



## Experimental Research Article

Korean J Anesthesiol 2022;75(5):437-444

<https://doi.org/10.4097/kja.22240>

pISSN 2005-6419 • eISSN 2005-7563

Received: April 20, 2022

Revised: May 31, 2022 (1st); June 21, 2022 (2nd)

Accepted: July 12, 2022

### Corresponding author:

Mridul Dhar, M.D.

Department of Anesthesiology and Critical Care, All India Institute of Medical Sciences, Veerbhadra Road, Rishikesh 249203, India  
Tel: +91-9717778374

Email: [mridul.anaes@aiimsrishikesh.edu.in](mailto:mridul.anaes@aiimsrishikesh.edu.in)

ORCID: <https://orcid.org/0000-0002-1913-2586>

Previous presentation in conferences:

Initial data presented as a virtual poster in the World Congress of Anesthesia, Prague, 2021.

Abstract published in *Anesthesia & Analgesia* 133 (3 s\_suppl), 1827-1828.

# Use of a human patient simulator for apnea studies: a preliminary in vitro trial

Debendra Kumar Tripathy<sup>1</sup>, Mridul Dhar<sup>1</sup>,  
Bharat Bhushan Bhardwaj<sup>2</sup>, K Hemanthkumar<sup>3</sup>, Praveen  
Talawar<sup>1</sup>, Shalinee Rao<sup>3,4</sup>

<sup>1</sup>Department of Anesthesiology and Critical Care, <sup>2</sup>Department of Emergency Medicine, <sup>3</sup>Advanced Center for Simulation and Skills, <sup>4</sup>Department of Pathology, All India Institute of Medical Sciences, Rishikesh, India

**Background:** Modern human patient simulators (HPSs) could be used for researching critical scenarios such as apnea oxygenation. We aimed to study the use of a high-fidelity HPS to assess prolonged apnea using various oxygenation strategies with a simple high-flow nasal cannula (15 L/min).

**Methods:** An experimental simulation study using an HPS (CAE Healthcare™) was conducted after obtaining approval from the Institutional Review Board. The HPS responded according to real-time physiologically modeled responses to external gases, such as oxygen (O<sub>2</sub>). Apnea experiments were performed with different physiological settings, such as shunt fraction (5%) and O<sub>2</sub> consumption (250, 500, and 750 ml/min). The following four apnea experiments were conducted: no oxygenation (NO), apnea oxygenation alone (AO), preoxygenation alone (PO), and para-oxygenation (PAO). The time to 92%, 75%, and 50% saturation was recorded. Alveolar and arterial gas levels were recorded till 50% saturation.

**Results:** At 250 ml/min, PO (1121 s) and PAO (1274.5 s) had a significantly longer time to 50% saturation (400% increase) compared to NO (222.5 s) and AO (239 s). A similar trend was observed for the time to 92% and 75% saturation. At higher O<sub>2</sub> consumption rates, a shorter time to desaturation was observed.

**Conclusions:** Apnea trends in the HPS correlated with similar prior human experiments. AO without preoxygenation was found to provide no additional benefit. Preoxygenation with high-flow O<sub>2</sub> via nasal cannula prolonged the time to desaturation in the PAO more than PO scenario. Therefore, HPSs can be used in future studies where patient safety is a concern.

**Keywords:** Apnea; Hypoxia; Nasal cannula; Oxygen inhalation therapy; Oxygen saturation; Patient simulation.



## Introduction

The use of simulations in medical practice is an exciting new sub-specialty that is being widely used for teaching, especially to simulate rare events and prepare students for real-life emergency scenarios. Simulations have been used effectively for procedural training, with mannequins replacing real patients, to avoid exposing novice students to patients for learning [1,2]. The use of simulations in research is still limited to statistical models and a few experimental studies, although there are many unexplored potential applications [2,3].

© The Korean Society of Anesthesiologists, 2022

© This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

With the availability of human patient simulator (HPS) machines that can precisely simulate various physiological and pathological conditions through input from computer-based software, the role of simulators in anesthesia has expanded to an advanced level [4]. Newer types of HPSs are based on physio-pharmacological models, which include real-time monitoring and feedback while interventions are performed on the simulator. HPSs are therefore ideal for complex critical scenarios and, thus, an appropriate tool for clinical research based on such scenarios.

Preoxygenation and apnea oxygenation are established techniques for prolonging the duration of apnea during intubation attempts in operation rooms and intensive care units [5–8], but most studies have been performed only on certain oxygen ( $O_2$ ) saturation levels because of ethical issues related to exposing patients to apnea and potential hypoxia [9–11]. Recent literature has documented the efficacy of high-flow  $O_2$  administered through a nasal cannula to provide longer periods of apnea in operation rooms and to maintain oxygenation in patients with pulmonary pathologies [12–17].

Through this experimental study, we aimed to investigate the effect of  $O_2$  therapy on prolonged apnea using a high-fidelity HPS. This allowed for longer periods of apnea to be studied and analyzed without risking patient safety. The primary objective of our study was to assess the utility of an HPS for apnea simulation and  $O_2$  therapy research, and the validity of extrapolating the data to human patients. The secondary objective was to compare the efficacy of different oxygenation strategies using a simple nasal cannula during apnea in terms of the time to desaturation.

## Materials and Methods

### Setup

After approval from the Institutional Review Board (IRB no. 261/IEC/IM/NF/2019), an experimental simulation study using an HPS was planned over four months. The HPS (CAE Healthcare™, USA) is equipped to detect delivered  $O_2$  and is used along with an anesthesia workstation and monitor with hemodynamic and oxygenation parameters.

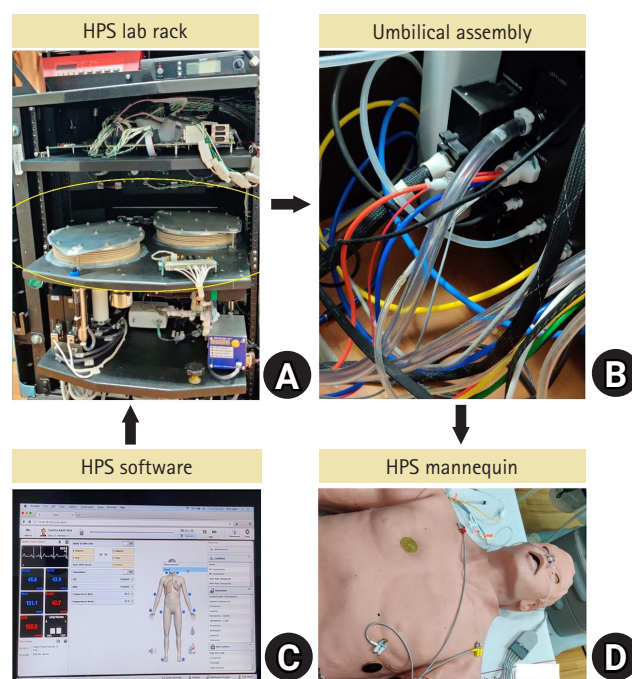
### Functioning of the HPS

The study object was a high-fidelity HPS. The basic components of this HPS are a mannequin attached to a central control unit or lab rack (Fig. 1A) through an umbilical assembly (Fig. 1B). The lab rack is driven by various gases, such as  $O_2$ , nitrogen ( $N_2$ ), carbon dioxide ( $CO_2$ ), and compressed air. A specific software

(Müse, CAE Healthcare™, USA) is used to control the functioning of the HPS (Fig. 1C). Circulation and respiration are simulated through the lab rack. Two bellows inside the lab rack serve the function of the lungs (Fig. 1A). Gas monitoring sensors are present at the level of the lab rack even though sampling is performed on the mannequin (Fig. 1D). Simulated hemodynamic measurements, such as non-invasive blood pressure, pulse oximetry for  $O_2$  saturation ( $SpO_2$ ), and electrocardiography, can also be obtained from the mannequin using actual monitors.

### Software

The HPS software, allows for two modes of functioning (Fig. 1C). In the first mode, the HPS response is controlled by an operator at the computer interface, whereas with the second mode, responses are modeled based on normal adult physiology. Several parameters are set for normal adult physiology, such as the shunt fraction (set at 5% for this study),  $O_2$  consumption, lung volume, and respiratory quotient, among others. Table 1 shows a list of all the parameters that were set using the default values [4]. The clinical hemodynamic and blood gas parameters, such as partial pressure of alveolar (PA), arterial (Pa), and venous (Pv)  $O_2$  and  $CO_2$ , are visible on a separate screen, which can either be a fixed expected response based on the experiment, a setting that is applied in the software, or a modeled response after synchronizing the monitors with the HPS mannequin. Once in the modeled mode,



**Fig. 1.** Schematic of the components and functions of the HPS system. HPS: human patient simulator.

**Table 1.** List of Respiratory Parameters That Can Be Adjusted in the Software

Basic parameters	
Swollen tongue	Shunt fraction
Airway occluder	SpO <sub>2</sub>
Laryngospasm	NMB
Needle decompression	Tidal volume
Bronchial occlusion (left and right)	Intrapleural volume: left
Respiratory rate	Intrapleural volume: right
Respiratory rate factor	Fraction of inspired O <sub>2</sub>
ETCO <sub>2</sub>	Chest tube flow
Additional parameters	
Respiratory rate	Chest wall compliance factor
Tidal volume	Distended chest wall compliance factor
Tidal volume factor	Functional residual capacity
pH shift	Lung compliance factor: left
PEEP	Lung compliance factor: right
Chest tube	Venous CO <sub>2</sub> shift
Chest tube flow	Bronchial resistance factor: left
Chest tube air leak	Bronchial resistance factor: right
O <sub>2</sub> consumption	Alveolar enflurane
CO <sub>2</sub> production factor	Fraction of inspired enflurane
PaCO <sub>2</sub> set-point	Alveolar halothane
PaO <sub>2</sub> set-point	Fraction of inspired halothane
I to E ratio (1:X)	Alveolar isoflurane
PetCO <sub>2</sub> -PaCO <sub>2</sub> factor	Fraction of inspired isoflurane
Respiratory gain factor	Alveolar nitrous oxide
Respiratory quotient	Fraction of inspired nitrous oxide
Volume/rate control factor	Alveolar sevoflurane
Chest wall capacity	Fraction of inspired sevoflurane

SpO<sub>2</sub>: oxygen saturation, NMB: neuromuscular block, ETCO<sub>2</sub>: end-tidal carbon dioxide, PEEP: positive end expiratory pressure, PaCO<sub>2</sub>: partial pressure of arterial carbon dioxide, PaO<sub>2</sub>: partial pressure of oxygen in arterial blood, PetCO<sub>2</sub>: pressure end-tidal carbon dioxide.

the HPS behaves like an independent unit from the fixed software and responds physiologically to real-time interventions, such as external O<sub>2</sub> or anesthetic agents. For this particular study, we were specifically interested in the functioning of the respiratory system, simulation of lung function, and gas-sensing mechanisms. For gas monitoring, alveolar O<sub>2</sub> and CO<sub>2</sub> values were sensed at the level of the lab rack, and for all other arterial parameters, including pulse oximetry, the values were determined based on set physiological parameters. Fig. 1 shows a schematic of the components and functions of the HPS system.

## Experiments

Apnea settings were applied from baseline values, and changes

in hemodynamic and blood gas parameters (PAO<sub>2</sub>, PaO<sub>2</sub>, PACO<sub>2</sub>, PaCO<sub>2</sub>, SpO<sub>2</sub>, pH) were recorded until the end of the experiment, which was defined as the attainment of 50% SpO<sub>2</sub>. The following four experiments were conducted with apnea: 1) no oxygenation (NO): only apnea was applied, 2) only apnea oxygenation (AO): 15 L/min O<sub>2</sub> was provided via simple nasal cannula after apnea was applied, 3) only preoxygenation (PO): O<sub>2</sub> was provided until the PAO<sub>2</sub> reached 400 mmHg, at which time apnea was applied with no O<sub>2</sub> during apnea; and 4) para-oxygenation (PAO): preoxygenation was provided until the PAO<sub>2</sub> reached 400 mmHg, at which time apnea was applied and 15 L/min O<sub>2</sub> was administered via simple nasal cannula during apnea. Alveolar and arterial gas levels were noted every 1 min from the beginning of the apnea period till 50% SpO<sub>2</sub> was reached. Time to desaturation was noted for 92%, 75%, and 50% SpO<sub>2</sub>.

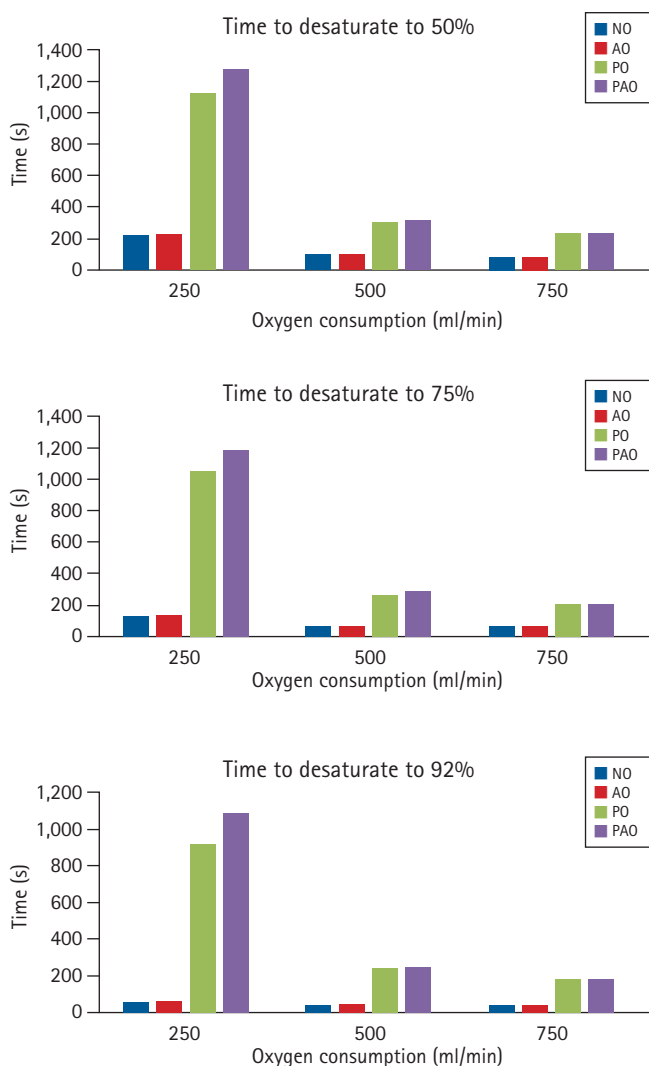
## Settings and analysis

Initial O<sub>2</sub> consumption was set at 250 ml/min. Each apnea experiment was repeated three times (at different sittings), and the mean values of the three recordings were used for the comparative analysis. Each set of four experiments was performed on different days to allow the machine to restart and equilibrate to baseline physiological values. This allowed us to maintain a quality check on the data and avoid erroneous readings. All experiments were then performed again at O<sub>2</sub> consumption rates of 500 and 750 ml/min. The apnea trends were compared among all four experiments (NO, AO, PO, and PAO). The time to desaturation was compared between the experiments and between the different O<sub>2</sub> consumption rates.

## Results

Fig. 2 shows a comparison of the desaturation time to 50%, 75%, and 92% SpO<sub>2</sub> among the four experimental settings at O<sub>2</sub> consumptions of 250, 500, and 750 ml/min. At 250 ml/min, NO (222.5 s) and AO (239 s) had a similar desaturation time to 50% SpO<sub>2</sub>. PAO (1274.5 s) had a longer desaturation time to 50% SpO<sub>2</sub> than PO (1121 s), which was a 400% increase compared to NO. At higher O<sub>2</sub> consumption rates, the desaturation times were shorter. At 500 ml/min, the desaturation time to 50% SpO<sub>2</sub> for NO and AO was 97 s and 98 s, respectively. Compared with NO, the desaturation time to 50% SpO<sub>2</sub> for PO and PAO was 300 s and 316 s, respectively, which was an increase of approximately 200%. Similar comparative trends were observed for the desaturation time to 92% and 75% SpO<sub>2</sub> (Fig. 2).

Fig. 3 shows a graphical trend of the partial pressure of O<sub>2</sub> in



**Fig. 2.** Time to 50%, 75%, and 92% saturation among all four experimental settings at oxygen consumptions of 250, 500, and 750 ml/min. NO: no oxygenation, AO: apnea oxygenation alone, PO: pre-oxygenation alone, PAO: para-oxygenation.

the alveoli (dashed line) and arterial blood (solid line) until the end of the each of the four experiments (i.e., once 50% SpO<sub>2</sub> was reached). The results are shown for all three O<sub>2</sub> consumption rates 250, 500, and 750 ml/min.

Table 2 shows the “end of experiment” values of PaCO<sub>2</sub> and pH for all four experiments and different O<sub>2</sub> consumption rates. Because of the shorter time to 50% SpO<sub>2</sub> at 250 ml/min O<sub>2</sub> consumption, the maximum PaCO<sub>2</sub> achieved was lower with NO (52.13 mmHg) and AO (52.9 mmHg) than with PO (72.5 mmHg) and PAO (75.1 mmHg), which allowed for longer apnea times and higher PaCO<sub>2</sub> values (Table 2). Thus, lower pH values were observed with PO (7.2) and PAO (7.18), primarily due to respiratory acidosis. Similarly, experiments at higher O<sub>2</sub> consumption rates also had lower PaCO<sub>2</sub> and higher pH values than the 250 ml/min experi-

ments due to the shorter times to desaturation (Table 2).

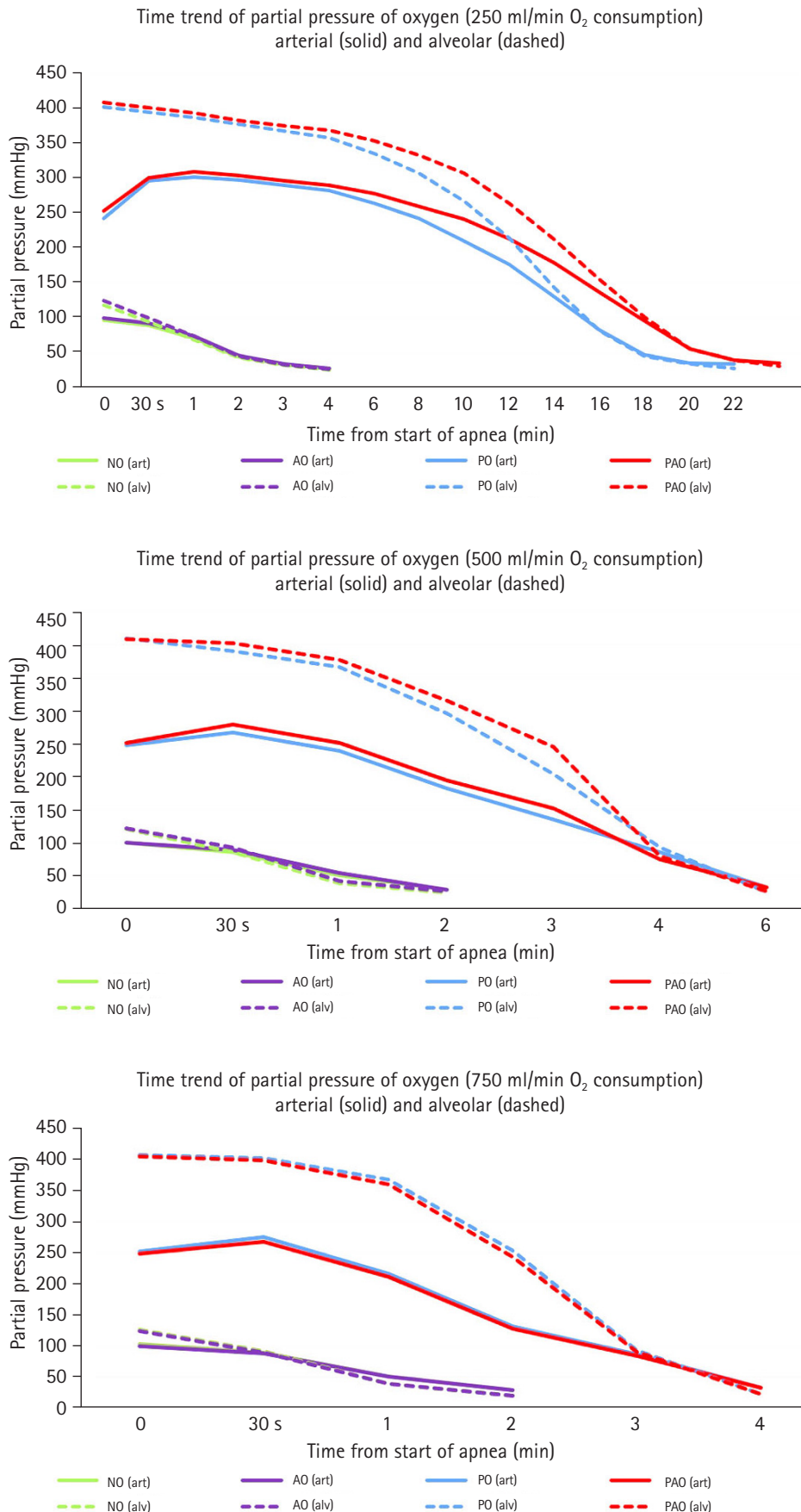
## Discussion

Recently, there has been growing interest in simulation/mannequin-related research. One advantage of such in vitro studies includes being able to perform research on complex clinical scenarios that are rarely encountered in practice or that would be a potential health risk to the patient [2,3]. One such scenario is apnea oxygenation. Also described as “apneic diffusion oxygenation,” this technique primarily involves drawing ambient O<sub>2</sub> “en masse” into the lungs by providing continuous flow through the airways [18]. Devices such as nasal cannula have conventionally been used, though higher flow devices such as transnasal humidified rapid-insufflation ventilatory exchange (THRIVE), which allow for the toleration of longer apnea times in clinical situations, have been developed [16].

Apnea oxygenation has been studied in humans since 1959. In one of the first studies, conducted by Frumin et al. [18], patients undergoing elective surgeries under general anesthesia with neuromuscular blockades were subjected to prolonged apnea following a period of preoxygenation and de-nitrogenation. Although the apnea termination point was not fixed, periods of apnea ranged from 15 to 55 min, during which arterial samples were monitored for blood gas analysis and catecholamine levels. The lowest SpO<sub>2</sub> level reached was 98%, the lowest pH was 6.88, and the highest PaCO<sub>2</sub> was 250 mmHg. A similar study would be very difficult to perform in modern research settings due to the ethical issues of subjecting patients to such high levels of respiratory acidosis and CO<sub>2</sub>. In the current study, a normal physiologically modeled HPS was used to study various oxygenation strategies during apnea to an extent that would not be feasible for real subjects (50% SpO<sub>2</sub>). The lowest pH reached was 7.18 and the highest PaCO<sub>2</sub> value was 75 mmHg (250 ml/min O<sub>2</sub> consumption) at 50% SpO<sub>2</sub>.

Another in vitro study conducted by Struys et al. [3] compared the time course of inhaled anesthetic drug delivery between two types of anesthesia machine circuits using test lungs. Different combinations of settings (e.g., flow) were applied to observe various patterns of anesthetic delivery and end-tidal concentrations. Such studies can also be performed using an HPS and would even be more accurate than a test lung due to its more advanced real-time gas-sensing mechanisms once synchronized to the modeled mode. A substantial amount of anesthesia-related simulation research has been conducted in the field of airway management, with various studies involving airway techniques and devices [2]. Although such studies are criticized for seldom following up with





**Fig. 3.** Graphical trend of partial pressure of oxygen in the alveoli and arterial blood among all four experiments across time until 50% SpO<sub>2</sub>, at oxygen consumption rates of 250, 500, and 750 ml/min. NO: no oxygenation, AO: apnea oxygenation alone, PO: pre-oxygenation alone, PAO: para-oxygenation, alv: alveolar, art: arterial.

**Table 2.** Maximum Values of Measured Parameters at the End of the Experiments (50% Saturation)

Experiment	NO	AO	PO	PAO
PaCO <sub>2</sub> * (mmHg)				
250 ml/min	52.13	52.90	72.50	75.10
500 ml/min	50.67	50.77	62.10	63.17
750 ml/min	51.87	50.97	64.57	63.90
pH*				
250 ml/min	7.35	7.34	7.20	7.18
500 ml/min	7.36	7.36	7.28	7.27
750 ml/min	7.35	7.36	7.26	7.26

\*Mean of 3 readings. NO: no oxygenation, AO: apnea oxygenation alone, PO: pre-oxygenation alone, PAO: para-oxygenation, PaCO<sub>2</sub>: partial pressure of arterial carbon dioxide.

patient-based studies to validate the simulation data, apnea oxygenation scenarios can only be ethically conducted to a certain level of acceptable desaturation in actual patients. Such experimental simulation-based studies should offer insights into the mechanisms and a preliminary understanding of new interventions.

Patient studies involving apnea oxygenation have been performed primarily in the operative, emergency, and critical care settings [7,8,10]. Outcome parameters range from time to desaturation, incidence of desaturation, lowest mean saturation reached during intubation, and mean saturation in respiratory failure, among others [7,9–11,13,14,17]. A study on apneic oxygenation comparing trans nasal humidified O<sub>2</sub> therapy versus conventional nasal oxygenation conducted by Rajan et al. [16] found a longer time to 90% desaturation in the transnasal humidified group (796 s vs. 444 s). Similar time to desaturation (to 92%) was observed in the present simulation study at 250 ml/min O<sub>2</sub> consumption (915 s for PO, 1087 s for PAO) using a nasal cannula at 15 L/min. Other studies based on lower apnea oxygenation flows of 5–10 L/min had times to desaturation (92–95%) ranging from 408 s to 587 s [19–21]. Assuming that the O<sub>2</sub> consumption/pulmonary shunt fraction will be slightly more than ideal in real patients and considering the differences in flow rates used, the experimental HPS data correlated well with patient data from previous human apnea oxygenation studies.

In the present study, we compared different nasal oxygenation strategies on an HPS mannequin that varied from no oxygenation to apnea oxygenation alone to para-oxygenation, to assess the time to 92%, 75%, and 50% SpO<sub>2</sub>. Across all settings, no oxygenation and oxygenation only during apnea showed similar times to desaturation, and para-oxygenation produced marginally longer times to desaturation compared to preoxygenation alone, both of

which were significantly longer than those in the earlier two settings. The above findings highlight that, without preoxygenation, apnea oxygenation alone does not provide any additional benefit, and that para-oxygenation can be used to maximize the duration of safe apnea.

The four experimental settings were also applied at O<sub>2</sub> consumption rates of 250, 500, and 750 ml/min to evaluate the performance of the HPS at different O<sub>2</sub> settings, which can be further extrapolated to varied O<sub>2</sub> demand situations. The comparative findings were similar across all consumption rates. In the current study, only the shunt fraction and O<sub>2</sub> consumption rate were manipulated; however, complex pulmonary pathologies may be simulated by adjusting various physiological parameters to estimate how an actual patient might behave under various conditions, such as anesthesia and surgery [4]. For example, chest wall compliance and bronchial resistance factors can be used to simulate restrictive and obstructive lung pathologies, respectively. Different flow rates of nasal oxygenation could also be compared on the HPS, similar to the protocol proposed by Theiler et al. [22].

The major and obvious limitation of the study is that the results obtained with any simulator experiment cannot with absolute certainty be compared to human data. Only its proximity to reality, as much as possible, can be ascertained, as was done in the present study. Another limitation is that the full spectrum of the software modifiable physiological factors could not be explored in the present study. This can be planned in future projects.

In conclusion, apnea trends in the HPS in the current study correlated well with similar prior human experiments, providing support for the use of HPS in similar future research and extrapolation of data to human patients. Through simulation experiments, we deduced that AO alone without preoxygenation provides no additional benefit to NO. High-flow O<sub>2</sub> via nasal cannula prolonged the time to desaturation in the PAO scenario more than in the PO scenario. Complex, rare, and potentially dangerous scenarios, such as apnea oxygenation, can be easily performed using HPS to study the patterns of various new interventions without the ethical concerns of exposing real patients.

## Funding

None.

## Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

## Author Contributions

Debendra Kumar Tripathy (Conceptualization; Formal analysis; Project administration; Resources; Supervision; Validation; Writing – review & editing)

Mridul Dhar (Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Software; Writing – original draft; Writing – review & editing)

Bharat Bhushan Bhardwaj (Conceptualization; Investigation; Methodology; Project administration; Supervision; Validation; Writing – review & editing)

K Hemanthkumar (Data curation; Investigation; Methodology; Resources; Software; Supervision)

Praveen Talawar (Conceptualization; Investigation; Software; Supervision; Writing – review & editing)

Shalinee Rao (Formal analysis; Project administration; Resources; Software; Supervision; Writing – review & editing)

## ORCID

Debendra Kumar Tripathy, <https://orcid.org/0000-0003-0346-1374>

Mridul Dhar, <https://orcid.org/0000-0002-1913-2586>

Bharat Bhushan Bhardwaj, <https://orcid.org/0000-0002-0899-5204>

K Hemanthkumar, <https://orcid.org/0000-0002-4521-7209>

Praveen Talawar, <https://orcid.org/0000-0002-9931-2316>

Shalinee Rao, <https://orcid.org/0000-0002-9833-5305>

## References

1. Bhagwat M. Simulation and anaesthesia. *Indian J Anaesth* 2012; 56: 14-20.
2. Rai MR, Popat MT. Evaluation of airway equipment: man or manikin? *Anaesthesia* 2011; 66: 1-3.
3. Struys MM, Kalmar AF, De Baerdemaeker LE, Mortier EP, Rolly G, Manigel J, et al. Time course of inhaled anaesthetic drug delivery using a new multifunctional closed-circuit anaesthesia ventilator. In vitro comparison with a classical anaesthesia machine. *Br J Anaesth* 2005; 94: 306-17.
4. HPS User Guide v 2.7.1 (English). CAE Healthcare [serial on the internet]. Sarasota (FL): CAE Healthcare; 2016 [cited Jan 2022]. Available from [https://www.caehealthcare.com/media/files/User\\_Guides/CAE\\_HPS\\_User\\_Guide.pdf](https://www.caehealthcare.com/media/files/User_Guides/CAE_HPS_User_Guide.pdf)
5. Nimmagadda U, Salem MR, Crystal GJ. Preoxygenation: physiologic basis, benefits, and potential risks. *Anesth Analg* 2017; 124: 507-17.
6. Fong KM, Au SY, Ng GW. Preoxygenation before intubation in adult patients with acute hypoxemic respiratory failure: a network meta-analysis of randomized trials. *Crit Care* 2019; 23: 319.
7. Jaber S, Monnin M, Girard M, Conseil M, Cisse M, Carr J, et al. Apnoeic oxygenation via high-flow nasal cannula oxygen combined with non-invasive ventilation preoxygenation for intubation in hypoxaemic patients in the intensive care unit: the single-centre, blinded, randomised controlled OPTINIV trial. *Intensive Care Med* 2016; 42: 1877-87.
8. Peters SG, Holets SR, Gay PC. High-flow nasal cannula therapy in do-not-intubate patients with hypoxemic respiratory distress. *Respir Care* 2013; 58: 597-600.
9. Pavlov I, Medrano S, Weingart S. Apneic oxygenation reduces the incidence of hypoxemia during emergency intubation: a systematic review and meta-analysis. *Am J Emerg Med* 2017; 35: 1184-9.
10. Binks MJ, Holyoak RS, Melhuish TM, Vlok R, Bond E, White LD. Apneic oxygenation during intubation in the emergency department and during retrieval: a systematic review and meta-analysis. *Am J Emerg Med* 2017; 35: 1542-6.
11. Caputo N, Azan B, Domingues R, Donner L, Fenig M, Fields D, et al. Emergency department use of apneic oxygenation versus usual care during rapid sequence intubation: a randomized controlled trial (The ENDAO Trial). *Acad Emerg Med* 2017; 24: 1387-94.
12. Nishimura M. High-flow nasal cannula oxygen therapy in adults. *J Intensive Care* 2015; 3: 15.
13. Leeies M, Flynn E, Turgeon AF, Paunovic B, Loewen H, Rabbani R, et al. High-flow oxygen via nasal cannulae in patients with acute hypoxemic respiratory failure: a systematic review and meta-analysis. *Syst Rev* 2017; 6: 202.
14. Lee CC, Mankodi D, Shaharyar S, Ravindranathan S, Danckers M, Herscovici P, et al. High flow nasal cannula versus conventional oxygen therapy and non-invasive ventilation in adults with acute hypoxemic respiratory failure: a systematic review. *Respir Med* 2016; 121: 100-8.
15. Schwabbauer N, Berg B, Blumenstock G, Haap M, Hetzel J, Riessen R. Nasal high-flow oxygen therapy in patients with hypoxic respiratory failure: effect on functional and subjective respiratory parameters compared to conventional oxygen therapy and non-invasive ventilation (NIV). *BMC Anesthesiol* 2014; 14: 66.
16. Rajan S, Joseph N, Tosh P, Kadapamannil D, Paul J, Kumar L. Effectiveness of transnasal humidified rapid-insufflation ventilatory exchange versus traditional preoxygenation followed by apnoeic oxygenation in delaying desaturation during apnoea: a preliminary study. *Indian J Anaesth* 2018; 62: 202-7.
17. Gleason JM, Christian BR, Barton ED. Nasal cannula apneic oxygenation prevents desaturation during endotracheal intubation:

- an integrative literature review. *West J Emerg Med* 2018; 19: 403-11.
18. Frumin MJ, Epstein RM, Cohen G. Apneic oxygenation in man. *Anesthesiology* 1959; 20: 789-98.
  19. Grude O, Solli HJ, Andersen C, Oveland NP. Effect of nasal or nasopharyngeal apneic oxygenation on desaturation during induction of anesthesia and endotracheal intubation in the operating room: a narrative review of randomized controlled trials. *J Clin Anesth* 2018; 51: 1-7.
  20. Teller LE, Alexander CM, Frumin MJ, Gross JB. Pharyngeal insufflation of oxygen prevents arterial desaturation during apnea. *Anesthesiology* 1988; 69: 980-2.
  21. Achar SK, Pai AJ, Shenoy UK. Apneic Oxygenation during simulated prolonged difficult laryngoscopy: comparison of nasal prongs versus nasopharyngeal catheter: a prospective randomized controlled study. *Anesth Essays Res* 2014; 8: 63-7.
  22. Theiler L, Schneeberg F, Riedel T, Kaiser H, Riva T, Greif R. Apnoeic oxygenation with nasal cannula oxygen at different flow rates in anaesthetised patients: a study protocol for a non-inferiority randomised controlled trial. *BMJ Open* 2019; 9: e025442.