpected serious adverse events, the study may be suspended or prematurely terminated, and the status of all enrolled patients will be assessed. Regular on-site monitoring will be conducted by research assistants to ensure adherence to the research plan and maintain the accuracy and integrity of the recorded data. Research participants will be informed of their right to request the comprehensive research results from the researchers on completion of the study. We expect to release the original data on the ResMan Chinese Clinical Trial Management Public Platform (http://www.medresman.org.cn) in February 2025, and the findings of this study will be disseminated through publication in peer-reviewed journals.

## DISCUSSION

Gastroscopy is considered the gold standard for the diagnosis and treatment of upper gastrointestinal tumours. Procedural sedation enhances the quality of gastrointestinal invasive examinations and patient comfort while also increasing the rate of positive diagnoses and improving patient compliance. An increasing number of patients are opting for painless gastroenteroscopy,[50 51] ensuring the safety of the perioperative period during painless gastrointestinal endoscopy has become an important issue of concern for anaesthetists.

During the painless gastroscopy procedure, when the endoscopist inserts the endoscope through the mouth, it shares the pharyngeal airway with anaesthesia and surgery. This situation complicates typical mask-positive pressure ventilation and inserts an oropharyngeal airway, increasing the challenge of airway management for anaesthetists. The introduction of the endoscope can lead to pharyngeal obstruction, while muscle relaxation induced by sedatives may cause upper airway collapse, potentially resulting in upper airway obstruction. The injection of gas during the procedure can compress the diaphragm, causing partial atelectasis of the lungs and a reduction in functional residual capacity, leading to hypoxaemia. Hypertensive patients can experience impaired transport and distribution of oxygen within the body due to changes in vascular structure and functional damage to target organs. Sudden fluctuations in blood pressure under anaesthesia may impact blood perfusion to vital organs, thereby affecting the delivery and utilisation of oxygen.[37] Neck and chest fat deposition, due to changes in airway anatomy, reduced residual amount of lung function and reduced chest wall compliance, which may lead to hypoxaemia under sedation or anaesthesia.[26 33] Patients with diabetes may experience microvascular and macrovascular complications that impair lung function and the transport and utilisation of oxygen in the body. Additionally, the neuropathy and autonomic dysfunction associated with diabetes may affect respiratory control and protective respiratory reflexes.[37 44] Furthermore, diabetes can cause acidosis in body fluids, reducing the affinity of haemoglobin for oxygen[37] and increasing the risk of hypoxaemia. Patients with coronary artery disease have weakened cardiac pumping function, possible cardiac insufficiency, affecting blood circulation and oxygen transport in the body, and reduced tolerance to hypoxaemia during endoscopy. Elderly patients often present multiple comorbidities such as chronic obstructive pulmonary disease and coronary heart disease, leading to a decline in the physiological reserve capacity of the respiratory and circulatory systems, thereby affecting the uptake and transport of oxygen. During the diagnostic and therapeutic procedures, sensitivity to sedatives or anaesthetics may increase, making it challenging to control the dosage of drugs and increasing the risk of respiratory depression.[49 52] In summary, patients with these factors are at a higher risk of developing hypoxaemia during painless gastroscopy, which may further lead to serious complications such as myocardial ischaemia, arrhythmia or cerebral hypoxaemia.

Changes in oxygen therapy are the primary way to reduce hypoxaemia, including HFNC, supraglottic jet oxygenation and ventilation (SJOV) and laryngeal mask for gastroscopy, which can decrease the incidence of hypoxaemia during painless gastroenteroscopy. HFNC therapy delivers high-flow oxygen (up to 60 L/min) to the nasopharynx and airways, generating positive airway pressure at the end of exhalation to enhance oxygenation and decrease the incidence of hypoxaemia.[18 39 53] However, HFNC did not demonstrate a significant difference compared with standard nasal intubation in obese colonoscopy patients undergoing sedation.[42] A nasopharyngeal injection tube (WNJ) performs SJOV through high flow and high drive pressure for fibreoptic bronchoscopy[54] and digestive endoscopy,[43 55–57] reducing the incidence of hypoxaemia. However, SJOV is associated with short-term adverse events such as sore throat, dry mouth and epistaxis.[43 58] In nine trials, a meta-analysis involving 2017 patients demonstrated that SJOV had no significant effect on low-risk patients (RR 0.29,95% CI 0.05 to 1.64, heterogeneity $I^2$=73%) and was associated with increased side effects (RR 5.25, 95% CI 2.29 to 12.02, heterogeneity $I^2$=0%). This indicates that SJOV in endoscopic surgery may be incomplete.[58] The LMA Gastro laryngeal mask features a dual-channel airway, providing both an unobstructed passage and positive pressure ventilation for digestive endoscopy.[59–62] However, the specialised laryngeal mask for gastroscopy, when used in invasive breathing mode, requires deep anaesthesia for insertion. The insertion process may result in throat damage, leading to symptoms such as throat pain and laryngospasm,[63] and it increases healthcare costs. A 2024 systematic review of 27 randomised controlled trials[64] suggests clinical equipoise persists regarding optimal non-invasive ventilation strategies for hypoxaemia prevention during procedural sedation. Therefore, based on previous study results[36 47], we expanded the indications for BPAP in a diverse high-risk population with a larger sample size, compared with traditional NC oxygen therapy, to verify its efficacy and safety in preventing hypoxaemia.

BPAP is a respiratory assist technique that features both inspiratory pressure (IPAP) and expiratory pressure (EPAP). The patient's spontaneous breathing is synchronised with BPAP, providing a high inspiratory pressure to ensure pressure support and an appropriate expiratory pressure to meet the patient's tidal volume needs. In the event of severe respiratory depression, the ventilator will provide artificial ventilation according to predetermined breathing parameters, using continuous positive airway pressure to improve airway patency, prevent upper airway collapse, reduce respiratory effort, enhance oxygenation, increase effective ventilation and consequently decrease the incidence of hypoxaemia.[36 46 65] The limited adoption of nasal masks in prehospital and emergency airway management is primarily attributed to their lower achievable positive airway pressure compared

with alternative interfaces. Research indicates that nasal mask ventilation provides superior ventilation efficacy compared with conventional orofacial masks during anaesthesia induction phases, particularly in patients with difficult airway anatomy.[66–68] The airway-opening mechanism involves a pressure gradient between the nasopharynx and oropharynx during nasal mask ventilation. This gradient counteracts gravitational forces on the soft palate and tongue, promoting forward movement and airway patency. In contrast, conventional masks apply uniform pressure to both cavities without establishing a gradient, allowing gravitational collapse of pharyngeal structures and subsequent obstruction.[69] The nasal mask is highly effective for upper gastrointestinal endoscopic anaesthesia, providing high oxygen concentrations and positive pressure ventilation. This improves oxygenation, reduces the need for airway interventions and prevents hypoxaemia during procedures.[45 70] In the event of emergencies such as gastrointestinal reflux or severe respiratory tract obstruction, the nasal mask facilitates easier suctioning and placement of oropharyngeal airways, thereby enhancing the safety and convenience of gastroscopy anaesthesia. In light of these considerations, a nasal mask will be selected as the primary interface for delivering bilevel ventilation throughout this clinical investigation. Previous studies have demonstrated the efficacy of BPAP ventilation strategy in gastroenterology; however, there are some limitations of small sample size and population limitation. Therefore, we conducted this study to include all people at risk of hypoxaemia and expand the sample size, aiming to further verify the efficacy of bilevel positive pressure ventilation in preventing hypoxaemia during painless gastroscopy.

## Strengths of the study

First, due to the inhibitory effects of propofol on the respiratory and circulatory system,[17 22 48] this study strictly controls the administration rate and dosage of propofol. Both groups of patients receive propofol intravenously at an infusion rate of 2 mg/s. The initial dose is set at 1.0 mg/kg for patients older than 50 years and 1.5 mg/kg for individuals younger than 50 years. Subsequent doses of 10–20 mg of propofol are titrated until the patient's MOAA/S score is ≤1 for painless gastroscopy.[60] Second, BIS monitoring was employed during the anaesthesia maintenance period (60–80) to guide the sedation depth of patients undergoing painless gastroscopy and to prevent both insufficient and excessive sedation.

## Limitations

First, the study lacked a blinding design. Given the nature of the airway intervention, patients in both groups could easily identify the supplemental oxygen devices. To mitigate information bias, postoperative outcome assessments and statistical analyses will be conducted by independent researchers who remain unaware of the group assignments. Second, $P_{ET}CO_2$ monitoring was not conducted for patients in either group. This omission was due to the oxygen delivery method used in the experimental group with BPAP, as well as limitations of the central conditions, which rendered suitable equipment for monitoring $P_{ET}CO_2$ unavailable.

In conclusion, this study is an investigator-initiated prospective, randomised, controlled trial involving a population at risk of painless gastroscopy, aimed at verifying the efficacy and safety of the BPAP ventilation strategy in preventing hypoxaemia during the procedure.

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**Contributors** HL and JW conceived the study. DC and YL assisted HL and JW in writing the manuscript. HL is the principal investigator of the study. QM, QZ and YY completed the ethical approval. JC, PL and JG completed the registration of the study. This study will be supervised by NX and SW. NX is the guarantor. All authors have critically reviewed, revised and approved the submitted version.

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**Competing interests** None declared.

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