



# Oxygen concentration titration guided by oxygen reserve index during pediatric laryngeal surgery with high-flow nasal cannula oxygen: a randomized controlled trial

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## Abstract

**Purpose** The objective of this study was to evaluate whether adjusting the oxygen concentration guided by the Oxygen Reserve Index (ORI) during pediatric laryngeal surgery with High Flow Nasal Cannula Oxygen (HFNO) could achieve postoperative  $PaO_2$  close to physiological levels while ensuring adequate oxygenation in surgery.

**Methods** Sixty pediatric patients undergoing laryngeal surgery or examination were randomly assigned to two groups. The ORI group received oxygen concentration adjustments every 5 min to maintain a target ORI value of 0.21, whereas the control group did not undergo any adjustments. Postoperative  $PaO_2$ , time weighted average fraction of inspired oxygen ( $FiO_2$ ), and mean Peripheral Oxygen Saturation ( $SpO_2$ ) were compared between groups. Finally, some analyses were conducted to examine the relationship of ORI with  $PaO_2$ .

**Results** In general, the postoperative  $PaO_2$  was  $164.9 \pm 48.8$  mmHg in ORI group and  $323.0 \pm 87.7$  mmHg in control group ( $P < 0.01$ ). The time weighted average  $FiO_2$  in the ORI group was 85.9 [81.8–92.7] %. There was no significant difference in mean  $SpO_2$  between the two groups (ORI vs. control: 98.4 [97.7–99.2] vs. 98.8 [97.7–99.5];  $P = 0.36$ ). According to the analyses, the optimal cut value for ORI was determined to be 0.195 when  $PaO_2$  was 150 mmHg.

**Conclusions** In pediatric laryngeal surgery with HFNO, reducing oxygen concentration guided by ORI helped achieve postoperative  $PaO_2$  levels closer to physiological norms without compromising intra-operative oxygenation.

**Keywords** High-flow nasal cannula oxygen · Laryngeal surgery · Hyperoxemia · Oxygenation · Airway management

## Introduction

Recently, High Flow Nasal Cannula Oxygen (HFNO) has gained popularity in pediatric anesthesia. Several studies indicate HFNO can replace conventional oxygenation in laryngeal surgeries with spontaneous breathing, enhancing airway safety and optimizing surgical conditions [1–4]. However, there is a limited number of studies on the application of HFNO in pediatric laryngeal surgery. In surgery, the common practice involves selecting an age-appropriate nasopharyngeal airway for the child, with an oxygen flow rate of 2 L/kg/min and fraction of inspired oxygen ( $FiO_2$ ) of 1.0 [1, 2, 5]. Extended exposure to pure oxygen may cause lung atelectasis, reduced arterial oxygen saturation, respiratory depression, systemic vasoconstriction, and diminished cardiac output, impacting pediatric patients' prognosis [6–8].

Pulse oximetry monitoring has limited capabilities in assessing hyperoxemia, and arterial blood gas analysis cannot provide continuous evaluation of hyperoxygenation

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status. Repeated vascular punctures may pose risks of harm to pediatric patients. The Oxygen Reserve Index (ORI) is a novel non-invasive monitoring tool that utilizes a multi-wavelength pulse co-oximetry to measure the oxygen reserve in the blood (Masimo Corp, Irvine, CA, USA) [9]. ORI has been found to correlate with real-time oxygen reserve status within the mild hyperoxia range (arterial oxygen partial pressure ( $PaO_2$ ) range 100–200 mmHg, ORI range 0.00–1.00) [10, 11]. ORI can be utilized to predict desaturation before significant changes in peripheral oxygen saturation ( $SpO_2$ ) occur, providing a window of time for anesthesiologists or surgeons to intervene. Using ORI enables monitoring of hyperoxia and prediction of hypoxia. It guides the continuous adjustment of oxygen concentration and providing personalized management for pediatric patients with diverse physiological states and surgical procedures, ensuring adequate oxygenation.

In a study, a critical threshold of 0.21 was obtained from the receiver operating characteristic (ROC) curve analysis to detect  $PaO_2 \geq 150$  mmHg [12]. The  $PaO_2$  value corresponding to 0.21 aligns with our desired mild hyperoxygenation state ( $100 \text{ mmHg} \leq PaO_2 \leq 200 \text{ mmHg}$ ). Therefore, we have chosen 0.21 as the target ORI reference value for adjusting oxygen concentration. This study aims to investigate the safety of adjusting HFNO oxygen concentration during pediatric laryngeal surgery guided by ORI, and whether postoperative  $PaO_2$  in children can approximate physiological levels. Additionally, we will explore the relationship between ORI and  $PaO_2$  in pediatric patients.

## Materials and methods

### Ethical considerations

The research protocol was approved by the Ethics Committee of Children's Hospital of Chongqing Medical University (Institutional Review Board#443/2022, Date of approval: November 16, 2022) and prospectively registered in the Chinese Clinical Trial Registry (Registration Number: CHICTR2300067820, Date of registration: January 28, 2023). The first participant was enrolled on January 30, 2023. In accordance with the ethical principles of the Helsinki Declaration, this study was conducted at Children's Hospital of Chongqing Medical University. Prior to enrollment, written informed consent was obtained from all patients' parents or legal guardians.

### Subjects

From January to September 2023, we enrolled children aged 3 months to 6 years, classified as ASA I-III, undergoing

laryngeal surgery or examination. Patients were grouped based on the use of ORI to adjust oxygen concentration: ORI group and control group. Exclusion criteria involved severe facial fractures, challenges with mask ventilation and intubation, inhalation risks, invasive mechanical ventilation, or severe cardiopulmonary diseases.

### Randomization

Participants were randomly assigned to either the ORI group or the control group using a computer-generated table of random numbers. Researchers recording data and anesthesiologists administering anesthesia remained blind to the group assignments. Participant codes were concealed in sealed opaque envelopes, revealed only on the surgery day. The same surgical team conducted all surgeries on the children.

### Anesthesia

Upon arrival in the operating room, the patient was monitored using pulse oximetry, non-invasive blood pressure, electrocardiogram, brainwave bispectral index (BIS) and transcutaneous carbon dioxide partial pressure ( $TcPCO_2$ , Combim™, Radiometer, Denmark). The intravenous access had been established in the ward, and preoxygenation via a mask was conducted prior to induction (5 L/min). Intravenous induction was initiated with midazolam (dose: 0.1 mg/kg, i.v.), penehyclidine hydrochloride (dose: 0.01 mg/kg, i.v.), sufentanil (dose: 0.1 µg/kg, i.v.), and propofol (dose: 2 mg/kg, i.v.) to maintain spontaneous breathing. After the disappearance of the eyelash reflex, 1% lidocaine was applied for oropharyngeal and tracheal surface anesthesia. Anesthesia depth (BIS range, 40–60) is maintained consistently with target-controlled infusion of propofol (Paedfusor model, Initial target plasma concentration: 3 µg/ml, TCI-V, Veryark, China) [13]. Following induction, oral secretions were cleared, and the HFNO nasal cannula was securely fixed to commence ventilation. Arterial catheterization (radial artery) was performed, with monitoring of arterial blood gases during the procedure, and the catheter was removed at the end of the surgery. During laryngeal surgery with HFNO, emergency mechanical ventilation, such as mask ventilation or endotracheal intubation, was promptly initiated if adequate oxygen saturation could not be maintained. Postoperatively, oral and airway secretions were suctioned again, and collaborative assessment with the surgical team determined the need for transfer to the intensive care unit (ICU) for additional supportive interventions.

## Interventions

In addition to routine anesthesia monitoring, both groups used the same ORI sensor (Rainbow Pulse CO-Oximetry sensor, Masimo), which was connected to the patient's thumb. The sensor was isolated from ambient light. ORI values were displayed on the Root monitor screen. In the ORI group, starting at 100%,  $FiO_2$  decreased by 5% every five minutes to maintain a target ORI value of 0.21. If ORI reached 0,  $FiO_2$  reverted to 100%. Once the ORI value stabilized,  $FiO_2$  was adjusted as before to achieve the target value of 0.21. The control group received continuous pure oxygen. Emergency ventilation (high-flow oxygen mask or endotracheal intubation) was initiated if  $SpO_2$  fell below 92% with  $FiO_2$  at 1.0 and did not recover spontaneously. Arterial blood gas analysis was performed at the beginning and end of the HFNO procedure in both groups.

## Outcomes

The primary outcome measure was the postoperative  $PaO_2$ . Secondary outcome measures included time weighted average  $FiO_2$ , mean  $SpO_2$ , mean ORI value, the incidence of severe hyperoxemia ( $PaO_2 > 200$  mmHg), lowest  $SpO_2$ , highest  $TcPCO_2$ , incidence of rescue ventilation, incidence of hypoxemia ( $SpO_2 < 92\%$ ), operation time and post anesthesia care unit (PACU) time. The time weighted average  $FiO_2$  was calculated as ( $FiO_2$  measured at 0 min in HFNO  $\times$  5 min +  $FiO_2$  measured at 5 min in HFNO  $\times$  5 min +  $FiO_2$  measured at 10 min in HFNO ... + final  $FiO_2$  before the end of HFNO  $\times$  5 min) divided by the duration of HFNO in minutes. Postoperative linear regression analysis, ROC analysis, and multivariate regression analysis were conducted to evaluate the correlation between ORI and  $PaO_2$ .

## Sample size and statistical analysis

The calculation of the sample size was based on a preliminary study, where the average postoperative  $PaO_2$  in the control group was 299.52 mmHg with a standard deviation of 85.62 mmHg, and the average postoperative  $PaO_2$  in the ORI group was 223.75 mmHg with a standard deviation of 72.53 mmHg. The sample size of 30 individuals per group is required to achieve 95% power at a two-sided significance level of 0.05. We plan to recruit 35 subjects per group to account for potential participant withdrawals or exclusions. The normality of the data was assessed using the Shapiro–Wilk test. Independent t-tests were used to evaluate postoperative  $PaO_2$  and highest  $TcPCO_2$ . The Mann-Whitney U test was used to assess time weighted average  $FiO_2$ , mean  $SpO_2$ , mean ORI, lowest  $SpO_2$ , operation time, and PACU

time. Proportions were compared using the chi-square test or Fisher's exact test.

According to previous studies, a threshold of  $PaO_2 \leq 240$  mmHg ( $n = 59$ ) was selected for simple linear regression analysis to examine the relationship between ORI and  $PaO_2$ . To determine the optimal cut ORI value for detecting  $PaO_2 \geq 150$  mmHg, receiver operating characteristic (ROC) curve analysis was performed. To assess the predictive ability and diagnostic performance of the ROC curve, the area under the curve (AUC) and its 95% confidence interval (95% CI) were calculated. Finally, multiple linear regression analysis was conducted on the relevant variables (Weight,  $PaO_2$ ,  $PaCO_2$ ,  $SpO_2$ , Operation time) that underwent univariate screening ( $P \leq 0.20$ ), to explore the factors influencing ORI values.

Continuous variables are presented as mean  $\pm$  SD, median [IQR], while categorical variables are presented as numbers (%). All  $P$  values were two-sided, and  $P < 0.05$  was considered statistically significant. IBM SPSS (v25; IBM) was used for all analyses.

## Results

### Demographic characteristics

Recruitment was halted after enrolling 70 patients from January 2023 to September 2023, with 7 patients not meeting inclusion criteria, and 3 patients declining to participate. Consequently, 60 patients were randomized into two groups. Figure 1 provides an overview of patient recruitment and the study process. Baseline characteristics for both groups are summarized in Table 1, demonstrating no significant differences between the groups at baseline.

### Primary and secondary outcome measures

Regarding primary outcome, the postoperative  $PaO_2$  in the ORI group was significantly lower than that in the control group (ORI vs. control:  $164.9 \pm 48.8$  vs.  $323.0 \pm 87.7$ ;  $P < 0.01$ ). For secondary outcomes, the time weighted average  $FiO_2$  in the ORI group remained within the specified range: 85.9 [81.8–92.7] %. There was no significant difference in mean  $SpO_2$  between the ORI group and the control group (ORI vs. control: 98.4 [97.7–99.2] vs. 98.8 [97.7–99.5];  $P = 0.36$ ). However, the mean ORI value in the ORI group was significantly lower than that in the control group (ORI vs. control: 0.24 [0.20–0.32] vs. 0.52 [0.41–0.64];  $P < 0.01$ ; Table 2).

In postoperative arterial blood gas analysis, 33 patients in both groups experienced hyperoxemia ( $PaO_2 > 200$  mmHg), with significantly fewer cases in the

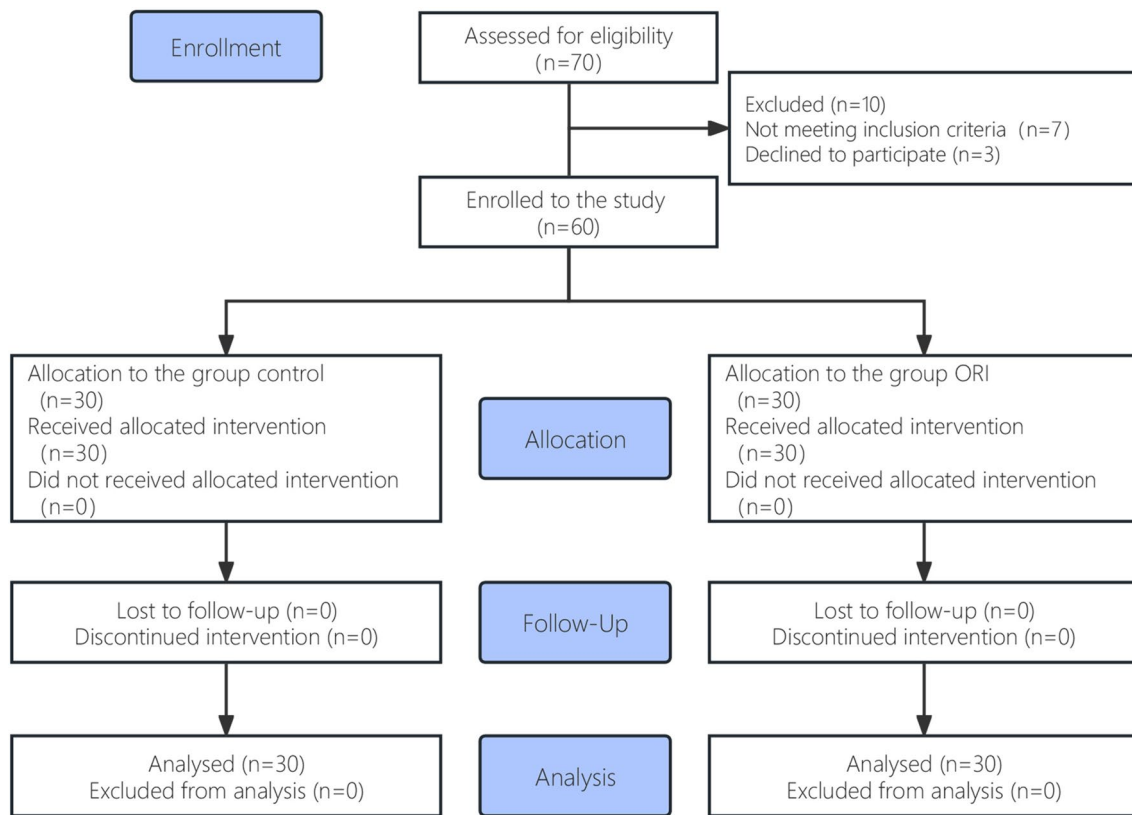


Fig. 1 CONSORT flow diagram of the study

Table 1 Baseline between ORI and control groups

| Variables                | Group ORI (n=30)  | Group control (n=30) | P value |
|--------------------------|-------------------|----------------------|---------|
| Sex                      |                   |                      |         |
| Male: Female             | 20:10             | 23:7                 | 0.39    |
| Age (months)             | 29.9 ± 19.0       | 27.7 ± 15.3          | 0.63    |
| ASA status               |                   |                      |         |
| II: III                  | 10:20             | 8:22                 | 0.57    |
| Weight (kg)              | 12.5 ± 4.8        | 10.8 ± 3.9           | 0.15    |
| Preoperative             |                   |                      |         |
| PaO <sub>2</sub> (mmHg)  | 245.7 ± 88.6      | 286.1 ± 108.6        | 0.12    |
| PaCO <sub>2</sub> (mmHg) | 49.2 ± 10.0       | 52.8 ± 10.0          | 0.16    |
| SpO <sub>2</sub> (%)     | 99.0 [97.0–100.0] | 98.0 [97.0–98.0]     | 0.11    |
| Oxygen therapy           | 2 (7%)            | 2 (7%)               | 1.00    |
| Postoperative            |                   |                      |         |
| PaCO <sub>2</sub> (mmHg) | 51.3 ± 10.2       | 53.9 ± 10.2          | 0.32    |

Values are presented as mean ± SD, median [IQR] or Number (%)

ORI Oxygen Reserve Index, ASA American society of anesthesiologists, PaO<sub>2</sub> Arterial oxygen partial pressure PaCO<sub>2</sub> Arterial carbon dioxide partial pressure SpO<sub>2</sub> Peripheral oxygen saturation

ORI group (n = 5, 17%) compared to the control group (n = 28, 93%). Although the lowest SpO<sub>2</sub> in the ORI group was lower than that in the control group (ORI vs. control: 94.5 [93.0–97.0] vs. 97.5 [95.0–99.0]; P = 0.03), the incidence of hypoxemia during HFNO (SpO<sub>2</sub> < 92%) was low in both groups (n = 3, 10%). There was no significant difference in the highest TcPCO<sub>2</sub> between the two groups (ORI vs. control: 58.4 ± 10.6 vs. 59.9 ± 10.6; P = 0.58). Emergency ventilation occurred in both groups (ORI: n = 2, 7%; control: n = 1, 3%). Operation time (ORI vs. control: 55 [45–63.8] vs. 65 [45–85]; P = 0.20) and PACU time (ORI vs. control: 40 [35–45] vs. 42.5 [35–50]; P = 0.42) did not differ significantly between the groups (Table 2).

There were no significant statistical differences in preoperative diagnoses, surgical procedures, and postoperative complication rates between the two groups of children. However, the ORI group had a shorter length of hospital stays (ORI vs. control: 5 [5.0–7.0] vs. 6 [5.3–7.8]; P = 0.048; Table 3).

### The relationship between ORI and PaO<sub>2</sub>

Through multiple linear regression analysis exploring factors influencing ORI values, it was found that PaO<sub>2</sub>

**Table 2** Primary and secondary outcome measures

| Variables  | Group ORI ( <i>n</i> = 30) | Group control ( <i>n</i> = 30) | <i>P</i> value |
|--|----------------------------|--------------------------------|----------------|
| Primary outcome measure                          |                            |                                |                |
| Postoperative <i>PaO</i> <sub>2</sub> (mmHg)     | 164.9 ± 48.8               | 323.0 ± 87.7                   | < 0.01         |
| Secondary outcome measures                       |                            |                                |                |
| Time weighted average <i>FiO</i> <sub>2</sub>    | 85.9 [81.8–92.7]           | 100.0 [100.0–100.0]            | < 0.01         |
| Mean <i>SpO</i> <sub>2</sub> (%)                 | 98.4 [97.7–99.2]           | 98.8 [97.7–99.5]               | 0.36           |
| Mean ORI   | 0.24 [0.20–0.32]           | 0.52 [0.41–0.64]               | < 0.01         |
| Postoperative <i>PaO</i> <sub>2</sub> > 200 mmHg | 5 (17%)                    | 28 (93%)                       | < 0.01         |
| Lowest <i>SpO</i> <sub>2</sub> (%)               | 94.5 [93.0–97.0]           | 97.5 [95.0–99.0]               | 0.03           |
| Highest <i>TcPCO</i> <sub>2</sub> (mmHg)         | 58.4 ± 10.6                | 59.9 ± 10.6                    | 0.58           |
| Rescue ventilation                               | 2 (7%)                     | 1 (3%)                         | 1.00           |
| <i>SpO</i> <sub>2</sub> < 92%                    | 3 (10%)                    | 3 (10%)                        | 1.00           |
| Operation time (min)                             | 55 [45–63.8]               | 65 [45–85]                     | 0.20           |
| PACU time (min)                                  | 40 [35–45]                 | 42.5 [35–50]                   | 0.42           |

Values are presented as mean ± SD, median [IQR] or Number (%)

*ORI* Oxygen Reserve Index, *PaO*<sub>2</sub> Arterial oxygen partial pressure, *FiO*<sub>2</sub> Fraction of inspired oxygen, *SpO*<sub>2</sub> Peripheral oxygen saturation, *TcPCO*<sub>2</sub> Transcutaneous carbon dioxide partial pressure, *PACU* Post anesthesia care unit

**Table 3** Diagnosis, procedure and postoperative complications

| Variables                       | Group ORI ( <i>n</i> = 30) | Group control ( <i>n</i> = 30) | <i>P</i> value |
|---------------------------------|----------------------------|--------------------------------|----------------|
| Diagnosis                       |                            |                                | 0.84           |
| Laryngostenosis                 | 2 (7%)                     | 5 (17%)                        |                |
| Subglottic stenosis             | 12 (40%)                   | 7 (23%)                        |                |
| Tracheomalacia                  | 4 (13%)                    | 6 (20%)                        |                |
| Laryngomalacia                  | 5 (17%)                    | 6 (20%)                        |                |
| Pharyngeal malacia              | 4 (13%)                    | 5 (17%)                        |                |
| Laryngeal cleft                 | 3 (10%)                    | 6 (20%)                        |                |
| Laryngeal papilloma             | 0 (0%)                     | 1 (3%)                         |                |
| Laryngeal tumour                | 2 (7%)                     | 1 (3%)                         |                |
| Bronchial foreign body          | 1 (3%)                     | 0 (0%)                         |                |
| Tracheoesophageal fistula       | 3 (10%)                    | 3 (10%)                        |                |
| Bilateral vocal cord paralysis  | 12 (40%)                   | 14 (47%)                       |                |
| Procedure                       |                            |                                | 1.00           |
| Examination                     | 30 (100%)                  | 30 (100%)                      |                |
| Excision of neoplasm            | 7 (23%)                    | 9 (30%)                        |                |
| Vocal cord abducent and fixed   | 3 (10%)                    | 1 (3%)                         |                |
| Excision of laryngeal papilloma | 1 (3%)                     | 1 (3%)                         |                |
| Supraglottoplasty               | 3 (10%)                    | 2 (7%)                         |                |
| “T” tube placement              | 2 (7%)                     | 3 (10%)                        |                |
| Laryngeal Cleft repair          | 3 (10%)                    | 1 (3%)                         |                |
| Balloon Dilation                | 1 (3%)                     | 3 (10%)                        |                |
| Postoperative complications     | 2 (7%)                     | 6 (20%)                        | 0.25           |
| Hospital stays (days)           | 5 [5–7]                    | 6 [5.3–7.8]                    | 0.048          |

Values are presented as median [IQR] or Number (%)

is positively correlated with ORI values (with each 1 mmHg increase in *PaO*<sub>2</sub>, ORI values increased by 0.002; *P* < 0.001; Table 4), while the correlation with other factors was relatively small.

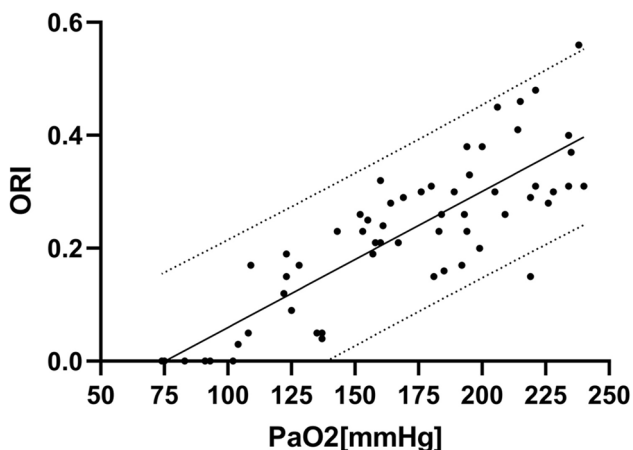
Finally, Fig. 2 illustrates a scatter plot depicting the relationship between ORI and *PaO*<sub>2</sub> ≤ 240 mmHg (*n* = 59). Linear regression analysis revealed a robust positive correlation (*r*<sup>2</sup> = 0.69, *P* < 0.01; ORI = −0.1819 + 0.0024 × *PaO*<sub>2</sub>;

**Table 4** Multiple linear regression analysis

| Model                    | B      | S.E    | P value |
|--------------------------|--------|--------|---------|
| Weight                   | 0.004  | 0.005  | 0.444   |
| PaO <sub>2</sub> (mmHg)  | 0.002  | <0.001 | <0.001  |
| PaCO <sub>2</sub> (mmHg) | 0.001  | 0.002  | 0.794   |
| SpO <sub>2</sub> (%)     | 0.007  | 0.018  | 0.679   |
| Operation time (min)     | <0.001 | 0.001  | 0.839   |

Dependent variable: ORI  $R^2=0.672$

PaO<sub>2</sub> Arterial oxygen partial pressure, PaCO<sub>2</sub> Arterial carbon dioxide partial pressure, SpO<sub>2</sub> Peripheral oxygen saturation

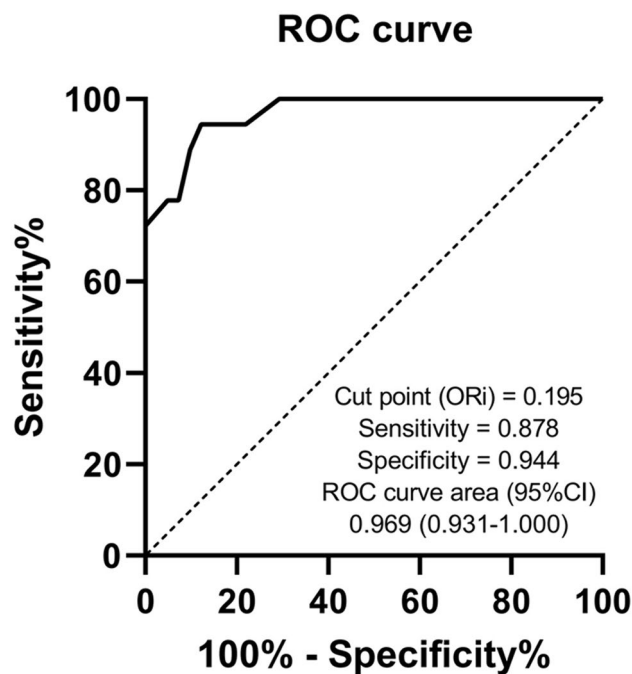


**Fig. 2** Correlation between ORI and PaO<sub>2</sub> ( $\leq 240$  mmHg). Linear regression lines with 95% predicted values are given. ( $r^2=0.69$ ;  $P < 0.01$ ;  $ORI = -0.1819 + 0.0024 \times PaO_2$ )

Fig. 2). Moving on to Fig. 3, the ROC curve displays the optimal cut value of ORI for detecting PaO<sub>2</sub>  $\geq 150$  mmHg. The area under the ROC curve (AUC) is 0.969 (95% CI 0.931–1.000), and the derived cutoff value from the ROC analysis is 0.195 (sensitivity 0.878, specificity 0.944; Fig. 3).

**Discussion**

In this randomized controlled trial, our findings suggest that reducing FiO<sub>2</sub> through continuous ORI monitoring facilitates a smooth surgical procedure in pediatric patients without compromising oxygenation. Prolonged high-concentration oxygen settings during HFNO may not be necessary. Dynamic adjustment of oxygen concentration has the potential to mitigate peri-operative hyperoxemia in children, thereby offering possible advantages in reducing peri-operative complications [8]. Currently, there are no established standards for setting the optimal FiO<sub>2</sub> during general anesthesia. Low oxygen levels can lead to vital organ hypoxia, while high oxygen levels may result in systemic



**Fig. 3** The ROC curve identifies the best ORI value to detect PaO<sub>2</sub>  $\geq 150$  mmHg. Optimal cut point is where sensitivity and specificity on the ROC curve maximize

vasoconstriction, atelectasis, brain injury, and other complications [6]. Therefore, finding the appropriate FiO<sub>2</sub> during the peri-operative period is crucial for improving pediatric outcomes [14]. In pediatric laryngeal surgeries with HFNO, oxygen concentration is often inclined towards pure oxygen to maintain intra-operative oxygenation. Oxygen concentration is only reduced during airway interventions to prevent the risk of airway fires [4]. Oxygen requirements in pediatric laryngeal surgery are dynamic, so why not adjust FiO<sub>2</sub> based on the surgical process to prevent unnecessary hyperoxygenation?

ORI is a novel noninvasive indicator that reflects oxygenation within the range of mild hyperoxia (PaO<sub>2</sub> 100–200 mmHg, ORI 0–1) [10, 11, 15]. Many case reports have demonstrated the value of ORI in oxygenation monitoring, ORI has been utilized as an early warning tool, assisting healthcare professionals in early identification of both hypoxemia and hyperoxemia, and aiding in the adjustment of oxygen concentration [16–20].

Under stable surgical conditions, adjusting oxygen concentration has minimal impact on SpO<sub>2</sub>. However, certain situations, such as increased surgical stimulation, respiratory secretions, airway obstruction due to bleeding, and laryngospasm resulting from light anesthesia, may lead to a decline in SpO<sub>2</sub>. Generally, after suspending surgery, clearing the airway, and deepening anesthesia, SpO<sub>2</sub> tends to recover spontaneously within a short time without the

need to change oxygen concentration. Once familiar with the surgical procedure, our focus shifts to specific time points for adjusting oxygen concentration based on ORI to prevent  $SpO_2$  decline. For longer-duration laryngeal surgeries where arterial blood gas analysis is necessary, we opt for arterial cannulation to reduce the frequency of arterial punctures, thus protecting the child. Adjusting  $FiO_2$  guided by ORI can also help avoid the harm associated with arterial punctures.

The pre-operative oxygen partial pressure did not differ significantly between the two groups. However, the ORI group demonstrated significantly lower postoperative oxygen partial pressure compared with the control group, along with a shorter hospital stay. The median average weighted  $FiO_2$  in the ORI group was 85.9%, this discrepancy may be influenced by the adjustment time and magnitude. Our approach involved initiating with 100%  $FiO_2$  and adjusting it by 5% every five minutes. Increasing the adjustment magnitude or shortening the adjustment time could potentially result in a lower average weighted  $FiO_2$ . We selected pure oxygen as the initial concentration due to uncertainty regarding whether HFNO could ensure intra-operative oxygenation while maintaining spontaneous respiration. In children with throat diseases and chronic hypoxia, high  $FiO_2$  during surgery are non-physiological. By addressing airway defects and adjusting oxygen concentration accordingly, the ORI group achieved peri-operative  $PaO_2$  levels within the normal physiological range. This likely contributed to the lower complication rate and shorter hospital stay observed in the ORI group.

Due to the diverse characteristics of pediatric patients, including variations in age, weight, duration of surgery, and surgical procedures, which could potentially impact ORI value changes and interpretation, we conducted a multiple linear regression analysis to explore the influencing factors. The results indicated that the only factor affecting the variation in ORI values in pediatric patients was  $PaO_2$  (Table 4). This suggests that during pediatric HFNO procedures, ORI values may, to some extent, indicate corresponding  $PaO_2$  values. However, previous research has shown that the relationship between ORI and  $PaO_2$  is not a simple linear one. Applegate et al. [21]. compared 485 pairs of ORI and  $PaO_2$  values and found a positive correlation when  $PaO_2$  was below 240 mmHg ( $r^2=0.536$ ). In our collected data, we have only 59 data points that meet the condition of  $PaO_2 \leq 240$  mmHg. The linear regression analysis conducted on the collected 59 data points showed a relatively strong positive correlation ( $r^2 = 0.69$ ;  $P < 0.01$ ;  $ORI = -0.1819 + 0.0024 \times PaO_2$ ; Fig. 2). The ROC curve indicates that the optimal ORI threshold for  $PaO_2 \geq 150$  mmHg is 0.195, which differs from the previous result of 0.21 (Fig. 3). The limited data availability and the inclusion of pediatric patients who may

have experienced chronic hypoxia could be contributing factors to this observed difference.

One study suggests that closed-loop oxygen control improves oxygenation in pediatric patients receiving HFNO therapy and allows for more efficient use of oxygen resources [22]. The closed-loop system reduces the frequency of manual adjustments, thereby reducing the workload for healthcare providers. Monitoring ORI may potentially enable the automated titration of oxygen concentration by a system, offering a better and more automated approach to non-invasive airway management.

This study also has several limitations. First, the setting of  $FiO_2$  during the HFNO procedure may be lower compared with the actual  $FiO_2$  due to the influence of children not having a fully closed oral cavity. Second, the sensitivity of ORI is limited to the  $PaO_2$  range of 100–200 mmHg, while both groups started with 100%  $FiO_2$ .  $PaO_2$  measurements obtained at the beginning of the procedure with  $PaO_2 \geq 200$  mmHg exceeded the sensitive range of ORI. Caution is needed when interpreting ORI readings as they do not directly equate to  $PaO_2$ . Third, our study did not collect complete data on children's atelectasis, and further investigation is needed to determine whether dynamic adjustment of oxygen concentration during HFNO can reduce the occurrence of atelectasis. Finally, the sample size of 60 cases is relatively small, and larger double-blind randomized controlled trials may be required to further validate our findings.

In summary, lowering  $FiO_2$  during pediatric laryngeal surgery with HFNO through continuous monitoring of ORI is feasible. This monitoring method holds potential for use in the peri-operative period. However, ORI cannot entirely replace arterial blood gas analysis for  $PaO_2$ , so caution is necessary when interpreting ORI readings.

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**Data availability** The data that support the findings of this study are available from the corresponding author, upon reasonable request.

## Declarations

**Conflict of interest** The authors declare no potential conflicts of interest related to commercial or financial relationships in this study.

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