Obesity Surgery (2019) 29:3992–3999
https://doi.org/10.1007/s11695-019-04077-y

ORIGINAL CONTRIBUTIONS

Apneic Oxygenation During Prolonged Laryngoscopy in Obese Patients: a Randomized, Double-Blinded, Controlled Trial of Nasal Cannula Oxygen Administration

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Published online: 16 July 2019

Abstract

Background Obese patients have a propensity to desaturate during induction of general anesthesia secondary to their reduced functional residual capacity and increased oxygen consumption. Apneic oxygenation can provide supplemental oxygen to the alveoli, even in the absence of ventilation, during attempts to secure the airway. In this study, we hypothesized that oxygen administration through a nasopharyngeal airway and standard nasal cannula during a simulated prolonged laryngoscopy would significantly prolong the safe apneic duration in obese patients.

Methods One hundred thirty-five obese patients undergoing non-emergent surgery requiring general anesthesia were randomized to either the control group or to receive apneic oxygenation with air versus oxygen. All patients underwent a standard intravenous induction. For patients randomized to receive apneic oxygenation, a nasopharyngeal airway and standard nasal cannula were inserted. A simulated prolonged laryngoscopy was performed to determine the duration of the safe apneic period, defined as the beginning of laryngoscopy until the peripheral oxygen saturation (SpO_2) reached 95%.

Results The oxygen group had a median safe apneic duration that was 103 s longer than the control group. The lowest mean SpO_2 value during the induction period was 3.8% higher in the oxygen group compared to the control group. Following intubation, patients in the oxygen group had a mean end tidal carbon dioxide ($ETCO_2$) level that was 3.0 mmHg higher than patients in the control group.

Conclusions In obese patients, oxygen insufflation at 15 L/min through a nasopharyngeal airway and standard nasal cannula can significantly increase the safe apneic duration during induction of anesthesia.

Keywords Obesity · Apneic oxygenation · Laryngoscopy · Airway management · Difficult intubation

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Introduction

The most recent Global Health Observatory data shows that half a billion adults are obese, and of the obese population, the morbidly obese segment is growing the most rapidly [1]. In obese patients, functional residual capacity (FRC) and respiratory compliance decrease as body mass index (BMI) increases. In addition, a larger proportion of oxygen consumption goes towards the work of breathing [2]. These changes predispose obese patients to rapid desaturation during induction of general anesthesia [3]. The time necessary for laryngoscopy and intubation may exceed the safe apneic duration, which is defined as the period of apnea before the peripheral oxygen saturation (SpO_2) decreases to 95% [4–8] and ranges from 2 to 4 min [4–6]. Exceeding this duration, such as may occur with a difficult intubation, increases the risk of hypoxia.

Apneic oxygenation can supply oxygen to the alveoli during a prolonged laryngoscopy, even while the patient is not being ventilated. During apnea, only one-tenth of the normal amount of carbon dioxide (CO_2) is returned from the bloodstream to the alveoli, since most of the CO_2 is buffered by the blood and tissues. This creates a negative pressure differential at the level of the alveoli, which entrains oxygen from the environment, provided no obstruction exists [7]. Various techniques for supplying oxygen during the apneic period have been described including nasopharyngeal airways, standard nasal cannula prongs, high-flow humidified nasal prongs, and modified endotracheal tubes [4, 5, 8–12]. The standard nasal cannula consists of a flexible tube with two short prongs that protrude into the patient's nares (Fig. 1). It is usually connected to an auxiliary oxygen source, which allows the main circuit of the anesthesia machine to be used for traditional preoxygenation with a face mask.

In this study, we hypothesized that oxygen administration through a nasopharyngeal airway and standard nasal cannula during a simulated prolonged laryngoscopy would significantly prolong the safe apneic duration in obese patients.

Materials and Methods

This randomized, controlled, double-blinded study was approved by the local institutional review board and performed at a public county teaching hospital. Written, informed consent was obtained from all patients prior to any study procedures.

Patients were included in the study if they were older than 18 years old, obese (BMI ≥ 30–39.9 kg/m^2) or morbidly obese (BMI ≥ 40–59.9 kg/m^2), and undergoing a non-emergent surgery requiring general anesthesia. They were excluded from the study for significant cardiopulmonary disease, active gastroesophageal reflux disease, concern for increased intracranial pressure, pregnancy or lactation, nasal obstruction, and known or suspected difficult airway. Patients were randomized using a random number sequence generator 1:1:1 to 3 groups: the control group, apneic oxygenation with 15 L/min oxygen, or apneic oxygenation with 15 L/min air. A member of the research team who was not involved in day-to-day research procedures (i.e., the statistician) created opaque envelopes containing index cards indicating to which group each subject had been randomized. Envelopes were opened in sequential order only after a subject had signed the consent form. A total of 189 patients were enrolled and 135 completed all study procedures (Fig. 2). Thirty-seven patients were enrolled and randomized but did not undergo any study procedures (e.g., surgery was canceled or rescheduled). An additional 17 patients did not complete study procedures (e.g., difficult airway, allergic reaction on induction, tank malfunction).

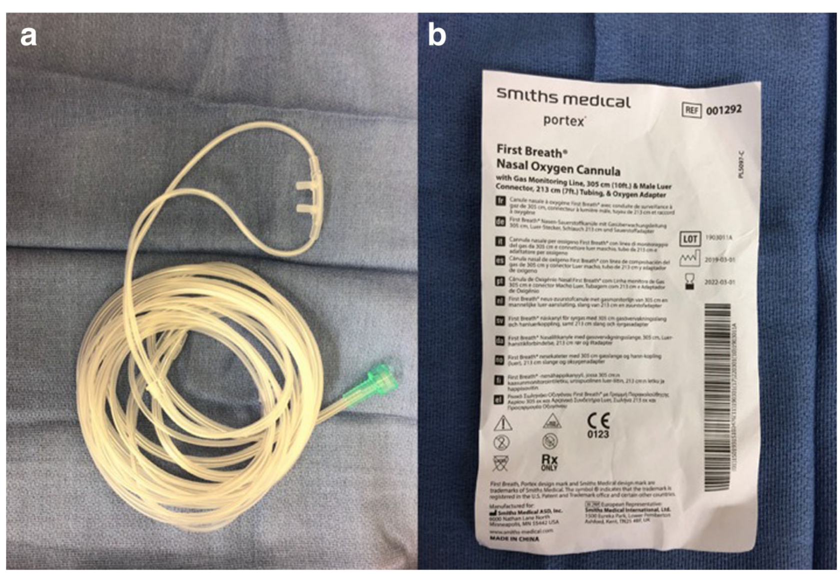

Fig. 1 **a** Standard nasal cannula. **b** First Breath® Nasal Oxygen Cannula product information

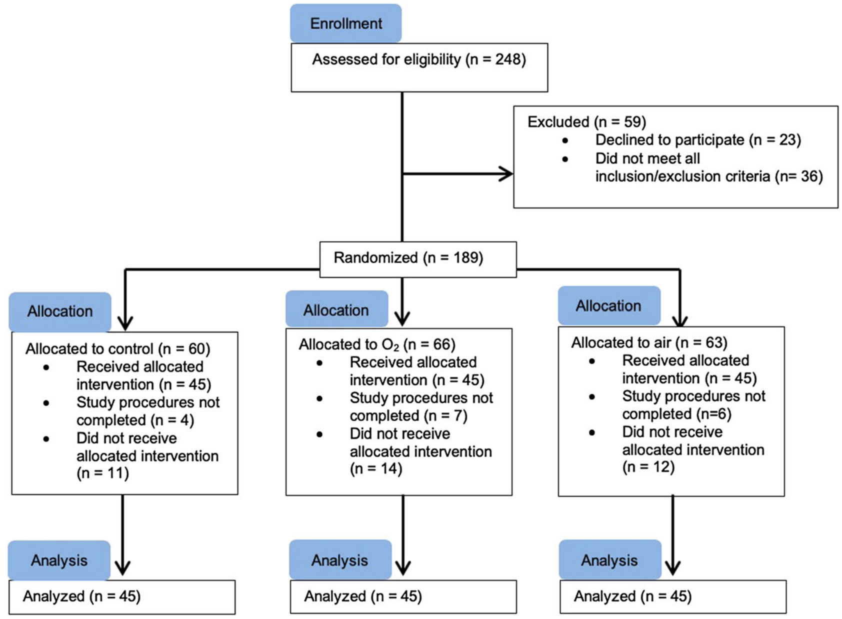

Fig. 2 Patient randomization flow diagram

The patients and all care providers were blinded. The only non-blinded personnel were anesthesia technicians who were educated on the study and given the sealed randomization envelopes after each subject was consented. They were instructed to read each card and bring a wrapped E-cylinder of the blinded gas (air vs. oxygen) that the card inside the envelope indicated. All tanks were covered with aluminum foil so that only the flow dial was visible to the anesthesia provider.

Prior to induction, standard monitors recommended by the American Society of Anesthesiologists (ASA) were applied. The default signal averaging time for the pulse oximetry was set to 5 s. Patients were placed in a ramped position with 25° reverse Trendelenburg for preoxygenation [13]. Preoxygenation using a tight-fitting face mask was initiated while the patient was breathing spontaneously and until the ETO_2 reached > 80% for at least 1 min. Flow from the nasal cannula did not commence until the beginning of the apneic period, which was defined as the time the face mask was taken off the face to begin laryngoscopy.

All patients underwent a standard intravenous induction with fentanyl (1 mcg/kg), lidocaine (50 mg), and propofol (1.5–2 mg/kg). Additional propofol was given in increments of 10 mg/min to prevent awareness during the apneic period. After mask ventilation was confirmed, rocuronium (0.6 mg/kg) was administered and a lubricated nasopharyngeal airway (Bard, Covington, GA) was placed into a nare. The nasal cannula (Smiths Medical, Minneapolis, MN) was then inserted into the patient's nares and was connected to the wrapped E-cylinder containing either oxygen or air (Figs. 1 and 3).

Providers were instructed to manually ventilate the patient at 10 breaths/min with a tidal volume of 8 mL/kg of ideal body weight (IBW). Real-time feedback from the ventilator was used to guide the manual ventilation. When 2 min had passed, the provider was asked to remove the mask from the patient's face and begin direct laryngoscopy. This marked the beginning of the apneic period (time-zero). At this time, the E-cylinder connected to the nasal cannula was turned to 15 L/m (air vs. oxygen). The anesthesia provider was asked to call out the Cormack-Lehane view seen [14]. If a grade III–IV view was seen, the provider was asked to take appropriate steps to secure the airway and further study procedures were ceased. If a grade I–II view was seen, the provider was asked to relax the laryngoscope to simulate a prolonged laryngoscopy with a grade III view and wait for the patient to desaturate to 95% or until 8 min had passed, whichever came first. At that time, the patient was immediately intubated and given 2 manual breaths at 20 cm water (H_2O) to confirm correct endotracheal tube position. The ventilator was then turned on to a preset tidal volume of 8 cc/kg IBW at a rate of 10 breaths/min and a positive end expiratory pressure (PEEP) of 5 cm H_2O. The safe apneic duration was recorded as the time from removal of the face mask until the SpO_2 reached 95% or until apnea was terminated at a maximum of 8 min. The time for resaturation was defined as the time from intubation until the SpO_2 reached 100%, or the highest the patient could reach and remain at for 1 min (Fig. 4).

The following information was recorded for each patient: age, gender, total body weight (TBW), IBW, BMI, serum bicarbonate, hemoglobin, ASA classification, smoking status, and baseline vital signs. Each patient was screened for obstructive sleep apnea (OSA) using the STOP-BANG questionnaire, which includes information regarding snoring, tiredness, observed apnea, high blood pressure, BMI, age, neck circumference, and gender. Peripheral oxygen saturation (SpO_2) was recorded at baseline on room air, at induction, at the start of apnea

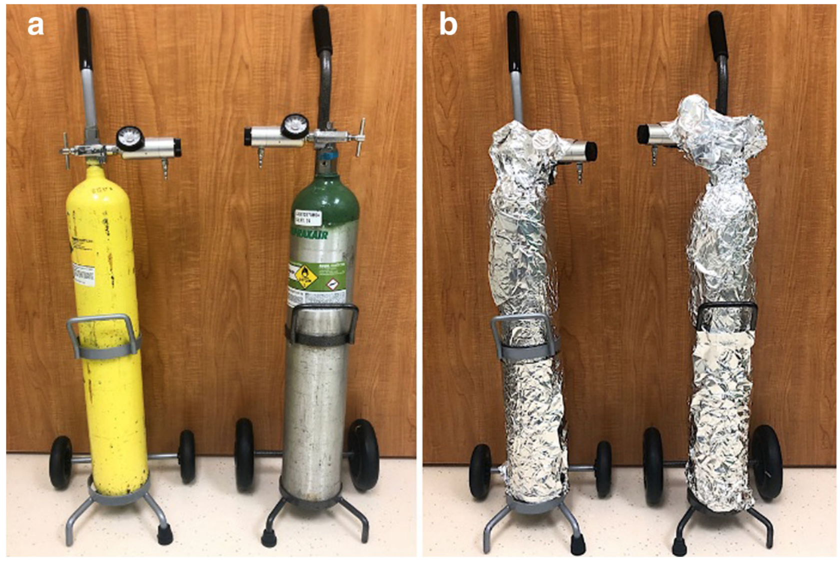

Fig. 3 **a** Air tank on left. Oxygen tank on right. **b** Air and oxygen tanks wrapped in aluminum foil for blinding purposes

(time-zero), and then continuously until termination of the study protocol. The end tidal O_2 (ETO_2) values at the start of induction and apnea were recorded. The safe apneic duration and the lowest SpO_2 during the induction period were also recorded. Upon successful intubation, the end tidal carbon CO_2 ($ETCO_2$) was recorded.

The primary outcome of the study was the safe apneic duration, defined as the time from the beginning of apnea until the SpO_2 fell to 95%. Apnea time was limited to a maximum length of 8 min for all patients. The secondary outcome measure was the resaturation time, defined as the time from intubation until the SpO_2 reached 100%, or the highest the patient could reach and remain at for 1 min.

Statistical Analysis

The study was designed to detect with 80% power an increase of 3 min in apnea time for patients in the oxygen group compared to those in the control group. The total observation time for both groups was limited to 8 min. Assuming a 2-min apnea time for obese patients in the control group, the study required a total of 72 obese patients in the 3 groups. Similarly, assuming a 1.5-min apnea time for morbidly obese patients in the control group, the study needed a total of 60 patients in the three groups. Accounting for loss to follow-up, a total of 68 patients were enrolled.

Data were summarized as mean ± standard deviation or median (interquartile range) and frequency and percentages. Kaplan-Meier survival curves were estimated and compared using stratified log-rank statistics where BMI class (obese and morbidly obese) was used as the stratification variable. Desaturation (survival) times are reported as medians with 95% confidence intervals.

Results

Patient Characteristics

Patient characteristics in each study group are summarized in Table 1. There were no significant differences between the groups.

Outcome Measures

The median (95% confidence interval) time before SpO_2 fell to 95% for patients in the oxygen group was 265 s (218, 331) compared with 162 s (134, 179) in the control group and 151 s (137, 176) in the air group (Table 2). A total of 10 patients in the oxygen group maintained their SpO_2 above 95% during 8 min of apnea, at which time the apneic period was terminated and they were intubated (Fig. 5). For statistical analysis, these patients' apnea times were recorded as 8 min, although they would have persisted for longer if apnea had been allowed to continue. The lowest SpO_2 during the induction period was significantly higher in the oxygen group compared to the control and air groups. Following intubation, patients in the oxygen group also had a higher $ETCO_2$ than patients in the control and air groups. Patients in the oxygen group were able to resaturate significantly faster compared to patients in the control group (Table 2).

Discussion

In this study, apneic oxygenation through a nasopharyngeal airway and standard nasal cannula significantly prolonged the safe apneic duration in obese patients during a simulated prolonged laryngoscopy. In addition, patients who received apneic oxygenation with 100% oxygen maintained a higher

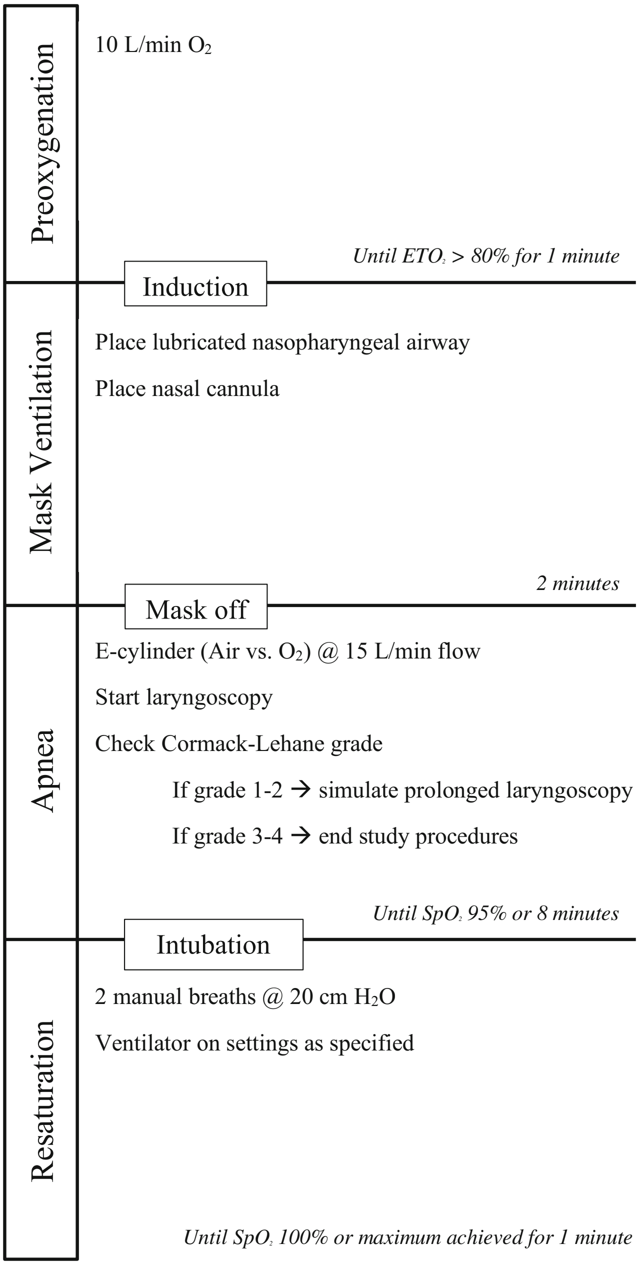

Fig. 4 Intraoperative timeline

SpO_2 throughout the induction period compared to the control and air groups. Furthermore, patients in the oxygen group were able to resaturate significantly faster than patients in the control group.

We chose the standard nasal cannula because it is inexpensive, readily available, and well tolerated. With a properly positioned nasal cannula, the anesthesia provider can place an oral airway, laryngeal mask airway, or laryngoscope and endotracheal tube without obstruction (Fig. 6). This technique also allows any increased pharyngeal pressure from the insufflation to be vented through the nares or open mouth during prolonged laryngoscopy, thus minimizing the risk of barotrauma.

In order for apneic oxygenation to be effective, the insufflated oxygen must reach the pharynx in order to provide oxygen enrichment. Thus, we chose to insert a nasopharyngeal airway in all patients in order to ensure that no obstruction was present. Obese patients are typically more difficult to mask ventilate [16], which can be ameliorated by the insertion of a nasopharyngeal airway. Flow rates were set to 15 L/min in order to maximize the amount of oxygen that would reach the pharynx. Previous studies have shown that rates of 15 L/min with a nasal cannula were well tolerated, especially for short periods of time, and did not produce any adverse events [17]. The Difficult Airway Society recommends the use of nasal cannula for oxygen insufflation at flows of 5–15 L/min [18].

Although previous studies have evaluated apneic oxygenation in the obese population, these studies were not double-blinded as they randomized to two groups: oxygen vs. control, which was easily distinguishable as the flow of oxygen is clearly audible. Thus, the providers caring for the patients knew which group each subject had been randomized to and may have been consciously or unconsciously biased in their actions towards a particular outcome. The present study was double-blinded with covered E-cylinders containing oxygen versus air, so that the providers did not automatically assume that presence of audible flow meant that insufflation was with oxygen. The control group was included to (1) determine the safe apneic duration of obese patients without any nasal cannula insufflation and (2) determine if insufflation of air through the nasal cannula prolonged the safe apneic duration compared to the control group.

Previous studies have excluded morbidly obese patients, but it is *precisely* this population that can benefit the most from the additional safe apnea time afforded by the use of apneic oxygenation [4, 8, 11]. Since these patients have a severely reduced FRC in conjunction with higher oxygen consumption, they are the most likely to desaturate during the induction period. Thus, the additional time afforded by apneic oxygenation may increase the first-pass intubation rate and decrease the incidence of repeated laryngoscopy in these patients.

Although this study adds to the body of literature supporting the use of apneic oxygenation, there are some limitations of the technique. Our study subjects were mostly women. We did not exclude men and enrolled all patients who met all inclusion and exclusion criteria, which resulted in the vast majority of participants being female. This is likely due to the fact that in the general population, obesity is more prevalent in women than in men, and many of the surgeries performed at our institution are gynecological in nature [19]. During apneic oxygenation, CO_2 levels continue to rise, which can lead to

Table 1 Patient characteristics. Data are expressed as means and standard deviations unless otherwise noted

Variable	Control ($n = 45$)	O_2 ($n = 45$)	Air ($n = 45$)
Age, years	46.1 (10.3)	47.1 (12.7)	46.9 (12.6)
Female sex, *n* (%)	34 (75.6%)	40 (88.9%)	42 (93.3%)
Hispanic ethnicity, *n* (%)	26 (57.8%)	33 (73.3%)	22 (48.9%)
BMI, kg/m^2	40.5 (7.9)	38.8 (6.7)	39.0 (6.5)
TBW, kg	108.2 (22.3)	101.3 (20.9)	103.8 (24.5)
STOP-BANG score [15]	3.3 (2.1)	2.7 (1.8)	2.8 (1.6)
Preoperative HCO_3^-, mmol/L	26.4 (2.4)	26.8 (2.6)	26.0 (2.1)
Preoperative Hgb, g/dL	13.4 (1.5)	12.4 (1.6)	12.4 (1.7)
Preoperative SpO_2[a]	98.4% (1.7)	98.7% (1.5)	98.8% (1.9)
Smoking status, *n* (%)			
Current	7 (15.6%)	3 (6.7%)	6 (13.3%)
Former	10 (22.2%)	10 (22.2%)	11 (24.4%)
Never	28 (62.2%)	32 (71.1%)	28 (62.2%)

BMI body mass index, *TBW* total body weight, HCO_3^- serum bicarbonate concentration, *Hgb* serum hemoglobin concentration, SpO_2 peripheral blood oxygen saturation

[a] SpO_2 at baseline on room air

respiratory acidosis. The levels of maximum CO_2 in prior studies utilizing apneic oxygenation have ranged widely with an average rate of rise of 2–3 mmHg/min [12, 20, 21]. Carbon dioxide retention during the apneic period may provide a limit to the ultimate duration of safe apneic oxygenation. Therefore, total apnea time was limited to 8 min in order to prevent further rises in CO_2. The presence of a nasal cannula during mask ventilation can cause a leak, which can decrease the effective tidal volume being delivered to the patient. However, for all enrolled patients, the anesthesia provider was able to achieve a tidal volume of 8 cc/kg IBW and reach an ETO_2 of > 80% at the start of the apneic period, suggesting that no significant leak occurred that interfered with mask ventilation.

The utility of apneic oxygenation may be limited in certain populations (e.g., healthy, non-obese patients) who already have a long safe apneic duration. Additionally, it is possible that apneic oxygenation is more useful for trainees who are less experienced at intubation than for expert intubators [22]. In such a setting, apneic oxygenation provides the opportunity for trainees to perform endotracheal intubation with a decreased risk of desaturation, thus allowing them more time to develop their airway management skills. However, even more experienced providers can benefit from the use of apneic oxygenation, especially in high-acuity patients with difficult airways who may need the additional safeguard against desaturation. Studies have shown that the majority of difficult intubations are unexpected, and thus apneic oxygenation may afford an additional margin of safety [23]. Since our study excluded patients with grade III–IV views, it is unknown if apneic oxygenation is of benefit in obese patients with difficult airways. We believe that it would be but for ethical reasons did not want to purposefully desaturate subjects with grade III-IV airways.

Table 2 Study outcome measures. Data are expressed as means and standard deviations unless otherwise noted

Outcome Measure	Control ($n = 45$)	O_2 ($n = 45$)	Air ($n = 45$)	*p* value
ETO_2[a]	92.0% (3.1)	93.2% (2.7)	92.2% (3.3)	0.11
Desaturation to SpO_2 95% (sec)[b]	162 (134, 179)	265 (218, 331)	151 (137, 176)	<0.001
Lowest SpO_2	88.7% (3.4)	92.5% (3.1)	88.6% (5.1)	<0.001
$ETCO_2$[c]	47.1 (4.0)	50.1 (6.3)	48.3 (5.5)	<0.03
Resaturation (sec)[b]	71 (55, 106)	50 (41, 59)	59 (42, 79)	<0.02

Abbreviations: ETO_2, end-tidal oxygen concentration; SpO_2, peripheral blood oxygen saturation; $ETCO_2$, end-tidal carbon dioxide

[a] ETO_2 at start of apneic period

[b] Represented as median and 95% confidence interval

[c] $ETCO_2$ upon intubation

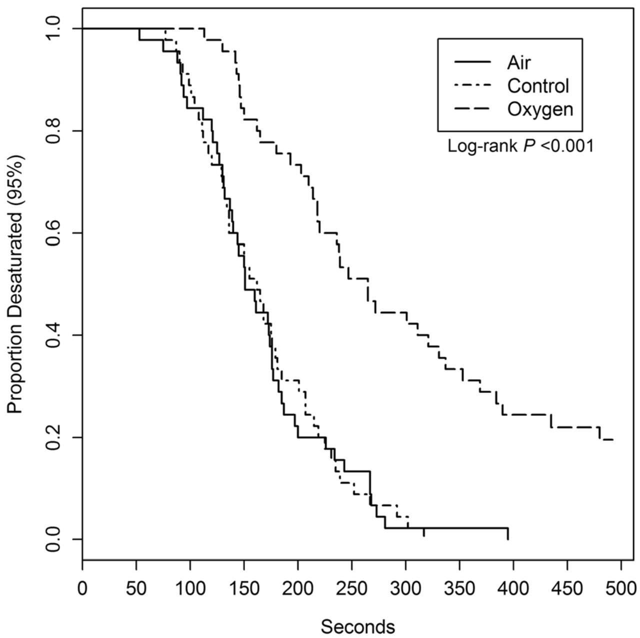

Fig. 5 Survival curves illustrating desaturation to SpO_2 95% in each patient group

In summary, this study shows that in obese patients, oxygen administration through a nasopharyngeal airway and standard nasal cannula can significantly increase the safe apneic duration during induction of anesthesia. In this patient population that is susceptible to rapid desaturation, apneic oxygenation can provide additional time for the airway to be secured before hypoxia occurs. The relative simplicity and safety of apneic oxygenation in this manner has the potential to make induction of general anesthesia and intubation a safer procedure, with a higher success rate and fewer complications. Therefore, we recommend that apneic oxygenation be considered for all obese patients undergoing general anesthesia.

Fig. 6 Patient undergoing apneic oxygenation during laryngoscopy and intubation

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the local institutional review board (STU 022017–074).

Consent Statement Informed consent was obtained from all individual participants included in the study.

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