Modelling Nasal High Flow Therapy Effects on Upper Airway Resistance and Resistive Work of Breathing

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Abstract

Aim: The goal of this paper is to quantify upper airway resistance with and without nasal high flow (NHF) therapy. For adults, NHF therapy feeds 30 to 60 L/min of warm humidified air into the nose through short cannulas which do not seal the nostril. NHF therapy has been reported to increase airway pressure, increase tidal volume (V_t) and decrease respiratory rate (RR), but it is unclear how these findings affect the work done to overcome airway resistance to air flow during expiration. Also, there is little information on how the choice of nasal cannula size may affect work of breathing. In this paper, estimates of airway resistance without and with different NHF flow (applied via different cannula sizes) were made. The breathing efforts required to overcome airway resistance under these conditions were quantified.

Method: NHF was applied via three different cannula sizes to a 3-D printed human upper airway. Pressure drop and flow rate were measured and used to estimate inspiratory and expiratory upper airway resistances. The resistance information was used to compute the muscular work required to overcome the resistance of the upper airway to flow.

Results: NHF raises expiratory resistance relative to spontaneous breathing if the breathing pattern does not change but reduces work of breathing if peak expiratory flow falls. Of the cannula sizes used, the large cannula produced the greatest resistance and the small cannula produced the least. The work required to cause tracheal flow through the upper airway was reduced if the RR and minute volume are reduced by NHF. NHF has been observed to do so in COPD patients (Braunlich et al, 2013). A reduction in I:E ratio due to therapy was found to reduce work of breathing if the peak inspiratory flow is less than the flow below which no inspiratory effort is required to overcome upper airway resistance.

Conclusion: NHF raises expiratory resistance but it can reduce the work required to overcome upper airway resistance via a fall in inspiratory work of breathing, RR and minute volume.

keywords: nasal high flow therapy; work of breathing; zero pressure inspiratory flow

1 Introduction

NHF involves the administration of warmed and humidified air, which may be enriched with oxygen, at flow rates up to 60 L/min for adults and 8 L/min for neonates.[1234] The conditioned air is supplied to the patient via a nasal cannula having soft nasal prongs which do not seal the nostril. The NHF flow is often greater than the peak inspiratory demand. Surplus air is expelled through the gap between prong and nares, and through the mouth if open. NHF is applied to critically ill patients suffering from conditions such as chronic airway disorders, mild obstructive sleep apnoea, acute hypoxemic respiratory failure and post operative hypoxemia.[5678]

In the last decade, the paucity of information on the mechanisms of action of NHF therapy prompted Dysart et al.[9] to postulate mechanisms of action of NHF. These include a reduction in mechanical work of breathing (WOB) - the muscular effort which drives breathing. Dysart et al.[9] suggested that inspiratory WOB was reduced as NHF provides air flow, which supplies inspiratory flow without effort by the patient. A popular surrogate for effort of breathing is the pressure rate product (PRP) which is usually calculated as the product of the breathing frequency and esophageal pressure change (between end of expiration and end of inspiration). Rubin et al.[10] , Willis et al.[11] and Pham et al.[12] used the PRP to quantify WOB under conditions of NHF in a population of neonates and children and reported a decrease in WOB. Using the electrical impedance tomography technique, Pham et al.[12] observed a reduction in the diaphragmatic electrical activity of 24 infants (age = 1 - 12 months) during NHF - suggesting, in some sense, the offloading of the diaphragmatic muscular effort and hence a reduction in mechanical work of breathing.

Whilst these studies provide insights into the benefits derived from NHF from the energy cost standpoint, PRP is a surrogate rather than the true work of breathing and these studies considered only the inspiratory aspect of breathing. Saslow et al.[13] used the gold standard method of computing WOB i.e. finding the area under the pressure-volume curve and found that the neonatal WOB associated with NHF of 3 - 5 L/min and CPAP of 6 cmH_2O are comparable. The WOB prior to the administration of NHF and the effect of cannula size

were not studied.

The questions we seek to answer are in three parts. Firstly, when NHF is applied, how much change occurs in the upper airway resistance in the inspiration and expiration directions? Secondly, how much breathing effort is required to overcome these resistances; and thirdly how does cannula size affect these quantities? An anatomically representative rigid model of the upper airway, from the trachea to the nares was used - according to Ferris et al.,[14] this section typically constitutes about two-thirds of the total airway resistance. Using a refined model based on the work of Otis et al.,[15] the effort to overcome upper airway resistance to air flow is calculated for a range of NHF and cannula sizes. As the interest lies in how NHF affects upper airway resistance, the lower airway (below the trachea) is not included in the experimental setup. The resistance of the lower airway has been reported to be linear (independent of flow) up to 120 L/min.[14] As the peak inspiratory flow during spontaneous breathing in young male adults is < 60 L/min,[16,17,18] it is reasonable to assume that for the same minute volume, there will be no change in resistance of the lower airway during NHF. If NHF changes the minute volume, the change in work done in the lower airways will have the same trend as the work done in the upper airway.

2 Materials and Methods

2.1 Upper Airway Model (UAM)

Computed tomography (CT) images of the upper airway of a 44 year old male adult, with no apparent airway abnormality, and in a mouth open resting state, were segmented to extract the airway. The sinuses were deleted and terminated at the trachea. A 3D model was 3D printed in acrylic (Visijet EX200) - Fig. 1. To study mouth closed breathing, which is recommended for NHF, the oral opening was sealed. Tests on models made from scans of subjects with their mouth closed, and subjects scanned with their mouth open, but with the oral cavity of the model sealed closed, showed these to have a similar resistance to flow. A complete description of model making methods can be found in the report by Geoghegan et

al.[19] A hole of diameter 1 mm was drilled directly into the trachea for pressure measurement. A positive displacement programmable piston pump (PP) (Van Hove et al.[20]) was connected to the UAM (Fig. 1). The PP is able to produce bidirectional flows up to 60 L/min. A TSI 4000 flow meter (industry calibrated) was used to confirm the flow delivered by the PP was as expected from the piston velocity. A difference of 6.4 % was found thus all piston flows were multiplied by a factor of 1.064. An AIRVO^{TM}2 nasal high flow device (manufactured by Fisher & Paykel Healthcare Limited, Auckland, New Zealand) was used to administer NHF via a breathing circuit and nasal cannula (Fisher & Paykel Healthcare Ltd, Optiflow). A pressure transducer (AMS 5915, Analog Microelectronics GmbH, Germany) was connected to the pressure tap in the trachea (P_1 in Fig. 1). P_2 is the atmospheric pressure.

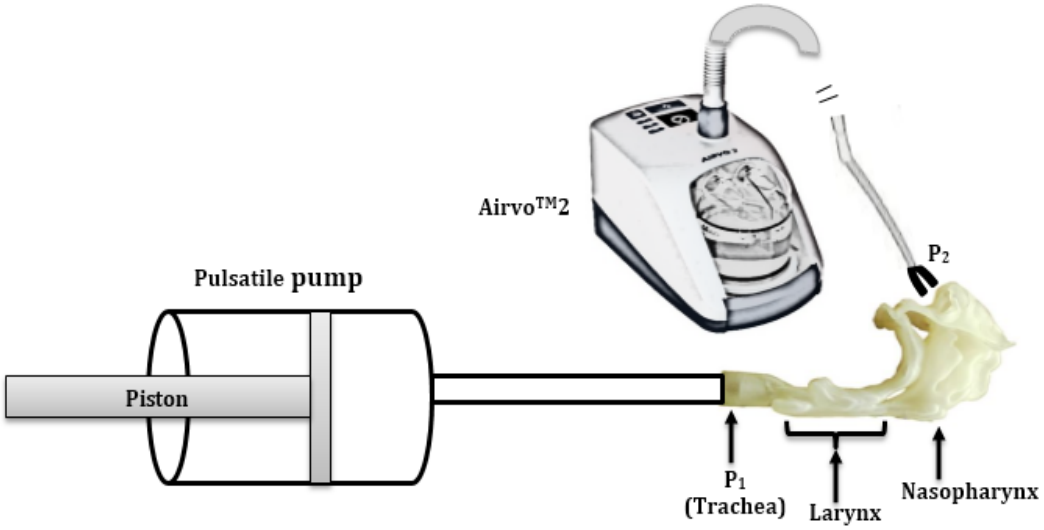


Figure 1: The experimental setup shows the upper airway model connected to the PP and the AIRVO^{TM}2. Tracheal pressure is sampled from point P_1. P_2 is the atmospheric pressure

2.2 Experimental procedure

The resistance of the UAM itself was first determined by pushing steady flow rates (F) ranging from -50 L/min to 50 L/min through the UAM. Negative flow rates denote inspiration. Rohrer's equation,[15] Eq.1, describes the relationship between air flow and the driving

pressure (P_{ru})

$$P_{ru} = K_1 F + K_2 F^2 \tag{1}$$

where K_1 and K_2 are resistance coefficients. K_1 and K_2 in Eq.1 are determined by least-squares fitting to the recorded flow (F) and differential pressure data ($P_{ru} = P_2 - P_1$). Airway resistance, R, is defined as $R = P_{ru}/F$ (Eq.2)

$$R = K_1 + K_2 F \tag{2}$$

Due to the second term in Eq.2, airway resistance depends on flow rate. Tracheal pressure was recorded with no NHF applied to the UAM. NHF was then applied via each of the three nasal cannulas: the small (OPT842), medium (OPT844) and large (OPT846) cannula (Fisher & Paykel Healthcare). For each cannula, the flow rate through the cannula (NHF flow rate) was set at 20 L/min (NHF20), 40 L/min (NHF40) and 60 L/min (NHF60) in turn. The PP was used to deliver rectangular flow waves in which the steady flow ranged from -50 to 50 L/min in steps of 10 L/min. At these pressures, the air density is virtually constant and the piston motion determines the tracheal flow.

3 Results

3.1 Upper airway pressure-flow characteristics

Fig. 2 shows the pressure-flow data obtained via the medium cannula for both breathing directions, inspiration and expiration during NHF20, NHF40 and NHF60. That of the zero-therapy state, ZT, (no cannula in place, no NHF flow) is also shown. The pressure rises quadratically with flow rate i.e. the K_2 term in Eq.1 cannot be neglected. Note that on Fig. 2, at zero tracheal flow (piston not moving), the inflow through the cannula is balanced by outflow through the leak area between the nares and cannula prongs. The pressure (P_2) at zero net flow is non-zero for all NHF and increases with increasing NHF. These pressures are produced by the stagnation of the cannula jet in the upper airway.

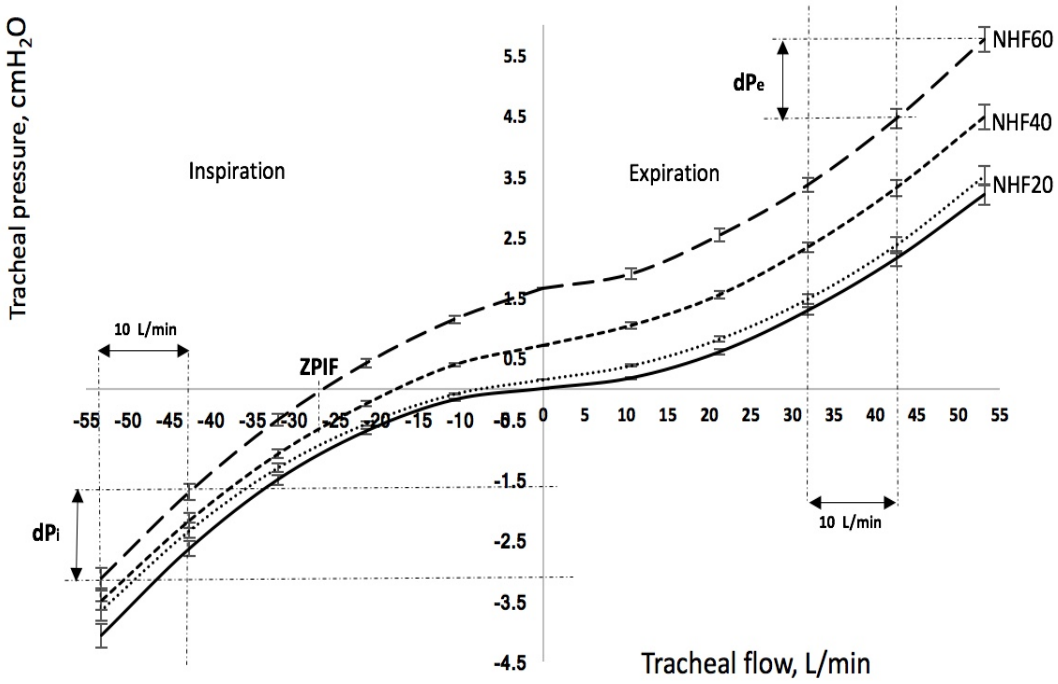


Figure 2: Pressure-flow relationship for adult UAM during inspiration and expiration at ZT and NHF20, NHF40 and NHF60, administered via the medium cannula. The error bars represent two standard deviations in pressure measurement.

It is observed that at NHF60, as tracheal flow increases (in both directions) expiration requires more pressure compared to inspiration whilst at ZT, inspiratory tracheal pressure eventually becomes greater than expiratory tracheal pressure as tracheal flow increases. From ZT towards NHF60, the changeover from a greater inspiratory effort to a greater expiratory effort occurs after NHF20. Nonetheless, at NHF60, the pressure difference required to produce a difference in tracheal flow is greater during inspiration. As shown in Fig. 2, the change in inspiratory pressure (dP_i) required to increase tracheal flow by 10 L/min is greater than the pressure (dP_e) required during expiration to increase tracheal flow by the same amount. This suggests a greater inspiratory resistance.

At the flow rate named zero pressure inspiration flow (ZPIF) in Fig. 2, the pressure at the trachea required to drive inspiratory flow is zero. As NHF increases the ZPIF also rises. At flow rates between ZPIF and zero, no muscular effort is required to drive inspiration against upper airway resistance. In this state, inspiration is driven by NHF.

In Fig. 3, the breathing flow of a male adult (age = 24 years) is shown. Tobin et al.[21] measured the breathing pattern of 65 normal subjects from 20 to 81 years of age and found no effect of age on the mean values of various breathing pattern components nor any significant correlation with body height. Negative flows represent tracheal flows in the inspiratory direction. Fig. 3 is the tracheal flow used in ZT and NHF > 0 cases studied here with NHF-induced modulations in amplitude and period defined for each case. The horizontal lines

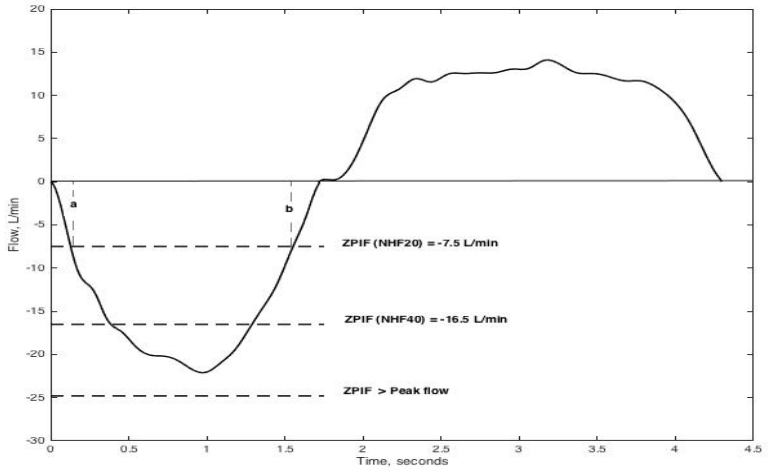


Figure 3: A breathing flow pattern of a male adult (age = 24). The ZPIF for NHF20, NHF40 and NHF60 found for the UAM are shown.

represent the ZPIF. When NHF20 is applied, for instance, from the start of inspiration up to a flow rate of -7.5 L/min (ZPIF), no respiratory effort will be required to overcome upper airway resistance but that needed to overcome lower airway resistance and lung elastance. Muscular effort is only required to overcome upper airway resistance between time = **a** and time = **b** until expiration begins. As NHF flow rate increases, ZPIF rises and less effort is required over the inspiratory phase. Note that the ZPIF can be greater than the peak inspiratory flow suggesting effortless inspiratory breathing across the upper airway.

Table 1 shows the K_1 and K_2 values fitted to inspiration and expiration during ZT, NHF20, NHF40 and NHF60. These values are used in all subsequent calculations.

Table 1: The K_1 and K_2 values of the UAM for inspiration and expiration during ZT, NHF20, NHF40 and NHF60. The R^2 values denote the coefficient of determination of the least squares fit of the pressure-flow plots to Rohrer's equation (Eq.1).

	Inspiration			**Expiration**		
	K_1 $(cmH_2O/L/s)$	K_2 $(cmH_2O/L^2/s^2)$	R^2	K_1 $(cmH_2O/L/s)$	K_2 $(cmH_2O/L^2/s^2)$	R^2
ZT	0.04	4.32	0.99	0.20	3.61	0.99
NHF20	0.45	4.32	1.00	0.57	3.62	0.99
NHF40	1.32	3.88	0.99	1.18	3.47	0.99
NHF60	2.14	3.65	1.00	1.07	4.09	1.00

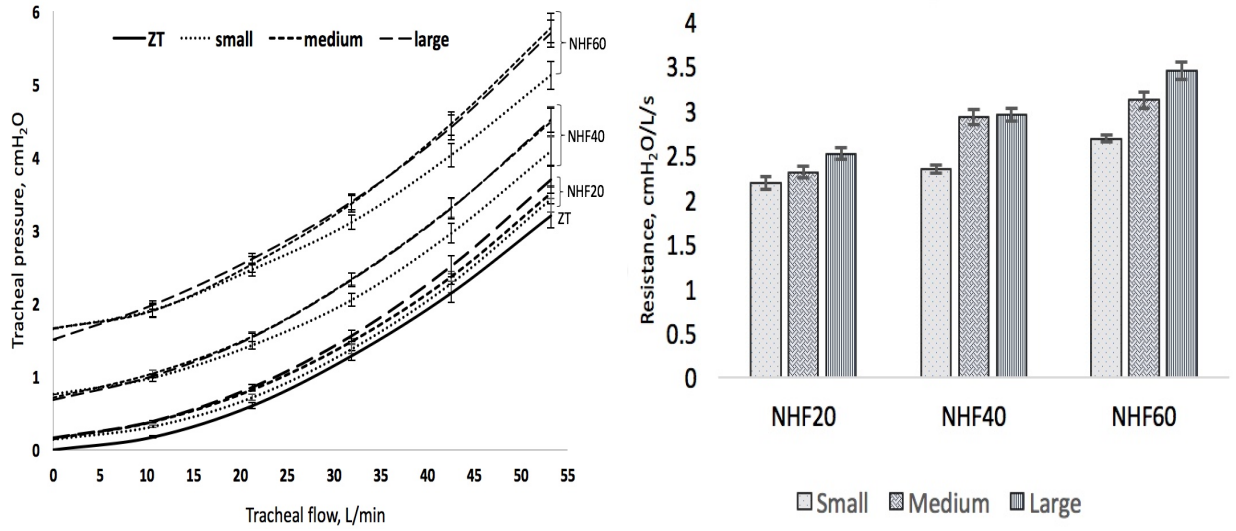
3.2 Effect of cannula size on resistance

Fig. 4a shows the expiratory pressure-flow plots at ZT, NHF20, NHF40 and NHF60 for all cannula and the flow rates induced by the piston motion (tracheal flow). The error bars represent two standard deviations in pressure calculated over 5 cycles. Except for NHF20, the pressure produced by the medium cannula is almost the same as that of the large cannula. NHF rates have a greater effect on pressure than cannula size does. The differences in pressure between small and large cannula increases with tracheal flow. The K_1 and K_2 deduced from each of the curves shown in Fig. 4a were used to compute the resistance at a tracheal flow of 30 L/min (Fig. 4b).

Though the large cannula tends to produce the greatest resistance at all NHF values, the error bars of the large and medium cannula overlap. Replacing the large cannula with the small cannula reduces expiratory resistance by 13 %, 20 % and 22%, respectively corresponding to NHF20, NHF40 and NHF60.

3.3 Resistive work of breathing

Having estimated the upper airway resistances (for inspiration and expiration) under NHF conditions, the metabolic energy cost required for tracheal flow under NHF conditions is now estimated. Eq.3 defines the breathing flow waveform, F. The work done per breath



(a) Expiratory pressure-flow plot (all cannula sizes)

(b) Upper airway resistance at 30 L/min

Figure 4: (a) The expiratory pressure-flow relationship for the UAM at ZT, NHF20, NHF40 and NHF60 administered via the small, medium and large cannula. The error bars represent two standard deviations in pressure measured over 5 cycles (b) A plot of the resistance of the UAM at a tracheal flow of 30 L/min when NHF20, NHF40 and NHF60 were administered via the small, medium and large cannula sizes. The standard errors in resistance due to errors in flow and pressure are shown by the error bars

comprises of the pressure used to overcome the resistance of the lung to inflation (elastance) - designated here as P_e - plus the pressure that overcomes upper airway resistance (P_{ru}) and lower airway resistance (P_{rl}). Eq.4 defines the mechanical work done per breath (WOB), as first used by Otis et al.[15]

$$F = \frac{dV}{dt} \tag{3}$$

$$WOB = \int (P_{ru} + P_{rl} + P_e)dV = \int (P_{ru} + P_{rl} + P_e)Fdt \tag{4}$$

Per the scope of the present experimental work, only the P_{ru} term of Eq. 4 is used and by substituting Eq. 1 into Eq. 4, Eq. 5 describes the total mechanical work done (rWOB) on inspiratory and expiratory tracheal flow via the upper airway in one minute.

$$rWOB = RR(\{\int_a^b (K_1F^2 + K_2F^3)dt\}_{inspiration} + \{\int_0^{T_e} (K_1F^2 + K_2F^3)dt\}_{expiration}) \tag{5}$$

where a and b are the times corresponding to the two intercepts of the ZPIF with the flow waveform (Fig. 3) and T_e is the expiratory time. Respiratory rate (RR) is in breaths

per minute (bpm). rWOB is also the average power of working against the upper airway resistance, expressed in J/min.

Nasal high flow therapy (NHF) has been widely reported to reduce RR[22,23] but its effect on tidal volume (V_t) and minute volume (MV) is complicated by disease state,[23] and wakefulness.[24] The effect of NHF on I:E ratio has been investigated by Fraser et al.[25] The results were used to infer how variation in I:E ratio might affect rWOB. In what follows, rWOB is investigated in three categories of subjects administered with NHF namely: (1) subjects in whom RR and V_t do not change with NHF (2) subjects with NHF-dependent RR and V_t but I:E ratio remains constant (3) subjects with NHF-dependent RR, V_t and I:E ratio.

3.3.1 Subject in whom RR and V_t do not change

Here, rWOB was calculated using the typical young adult resting state RR of 15 bpm and V_t of 0.5 L.[26,27] The mean I:E ratio for 47 young adults without NHF (age = 28.6 ± 5.3) found by Tobin et al.[21] to be 0.74 was used in the calculation of rWOB. The change in rWOB due to NHF ($rWOB_{NHF}$), is calculated as a percentage of the ZT rWOB ($rWOB_{ZT}$) i.e. $\%\Delta = 100(rWOB_{NHF} - rWOB_{ZT})/rWOB_{ZT}$. The results are presented in Table 2. The net effect is that rWOB rises with NHF up to NHF40 but at NHF60 rWOB falls. The rWOB at NHF60 falls below that at NHF40 because at NHF60, the ZPIF produces a greater reduction in inspiratory effort done it does at NHF40.

3.3.2 Subject with NHF-dependent RR and V_t

The observed respiratory response to NHF where there is a fall in RR,[22,28,29] a rise in V_t[28,22] but a general fall in MV[23] was considered. Braünlich et al.[23] reported that 20 L/min NHF reduced MV by approximately 1 L in 15 patients suffering from COPD (mean age = 67.7 years). Corley et al.[22] studied 20 COPD patients (mean age = 65 years), who were prescribed 50 L/min NHF, and observed a 3.4 bpm reduction in RR. Based on these observations, MV was reduced by 1 L for every 20 L/min of NHF and RR was reduced by 3.4 bpm for every 50 L/min NHF. The I:E ratio was 0.74.[21]

Table 2: The rWOB at ZT, NHF20, NHF40 and NHF60 for inspiration (rWOBi) and expiration (rWOBe). rWOB represents the sum of inspiratory and expiratory rWOB and %Δ is the percentage change in rWOB relative to ZT. rWOBi* is the rWOBi if the ZPIF effect is ignored

	Inspiration		**Expiration**	**Total**	
	rWOBi* **(J/min)**	**rWOBi** **(J/min)**	**rWOBe** **(J/min)**	**rWOB** **(J/min)**	%Δ
ZT	0.54	0.54	0.22	0.76	-
NHF20	0.67	0.66	0.28	0.94	24
NHF40	0.89	0.81	0.38	1.19	57
NHF60	1.12	0.45	0.39	0.84	11

209 In Table 3 the inspiratory, expiratory and total rWOB are shown. The percentage change
210 in rWOB relative to ZT (as was done in the previous case) is also shown with the negative sign indicative of a reduction. It is noticeable that rWOB during NHF falls below rWOB at

Table 3: Inspiratory WOB (rWOBi), expiratory WOB (rWOBe), total WOB (rWOB) and percentage change (%Δ) in rWOB relative to the ZT rWOB (shown in Table 2) when RR and MV falls but I:E ratio remains unchanged. rWOBi* is the rWOBi if the ZPIF effect is ignored.

	rWOBi* **(J/min)**	**rWOBi** **(J/min)**	**rWOBe** **(J/min)**	**rWOB** **(J/min)**	%Δ
NHF20	0.45	0.45	0.19	0.64	-16
NHF40	0.41	0.27	0.18	0.44	-42
NHF60	0.34	0.13	0.11	0.24	-68

211

212 ZT for all considered NHF. It is concluded that at least for the upper airway, irrespective of
213 breathing direction (inspiration or expiration), NHF increases rWOB (work done on tracheal
214 flow in a minute) when MV remains unchanged but it produces a significant fall in rWOB
215 when MV falls.

3.3.3 Subject with NHF-dependent RR, V_t I:E ratio

Fraser et al.[25] found that administering NHF of 30 L/min caused a reduction in I:E ratio of about 13 % in 30 males. To the authors knowledge, this is the only report of I:E ratio variation with NHF to date and was used to scale the I:E ratio with NHF (13 % fall in I:E ratio for every 30 L/min NHF). The relationship between NHF, MV, V_t and RR was the same as in Section 3.3.2. The results are shown in Table 4.

Table 4: Inspiratory rWOB (rWOBi), expiratory rWOB (rWOBe), total rWOB (rWOB) and percentage change (%Δ) in rWOB relative to the ZT rWOB (shown in Table 2) when RR and MV falls and NHF changes I:E ratio. rWOBi* is the rWOBi if the ZPIF effect is ignored.

	rWOBi* (J/min)	**rWOBi (J/min)**	**rWOBe (J/min)**	**rWOB (J/min)**	%Δ
NHF20	0.52	0.52	0.17	0.69	-9
NHF40	0.54	0.43	0.15	0.58	-24
NHF60	0.52	0.27	0.08	0.35	-54

It is observable that relative to the previous case the rWOB (for NHF dependent I:E ratio) increases for NHF20, NHF40 and NHF60. This happens because reducing I:E ratio means reducing inspiratory time but increasing expiratory time. This leads to a fall in peak expiratory flow, a rise in peak inspiratory flow and the widening of the difference between the ZPIF and the peak inspiratory flow. If after a fall in I:E ratio the ZPIF remains greater than peak inspiratory flow, rWOB will be further reduced because expiratory effort will fall and inspiration will be effortless.

4 Discussion

4.1 Effect of NHF on airway pressure during expiration

Mundel et al.[24] found that NHF of 15 L/min produced a greater nasal pressure with the large cannula compared to the small cannula.[24] Their model was simpler than the current one, with an axis-symmetric passage including a constriction that simulated the nasal valve. Their results and the present results agree qualitatively.

The present work is the first measurement of the resistance due to the cannula in an anatomically realistic geometry. As expected, the large cannula was found to produce a greater resistance than the small cannula. At NHF40 and tracheal flow of 30 L/min for instance, the expiratory resistance due to NHF administration via the large cannula was 20 % higher than when delivered through the small cannula. The leak area between the cannula prong and the nostril contributes to the rise in pressure with cannula size as the expired flow must pass through a smaller area with greater pressure loss.

Several researchers[30,31,32,33] have reported on the increase of airway pressure with increasing NHF as found in the present study. The present results suggest that whilst it may be possible to increase the extrinsic positive end-expiratory pressure (ePEEP) to reduce atelactasis by increasing cannula size, such a decision should be weighed against the possible rise in the expiratory effort of breathing.

4.2 Effect of NHF on resistive work of breathing

Dysart et al.[9] postulated that matching NHF with inspiratory flow demand may attenuate nasopharyngeal resistance and lead to reduction of work of breathing. Further, the nasal cannula is designed to reach past the nasal valve (which has significant resistance) leading to a reduction of inspiratory work of breathing. The fall in inspiratory work of breathing due to NHF can be explained in terms of the NHF-induced rise of the ZPIF, below which inspiration through the upper airway requires no respiratory effort.

Information on expiratory effort against a cannula jet is scarce in the literature.[9] The

present study indicates a rise in expiratory resistance to flow when NHF is applied. The expiratory flow must negate the momentum of the jet, leading to a rise in static pressure towards stagnation pressure. It follows that the greater the NHF, the greater the jet stagnation pressure and the effort that will be required to overcome and reverse the jet flow. If NHF raises the total volume of air to be expelled, a rise in flow rate through the leak area and a consequent rise in expiratory pressure is expected.

In spite of the longer expiratory time (I:E ratio < 1), rWOBe was lower than rWOBi because the peak expiratory flow was lower than the peak inspiratory flow. Also the resistance coefficients for inspiration were found to be greater. When RR and V_t remain unchanged, NHF dependent increase in rWOB (work required for tracheal flow through the upper airway per minute or power of breathing in J/min) was observed (Table 2) due to the increased inspiratory and expiratory resistance. At a constant I:E ratio, the fall in RR and consequently MV produced a reduction in rWOB in an NHF dependent manner (Table 3) partly due to the rise in ZPIF with NHF and a fall in peak expiratory flow with NHF. rWOB will further reduce if the ZPIF remains above the peak inspiratory flow after a fall in I:E ratio.

It has been reported that chronic obstructive pulmonary disease (COPD) and airway restrictive diseases are characterised by a rise in RR.[34,21] Since COPD augments expiratory resistance, which in turn demands a greater breathing effort, the fall in RR[23,35,36] coupled with the possible decrease in work of breathing upon the application of NHF may provide a significant relief to the respiratory musculature of COPD patients.

Though RR has been widely reported to fall with NHF,[22,23,29] varied findings exists as to how NHF impacts V_t and MV. Braünlich et al.[23] observed a general decrease in MV due to a decrease in RR for healthy subjects, idiopathic pulmonary fibrosis (IPF) patients and chronic obstructive pulmonary disease patients (COPD) upon the administration of 20 L/min NHF, however, V_t decreased amongst the healthy subjects, increased amongst the COPD patients and remained unchanged in the IPF patients. In a study performed on 10 healthy adults by Mundel et al.,[24] it was found that application of NHF did not change MV during wakefulness (as RR was offset by a rise in V_t), however it decreased MV during sleep

(by decreasing V_t, no change in RR was observed). Using electrical impedance tomography, Diab et al.[35], Riera et al.[28] and Corley et al.[22] reported a rise in V_t in response to NHF. Diab et al.[35] however measured MV as well, finding no change in it.

Wakefulness and disease state complicate the influence of NHF on V_t and MV. Given the convincing body of evidence supporting a fall in RR, if MV rises due to NHF, a rise in V_t traceable to an increase in inspiratory flow is suggested. Under such circumstances, work of breathing may be higher with NHF than without. Also, work of breathing may be expected to fall below that at ZT if MV falls due to a fall in both RR and V_t. Nonetheless, the interpretation of the therapeutic benefit of NHF to a patient must be comprehensive and not restricted to work of breathing alone as other parameters such as dyspnea, mouth dryness,[7] functional residual capacity,[35 22] end-tidal and blood arterial CO_2 concentration[37] also indicate the well being of patients in response to NHF.

4.3 Limitations of this study

There are some limitations associated with the present work. Measurement of resistance coefficients was limited to one individual adult airway. From study of a database of 180 scans (Nejati et al.[38]), we believe the airway used have no abnormalities, and to have dimensions within the one standard deviation of the population studied. Nevertheless, studies of person-to-person variation are needed.

The upper airway model used lacks the mucosal layer and compliance which the biological upper airway possesses. Though changes in airway surface properties may affect flow via development of viscous forces, the thin mucosal layer present in the healthy individual is reported to produce little effect on flow.[39] Also, a significant upper airway compliance may require an extra pressure drop but the small compliance of the upper airway (≈ 3 ml/cmH_2O[40]) limits this effect. It is plausible however that under conditions of high airway compliance and thick mucosal lining, upper airway resistance may differ from those presented here.

The CT on which the model was based was taken in the supine position, but NHF may

be administered to patients in a sitting or semi-reclined position. Curvature of the spine and thorax affects lung volume and resistance of the chest wall. However, the present study focusses on results of the upper airway. Weber et al.[41] found that there was no association between head posture and resistance to nasal airflow.

A single healthy breathing pattern has been used, and studies of the effect of breathing pattern variation from individual to individual, and with disorders such as COPD, are needed.

Furthermore, the evaluation of the resistive component of mechanical work of breathing has been restricted to only the upper airway, and the lower airway work has been assumed to be the same with or without NHF as mentioned in Section 1.

5 Conclusions

In conclusion, an increase in cannula size can increase airway pressure but this may come with an increase in expiratory resistance. NHF increases expiratory resistance but reduces overall resistive work of breathing through a fall in inspiratory work of breathing, respiratory rate and minute volume. An NHF-induced fall in I:E ratio may cause a rise in resistive work of breathing.

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