

# High oxygen fraction during airway opening is key to effective airway rescue in obese subjects

Marianna Laviola, Christian Niklas, Husam Alahmadi, Anup Das, Declan G Bates, Jonathan G Hardman

**Abstract**— Apnea is common after induction of anesthesia and may produce dangerous hypoxemia, particularly in obese subjects. Optimal management of airway emergencies in obese, apneic subjects is complex and controversial, and clinical studies of rescue strategies are inherently difficult and ethically-challenging to perform.

We investigated rescue strategies in various degrees of obesity, using a highly-integrated, computational model of the pulmonary and cardiovascular systems, configured against data from 8 virtual subjects (body mass index [BMI] 24–57 kg m<sup>-2</sup>). Each subject received pre-oxygenation with 100% oxygen for 3 min, and then apnea with an obstructed airway was simulated until SaO<sub>2</sub> reached 40%. At that time, airway rescue was simulated, opening of the airway with the provision of various patterns of tidal ventilation with 100% oxygen.

Rescue using tidal ventilation with 100% oxygen provided rapid re-oxygenation in all subjects, even with small tidal volumes in subjects with large BMI. Overall, subjects with larger BMI pre-oxygenated faster and, after airway obstruction, developed hypoxemia more quickly.

Our results indicate that attempts to achieve substantial tidal volumes during airway rescues are probably not worthwhile (and may be counter-productive); rather, it is the assurance of a high-inspired oxygen fraction that will prevent critical hypoxemia.

## I. INTRODUCTION

During anesthesia, patients are often rendered apneic; the anesthetist provides a patent airway through airway manipulation, facilitating pulmonary ventilation. Failure to manage the airway effectively may result in prolonged, and potentially lethal, apnea. A worst-case scenario results in a “Can’t intubate, can’t oxygenate” situation. Oxygen stores are depleted and carbon dioxide accumulates during apnea. However, our understanding of the factors affecting the progression of these pathophysiological abnormalities in various clinical contexts is incomplete.

Previous clinical investigations have highlighted obesity as an important risk factor that may radically change the progression of hypoxemia during apnea, due to reduction of functional residual capacity (FRC) in obese patients [1-3] and higher metabolic oxygen consumption. [4] Equally a high body mass index (BMI) and associated factors like a

short, thick neck and obstructive sleep apnea are recognized predictors for difficult mask ventilation and difficult laryngoscopy. [5] [6] However, the optimal management of airway emergencies is unclear even in healthy subjects, and the optimal management of obese, apneic subjects is complex and controversial. *In vivo* studies have been difficult and ethically-challenging to perform, and thus evidence to inform this issue is scarce.

This paper uses a high-integrated computational modelling of cardiovascular and pulmonary systems to evaluate different patterns of tidal ventilation achieving re-oxygenation following airway rescue (i.e. re-opening). We investigated different degrees of obesity, examining the rate of progression of hypoxemia, and the impact on re-oxygenation of following the opening of an obstructed airway and the application of various patterns of tidal ventilation.

## II. METHODS

### A. Computational Model

We used the Interdisciplinary Collaboration in Systems Medicine (ICSM) suite of physiological simulations that consists of highly-integrated computational models of the pulmonary and cardiovascular systems. [7-11] The model has been widely validated for investigation of pre-oxygenation, apnea and hypoxemia in adults, [12, 13] parturients [14] and children. [15]

The model includes a series deadspace volume, 100 independently-configurable alveolar compartments and 19 in-series cardiovascular compartments. The series deadspace (SD) is located between the airway and the alveolar compartments and it is simulated as a series of stacked, rigid laminae of equal volume ( $N_{lam}$ ). The static total volume of the series deadspace is set to 150 ml and each lamina,  $j$ , has a known fraction ( $f_{(SD,j)}^x$ ) of gas  $x$ . The pressure (above atmospheric) within each alveolar compartment is described by the following cubic function:

$$p_i = \begin{cases} \left( \frac{(10 \cdot v_i - 300)^3}{6600} \right) - P_{ext,i} & v_i > 0 \text{ for } i=0, \dots, N_{alv} \\ p_i = 0 & \text{otherwise} \end{cases} \quad (1)$$

In the equation (1),  $p_i$  is the alveolar pressure in cmH<sub>2</sub>O for the  $i^{th}$  of  $N_{alv}$  alveolar compartments for the given volume of alveolar compartment,  $v_i$ , in millilitres.  $P_{ext,i}$  (per alveolar unit, in cmH<sub>2</sub>O) represents the effective net pressure generated by the sum of the effects of factors outside each alveolus.

We recently developed and validated additional modules in the ICSM simulation suite in order to include: (i) cardiogenic

M. Laviola\* and H. Alahmadi, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, UK (\*corresponding author; email: marianna.laviola@nottingham.ac.uk; husam.alahmadi@nottingham.ac.uk).

C Niklas and J.G. Hardman, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham (UK) and Nottingham University Hospitals NHS Trust, Nottingham (UK) (e-mail: christian.niklas@posteo.de and J.Hardman@nottingham.ac.uk).

A. Das and D.G. Bates, School of Engineering, University of Warwick, UK (e-mail: anup.das@warwick.ac.uk, d.bates@warwick.ac.uk).

pulsation affecting intrathoracic gas spaces, (ii) augmented gas-mixing within the conducting respiratory deadspaces, (iii) oxygen insufflation into the trachea, larynx or supraglottic space and (iv) pharyngeal pressure oscillation (e.g. occurring as a result of high-flow nasal oxygen administration). [16, 17]

For the purpose of this paper, we used the following modules:

- *Cardiogenic oscillations module*

We described the effect of cardiac oscillations on alveolar compartments by the following equation:

$$P_{osc,i} = K_{osc} \cdot \varphi \quad \text{for } i = 0, \dots, N_{osc} \quad \text{where } N_{osc} \leq N_{alv} \quad (2)$$

where  $P_{osc,i}$  represents the pressure of the heart acting on the alveolar compartment  $i$ . This additional pressure, in combination with existing pressure values of the alveolar compartments, creates a pressure difference between the mouth and the alveolar compartments, across which the flow of gas can occur. The parameter  $K_{osc,i}$  is a constant, representing the strength of the effect of cardiogenic oscillations on alveolar ventilation, due to the alveoli being compressed by the heart and/or trans-alveolar blood volume.  $N_{osc}$  is the number of alveolar compartments that are affected by cardiogenic oscillations and  $N_{alv}$  represents the number of alveolar compartments. The function  $\varphi$ , described by a squared half-sine wave, is the ventricular activation function, equal to 1 at the peak of systolic contraction and 0 during maximal diastolic relaxation.

Thus, the final equation describing the pressure of each alveolar compartment is:

$$p_i = \begin{cases} \left( \frac{(10 \cdot v_i - 300)^3}{6600} \right) - P_{ext,i} - P_{osc,i} & v_i > 0 \quad \text{for } i=0, \dots, N_{alv} \\ p_i = 0 & \text{otherwise} \end{cases} \quad (3)$$

- *Anatomical deadspace gas-mixing module*

In order to represent the proportion of gas mixing between adjacent laminae of the anatomical deadspace, a variable parameter ( $\sigma$ ) is introduced to the calculation of  $f_{SD,j}^x$ .

This new parameter allows various degrees of mixing:  $\sigma = 1$  would indicate a complete mixing of gases between layers, representing the effects of extreme turbulent flow of air, while  $\sigma = 0$  would indicate no mixing of gases. Thus:

$$f_{(SD,j)}^x = \left( (1 - \sigma) f_{SD,j}^x \right) + \sigma f_{(SD,j+1)}^x \quad \text{where } j < N_{lam} \quad (4)$$

where  $f_{(SD,j)}^x$  is the fraction of gas  $x$  in lamina  $j$  and  $f_{(SD,j+1)}^x$  is the fraction of gas  $x$  in the next lamina.

B. *Virtual subjects, protocol and data*

For this study, we created 8 virtual (*in-silico*) subjects with BMI between 24 and 57 kg m<sup>-2</sup>, describing various degrees of obesity. Physiological variables relating to tidal ventilation, respiratory rate, FRC and oxygen consumption were calculated for each virtual subject using data from previously published papers [3, 4, 18, 19] and were used to

configure the ICSM model to create a simulation of each patient. The physiological descriptors used are provided in Table I. Resting tidal volume was configured as decreased in subjects with larger BMI; respiratory rate similarly increased with increasing BMI. Resting oxygen consumption (VO<sub>2</sub>) was configured as follows:

$$VO_2 = 138 + 1.47 \cdot \text{bodyweight} \quad (5)$$

where VO<sub>2</sub> is expressed in ml min<sup>-1</sup> and body weight is expressed in kg. [4] During the induction of anesthesia, the FRC was configured as decreasing by 20% in subjects with BMI < 30 kg m<sup>-2</sup> and by 50% in subjects with BMI 32–57 kg m<sup>-2</sup>. [3, 19]

Each virtual subject underwent pulmonary denitrogenation (i.e. ‘pre-oxygenation’) during resting, tidal breathing with an inspired oxygen fraction (FiO<sub>2</sub>) of 100% for 3 min. Induction of general anesthesia then occurred, and apnea commenced. The upper airway became obstructed immediately upon loss of consciousness. Apnea continued until the arterial oxygen saturation (SaO<sub>2</sub>) reached 40%. At that time, for all virtual subjects, we simulated an airway rescue maneuver that consisted of the opening of the airway and provision of various patterns of tidal ventilation with 100% oxygen. These ventilation patterns simulated varying degrees of success in re-instituting tidal ventilation; they were: 500 ml min<sup>-1</sup> (50 ml x 10 min<sup>-1</sup>), 2000 ml min<sup>-1</sup> (200 ml x 10 min<sup>-1</sup>) and 5000 ml min<sup>-1</sup> (500 ml x 10 min<sup>-1</sup>).

The following simulation outputs were recorded every 5 msec: arterial partial pressure of oxygen (PaO<sub>2</sub>), arterial partial pressure of carbon dioxide (PaCO<sub>2</sub>) and SaO<sub>2</sub>.

Model simulations were run using a 64-bit Intel Core i7 3.7 GHz Windows 7 personal computer, running Matlab version R2018a.v9 (MathWorks Inc. MA, USA).

### III. RESULTS

Fig. 1 shows the time courses of PaO<sub>2</sub> and PaCO<sub>2</sub> from the start of pre-oxygenation to the end of obstructed-airway apnea (SaO<sub>2</sub> 40%). All subjects showed a rapid increase in PaO<sub>2</sub> during pre-oxygenation; subjects with greater BMI pre-oxygenated more quickly. The progression of hypoxemia during apnea was consistently accelerated by increasing BMI, with the apnea-time to reach SaO<sub>2</sub> 40% in the BMI 57 kg m<sup>-2</sup> subject being only 47% of that seen in subjects with BMI < 30 kg m<sup>-2</sup>. Carbon dioxide accumulation was effectively linear and was slightly slower with increasing BMI.

Fig. 2 shows the effect of airway rescue involving airway opening and the application of various patterns of tidal ventilation using 100% oxygen. Rescuing apneic subjects with tidal ventilation provided rapid re-oxygenation for all subjects; increasing minute volume during rescue provided marginally faster re-oxygenation, but even very small volumes of 100% oxygen achieved effective (i.e. life-preserving) rescue. Post-intervention re-oxygenation was slightly slower in subjects with greater BMI.

The time from airway rescue to achieving PaO<sub>2</sub> 8 kPa in the various configurations is reported in Table II, representing the rapidity of rescue from critical hypoxemia.

TABLE I. PHYSIOLOGICAL PARAMETERS OF VIRTUAL SUBJECTS

Subjects	BMI (kg · m <sup>-2</sup> )	Body weight (kg)	Tidal volume (ml)	Respiratory rate (breaths · min <sup>-1</sup> )	FRC (l)	VO <sub>2</sub> (ml · min <sup>-1</sup> )
BMI 24	24	70.0	420	12.0	3.00	250
BMI 27	27	76.8	415	12.5	2.87	251
BMI 32	32	89.3	410	13.0	2.73	269
BMI 37	37	102.0	400	14.5	2.57	288
BMI 42	42	113.0	390	15.5	2.06	304
BMI 47	47	134.6	385	16.5	1.99	336
BMI 52	52	139.7	375	18.0	1.89	343
BMI 57	57	152.0	365	19.0	1.80	361

BMI body mass index; VO<sub>2</sub> resting oxygen consumption; FRC function residual capacity before induction of anesthesia

#### IV. DISCUSSION

We have performed a comprehensive modelling investigation into apnea tolerance and rescue strategies in subjects with different degrees of obesity. We observed that de-oxygenation during obstructed-airway apnea was significantly accelerated in subjects with greater BMI, and for each tidal ventilation pattern used a degree of re-oxygenation was achieved.

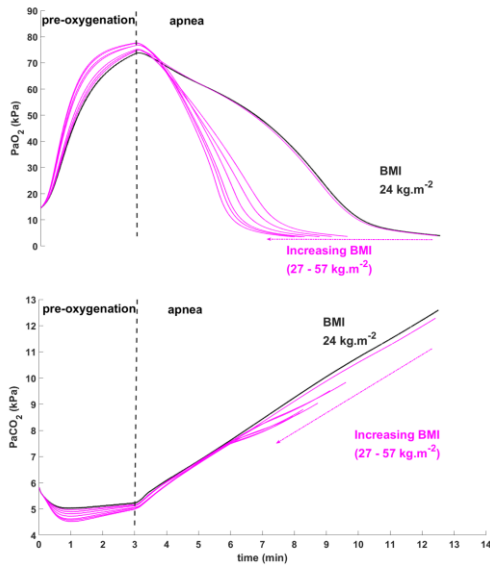


Figure 1. Time-course of PaO<sub>2</sub> (upper panel) and PaCO<sub>2</sub> (lower panel) during pre-oxygenation and apnea with airway obstruction (black curve BMI 24 kg m<sup>-2</sup>; magenta curves: BMI 27–57 kg m<sup>-2</sup>). All curves end when SaO<sub>2</sub> reaches 40%. The vertical, black, dashed line marks the beginning of apnea.

TABLE II. TIME TO REACH PaO<sub>2</sub> 8 kPa FOLLOWING TIDAL VENTILATION AIRWAY RESCUE

Subjects	Minute Ventilation (ml · min <sup>-1</sup> )		
	500	2000	5000
	Time (sec)		
BMI 24	25	25	25
BMI 27	25	25	25
BMI 32	35	35	35
BMI 37	37	36	36
BMI 42	45	44	44
BMI 47	47	46	46
BMI 52	49	48	48
BMI 57	51	50	49

BMI: body mass index

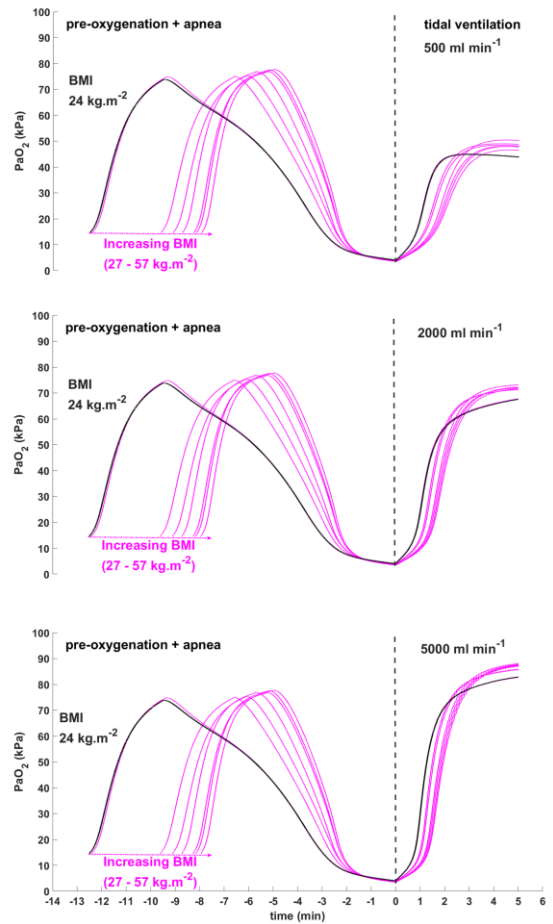


Figure 2. Time-course of PaO<sub>2</sub> during pre-oxygenation, apnea with airway obstruction, and rescue with airway opening and tidal ventilation: minute ventilations of 500 ml min<sup>-1</sup> (upper panel), 2000 ml min<sup>-1</sup> (middle panel) and 5000 ml min<sup>-1</sup> (lower panel) (black curve BMI 24 kg m<sup>-2</sup>; magenta curves: BMI 27–57 kg m<sup>-2</sup>). The vertical, black, dashed line marks airway-opening and rescue tidal ventilation.

We observed that re-oxygenation was slightly slower with increasing obesity, with a maximum delay of 26 sec to reach 8 kPa between the subjects with the highest and the lowest BMI. These findings are consistent with clinical experience, where it is often noted that rapid de-oxygenation may occur during apnea in the obese patient, and that re-oxygenation may be slowed. [1, 3]

After simulated airway rescue, subjects did not re-oxygenate faster when receiving ventilation with larger tidal volumes compared to smaller ones. This has clear implications for clinical practice, in that attempts to achieve substantial tidal volumes during airway rescues are probably not worthwhile and may be counter-productive. The extra effort required to deliver large tidal volumes may result in gastric distension, with consequent diaphragmatic splinting and regurgitation; rather, it is the assurance of a high-inspired oxygen fraction that will prevent critical hypoxemia.

We chose to consider tidal ventilation with only one inspired oxygen fraction (i.e. 100%). The reason not to consider other inspired oxygen fractions was that, during airway rescue, if one can ventilate then it will always be with 100% oxygen. However, in an airway crisis most instances of airway *opening* are achieved with a local oxygen fraction of 21% (i.e. there is no provision of a high concentration of oxygen at the airway while it is manipulated). Thus, this study could inform clinical consideration for safe airway management in obese subjects undergoing anesthesia.

Despite extensive validation and very good reproduction of normal physiology and pathology [7-9, 11] the modelled scenario must be viewed with a degree of caution, since robust model validation is difficult due to the sparsity of clinical data describing scenarios of extreme physiological derangement. Prior validation of the model in less severe environments has been very encouraging, however, and given the lack of alternative methodologies to explore such crises, we believe that these results provide valuable insights into the management of apneic de-oxygenation and can usefully inform clinical practice and future research in such scenarios.

The next step will be that to investigate which combinations of tidal ventilation modalities assured safe intra-pulmonary pressures for airway resistances in small devices, while upper airway obstruction persists.

#### ACKNOWLEDGMENT

The authors acknowledge the EPSRC grant "Personalised Simulation Technologies for Optimising Treatment in the Intensive Care Unit: Realising Industrial and Medical Applications" (Grant No. EP/P023444/1).

#### REFERENCES

[1] M. C. Berthoud, J. E. Peacock, and C. S. Reilly, "Effectiveness of preoxygenation in morbidly obese patients," *Br J Anaesth*, vol. 67, no. 4, pp. 464-466, 1991.

[2] B. J. Dixon, J. B. Dixon, J. R. Carden, A. J. Burn, L. M. Schachter, J. M. Playfair, C. P. Laurie, and P. E. O'Brien, "Preoxygenation is more effective in the 25° head-up position than in the supine position in severely obese patients: a

randomized controlled study," *Anesthesiology*, vol. 102, no. 6, pp. 1110-1115, 2005.

[3] G. Damia, D. Mascheroni, M. Croci, and L. Tarenzi, "Perioperative changes in functional residual capacity in morbidly obese patients," *Br J Anaesth*, vol. 60, no. 5, pp. 574-578, 4/1, 1988.

[4] R. B. White, and J. K. Alexander, "Body oxygen consumption and pulmonary ventilation in obese subjects," *J Appl Physiol*, vol. 20, no. 2, pp. 197-201, 1965.

[5] S. Kheterpal, D. Healy, M. F. Aziz, A. M. Shanks, R. E. Freundlich, F. Linton, L. D. Martin, J. Linton, J. L. Epps, A. Fernandez-Bustamante, L. C. Jameson, T. Tremper, and K. K. Tremper, "Incidence, Predictors, and Outcome of Difficult Mask Ventilation Combined With Difficult Laryngoscopy: A Report From the Multicenter Perioperative Outcomes Group," *Survey of Anesthesiology*, vol. 59, no. 6, pp. 271-272, 2015.

[6] "Practice Guidelines for the Perioperative Management of Patients with Obstructive Sleep Apnea A Report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea," *Anesthesiology*, vol. 104, no. 5, pp. 1081-1093, 2006.

[7] J. G. Hardman, N. M. Bedforth, A. B. Ahmed, R. P. Mahajan, and A. R. Aitkenhead, "A physiology simulator: validation of its respiratory components and its ability to predict the patient's response to changes in mechanical ventilation," *Br J Anaesth*, vol. 81, no. 3, pp. 327-332, 1998.

[8] N. M. Bedforth, and J. G. Hardman, "Predicting patients' responses to changes in mechanical ventilation: a comparison between physicians and a physiological simulator," *Intens Care Med Exp*, vol. 25, no. 8, pp. 839-842, 1999.

[9] J. G. Hardman, and N. M. Bedforth, "Estimating venous admixture using a physiological simulator," *Br J Anaesth*, vol. 82, no. 3, pp. 346-349, 1999.

[10] A. Das, P. P. Menon, J. G. Hardman, and D. G. Bates, "Optimization of mechanical ventilator settings for pulmonary disease states," *IEEE T Bio-Med Eng*, vol. 60, no. 6, pp. 1599-1607, 2013.

[11] A. Das, Z. Gao, P. P. Menon, J. G. Hardman, and D. G. Bates, "A systems engineering approach to validation of a pulmonary physiology simulator for clinical applications," *J R Soc Interface*, vol. 8, no. 54, pp. 44-55, 2011.

[12] J. G. Hardman, J. S. Wills, and A. R. Aitkenhead, "Investigating hypoxemia during apnea: validation of a set of physiological models," *Anesth Analg*, vol. 90, no. 3, pp. 614-618, 2000.

[13] M. J. McNamara, and J. G. Hardman, "Hypoxaemia during open-airway apnoea: a computational modelling analysis," *Anaesthesia*, vol. 60, no. 8, pp. 741-746, 2005.

[14] S. H. McClelland, D. G. Bogod, and J. G. Hardman, "Pre-oxygenation and apnoea in pregnancy: changes during labour and with obstetric morbidity in a computational simulation," *Anaesthesia*, vol. 64, no. 4, pp. 371-377, 2009.

[15] J. G. Hardman, and J. S. Wills, "The development of hypoxaemia during apnoea in children: a computational modelling investigation," *Br J Anaesth*, vol. 97, no. 4, pp. 564-570, 2006.

[16] M. Laviola, A. Das, M. Chikhani, D. Bates, and J. G. Hardman, "Investigating the effect of cardiac oscillations and deadspace gas mixing during apnea using computer simulation," *Conf Proc IEEE Eng Med Biol Soc.*, pp. 337-340, 2017.

[17] M. Laviola, A. Das, M. Chikhani, D. G. Bates, and J. G. Hardman, "Computer simulation clarifies mechanisms of carbon dioxide clearance during apnoea," *Br J Anaesth*, In Press.

[18] M. G. Sampson, and A. E. Grassino, "Load compensation in obese patients during quiet tidal breathing," *J Appl Physiol*, vol. 55, no. 4, pp. 1269-1276, 1983.

[19] R. W. M. Wahba, "Perioperative functional residual capacity," *Can J Anaesth.*, vol. 38, no. 3, pp. 384-400, April 01, 1991.