Airway pressures generated by high flow nasal cannula in patients with acute hypoxemic respiratory failure: a computational study

Hossein Shamohammadi[1], Liam Weaver[1], Sina Saffaran[1], Roberto Tonelli[2], Marianna Laviola[3], John G. Laffey[4], Luigi Camporota[5], Timothy E. Scott[6], Jonathan G. Hardman[3,7], Enrico Clini[2*] and Declan G. Bates[1]

Abstract

Introduction and objectives High flow nasal cannula (HFNC) therapy is an increasingly popular mode of non-invasive respiratory support for the treatment of patients with acute hypoxemic respiratory failure (AHRF). Previous experimental studies in healthy subjects have established that HFNC generates flow-dependent positive airway pressures, but no data is available on the levels of mean airway pressure (mP_{aw}) or positive end-expiratory pressure (PEEP) generated by HFNC therapy in AHRF patients. We aimed to estimate the airway pressures generated by HFNC at different flow rates in patients with AHRF, whose functional lung volume may be significantly reduced compared to healthy subjects due to alveolar consolidation and/or collapse.

Materials and methods We developed a high-fidelity mechanistic computational model of the cardiopulmonary system during HFNC therapy using data from healthy subjects, and then measured the mP_{aw} and PEEP levels produced when different amounts of alveolar consolidation/collapse were incorporated into the model.

Results When calibrated to represent normal lung physiology in healthy subjects, our model recapitulates the airway pressures produced by HFNC at different flow rates in healthy volunteers who were breathing normally, with their mouths closed or open. When different amounts of alveolar consolidation/collapse are implemented in the model to reflect the pathophysiology of AHRF, the mP_{aw} and PEEP produced by HFNC at all flow rates increase as the functional lung volume decreases (up to a mP_{aw} of 11.53 and a PEEP of 11.41 cmH_2O at 60 L/min with the mouth closed when 50% of the model's alveolar compartments are non-aerated). When the model was matched to individual patient data from a cohort of 58 patients with AHRF receiving HFNC at 60 L/min, the mean (standard deviation) of the mP_{aw} / PEEP produced by HFNC in the models of these patients was 8.56 (1.50) / 8.92 (1.49) cmH_2O with mouths closed, and 1.73 (0.31) / 1.36 (0.36) cmH_2O with mouths open.

Conclusions Our results suggest that the airway pressures produced by HFNC in patients with AHRF could be higher than is currently assumed based on experimental data from healthy subjects, particularly in patients whose mouths remain closed. Higher levels of PEEP could be beneficial if they lead to alveolar recruitment and improved lung compliance, but could cause alveolar overdistension if they do not, motivating the close monitoring of the effects of

*Correspondence:
Enrico Clini
enrico.clini@unimore.it

Full list of author information is available at the end of the article

HFNC on lung mechanics. Further clinical studies are warranted to directly measure the airway pressures produced by HFNC in patients with different severities of AHRF.

Keywords High flow nasal cannula, Non-invasive respiratory support, Mathematical modelling, Computer simulation, Positive end expiratory pressure

Introduction

High flow nasal cannula (HFNC) therapy delivers heated and humidified air or oxygen to patients at high flow rates, typically between 20 and 60 L/min, via a nasal cannula interface [1, 2]. HFNC is an increasingly popular form of non-invasive respiratory support for the treatment of acute respiratory failure, particularly since the COVID-19 pandemic [3–6]. In contrast to other forms of non-invasive respiratory support such as continuous positive airway pressure (CPAP) or non-invasive ventilation (NIV), which use a tightly sealed mask or helmet to deliver positive pressure to the lungs, HFNC therapy provides a set flow rate of air or oxygen via a nasal cannula interface, with either symmetrical [1] or asymmetrical prongs [7, 8].

The ability of HFNC therapy to generate a flow-rate-dependent positive airway pressure is well accepted among clinicians. However, estimates made to date of the level of airway pressures produced by HFNC at different flow rates are based exclusively on measurements made in subjects who were not suffering from acute respiratory failure. In healthy subjects whose mouths were closed, a HFNC flow rate of 60 L/min (typically the maximum used in clinical practice) produced average mean airway pressures of 6.12 cmH_2O in [9] and 6.78 cmH_2O in [10], and an average expiratory pressure of 7.4 cmH_2O in [11]. Increased mean airway pressure compared to spontaneous breathing has been measured in patients with chronic obstructive pulmonary disease (COPD) at various HFNC flow rates up to 50 L/min. At 50 L/min, mean airway pressure increased to 3.01 ± 1.03 cmH_2O [12]. Similarly, in another study involving hypercapnic patients with interstitial lung disease (ILD), a flow-dependent increase in mean airway pressure was measured in the nasopharyngeal space, reaching a maximum of 3.1 ± 1.5 cmH_2O at 50 L/min [13].- See Table S1 of the Supplementary Material for a full review of relevant data from previous studies.

In contrast to the situations considered above, the functional lung volume is reduced in acute respiratory failure. Gattinoni [14] introduced the concept of the "baby lung" in acute respiratory distress syndrome (ARDS), based on computed tomography examinations which showed that some ARDS patients could have normally aerated lung tissue corresponding to the dimensions of the lung of a 5- to 6-year-old child (300–500 g of aerated tissue). Based on the standard relationship between pressure and volume in ideal gases (Pressure $\times$ Volume = Mass of gas $\times$ Gas constant $\times$ Temperature), we hypothesised that if the flow of air delivered by HFNC into the lungs is similar, smaller functional lung volumes in patients with AHRF could lead to HFNC providing higher airway pressures than that expected based on data from healthy subjects.

Methods

Patient and public involvement

No patients were involved in the study, all results are based on modelling of data from previously published studies.

Modelling a cohort of healthy subjects receiving HFNC

To investigate the relationship between functional lung volume and airway pressures produced by HFNC, we adapted a multi-compartmental computational simulator, previously employed to simulate patients with different conditions, such as COVID-19 [15], chronic obstructive pulmonary disease (COPD) [16], ARDS [17, 18] and AHRF [19]. The simulator offers several advantages including the ability to define multiple alveolar compartments with individually configurable mechanical characteristics such as alveolar collapse, consolidation and stiffening, gas-exchange disruption, pulmonary vasoconstriction, vasodilation, and airway obstruction. This allows for the representation of various clinical features including acute lung injury, ventilation-perfusion mismatch, physiological shunt, alveolar gas trapping with intrinsic positive end-expiratory pressure (iPEEP), and reopening of collapsed alveoli [20, 21]. Key mechanisms involved in the application of HFNC therapy, including carbon dioxide clearance from dead space, gas leakage, a friction factor for turbulent flow, and increases in airway resistance at high flow rates are included in the model presented here – full details are provided in Sect. 4 of the Supplementary Material.

We initially adapted this computational simulator to create a virtual cohort of ten subjects whose characteristics were representative of participants in four previous studies reporting mean airway pressures in healthy subjects at multiple HFNC flow rates [9, 10, 22, 23]. This virtual cohort consists of an equal number of males and females, with an average age of 33 years, height of 170 cm, and weight of 74 kg, all falling within the normal BMI range. Detailed information regarding the cohort is presented in Table S2 in the supplementary material. Healthy lung physiology and respiratory effort are

simulated in all cases, with compliance and airway resistance values varying within normal ranges.

Modelling reductions in functional lung volume in patients receiving HFNC therapy

To simulate alveolar consolidation/collapse (i.e., compartments with no participation in ventilation), the inlet resistance of a specified number of the alveolar compartments in the model is increased to a large value to preclude any airflow to the alveolus. In this part of the investigation, all other parameters pertaining to the subjects including FiO_2 were left unaltered, ensuring that the results are focused exclusively on elucidating the influence of the size of the functional lung volume on the pressures generated by HFNC.

Modelling a cohort of AHRF patients receiving HFNC therapy

To estimate the PEEP produced by HFNC in actual AHRF patients, data were extracted from two studies [24, 25] reporting data on 60 non-COVID-19 patients with moderate-to-severe AHRF, conducted within a respiratory intensive care unit at the University Hospital of Modena, Italy, from 2016 to 2021. These comprised a comprehensive set of physiological measurements for each patient during their HFNC therapy, including gender, age, height, weight, fraction of inspired oxygen, and HFNC flow rate, all of which served as inputs for the cardiopulmonary simulator. Using global optimization algorithms, the simulator's parameters were calibrated so that its outputs matched as closely as possible the responses of individual patients to HFNC therapy, encompassing partial pressures of oxygen (PaO_2) and carbon dioxide ($PaCO_2$) in the arterial blood, oesophageal pressure swings (ΔP_{es}, measured by a dedicated oesophageal pressure transducer), and expiratory tidal volume (VT, measured by numerical integration of respiratory flow

measured by a pneumotachograph) – for full details of the model matching process, see the supplementary material. Two patients were excluded from the analysis due to concerns regarding abnormally high VT measurements, potentially stemming from erroneous integration of a portion of the flow directed to the patient into the integrated flow signal.

Calculating PEEP and mean airway pressure during HFNC therapy

Previous experimental studies [9, 10, 22, 23], have measured mean airway pressure (mP_{aw}) produced by HFNC at the participants' pharynx. In our model, tracheal pressure serves as the reference for calculating both PEEP and mP_{aw}. Specifically, PEEP is determined as the positive end-expiratory pressure calculated at the trachea, while mP_{aw} represents the mean tracheal pressure throughout one complete breathing cycle.

Results

The cardiopulmonary simulator recapitulates airway pressures measured in healthy subjects receiving HFNC at different flow rates

The cardiopulmonary simulator effectively replicates airway pressures observed in healthy subjects undergoing HFNC therapy across various flow rates, in both mouth closed and open conditions. As shown in Table 1, the simulated mP_{aw} values closely match those reported in the experimental studies. Study [9] reported mP_{aw} in a closed-mouth condition at set flow rates ranging from 30 to 100 L/min, while another study [10] reported mP_{aw} in an open-mouth condition at set flow rates of 20, 40, and 60 L/min.

At fixed HFNC flow rates, PEEP increases as the functional lung volume decreases

In our model, at fixed HFNC flow rates, PEEP increases as the percentage of consolidated/collapsed lung volume increases (Table 2). For instance, at a HFNC flow rate of 60 L/min PEEP ranges from 6.19 ± 1.13 and 0.75 ± 0.19 cmH_2O in healthy subjects to 11.41 ± 2.56 and 1.55 ± 0.51 cmH_2O in subjects with 50% consolidated/collapsed lung, with the mouth closed and open, respectively.

### PEEP in models of 58 AHRF patients receiving HFNC at 60 L/min

Figure 1 compares the simulator outputs against individual measurements of PaO_2, $PaCO_2$, tidal change in pleural pressure (ΔP_{pl}), and VT in 58 patients during HFNC therapy at 60 L/min flow rate [24, 25]. In the case of ΔP_{pl}, we compare the actual tidal change in pleural pressure obtained from the model with its surrogate, ΔP_{es}. Across the cohort, the mean absolute percentage errors between

Table 1 Simulated Mean Airway pressure (mP_{aw}) in 10 healthy subjects at different HFNC flow rates compared to data from [9, 10] (*S.D. not reported)

Mouth condition	HFNC flow rate (L/min)	Experimental $mP_{aw}\pm SD$ (cmH_2O)	Simulated $mP_{aw}\pm SD$ (cmH_2O)
closed	30	2.71 ± 0.74	2.75 ± 0.59
	40	3.79 ± 0.84	3.92 ± 0.80
	50	4.95 ± 1.09	5.03 ± 0.96
	60	6.12 ± 1.37	6.37 ± 1.12
	70	7.69 ± 1.46	7.80 ± 1.34
	80	9.00 ± 1.89	9.33 ± 1.74
	90	10.05 ± 2.11	10.62 ± 1.99
	100	11.88 ± 2.73	12.50 ± 2.63
open	20	$0.18*$	0.19 ± 0.06
	40	$0.54*$	0.57 ± 0.12
	60	$0.75*$	0.77 ± 0.16

Table 2 mP_{aw} and PEEP at different HFNC flow rates with varying percentages of consolidated/collapsed lung volume

HFNC flow rate (L/min)	Mouth condition	Pressures (cmH₂O)	Lung consolidation/collapse (%)					
			0	10	20	30	40	50
30	closed	$mP_{aw} \pm SD$	2.75 ± 0.59	2.99 ± 0.65	3.28 ± 0.73	3.66 ± 0.84	4.18 ± 0.98	4.91 ± 1.18
		PEEP ± SD	2.62 ± 0.60	2.87 ± 0.66	3.17 ± 0.74	3.57 ± 0.84	4.10 ± 0.99	4.85 ± 1.18
40	closed	$mP_{aw} \pm SD$	3.92 ± 0.80	4.22 ± 0.88	4.62 ± 0.99	5.13 ± 1.14	5.84 ± 1.33	6.82 ± 1.59
		PEEP ± SD	3.72 ± 0.81	4.06 ± 0.89	4.47 ± 1.00	5.01 ± 1.14	5.73 ± 1.33	9.74 ± 1.60
	open	$mP_{aw} \pm SD$	0.57 ± 0.12	0.65 ± 0.15	0.72 ± 0.17	0.81 ± 0.20	0.93 ± 0.23	1.10 ± 0.28
		PEEP ± SD	0.54 ± 0.13	0.63 ± 0.17	0.71 ± 0.21	0.80 ± 0.19	0.92 ± 0.22	1.24 ± 0.46
50	closed	$mP_{aw} \pm SD$	5.03 ± 0.96	5.69 ± 1.14	6.20 ± 1.28	6.87 ± 1.46	7.78 ± 1.71	9.05 ± 2.06
		PEEP ± SD	4.87 ± 0.95	5.49 ± 1.15	6.03 ± 1.29	6.72 ± 1.47	7.65 ± 1.72	8.95 ± 2.06
60	closed	$mP_{aw} \pm SD$	6.37 ± 1.12	7.37 ± 1.41	8.01 ± 1.59	8.84 ± 1.81	9.96 ± 2.12	11.53 ± 2.55
		PEEP ± SD	6.19 ± 1.13	7.13 ± 1.42	7.80 ± 1.60	8.65 ± 1.83	9.81 ± 2.13	11.41 ± 2.56
	open	$mP_{aw} \pm SD$	0.77 ± 0.17	0.86 ± 0.20	0.95 ± 0.23	1.08 ± 0.26	1.25 ± 0.31	1.47 ± 0.37
		PEEP ± SD	0.75 ± 0.19	0.83 ± 0.22	0.93 ± 0.23	1.08 ± 0.28	1.24 ± 0.31	1.55 ± 0.51
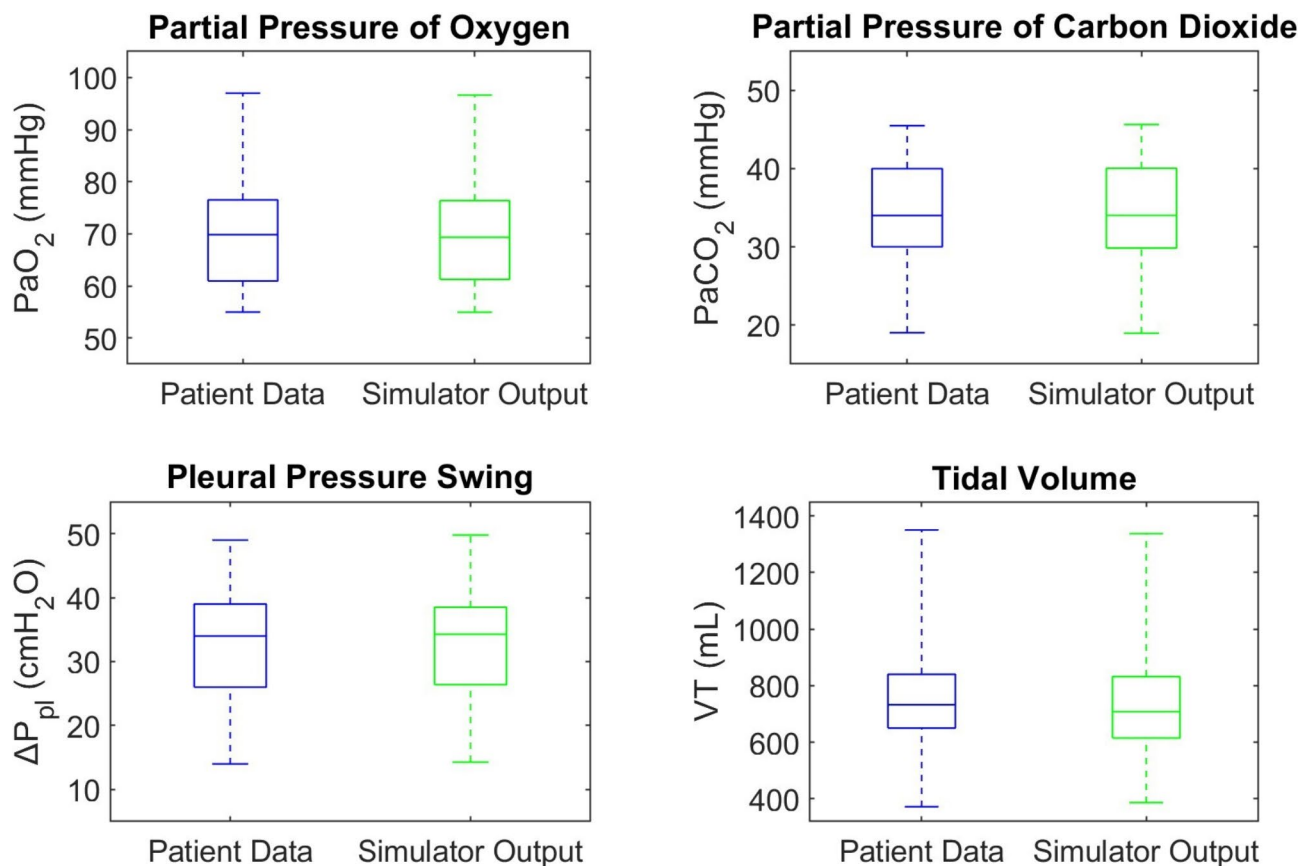
Fig. 1 Patient data distributions compared to simulator outputs while on HFNC, median, interquartile ranges, and actual ranges

the patient data and simulator outputs were 0.5% for PaO_2, 0.6% for $PaCO_2$, 2.5% for ΔP_{pl}, and 4.5% for VT.

The mean (standard deviation) of mP_{aw} and PEEP calculated in the models across the cohort of 58 patients with AHRF, all of whom were receiving HFNC therapy at 60 L/min with their mouths closed, was 8.56 (1.50) and 8.92 (1.49) cmH_2O, respectively. When simulated in the open mouth condition, the mP_{aw} and PEEP recorded in the model were 1.73 (0.31) and 1.36 (0.36) cmH_2O,

respectively. The mean (standard deviation) percentage of consolidated/collapsed compartments in the models was 20 (8.53) in the closed mouth condition and 34.5 (10.9) in open mouth condition (see Fig. 2).

Discussion

The ability of HFNC to produce a flow-dependent positive airway pressure in healthy subjects has been conclusively demonstrated in multiple studies [9, 10, 22, 23].
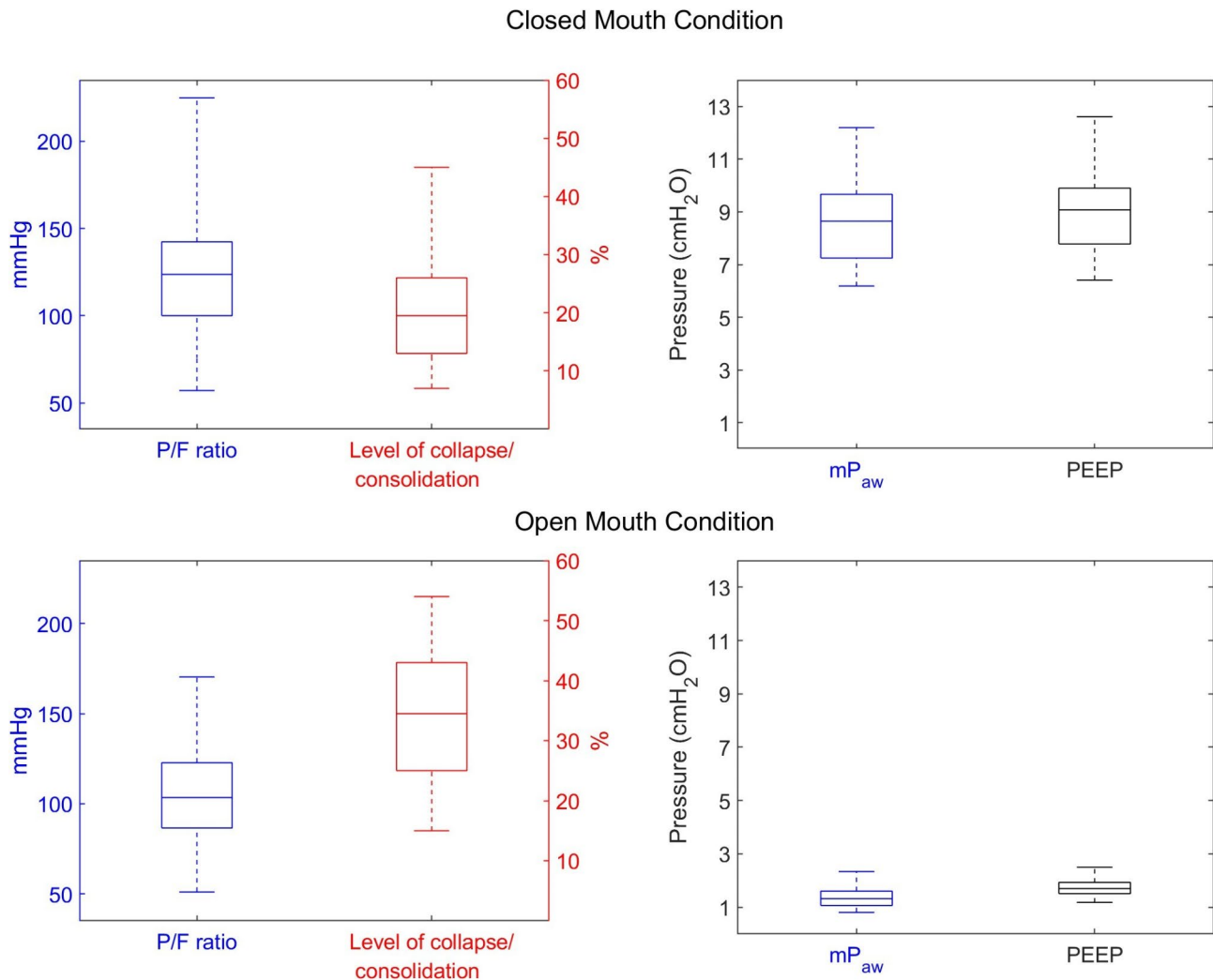
Closed Mouth Condition

Open Mouth Condition

Fig. 2 P/F ratio, level of consolidated/collapsed lung, mP_{aw}, and PEEP in the 58 models of patients receiving HFNC at 60 L/min under closed and open mouth condition, median, interquartile ranges, and actual ranges

However, no studies to date have measured the PEEP produced by HFNC in actual AHRF patients. The results presented here suggest that the PEEP produced by HFNC in AHRF patients may be 40% higher than that produced in healthy subjects, on average, with significantly greater differences being possible in some patients. These results were produced using a model which, when calibrated to represent healthy lung physiology, reproduces the pressures measured in previous human studies at multiple HFNC flow rates, in both mouth closed and open conditions. When this model is adjusted to reflect different levels of alveolar consolidation/collapse within the lung, PEEP increases with the amount of non-functional lung, at all flow rates. When the model parameters are adjusted so that they match data from 58 individual moderate-to-severe AHRF patients receiving HFNC therapy at 60 L/min [24, 25], it suggests the average PEEP was 8.92

cmH_2O across this cohort, with some patients receiving a PEEP of more than 12 cmH_2O.

Interestingly, a recent experimental study of the effect of different prong/nare ratios in HFNC which used a three-dimensionally printed bench model measured a PEEP of approximately 11 cmH_2O at 60 L/min flow rate and a prong/nare ratio of 0.51 [26]. Greater occlusion of the nares by the nasal cannula prongs can increase the resistance to flow and lead to higher generated pressure – in the studies involving the 58 AHRF patients whose data is used here, the largest prongs available were used in an attempt to provide the maximum possible level of support (all patients subsequently failed HFNC therapy and were consecutively given a trial of NIV. Another recent bench study using a mechanical lung respiratory simulation system with a prong/nare ratio of 0.63 reported a PEEP value of 10.3 cmH_2O at a HFNC flow rate of 60 L/min [27], while PEEP values of up to 36 cmH_2O were

measured at flows of 60 L/min in a mechanical model of the paediatric lung [28].

Two recent physiological studies comparing the effects of HFNC at 50–60 L/min flow rates with NIV or CPAP [29, 30] in AHRF patients found large differences in terms of gas exchange and end-expiratory lung volume (EELV). PEEP was not measured during HFNC in these studies, but the PEEP applied during NIV (10–12 cmH$_2$O plus additional inspiratory pressure support) and CPAP (14 cmH$_2$O) were higher than our estimates for that produced by HFNC. These differences, together with the fact that some patients receiving HFNC may have had their mouths open (data not reported), may explain the differences in gas exchange and EELV found in those studies. Lower PEEP levels were measured previously in healthy volunteers whose mouths were open during HFNC (Table S1) – our results suggest that the reduction in PEEP caused by opening the mouth may be even greater in patients with AHRF.

In our models of patients with AHRF, HFNC produces higher pressures than previously observed in healthy subjects because the functional volume of the lungs is reduced due to alveolar consolidation/collapse – across the models of 58 AHRF patients the average level of non-aerated lung volume produced by the process of matching the models to data of patients was 20%. In the context of invasive mechanical ventilation of patients with ARDS, it is by now well established that ventilator-induced lung injury (VILI) essentially corresponds to the application of excessive stress and strain to the "baby lung" [14] – the smaller the "baby lung" the greater the potential for VILI. Appropriate levels of PEEP may keep open portions of the lung that are prone to consolidation/collapse, increasing the resting end expiratory lung volume and reducing stress and strain [31]. If PEEP does not recruit collapsed alveoli, however, it may overdistend already open alveoli, increasing stress and strain [32]. In patients with AHRF who are spontaneously breathing, the PEEP effect of HFNC primarily arises from increased respiratory system resistance during the expiratory phase. This prevents the collapse of alveoli during exhalation and leads to an improvement in overall end-expiratory lung impedance with reduced gas shifting and pendelluft [33]. However, it can also potentially cause overdistension, particularly in non-dependent lung regions, when the lung is non-homogeneous. In this context, the detrimental effects of excessive PEEP are likely to be more dependent on the type of lung injury, and to be primarily generated during the expiratory phase when elastic recoil increases airway resistance. Our study suggests that managing this difficult balancing act may be an important element of achieving positive outcomes in the context of spontaneously breathing patients receiving non-invasive respiratory support therapies such as HFNC.

Our study has some limitations. The model was calibrated to patient data from two studies conducted at the same centre, involving patients with moderate-to-severe AHRF, all of whom were subsequently escalated to non-invasive or invasive mechanical ventilation. No data were available with which to directly estimate the level of alveolar consolidation/collapse in these patients – the size of the functional lung volume used in our models is the result of adjusting its parameters so that it optimally reproduces the measurements of PaO$_2$, PaCO$_2$, oesophageal pressure swing and tidal volume made in each patient.

Conclusions

The results of this study suggest that the positive airway pressures produced by HFNC in patients with AHRF who have reduced functional lung volumes due to alveolar consolidation/collapse might be significantly higher than is currently assumed based on the available experimental data from healthy subjects. In our model, at fixed HFNC flow rates, PEEP increased as the functional lung volume decreased. Higher levels of PEEP could be beneficial if they lead to alveolar recruitment and improved lung compliance, but if they do not produce recruitment then they could increase the risk of lung injury due to alveolar overdistension. While our results are logical consequences of standard gas pressure-volume relationships, further confirmatory clinical studies are warranted to directly measure the airway pressures produced by HFNC in patients with AHRF.

Abbreviations

HFNC	High Flow Nasal Cannula
AHRF	Acute Hypoxemic Respiratory Failure
mP$_{aw}$	Mean Airway Pressure
PEEP	Positive End Expiratory Pressure
CPAP	Continuous Positive Airway Pressure
COPD	Chronic Obstructive Pulmonary Disease
ARDS	Acute Respiratory Distress Syndrome
ICU	Intensive Care Unit
PaO$_2$	Partial Pressure of Arterial Oxygen
PaCO$_2$	Partial Pressure of Arterial Carbon Dioxide
ΔPpl	Tidal Change in Pleural Pressure
VT	Tidal Volume
NIV	Non-Invasive Ventilation
VILI	Ventilator Induced Lung Injury
EELV	End Expiratory Lung Volume

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12931-025-03096-x.

Supplementary Material 1

Data availability

All data generated or analysed during this study are included in this published article and its supplementary information files.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]School of Engineering, University of Warwick, Coventry CV4 7AL, UK
[2]Respiratory Diseases Unit, Department of Medical and Surgical Sciences, University Hospital of Modena, University of Modena and Reggio Emilia, Modena, Italy
[3]Anaesthesia and Critical Care, Injury Inflammation and Recovery Sciences, School of Medicine, University of Nottingham, Nottingham NG7 2UH, UK
[4]Anaesthesia and Intensive Care Medicine, School of Medicine, Galway University Hospitals, University of Galway, Galway H91 TK33, Ireland
[5]Intensive Care Medicine, Division of Asthma Allergy and Lung Biology, Guy's and St Thomas' NHS Foundation Trust, King's College London, London, UK
[6]Centre for Biomechanics and Rehabilitation Technologies, Stoke on Trent, University of Staffordshire, Stoke-on-Trent ST4 2DF, UK
[7]Nottingham University Hospitals NHS Trust, Nottingham NG7 2UH, UK

References

1. Carlucci A, Maggiore SM. High Flow Nasal Cannula: physiological effects and clinical applications. Springer Cham Springer Cham. 2021. https://doi.org/10.1007/978-3-030-42454-1. 1st ed.
2. Ricard JD, et al. Use of nasal high flow oxygen during acute respiratory failure. Intensive Care Med. 2020;46(12):2238–47. https://doi.org/10.1007/s00134-020-06228-7.
3. Battaglini D, et al. Noninvasive respiratory support and patient self-inflicted lung injury in COVID-19: a narrative review. Br J Anaesth. 2021;127(3):353–64. https://doi.org/10.1016/j.bja.2021.05.024.
4. Rochwerg B, et al. The role for high flow nasal cannula as a respiratory support strategy in adults: a clinical practice guideline. Intensive Care Med. 2020;46(12):2226–37. https://doi.org/10.1007/s00134-020-06312-y.
5. Grieco DL, et al. Effect of Helmet Noninvasive Ventilation vs High-Flow Nasal Oxygen on days Free of respiratory support in patients with COVID-19 and moderate to severe hypoxemic respiratory failure: the HENIVOT Randomized Clinical Trial. JAMA - J Am Med Association. 2021;325(17):1731–43. https://doi.org/10.1001/jama.2021.4682.
6. Schifino G, Vega ML, Pisani L, Prediletto I. Effects of non-invasive respiratory supports on inspiratory effort in moderate-severe COVID-19 patients. A randomized physiological study. Eur J Intern Med. 2022;100:110–8. https://doi.org/10.1016/j.ejim.2022.04.012.
7. Tatkov S, Rees M, Gulley A, van den Heuij LGT, Nilius G. 'Asymmetrical nasal high flow ventilation improves clearance of CO2 from the anatomical dead space and increases positive airway pressure', J Appl Physiol (1985), vol. 134, no. 2, pp. 365–377, 2023. https://doi.org/10.1152/japplphysiol.00692.2022
8. Slobod D, et al. Effects of an asymmetrical high flow nasal cannula interface in hypoxemic patients. Crit Care. Apr. 2023;27(1):145. https://doi.org/10.1186/s13054-023-04441-6.
9. Parke RL, Bloch A, McGuinness SP. Effect of very-high-flow nasal therapy on airway pressure and end-expiratory lung impedance in healthy volunteers. Respir Care. 2015;60(10):1397–403. https://doi.org/10.4187/respcare.04028.
10. Vieira F, et al. High-flow nasal cannula compared with continuous positive airway pressure: a bench and physiological study. J Appl Physiol. 2022;132(6):1580–90. https://doi.org/10.1152/japplphysiol.00416.2021.
11. Groves N, Tobin A. High flow nasal oxygen generates positive airway pressure in adult volunteers. Australian Crit Care. 2007;20(4):126–31. https://doi.org/10.1016/j.aucc.2007.08.001.
12. Bräunlich J, Köhler M, Wirtz H. 'Nasal highflow improves ventilation in patients with COPD'. Int J Chron Obstruct Pulmon Dis, pp. 1077–85, 2016.
13. Bräunlich J, Köhler M, Wirtz H. Nasal High-Flow (NHF) improves ventilation in patients with interstitial lung disease (ILD)—A physiological study. J Clin Med. 2023;12(18):5853.
14. Gattinoni L, Pesenti A. The concept of baby lung. Intensive Care Med. Jun. 2005;31(6):776–84. https://doi.org/10.1007/s00134-005-2627-z.
15. Das A et al. 'In Silico Modeling of Coronavirus Disease 2019 Acute Respiratory Distress Syndrome: Pathophysiologic Insights and Potential Management Implications', Crit Care Explor, vol. 2, no. 9, p. e0202, 2020. https://doi.org/10.1097/cce.0000000000000202
16. Saffaran S, et al. Inhaled sGC modulator can lower pH in patients with COPD without deteriorating oxygenation. CPT Pharmacometrics Syst Pharmacol. 2018;7(8):491–8.
17. Chikhani M, Das A, Haque M, Wang W, Bates DG, Hardman JG. High PEEP in acute respiratory distress syndrome: quantitative evaluation between improved arterial oxygenation and decreased oxygen delivery. Br J Anaesth. Nov. 2016;117(5):650–8. https://doi.org/10.1093/bja/aew314.
18. Saffaran S, Das A, Laffey JG, Hardman JG, Yehya N, Bates DG. 'Utility of Driving Pressure and Mechanical Power to Guide Protective Ventilator Settings in Two Cohorts of Adult and Pediatric Patients With Acute Respiratory Distress Syndrome: A Computational Investigation.', Crit Care Med, vol. 48, no. 7, pp. 1001–1008, Jul. 2020, https://doi.org/10.1097/CCM.0000000000004372
19. Weaver L, et al. Digital Twins of Acute Hypoxemic respiratory failure patients suggest a mechanistic basis for success and failure of noninvasive ventilation. Crit Care Med. May 2024. https://doi.org/10.1097/CCM.0000000000006337.
20. Weaver L, et al. High risk of patient self-inflicted lung injury in COVID-19 with frequently encountered spontaneous breathing patterns: a computational modelling study. Ann Intensive Care. 2021;11(1):1–8. https://doi.org/10.1186/s13613-021-00904-7.
21. Weaver L, et al. Optimising respiratory support for early COVID-19 pneumonia: a computational modelling study. Br J Anaesth. 2022;128(6):1052–8.
22. Ritchie JE, Williams AB, Gerard C, Hockey H. Evaluation of a humidified nasal high-flow oxygen system, using oxygraphy, capnography and measurement of upper airway pressures. Anaesth Intensive Care. 2011;39(6):1103–10. https://doi.org/10.1177/0310057x1103900620.
23. Miyazaki Y, Inoue S, Hirose H, Kooguchi K, Kotani J. High-velocity nasal insufflation increases nasopharyngeal pressure with flow-dependent manner compared with high flow nasal cannula in adult volunteers – a single-center prospective observational study. Kobe J Med Sci. 2021;67(3):92–7.
24. Tonelli R, et al. Early Inspiratory Effort Assessment by Esophageal Manometry predicts noninvasive ventilation outcome in De Novo Respiratory failure: a pilot study. Am J Respir Crit Care Med. 2020;202(4):558–67. https://doi.org/10.1164/rccm.201912-2512OC.
25. Tonelli R et al. 'Inspiratory Effort and Lung Mechanics in Spontaneously Breathing Patients with Acute Respiratory Failure due to COVID-19: A Matched Control Study.', American J Res Crit Care Med. 2021;204(6):725–728, United States. https://doi.org/10.1164/rccm.202104-1029LE
26. Pinkham MI et al. 'Effect of respiratory rate and size of cannula on pressure and dead-space clearance during nasal high flow in patients with COPD and acute respiratory failure', J Appl Physiol. 1985;132(2):553–563. https://doi.org/10.1152/japplphysiol.00769.2021

27. Sun Y-H, Dai B, Peng Y, Tan W, Zhao H-W. Factors affecting FiO(2) and PEEP during high-flow nasal cannula oxygen therapy: a bench study. Clin Respir J. Dec. 2019;13(12):758–64. https://doi.org/10.1111/crj.13087.

28. Ejiofor BD, Carroll RW, Bortcosh W, Kacmarek RM. PEEP generated by High-Flow Nasal Cannula in a Pediatric Model. Respir Care. Oct. 2019;64(10):1240–9. https://doi.org/10.4187/respcare.06470.

29. Grieco DL, et al. Physiological comparison of High-Flow Nasal Cannula and Helmet Noninvasive Ventilation in Acute Hypoxemic Respiratory failure. Am J Respir Crit Care Med. 2020;201(3):303–12. https://doi.org/10.1164/rccm.201904-0841OC.

30. Menga LS, et al. Respective effects of Helmet pressure support, continuous positive Airway pressure, and Nasal High-Flow in Hypoxemic Respiratory failure: a randomized crossover clinical trial. Am J Respir Crit Care Med. 2023;207(10):1310–23. https://doi.org/10.1164/rccm.202204-0629OC.

31. García-Prieto E et al. 'Impact of recruitment on static and dynamic lung strain in acute respiratory distress syndrome', Anesthesiology, 124, 2, pp. 443–52, 2016.

32. Chiumello D, et al. Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. Am J Respir Crit Care Med. 2008;178(4):346–55.

33. Yoshida T et al. Volume-controlled ventilation does not prevent injurious inflation during spontaneous effort. Am J Respir Crit Care Med. 2017;196(5):590–601.

Publisher's note