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STUDY PROTOCOL

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Apneic oxygenation with Transnasal Humidified Rapid-insufflation Ventilator Exchange (THRIVE) in obstructive sleep apnea patients: study protocol of a randomized controlled trial

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Abstract

Background Patients with obstructive sleep apnea (OSA) are at increased risks of rapid oxygen desaturation during anesthesia, highlighting the need for effective strategies to extend safe apnea time. This study aims to evaluate the efficacy of combining a nasopharyngeal airway (NPA) with transnasal humidified rapid-insufflation ventilator exchange (THRIVE) at 60L/min, compared to THRIVE alone, in prolonging the safe apnea duration and enhancing carbon dioxide elimination in apneic OSA patients.

Methods This single-center, prospective, double-blind, randomized controlled trial will include 56 adult patients with OSA scheduled for elective surgery under general anesthesia. Participants will be randomized in a 1:1 ratio to receive either NPA + THRIVE or THRIVE alone. Both groups will undergo standard anesthesia induction, including pre-oxygenation via face mask with 100% FiO_2at 10 L/min. During apnea, patients in both groups will receive oxygen via Optiflow THRIVE at 60 L/min. The primary outcome is the time from the initiation of nasal oxygenation to a peripheral oxygen saturation (SpO_2) of 95%. Secondary outcomes include the lowest SpO_2 during intubation, plateau end-tidal CO_2 ($EtCO_2$) values, rate of increase of transcutaneous CO_2 ($tcCO_2$), and time to regain baseline SpO_2 after resuming ventilation.

Discussion This trial is expected to provide insights into the effectiveness of combining THRIVE with NPA in prolonging safe apnea time and improving carbon dioxide elimination in OSA patients during anesthesia induction. Positive findings could support adoption THRIVE + NPA as a standard practice in managing OSA patients, potentially lowering perioperative risks associated with hypoxia and hypercapnia.

Trial registration This trial was registered on Clinical Trials.gov(NCT 06581588) on Sep 3, 2024.

Keywords Apneic oxygenation, THRIVE, Nasopharyngeal airway, Obstructive sleep apnea, Randomized controlled trial

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Background

With the increasing prevalence of obesity, the prevalence of obstructive sleep apnea (OSA) is also rising, ranging from 9 to 25% in the general adult population [1, 2]. Patients with OSA present unique challenges under general anesthesia due to their susceptibility to airway collapse, reduced functional residual capacity, and elevated oxygen consumption, all contributing to rapid desaturation during anesthesia induction [3–5]. Furthermore, compared to non-OSA patients, those with OSA have a three- to four-fold increased risk of difficult intubation, difficult mask ventilation, or both, making effective and strategies to extend safe apnea time particular crucial in this population [1, 2, 6, 7].

Apneic oxygenation strategies have gained attention with the advent of high-flow heated and transnasal humidified rapid insufflation ventilatory exchange (THRIVE) [8–10], which has been shown to prolong safe apnea times in diverse patient groups, including those with obesity [11–13]. However, the application of neuromuscular blockade during anesthesia induction significantly exacerbates upper airway collapsibility, potentially reducing THRIVE's effectiveness in maintaining oxygen saturation in paralyzed OSA patients. Despite its promise, no studies have specifically evaluated THRIVE in this context.

Consequently, there is a need to explore adjunctive methods to ensure consistent airway patency in paralyzed OSA patients. This study aims to address this gap by evaluating whether adding a nasopharyngeal airway (NPA) to THRIVE improves airway patency and extends safe apnea time compared to THRIVE alone. We hypothesize that combining THRIVE with an NPA will prolong time to hypoxia and enhance carbon dioxide clearance, optimizing perioperative airway management for this high-risk population.

Methods

Study design, ethics, and trial registration

This study is designed as a single-center, prospective, double-blind, randomized controlled clinical trial. This study received approval from the Clinical Research Ethics Committee of Beijing Tongren Hospital on June 20, 2024 (approval NO. TREC2024-KY069). The trial protocol adheres strictly to the SPIRIT 2023 guidelines for clinical trials and CONSORT 2010 guidelines for reporting randomized controlled trials. This trial was registered at https://clinicaltrials.gov/study/NCT06581588 with registration number NCT 06581588 on September 3, 2024.Written informed consent will be obtained from all participants before enrollment.

Patient inclusion and exclusion criteria

Inclusion criteria

(1) Adults aged 18 to 75 years.
(2) American Society of Anesthesiologists (ASA) physical status classification I-III.
(3) Diagnosed with OSA, defined by polysomnography (PSG) as an apnea–hypopnea index (AHI) ≥ 5 events/hour.
(4) Scheduled for elective surgery under general anesthesia.

Exclusion criteria

The patients will be excluded if they meet any of the following criteria: (1) presence of chronic respiratory diseases; (2) oxygen saturation below 98% while on supplemental oxygen; (3) anticipated difficulty with intubation; (4) uncontrolled hypertension; (5) ischemic cardiomyopathy; (6) congestive heart failure; (7) increased intracranial pressure; (8) uncontrolled gastroesophageal reflux disease; (9) known allergy to anesthetics; or (10) inability to use high-flow devices due to nasopharyngeal blockage.

Patient screening and baseline assessment

Investigators trained in standardized protocols will screen and enroll eligible participants preoperatively. No incentives, financial or otherwise, will be offered for participants. Patients will be fully informed about possible benefits, drawbacks, and any potential risks. Written consent will be obtained before baseline assessments, which include: (1) completion of the STOP-Bang questionnaire to quantify OSA risk; (2) collection of demographic data (age, gender, BMI), comorbidities, and relevant preoperative laboratory results.

Assignment of interventions

Randomization and allocation

A total of 44 patients will be randomly assigned (1:1 ratio) to either a THRIVE + NPA group or a THRIVE-alone group. A researcher not involved in patient care will generate the random sequence and place assignments in sequentially numbered, opaque, sealed envelopes. After verifying patient eligibility, the attending anesthesiologist will verify the participant's medical number, age, and gender before opening the envelope to confirm the allocation. The study flow chart is illustrated in Fig. 1. The study process and evaluation are reported in Table 1.

Blinding

Attending anesthesiologists cannot be blinded due to the physical nature of the intervention. Patients,

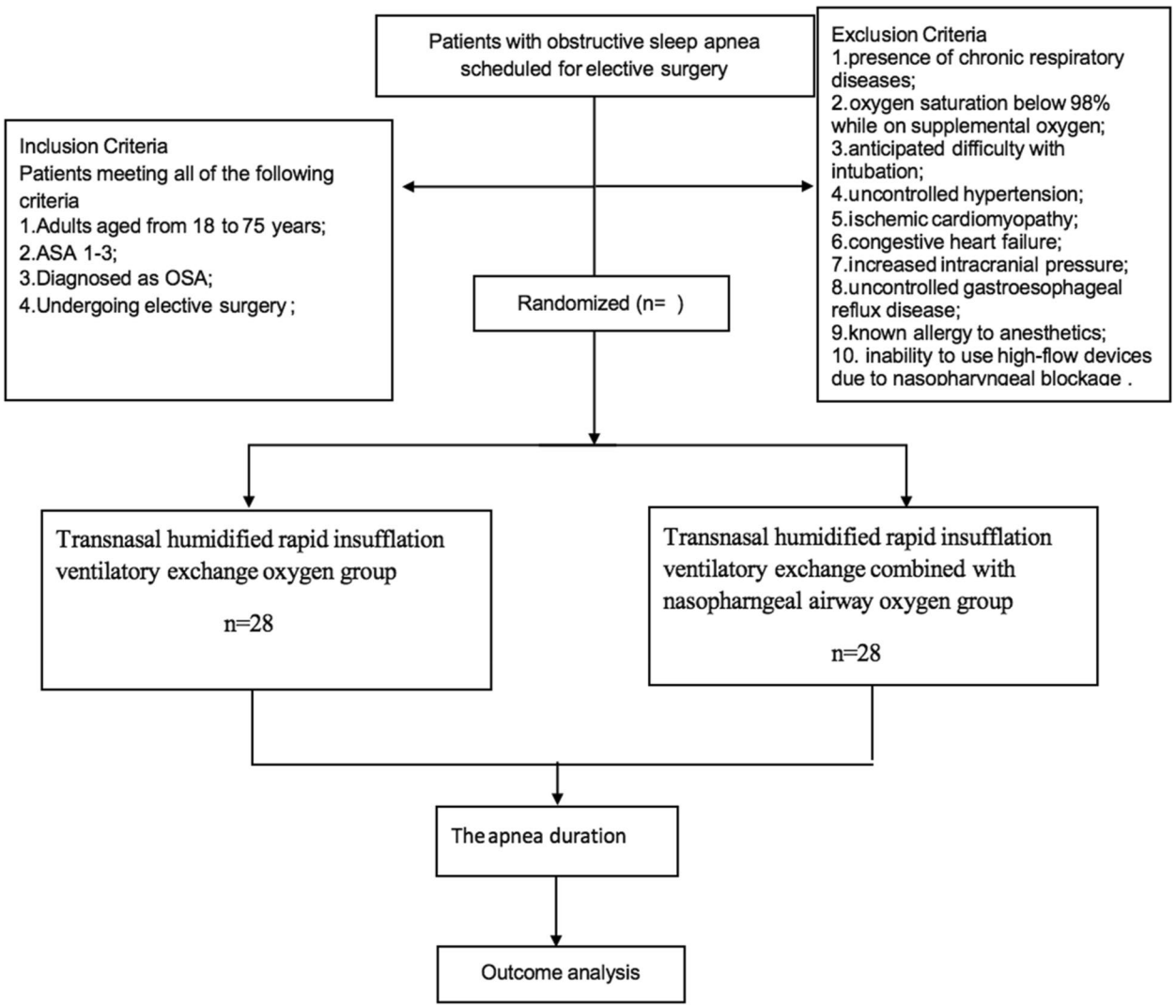

Fig. 1 Flowchart of the study

postoperative assessors, statisticians, and other study investigators involved in data analysis will remain blinded to group assignments. In the event of an adverse event or complication that requires discontinuation of the study intervention, outcome assessors will be unblinded as necessary.

Interventions

After obtaining written informed consent, patients will be randomly assigned to one of two intervention groups (as outlined in Fig. 1):

1. Intervention group (NPA+THRIVE):

A nasopharyngeal airway of appropriate size (measured from the nostril to the earlobe or the angle of the mandible) will be gently inserted. The NPA will provide a direct pathway for oxygen delivery to the upper airway, assisting in maintaining airway patency throughout the apneic period.

Participants will receive oxygen via a nasopharyngeal airway connected to a high-flow nasal oxygen system (Optiflow THRIVE; Fisher & Paykel Healthcare, Auckland, New Zealand) at a flow rate of 60 L/min, FiO_2 100%, heated to 37 °C.

2. The control group:

Participants will receive oxygen via the same high-flow system (60 L/min, FiO_2 100%, 37 °C) without NPA insertion.

Table 1 Schedule of assessments

	Enrolment	Allocation	Primary study period				Follow-up	
Time point	**- 1 d**	**0**	**Start of apnea**	**5 min after apnea**	**10 min after apnea**	**At the end of apnea**	**2 min following intubation**	**PACU**
Enrolments								
Eligibility screen	×							
Informed consent	×							
Allocation		×						
Interventions								
NPA + THRIVE			×					
THRIVE-alone			×					
Assessments								
Baseline information		×						
Apnea duration						×		
tcCO2	×		×	×	×	×		
Blood gas analysis	×		×	×	×	×		
Lowest end-tidal oxygen	×						×	
Highest end-tidal CO2	×						×	
Complications assessment						×	×	×

NPA nasopharyngeal airway, *THRIVE* transnasal humidified rapid-insufflation ventilator exchange, *PACU* post anaesthesia care unit

Anesthesia induction and maintenance

All patients will undergo pre-oxygenation via face mask with an FiO_2 of 1.0 at 10L/min, positioned in a 30-degree ramped position. Anesthesia induction will include an opioid, propofol, and rocuronium at doses selected by the anesthetist. Anesthesia was maintained with an infusion of intravenous propofol and remifentanil. Manual bag-mask ventilation with be performed with PEEP settings adjusted by the anesthetist. Laryngoscopy will be conducted using a CMAC videolaryngoscope, and the Cormack and Lehane laryngoscopy grade will be recorded. Patients who present with difficulties in manual ventilation or Grade 3 or 4 laryngoscopy views will be excluded at this stage. The videolaryngoscope will then be removed, and the patient will be manually ventilated to achieve an end-tidal oxygen level of 90%. Nasal oxygen therapy will then be applied according to the assigned group. Airway patency was maintained via jaw thrust.

The patient remained anesthetized and apneic until SpO_2 reading of 95% was obtained, or a time of 18 min was reached. At this point, nasal oxygen therapy was removed and the patient manually bag-mask ventilated and intubated after SpO_2 of 98% was achieved.

In both groups, the first operator will be a senior or a junior supervised by a senior. Clinical data will be collected throughout intubation, surgery and until discharge of the PACU.

Perioperative management

Both groups will receive identical perioperative management according to our center's standard surgical, anesthetic, and postoperative pain protocols. No modifications were made to these established practices.

Outcome measures

The primary outcome is defined as time (in seconds) from the initiation of nasal oxygenation to the point when peripheral oxygen saturation (SpO_2) drops to 95%. If a patients SpO2 does not decrease to 95% within 18 min, the duration will be recorded as 18 min.

The second outcome measures include: blood gas analysis at specific intervals: at the start of apnea, at five and ten minutes after apnea onset, and at the end of apneic period, the duration of oxygen desaturation will be documented, tracking the time spent at each SpO_2 threshold (100–99%,98%, and 95%), plateau end-tidal CO_2 ($ETCO_2$) value, lowest end-tidal oxygen (EtO_2) within the first 2 min following intubation, rate of transcutaneous CO_2 ($tcCO_2$) increase during the apneic period, highest $EtCO_2$ within the first 2 min following intubation, and time required to return to baseline Spo2 after ventilation resumes post-intubation. Additional secondary outcomes observed in the post-anesthesia care unit (PACU) include the lowest SpO_2, occurrence of morbidities (e.g. nausea, vomiting, inspiratory dyspnoea post-extubation), lowest SpO_2 post-extubation, incidences of desaturation < 90%

and severe desaturation < 80% after extubation, oxygen therapy requirement upon PACU discharge, length of stay in PACU, use of non-invasive ventilation, and re-intubation for respiratory failure).

Sample size calculation

The study was powered based on the primary outcome measure, which is the time to desaturation to 95%. Since no previous data exist for OSA patients receiving high-flow oxygen during apnea. We referenced a study [14] in which subjects receiving 70L/min of oxygen during apnea had a time to desaturation of 8.2 min. We used this to estimate time to desaturation in the THRIVE-alone group. We estimated that time to desaturation in the NPA group would be 15% longer. With a standard deviation of 1.3 min from Wong et al. [13], 1:1 randomization, a two-tailed alpha 0.05, and power of 90%, a sample size of 14 participants per group was calculated as sufficient to achieve statistical power for the primary outcome, but given the uncertainty in these estimates we doubled a sample size of 28 per group.

Data and statistical analysis

The primary outcome will be analyzed to determine the significance of difference between the groups. Secondary outcomes, including postoperative complications (such as respiratory, cardiovascular events, or mortality), will also be compared between the two groups. Both modified intention-to-treat and a per-protocol analyses will be applied for these comparisons. Differences in primary and secondary outcomes will be assessed using parametric and non-parametric testes, as suitable for the data. A *P*-value < 0.05 will be considered statistically significant. Statistical analyses will be conducted using PASS 24 software.

Data collection and monitoring

Data collection will be collected systematically throughout the study using standardized forms. To ensure study quality, all investigators will undergo training on Good Clinical Practice (GCP) and protocol-specific procedures. Subsequently, they must pass examinations-comprising both written and practical assessments administered through our institutional training program-to verify their proficiency in data collection and intraoperative monitoring. The trained investigator (LGY) who will be blinded to the allocation will collect intraoperative data. WLL,YSL, and YY will do the anesthesia procedures and collect intraoperative data, respectively; to avoid bias, they will not participate in postoperative data collection. All the statistical analyses will be performed by one of the corresponding authors (WGY).

A serious adverse event (SAE) is defined as any untoward medical occurrence that meets one or more of the following criteria: (1) results in death; (2) is life-threatening; (3) requires inpatient hospitalization or prolongation of existing hospitalization; (4) results in persistent or significant disability or incapacity; (5) results in a congenital anomaly or birth defect. In our study, any SAE will be immediately reported to the principal investigator. The principal investigator will subsequently report all SAEs or any unanticipated problems involving risks to participants to the research ethics board and the principal investigator at Beijing Tongren Hospital. If these problems are thought to be associated with participating in the trial, then they will also be reported to the research ethics.

The anticipated risks associated with this study are minimal. Possible discomforts include minor effects from high-flow nasal oxygen, such as skin irritation, dry mouth, or nasal congestion. The potential risks will be fully disclosed to participants during the informed consent process, and they will be able to report these risks during the preoperative adjustment period and 3 day postoperative follow up. Other potential risks include potential for breach of confidentiality.

Confidentiality

Participants' health information will be kept strictly confidential, accessible to the authorized research team members. Paper records will be stored securely in a locked cabinet, while electronic data will reside in a password-protected database. Each participant will be assigned a unique ID to ensure anonymity, with identifying information stored separately from study data. Access to the final dataset is limited to key investigators and the research statistician.

Data availability

Study findings will be published in a peer-reviewed journal. Interested researchers may contact the study principal investigator for data access requests.

Discussion

This randomized controlled trial protocol aims to investigate the clinical implications of combing a NPA with THRIVE specifically in patients with OSA. While prior studies have demonstrated that THRIVE extends safe apnea time in various populations [15–18], including those with obesity [12], airway collapse common in OSA may limit its effectiveness by impeding oxygen delivery to the alveoli [7, 19, 20]. Continuous oxygenation alone may not fully resolve the airway obstruction issues characteristic of OSA [3, 11, 21], emphasizing the practical necessity of an adjunct to maintain airway patency.

From an operational standpoint, integrating an NPA requires careful attention to sizing and insertion to avoid nasal trauma and ensure patient comfort. Standardizing these procedures within the study—through provider training and consistent placement techniques—aims to minimize complication rates and optimize efficacy. While the combined approach is hypothesized to mechanically support the airway and enhance oxygenation, its definitive benefit in perioperative care for OSA remains to be demonstrated.

Limitations include the single-center design, which may affect the external validity of our findings, and the variability in individual anatomy and response to THRIVE that might influence outcomes. Future multicenter trials are recommended to validate and generalize these findings across broader patient demographics and clinical settings.

In summary, this protocol directly addresses a practical clinical limitation of THRIVE in OSA patients by evaluating the operational feasibility and potential clinical benefits of integrating an NPA into routine airway management during anesthesia induction. Outcomes of this trial could substantially enhance perioperative patient safety in a population vulnerable to rapid desaturation.

Abbreviations

OSA	Obstructive sleep apnea
NPA	Nasopharyngeal airway
ASA	American Society of Anesthesiologists Classification
THRIVE	Transnasal humidified rapid-insufflation ventilator exchange
DMC	Data monitoring committee
SpO_2	Oxygen saturation
FiO_2	Fraction of inspired oxygen
$EtCO_2$	End-tidal carbon dioxide
$tcCO_2$	Transcutaneous carbon dioxide
$PaCO_2$	Arterial carbon dioxide pressure
PACU	Post anaesthesia care unit
PaO_2	Arterial oxygen partial pressure
BMI	Body weight index
PEEP	Positive end-expiratory pressure
SAE	Serious adverse event

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No.

Authors' contributions
GY L drafted the manuscript. All participated in revising the manuscript substantially. GY W provided administrative support. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study was approved by the institutional ethic committee of Beijing Tongren Hospital, Capital Medical University (NO. TREC2024 KY069 KY069). Informed consent will be obtained from all the participants in the study. All methods will be conducted in accordance with the ethical standards of the declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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