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RESEARCH ARTICLE **OPEN ACCESS**

Optimizing Preoxygenation in Anesthesia: A Clinical Trial of Tidal Volume and Deep Breathing Techniques

Erwin Mulyawan[1,*] and Clarissa Jasmine Aurelia[1]

[1]*Department of Anaesthesiology, Faculty of Medicine, Pelita Harapan University, Tangerang, Banten, 15810, Indonesia*

Abstract:

Introduction: Preoxygenation before anesthetic induction allows denitrogenation and delays oxygen desaturation. Existing studies show inconsistent results, likely due to differences in patient populations, anesthetic systems, and Fresh Gas Flow (FGF). This study compares commonly used techniques focusing on achieving target End-tidal Oxygen (ETO_2) levels.

Methods: This randomized crossover trial compared three preoxygenation techniques in 120 ASA I adults undergoing elective surgery: Tidal Volume Breathing (TVB) for 3 minutes at 5 L/min FGF, 4 deep breaths in 30 seconds at 5 L/min FGF, and 8 deep breaths in 1 minute at 10 L/min FGF, separated by 15-minute room-air washout periods. ETO_2, End-tidal Carbon Dioxide ($ETCO_2$), Inspired Oxygen ($InspO_2$), and respiratory rate were recorded.

Results: All 120 patients achieved ETO_2 ≥90% with TVB by 3 minutes, plateauing at 87% by 2.5 minutes. Four deep breaths in 30 seconds yielded suboptimal ETO_2 (78% at 5 L/min; 82% at 10 L/min). Eight deep breaths in 1 minute achieved ETO_2 of 81% at 5 L/min and 91% at 10 L/min, comparable to TVB.

Discussion: TVB for 3 minutes remains consistent with guidelines recommending ETO_2 ≥90% prior to induction. The suboptimal performance of 4 deep breaths confirms that duration is critical regardless of FGF. Higher FGF with 8 deep breaths partially compensates for shorter duration.

Conclusion: Tidal volume breathing for 3 minutes was the most consistent technique for achieving the ETO_2 ≥90% surrogate target in this cohort. Findings are limited to ASA I patients and warrant further study in higher-risk populations.

Keywords: Preoxygenation, General anesthesia, Anesthesia induction, Tidal volume breathing, End-tidal oxygen, Fresh gas flow.

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*Address correspondence to this author at the Department of Anaesthesiology, Faculty of Medicine, Pelita Harapan University, Tangerang, Banten, 15810, Indonesia; E-mail: erwin_mulys@yahoo.co.id

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1. INTRODUCTION

Despite advances in modern anesthesia, preoxygenation remains a fundamental step prior to anesthetic induction and tracheal intubation. This process facilitates denitrogenation, increases oxygen reserves, and delays the onset of oxygen desaturation during the apneic period [1-3]. Preoxygenation is particularly crucial in situations such as Rapid Sequence Induction (RSI), difficult airway management, and in patient populations with reduced oxygen reserve, including obese, critically ill, and pregnant patients [4-6].

In current practice, End-tidal Oxygen (ETO_2 ≥90%) is widely accepted as the most reliable marker of effective preoxygenation [2, 7]. However, this target may not always be achieved due to factors such as mask leak, inadequate fresh gas flow, or insufficient duration of preoxygenation [8, 9]. Preoxygenation *via* Tidal Volume Breathing (TVB) for three minutes is commonly used worldwide [10]. Nevertheless, its effectiveness is influenced by several factors, including fresh gas flow, patient cooperation, and breathing circuit design [9, 11, 12]. Alternative techniques, such as four or eight deep breaths within a short period, have been proposed and challenge the necessity of the traditional three-minute TVB method [13, 14].

Recent literature highlights additional strategies to optimize preoxygenation, including head-up positioning, application of Positive End-expiratory Pressure (PEEP), High-flow Nasal Oxygen (HFNO), and apneic oxygenation [6, 12, 15-17]. Despite these advances, the fundamental comparison between traditional and rapid breathing techniques under controlled conditions remains clinically relevant.

Existing literature comparing different preoxygenation techniques continues to yield variable findings, which may be attributable to methodological differences such as patient populations, anesthetic systems, and variations in Fresh Gas Flow (FGF) [2, 18-21]. This study aims to compare the effectiveness of commonly used preoxygenation techniques and evaluate the impact of fresh gas flow using a circle absorber system, with emphasis on achieving target ETO_2 levels.

2. MATERIALS and Methods

This randomized crossover trial was approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Pelita Harapan University, on November 14, 2025 (approval number: 247/K-LKJ/ETIK/XI/2025). This study was a single-center trial conducted from January–February 2026. Informed consent was obtained from all participants. This study was conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) extension for crossover trials [22] and the Declaration of Helsinki.

Figure **1** shows the CONSORT flow diagram for enrolment, randomization, and analysis of this study. A total of 120 adult patients aged 18–60 years with ASA Physical Status I, no known comorbidities, and a Body Mass Index (BMI) between 18 and 27 kg/m^2 were enrolled. All patients were non-smokers scheduled for minor peripheral elective surgeries. Patients were excluded if they had a BMI below 18 or above 27 kg/m^2, were smokers, or had a beard, as facial hair may compromise mask seal and affect fresh gas flow delivery and ETO_2 measurements. Additional exclusion criteria included anticipated difficult airway, pregnancy, presence of dentures or facial abnormalities that could interfere with mask fit, and administration of sedative or opioid premedication prior to induction, as these agents may alter respiratory rate and tidal volume, both of which are secondary outcome variables in this study.

Each patient underwent all three preoxygenation techniques: TVB for 3 minutes at 5 L/min FGF, DB for 1 minute at 5 L/min FGF, and DB for 1 minute at 10 L/min FGF in a randomized order. The sequence of techniques was generated by drawing lots. The investigator was responsible for sequence generation, patient enrollment, and assignment, which did not permit allocation concealment and is acknowledged as a limitation. A 15-minute period of room-air breathing separated each technique to allow washout, and baseline measurements were obtained during room-air breathing immediately before each test. As the breathing technique could not be concealed, blinding of participants and the administering clinician was not feasible. Outcome assessment and data analysis were also unblinded. Before anesthetic induction, all techniques were explained to patients to familiarize them with mask breathing and ensure an adequate mask seal. A standardized anesthesia machine (Aestiva 5/Compact; Datex-Ohmeda, Madison, WI) was used for all subjects. The breathing circuit consisted of a circle absorber system with an Ohmeda GMS absorber containing USP-grade sodium hydroxide lime, disposable 60-inch corrugated breathing tubes, and a 3-L natural latex reservoir bag pre-inflated using the oxygen flush valve. Preoxygenation was administered with 100% oxygen *via* a well-fitting face mask, with all subjects positioned supine.

During TVB, patients were cued to sustain normal tidal volume and respiratory rate. During DB, patients were prompted to take a deep breath every 7.5 seconds, corresponding to approximately 4 breaths by 30 seconds and 8 breaths by 60 seconds. $InspO_2$, ETO_2, $ETCO_2$, and Respiratory Rate (RR) were recorded continuously and are reported at 30-second intervals.

The predefined primary outcome was the proportion of patients achieving the target ETO_2 ≥90% within the observation period for each technique, reported with 95% confidence intervals. Secondary outcomes ($InspO_2$, $ETCO_2$, RR) were analyzed using repeated-measures ANOVA. Because TVB was measured at six timepoints (30–180 seconds) while the two DB conditions were measured only at 30 and 60 seconds, a 3(technique) × 2(time) repeated-measures ANOVA was used for between-technique comparisons at the two shared timepoints, and a separate one-way repeated-measures ANOVA characterized the

TVB time course across all six timepoints. Mauchly's test was used to assess sphericity; where violated, the Greenhouse-Geisser correction was applied. Pairwise post-hoc comparisons between techniques used paired Student's t-tests with Holm-Bonferroni correction for multiple comparisons [23] and are reported as mean difference with 95% confidence interval. Time to attainment of the target ETO_2 ≥90% was compared between FGF levels (5 *vs*. 10 L/min, within the DB technique) using Kaplan-Meier estimation and the log-rank test, as previously described by Baraka *et al*. [14]. The event was defined as ETO_2 first reaching ≥90%; patients not reaching this threshold within the observation window were censored at their last recorded timepoint. Assuming a paired (crossover) design, 80% power, a small-to-moderate standardized effect size (dz = 0.3), and a two-sided α of 0.0167 (Holm-adjusted for three pairwise comparisons), a minimum of 120 participants would be required. There were no missing data among the recorded measurements. All analyses were performed in SPSS. A p-value of <0.05 was considered statistically significant.

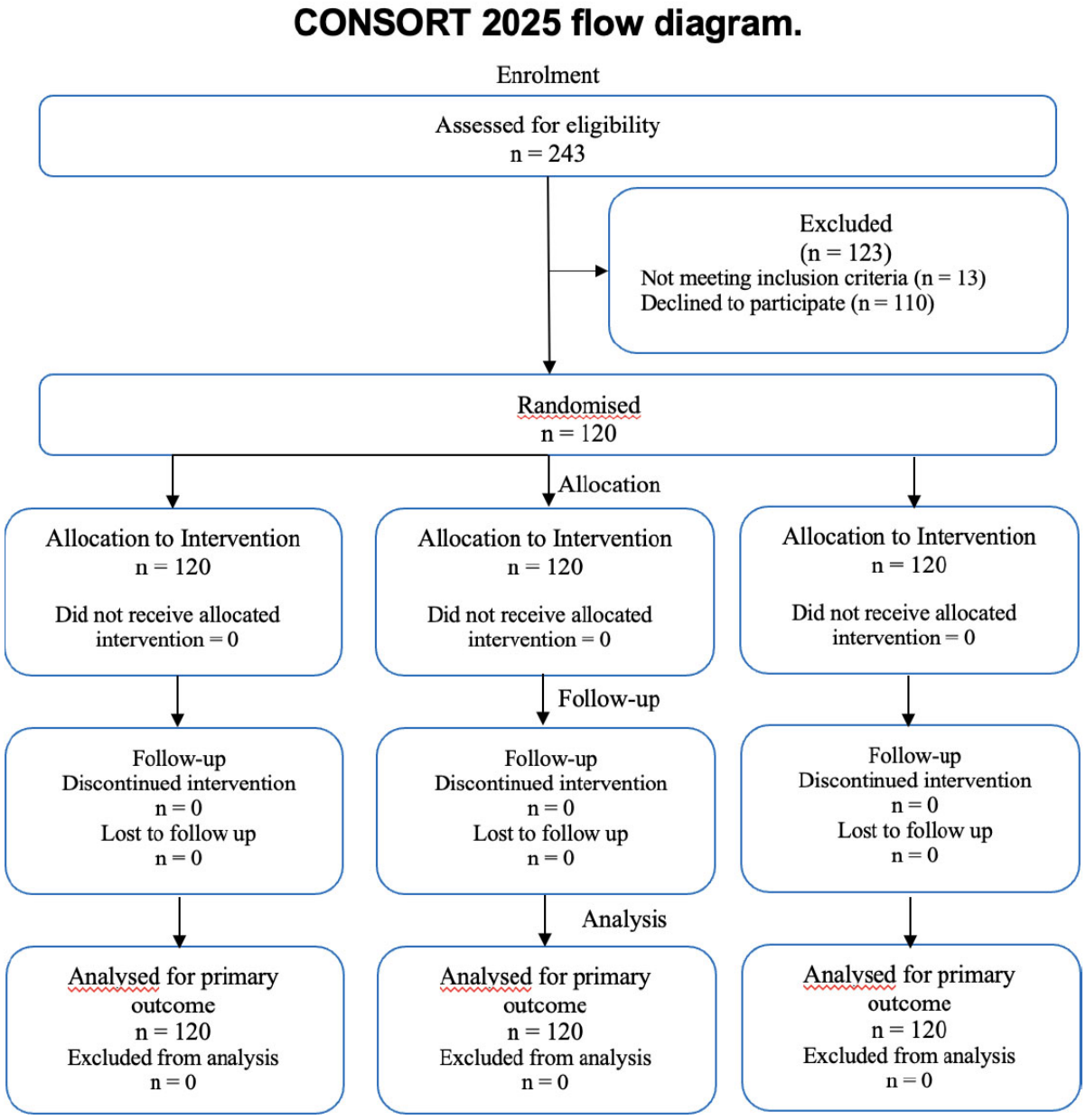


Fig. (1). CONSORT flow diagram of participant enrolment, randomization, allocation, follow-up, and analysis in this randomized crossover trial.

3. RESULTS

Following the inclusion and exclusion criteria, 120 patients with 60 females and 60 males were enrolled in this study, each undergoing all three preoxygenation techniques in a randomized order (Table **1**). Mean values of all measured variables at each time point are provided in Supplementary Table **S1**.

Table 1. Demographic characteristics of the study participants.

-	Total Population (N = 120)
Age (years)	29.60 ± 5.87
Weight (kg)	59.55 ± 7.03
Height (cm)	165.75 ± 6.20
BMI (kg/m^2)	21.60 ± 2.10

Note: Data are presented as mean ± standard deviation. BMI, body mass index.

Figure **2** shows that $InspO_2$ remained essentially unchanged throughout the 3-minute TVB observation period, with a mean of 94.75% at 5 L/min FGF. In contrast, deep breathing showed a significant FGF-dependent increase in $InspO_2$, rising from 80.29% to 87.63% at 30 seconds and from 83.63% to 92.58% at 60 seconds as FGF increased from 5 to 10 L/min. A 3(technique) × 2(time) repeated-measures ANOVA confirmed significant main effects of technique ($F(2,238) = 425.6$, $p < 0.001$) and time ($F(1,119) = 253.8$, $p < 0.001$), and a significant technique × time interaction ($F(5,595) = 16.1$, $p < 0.001$). Holm-corrected paired comparisons showed significantly higher $InspO_2$ with TVB than with either deep-breathing condition at 30 seconds (*vs*. DB-5 L/min: mean difference 9.71, 95% CI 8.94–10.48, $p < 0.001$; *vs*. DB-10 L/min: 2.38, 95% CI 1.95–2.80, $p < 0.001$) and at 60 seconds (*vs*. DB-5 L/min: 8.33, 95% CI 7.36–9.31, $p < 0.001$), but not significantly different from DB-10 L/min at 60 seconds (mean difference −0.62, 95% CI −1.63 to 0.38, $p = 0.21$). $InspO_2$ was also significantly higher with 10 L/min than 5 L/min FGF during deep breathing at both timepoints (30 s: mean difference −7.33, 95% CI −8.12 to −6.55, $p < 0.001$; 60 s: −8.96, 95% CI −10.16 to −7.76, $p < 0.001$).

Figure **3** shows the corresponding ETO_2 trends. All patients reached the target ETO_2 ≥90% by 3 minutes of TVB, with values rising from 60.83% at 30 seconds and plateauing at 87.08% by 2.5 minutes at a FGF of 5 L/min. Following 4 deep breaths in 30 seconds, ETO_2 increased to 78.29% at 5 L/min FGF and 82.67% at 10 L/min FGF, a statistically significant difference (mean difference 4.38, 95% CI 3.40–5.35, $p < 0.001$). When deep breathing was extended to 8 breaths over 1 minute, ETO_2 reached 91.29% at 10 L/min FGF, with all patients attaining the ≥90% target. This is comparable to 81.21% at 5 L/min FGF, where no patient reached the target within the 60-second observation window (mean difference 10.08, 95% CI 9.37–10.80, $p < 0.001$). Kaplan-Meier analysis showed that median time to reach ETO_2 ≥90% was 60 seconds with deep breathing at 10 L/min FGF, whereas the median was not reached within the 60-second observation window at 5 L/min FGF (log-rank $p < 0.0001$). The ETO_2 value at 8 deep breaths in 1 minute using 10 L/min (91.29%) showed no statistically significant difference from TVB at 3 minutes (91.63%; mean difference 0.34, $p = 0.9149$).

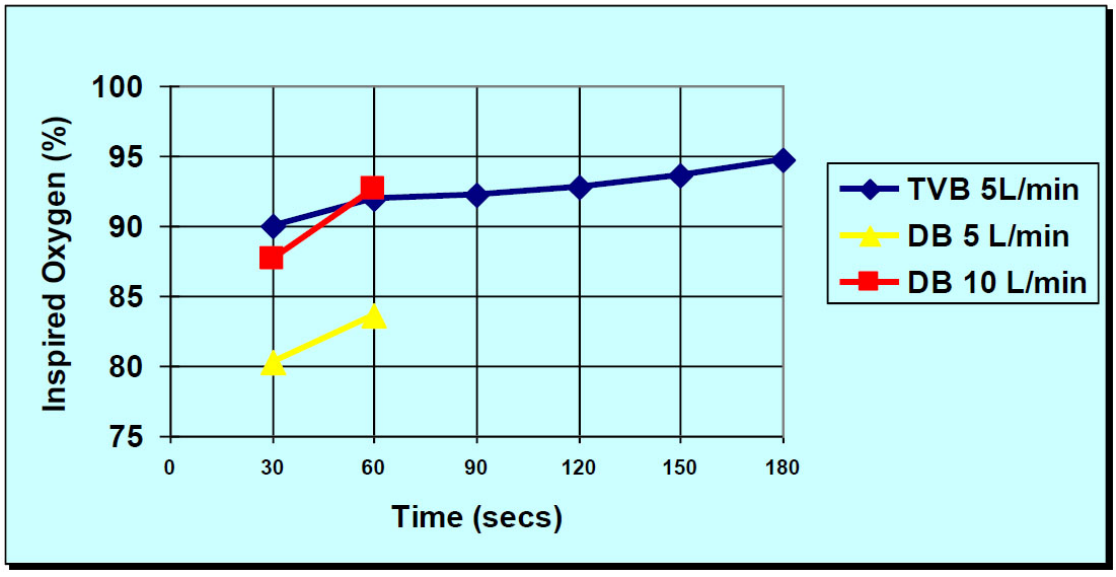


Fig. (2). Mean inspired oxygen concentration ($InspO_2$) over time during Tidal Volume Breathing (TVB) at 5 L/min and Deep Breathing (DB) at 5 and 10 L/min fresh gas flow.

Tidal volume breathing produced a significant decline in mean $ETCO_2$ over time (one-way repeated-measures ANOVA with Greenhouse-Geisser correction: $F(5,115) = 357.6$, $p < 0.001$), falling from 27.74 mmHg at 30 seconds to 21.00 mmHg at 180 seconds, but no significant change in respiratory rate ($F(5,115) = 2.45$, $p = 0.038$ uncorrected; $p = 0.094$ after Greenhouse-Geisser correction). Deep breathing elicited a more pronounced hypocapnic response than TVB, with $ETCO_2$ declining to 23.88 and 22.63 mmHg at 30 seconds using 5 and 10 L/min FGF, respectively (both significantly lower than TVB at the same timepoint, Holm-corrected $p < 0.001$), and to 22.25 and 20.63 mmHg at 60 seconds with 8 deep breaths (Fig. 4).

During observation in the recovery room, 5 of 120 patients experienced transient dizziness and 1 experienced transient nausea, both following the deep-breathing techniques. No other complications occurred.

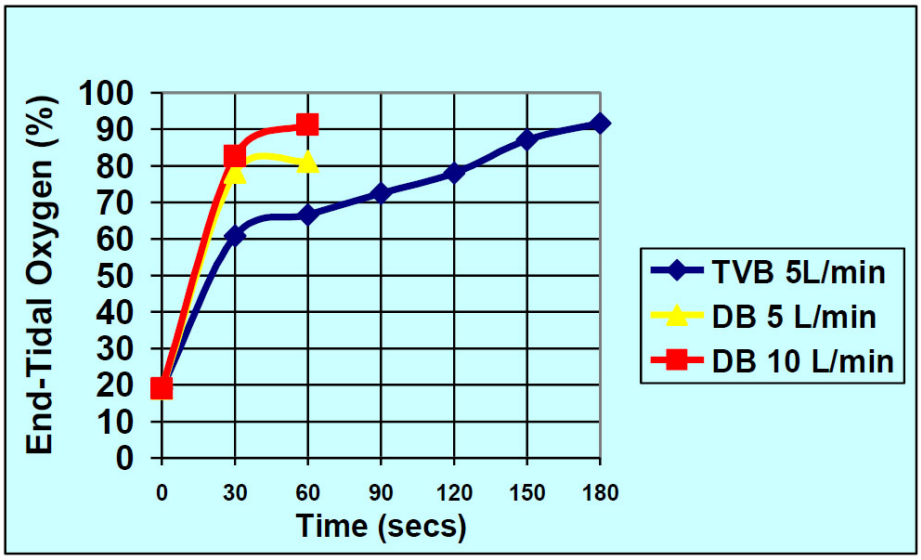


Fig. (3). Mean End-tidal Oxygen Concentration (ETO_2) over time during Tidal Volume Breathing (TVB) at 5 L/min and Deep Breathing (DB) at 5 and 10 L/min fresh gas flow.

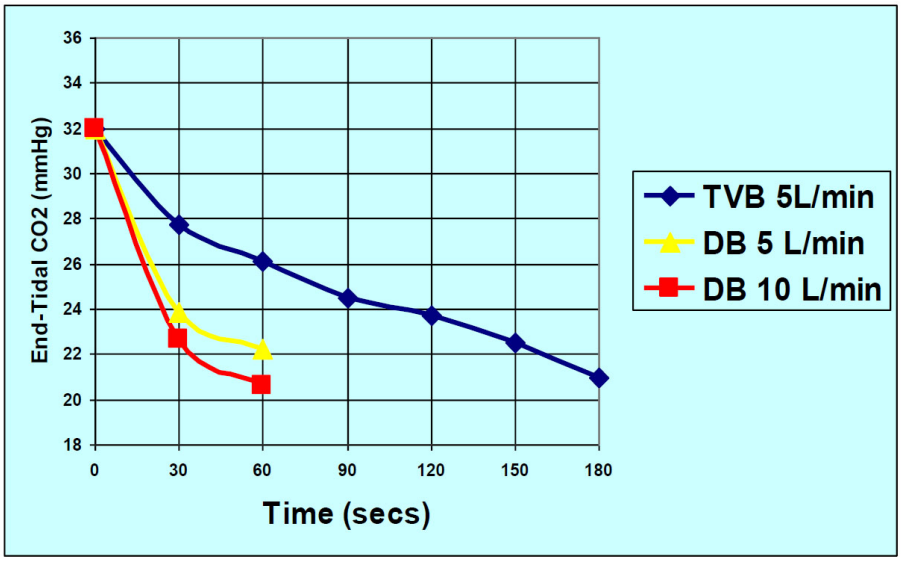


Fig. (4). Mean End-tidal Carbon Dioxide ($ETCO_2$) over time during Tidal Volume Breathing (TVB) at 5 L/min and Deep Breathing (DB) at 5 and 10 L/min fresh gas flow.

4. DISCUSSION

This study shows that tidal volume breathing for 3 minutes reliably achieves the ETO_2 ≥90% target, a widely used surrogate marker of preoxygenation adequacy, within this timeframe. This finding is consistent with existing literature [14, 20, 21] and supports the continued use of tidal-volume breathing as a commonly used technique, though ETO_2 attainment alone does not confirm improved safe apnea time or clinical outcomes. Increased Fresh Gas Flow (FGF) from 5 to 10 L/min did not significantly enhance ETO_2 during tidal volume breathing. In comparison, the 4-deep-breath-in-30-second checkpoint resulted in suboptimal preoxygenation, with none of the subjects achieving the target ETO_2 of ≥90%. This suggests that, although appealing in time-constrained situations, the technique does not allow sufficient time for complete denitrogenation, particularly in the tissue and venous compartments [24]. Additionally, increasing FGF did not significantly improve outcomes at this early checkpoint, likely due to a mismatch between high inspiratory demand and the available fresh gas flow, resulting in entrainment of exhaled gases and a reduced inspired oxygen concentration.

Extending deep breathing to the full one minute significantly improved preoxygenation efficiency, particularly when combined with higher FGF (10 L/min). Under these conditions, ETO_2 values showed no statistically significant difference from tidal volume breathing, though this was not formally tested for equivalence. This finding shows the importance of adequate duration and sufficient fresh gas flow in optimizing deep breathing techniques. The improved performance at higher FGF may be explained by reduced rebreathing and increased inspired oxygen concentration during periods of high minute ventilation [25].

An important physiological consideration is that effective preoxygenation involves not only alveolar oxygenation but also oxygen loading of tissue and venous compartments. Rapid breathing techniques can achieve high alveolar oxygen concentrations quickly, but the limited time may limit oxygen storage in peripheral compartments, resulting in faster desaturation during apnea [1, 3]. This may explain the inferior performance of the 4-deep-breath checkpoint despite relatively high inspired oxygen levels.

The incidence of transient dizziness observed with deep breathing is clinically notable and warrants closer consideration. This most likely reflects acute hypocapnia from hyperventilation exceeding metabolic CO_2 production, resulting in cerebral vasoconstriction and a transient reduction in cerebral blood flow [26]. A related but distinct concern is the Bohr effect: acute hypocapnia left-shifts the oxyhemoglobin dissociation curve, increasing hemoglobin's affinity for oxygen and potentially impairing its unloading to tissues. While these symptoms were transient and self-limited in this healthy ASA I cohort, the physiological basis for them raises a caution for populations in whom acute reductions in cerebral perfusion carry more risk, including patients with cerebrovascular disease, epilepsy, or raised intracranial pressure [27].

This study has several limitations. It was conducted in ASA I patients undergoing elective peripheral surgery with normal cardiopulmonary physiology, which may limit generalizability to patients with reduced functional residual capacity or impaired oxygenation. Furthermore, although this study has been ethically approved at our institution, it was not registered in any prospective clinical trial databases. Blinding of participants, the administering clinician, outcome assessors, and the statistician was not feasible given the nature of the interventions. Adverse events were not tracked by fresh gas flow condition, limiting mechanistic interpretation of the observed dizziness and nausea. Additionally, surrogate markers such as ETO_2 were used to assess preoxygenation efficacy rather than clinical outcomes such as time to desaturation. Future studies should address these limitations with a priori sample-size planning, independent allocation concealment, more diverse patient populations, and clinically meaningful endpoints. Furthermore, adjuncts that may also enhance oxygenation and prolong safe apnea time, such as head-up positioning, application of positive airway pressure (PEEP or CPAP), and apneic oxygenation using nasal cannula or High-flow Nasal Oxygen (HFNO), may also be investigated.

CONCLUSION

This study shows that tidal-volume breathing for 3 minutes was the most consistent method for achieving the ETO_2 ≥90% target in a circle absorber system. As ETO_2 is a physiological surrogate, this does not by itself demonstrate improved safe apnea time or clinical outcomes. Deep breathing showed no statistically significant difference from TVB in ETO_2 only when performed for the full 1 minute with high fresh gas flow. Further research with a priori sample-size planning, investigating adjuncts to optimize preoxygenation such as positioning, apneic oxygenation, and positive end-expiratory pressure, may also be conducted.

AUTHORS' CONTRIBUTIONS

C.J., E.M.: Study conception and design; E.M.: Data collection; EM, C.J.: Analysis and interpretation of results; C.J.: Draft manuscript; All authors reviewed the results and approved the final version of the manuscript.

LIST OF ABBREVIATIONS

ANOVA	=	Analysis of Variance
ASA	=	American Society of Anesthesiologists
BMI	=	Body Mass Index
CONSORT	=	Consolidated Standards of Reporting Trials
CPAP	=	Continuous Positive Airway Pressure
DB	=	Deep Breathing

$ETCO_2$	=	End-Tidal Carbon Dioxide
ETO_2	=	End-Tidal Oxygen
FGF	=	Fresh Gas Flow
FRC	=	Functional Residual Capacity
GMS	=	Gas Management System
HFNO	=	High-Flow Nasal Oxygen
$InspO_2$	=	Inspired Oxygen Concentration
IRB	=	Institutional Review Board
PEEP	=	Positive End-Expiratory Pressure
RR	=	Respiratory Rate
RSI	=	Rapid Sequence Induction
TVB	=	Tidal Volume Breathing
USP	=	United States Pharmacopeia

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study obtained ethical approval from the Institutional Review Board (Faculty of Medicine, Pelita Harapan University), headed by Prof. Dr. dr. Cucunawangsih, Sp.MK (K), in November 2025, with approval number 247/K-LKJ/ETIK/XI/2025.

HUMAN AND ANIMAL RIGHTS

All procedures involving human participants were conducted in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Informed consent from patients enrolled in this study has been obtained.

STANDARDS OF REPORTING

CONSORT guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

Data is available in the Pelita Harapan University database and may be obtained *via* personal and formal requests to the aforementioned party.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

SUPPLEMENTARY MATERIAL

Supplementary material is available on the publisher's website along with the published article.

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