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Effect of Inspiratory Time and Lung Compliance on Flow Bias Generated During Manual Hyperinflation: A Bench Study

Bradley G Bennett, Peter Thomas PhD, and George Ntoumenopoulos PhD

BACKGROUND: Manual hyperinflation can be used to assist mucus clearance in intubated patients. The technique's effectiveness to move mucus is underpinned by its ability to generate flow bias in the direction of expiration, and this must exceed specific thresholds. It is unclear whether the inspiratory times commonly used by physiotherapists generate sufficient expiratory flow bias based on previously published thresholds and whether factors such as lung compliance affect this. METHODS: In a series of laboratory experiments, we applied manual hyperinflation to a bench model to examine the role of 3 target inspiratory times and 2 lung compliance settings on 3 measures of expiratory flow bias. RESULTS: Longer inspiratory times and lower lung compliances were associated with improvements in all measures of expiratory flow bias. In normal compliance lungs, achievement of the expiratory flow bias thresholds were (1) never achieved with an inspiratory time of 1 s, (2) rarely achieved with an inspiratory time of 2 s, and (3) commonly achieved with an inspiratory time of 3 s. In lower compliance lungs, achievement of the expiratory flow bias thresholds was (1) rarely achieved with an inspiratory time of 1 s, (2) sometimes achieved with an inspiratory time of 2 s, and (3) nearly always achieved with an inspiratory time of 3 s. Peak inspiratory pressures exceeded 40 cm H_2O in normal compliance lungs with inspiratory times of 1 s and in lower compliance lungs with inspiratory times of 1 and 2 s. CONCLUSIONS: Inspiratory times of at least 3 s with normal compliance lungs and at least 2 s with lower compliance lungs appear necessary to achieve expiratory flow bias thresholds during manual hyperinflation. Inspiratory times shorter than this may lead to excessive peak inspiratory pressures. Verification of these findings in relation to the movement of mucus should be examined in further bench or animal models and/or human clinical trials. *Key words: intensive care; manual hyperinflation; physiotherapy; inspiratory time; lung compliance; flow bias; lung model; respiratory mechanics.* [Respir Care 0;0(0):1–•. © 0 Daedalus Enterprises]

Introduction

Manual hyperinflation is a technique used by physiotherapists in ICUs across Australia,[1] the United Kingdom,[1,2] Denmark,[3] and Brazil[4] to assist with mucus clearance in mechanically ventilated patients.[5] The existing evidence for manual hyperinflation demonstrates only some short-term improvements in lung function without any benefits in major patient outcomes,[6] and this may account for its limited practice in other regions.[7] There is also the potential for harm with circuit disconnection (loss of PEEP), the tidal volume (V_T) values and airway pressures generated, and the potential impact on cardiac output and blood pres-

Mr Bennett is affiliated with Australian Catholic University, North Sydney, New South Wales, Australia. Dr Thomas is affiliated with the Department of Physiotherapy, Royal Brisbane and Women's Hospital, Herston, Queensland 4006, Australia. Dr Ntoumenopoulos is affiliated with the School of Physiotherapy, Faculty of Health Sciences, Australian Catholic University.

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Correspondence: George Ntoumenopoulos PhD, Level 9, 33 Berry Street, North Sydney, New South Wales 2060, Australia. E-mail: George.Ntoumenopoulos@acu.edu.au.

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sure.[6] Retained mucus in the lower respiratory tract is associated with the development of nosocomial pneumonia[8] and may increase mortality in the ICU.[9] Administration of manual hyperinflation requires that the patient be disconnected from the mechanical ventilator and connected to a circuit where the physiotherapist can manually administer breaths to the patient by squeezing and releasing a reservoir bag.[10]

When manual hyperinflation is applied for the purpose of enhancing mucus clearance, it is recommended that the physiotherapist use a prolonged inspiratory time (by slowly squeezing the reservoir bag) and a short expiratory time (by rapidly releasing the reservoir bag).[11] This is because the mechanism by which manual hyperinflation is proposed to assist mucus clearance is through annular 2-phase gas-liquid flow,[12] whereby there is a transfer of momentum[13] from the breath to the mucus in the airways. A relatively slow inspiratory flow followed by a relatively fast expiratory flow is thought to cause a flow bias in the direction of expiration and cause the movement of mucus toward the mouth.

For manual hyperinflation to be effective in moving mucus, the generated flow bias may need to exceed various threshold values. A previous bench study examined the movement of mucus simulant in both vertical and horizontal tubes ventilated with bidirectional gas flow and found movement of mucus simulant only when the peak flow of gas moving in one direction was at least 10% faster than the peak flow of gas moving in the opposite direction.[14] The results of a later experiment examining the movement of mucus simulant in mechanically ventilated sheep corroborated this finding.[15] Consequently, it may be necessary for manual hyperinflation to be performed in a way such that the ratio between the peak inspiratory flow (PIF) and peak expiratory flow (PEF) is <0.9, and this has been used in some manual hyperinflation research as a theoretical benchmark for whether manual hyperinflation may have been effective in moving mucus.[16-18] More recent bench and animal studies suggest that threshold values for the absolute difference between the PIF and the PEF (PIF − PEF)[19] <−17 L/min (normal mucus simulant 1.5%) and <−22 L/min (thick mucus simulant 3.0%) and also possibly the difference between the mean inspiratory flow and the mean expiratory flow (MIF − MEF)[20] <−7.9 L/min may also be important thresholds for the movement of mucus. However, to the best of our knowledge, the proposed thresholds have not yet been verified in humans, and it remains unclear whether the precise threshold values can be directly extrapolated to the application of manual hyperinflation in the human lung. In addition, gravity[21]; mucus layer thickness[19]; and possibly also lung compliance, airway resistance, and patient expiratory effort may augment or impede mucus clearance during manual hyperinflation and/or mechanical ventilation.

QUICK LOOK

Current knowledge

Manual hyperinflation is a technique used by physiotherapists in ICUs to assist with mucus clearance in mechanically ventilated patients. The existing evidence for manual hyperinflation demonstrates only short-term physiologic improvements without outcome benefits. There is also the potential for harm with circuit disconnection, the V_T values and airway pressures generated, and the potential impact on cardiac output and blood pressure. Administration of manual hyperinflation requires disconnection of the patient from the ventilator and connection to a manual resuscitator. This practice is uncommon in North America.

What this paper contributes to our knowledge

Inspiratory times of at least 3 s with normal compliance lungs and at least 2 s with lower compliance lungs were necessary to achieve expiratory flow bias thresholds during manual hyperinflation of a lung model. Shorter inspiratory times led to excessive peak inspiratory pressures. Verification of these findings in relation to the movement of mucus should be examined in animal models and/or human clinical trials.

During manual hyperinflation, a number of variables can alter the flows, peak inspiratory pressure, and V_T value generated. The physiotherapist can influence a number of these variables, through determining the type of manual hyperinflation circuit utilized and the inspiratory/expiratory time and V_T delivered. These have the potential to alter the effectiveness of the procedure and/or adversely affect the patient if they are not regulated. Peak inspiratory pressures are recommended to be <40 cm H_2O to avoid risks of barotrauma.[22] No limits have been recommended for V_T during manual hyperinflation, but large V_T values may impede venous return[6] and could contribute to lung injury via volutrauma.

Recent research has largely focused on the controllable factors that assist with generating a faster expiratory flow, such as manual hyperinflation circuit design and the use of PEEP valves.[23-26] and expiratory release techniques[11,18] By comparison, less attention has been directed to ways in which a slower inspiratory flow can be generated, such as through a prolonged inspiratory time. Furthermore, it appears in practice that the typical inspiratory time taken to deliver a breath during manual hyperinflation may be much shorter than the early recommendations of 3 s.[10] Most studies suggest that 1–2 s of inspiratory time during manual hyperinflation is commonly used,[16,17,27] possibly due to the physiotherapist accommodating to minimize patient

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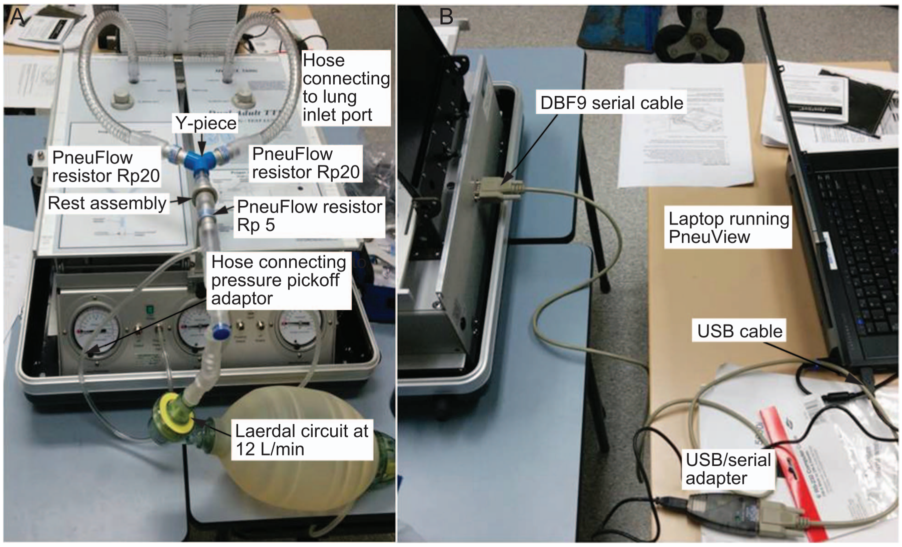

Fig. 1. Experimental setup, front view (A) and back view (B).

discomfort from a long inspiration[28] as a consequence of comparatively lighter sedation techniques that are used currently[29] compared with when the early recommendations were made. Prolonged inspiratory times may also reduce venous return to the heart and adversely impact cardiac function.[22] It is unclear whether a 1–2 s inspiratory time during manual hyperinflation compromises the effectiveness of the technique to generate an expiratory flow bias.

We hypothesized that inspiratory time and lung compliance during manual hyperinflation would affect the expiratory flow bias generated. In this experiment, we specifically investigated the effect of 3 inspiratory times and 2 lung compliance values on the generated flow bias during manual hyperinflation in a bench model.

Methods

Experimental Design

One experienced cardiothoracic physiotherapist performed manual hyperinflation on the bench model until 30 acceptable applications were recorded for all 6 experimental conditions, which were pairwise combinations of inspiratory time (1, 2, or 3 s) and lung compliance settings used in previous bench studies (0.05 L/cm H_2O to simulate normal lung compliance[11,18,26,30] or 0.02 L/cm H_2O to simulate lower lung compliance [to mimic lung compliance found in ARDS[26,31]]). Upper and lower airway resistance were standardized to simulate normal intubated adult airway resistance across all trials.

Equipment and Experimental Setup

The experiment was carried out at the Australian Catholic University, North Sydney Campus, James Carol Building, simulation center (Sydney, Australia). The bench model comprised a training/test lung model (Dual Adult PneuView model 5600i, Michigan Instruments, Grand Rapids, Michigan) set up as per Figure 1 in connection with a Laerdal silicone resuscitator bag with a 12-L/min constant supply of compressed air. Data from the training/test lung model was transmitted electronically where it was captured via the PneuView software application (Dual Adult PneuView model 5600i). Airway resistance was simulated by using a PneuFlo parabolic airway resistor of Rp5 for the upper airways and Rp20 for the lower airways as per the manufacturer's instructions. PneuFlo parabolic airway resistors exhibit parabolic characteristics with regard to pressure change as a function of flow (see the supplementary materials at http://www.rcjournal.com). We covered the compliance scale and the volume scale on the training/test lung model to blind the physiotherapist performing manual hyperinflation to the lung compliance settings. The computer was directed away from the participant such that they could not see the information on the screen. The PneuView software application had been calibrated previously with the training/test lung model as per the manufacturer's instructions. A setting of ATPX was selected in the PneuView software application to calibrate the software to the ambient conditions of 25°C air temperature and 760 mm Hg barometric pressure.

Measures

The PneuView software application was set to record the following measures for each manual hyperinflation application due to their potential to affect flow bias: V_T, inspiratory time, inspiratory hold time, expiratory time, proximal inspiratory pressure, MIF, PIF, MEF, and PEF

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for each breath. Measures of flow bias (PIF/PEF, PIF − PEF [L/min], and MIF − MEF [L/min]) were derived from MIF, PIF, MEF, and PEF.

Protocol

Each of the 6 pairwise combinations of inspiratory time and lung compliance was assigned a number from 1 to 6, which was then entered into a random number generator at www.random.org, which generated a permutation of these numbers in a random order. Experiments were performed in the order of this permutation.

Before the start of each experiment, the physiotherapist left the room, and the researcher adjusted the compliance setting on the training/test lung model as appropriate for the experimental condition and ensured that the manual hyperinflation circuit remained connected to the gas outlet with the flow on.

The physiotherapist was advised before the first experiment to perform manual hyperinflation for each experiment for the purpose of assisting mucus clearance and to insufflate a V_T of 1.4 L of air into the training/test lung model. The physiotherapist was advised only of the target inspiratory time at the beginning of each experiment.

A practice period was undertaken before data acquisition to familiarize the physiotherapist with the experimental condition. For each experiment, the physiotherapist continuously applied manual hyperinflation until data for 30 acceptable applications were recorded. Acceptable manual hyperinflation applications were within ± 0.25 s of the target inspiratory time, and V_T values were within 1.3–1.5 L. Real-time visual feedback was graphically displayed to the researcher via the PneuView software application about the inspiratory time and V_T. The researcher relayed this information to the physiotherapist via real-time verbal feedback as per Figure 2. The physiotherapist also self-monitored inspiratory time by verbally counting up by 1,000, with each number taking approximately 1 s to verbalize.

Statistical Analysis

The data from each experiment were manually transcribed from the PneuView software application into a Microsoft Excel document. Manual transcription was verified by a second person for a random sample of 2 of the 6 experiments for accuracy. The Microsoft Excel document was exported to SPSS 22 (IBM, Armonk, New York) to perform all statistical tests. The agreement between our target value and the value we achieved experimentally for inspiratory time and V_T was analyzed via 2 Bland and Altman mean-versus-difference plots. Two-way analysis of variance was used to examine whether there was a relationship between inspiratory time and lung compliance on measures of flow bias. Pearson's correlation coefficient

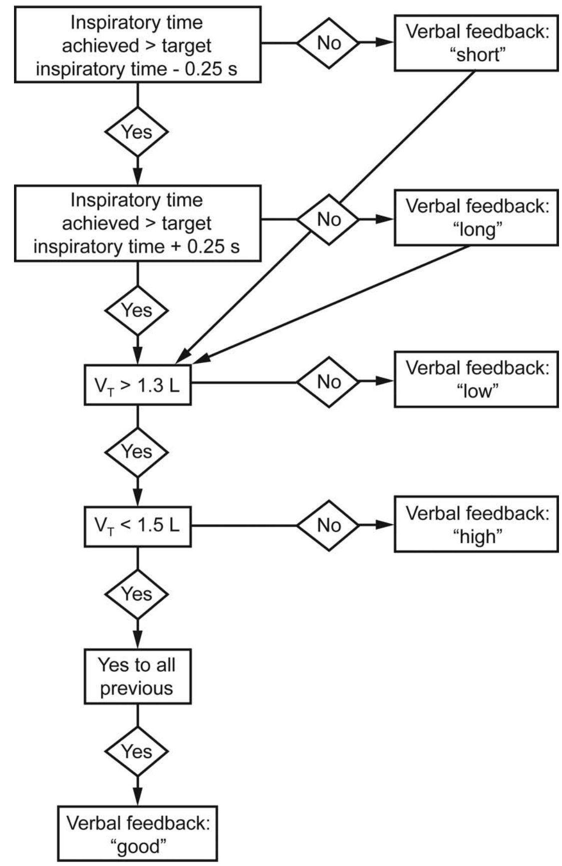

Fig. 2. Verbal feedback flow diagram. V_T = tidal volume (L).

was also used to examine the relationships between inspiratory time, lung compliance, V_T, proximal inspiratory pressure, expiratory time, PIF, and PEF and the measures of flow bias. To examine the predictors of flow bias, sequential forward linear regression was used only retaining variables in the model that had a *P* value of $<.05$. We also compared the flow bias generated during each manual hyperinflation application with the published threshold data. This included (1) PIF/PEF of <0.9, (2) PIF − PEF of <-17 L/min, (3) PIF − PEF of <-22 L/min, and (4) MIF − MEF <-7.9 L/min. Chi-square tests with Pearson's correlation coefficient were used to investigate whether the flow bias was significantly related to the published threshold data.

Results

Inspiratory Time, V_T, and Proximal Inspiratory Pressures

Inspiratory times were tightly controlled for in all experimental conditions as data points were within the limits of agreement >95% of the time (Fig. 3A), and this was similar for V_T values (Fig. 3B). Proximal inspiratory pres-

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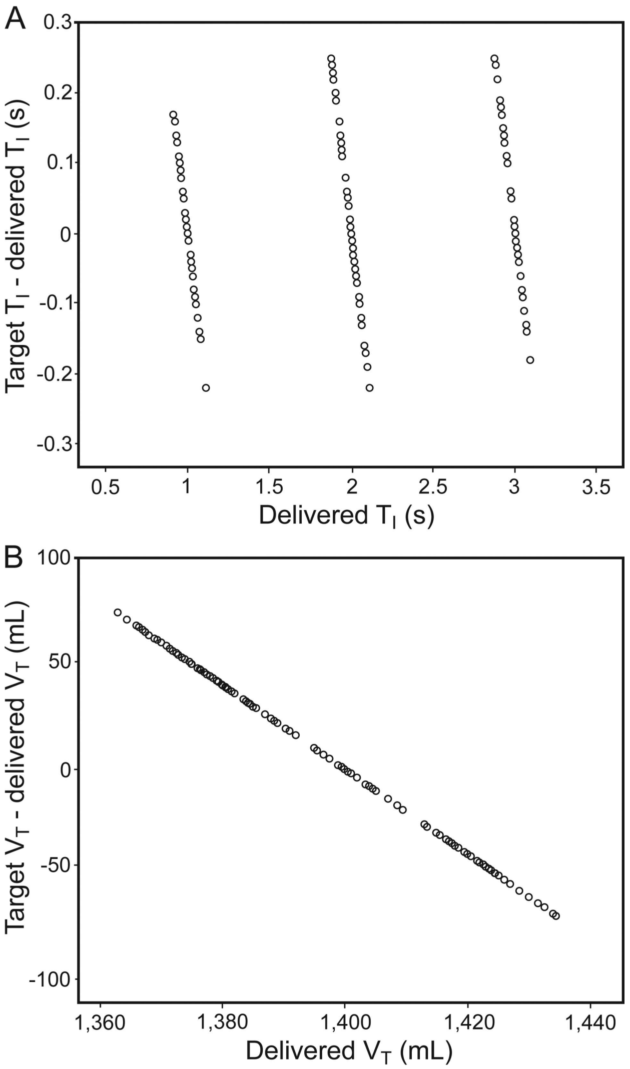

Fig. 3. Bland-Altman plots for mean versus difference of inspiratory time (A) and tidal volume (B). Horizontal lines show the mean, and dashed horizontal lines denote the limits of agreement. T_I = inspiratory time; target T_I = inspiratory time target that was aimed for during manual hyperinflation; delivered T_I = inspiratory time that was delivered during the experiment; V_T = tidal volume; target V_T = tidal volume target that was aimed for during manual hyperinflation; delivered V_T = tidal volume that was delivered during the experiment.

sures were >40 cm H_2O when inspiratory time was 1 s in the normal (Table 1) compliance setting and when inspiratory time was 1 and 2 s for the lower compliance setting (Table 2).

Interaction of Inspiratory Time and Compliance on Expiratory Flow Bias

There was a statistically significant relationship between the effects of inspiratory time and lung compliance on all 3 measures of flow bias (Tables 1–3). A simple main effects analysis showed that prolonging inspiratory time assists manual hyperinflation in generating an expiratory flow bias across all measures of expiratory flow bias. Each additional second increases expiratory flow bias independent of lung compliance (Tables 1 and 2). However, a lower lung compliance also appears to assist manual hyperinflation more than a normal lung compliance in generating larger expiratory flow bias independent of inspiratory time (Table 3).

Significant Factors Associated With Expiratory Flow Bias

The results of forward sequential linear regression for each expiratory flow bias measure are presented in Table 4. Inspiratory time was included in the model for PIF − PEF and MIF − MEF with a negative co-efficient that corroborates the finding from 2-way analysis of variance that prolonged inspiratory times assist in generating an expiratory flow bias. Inspiratory time was dropped out of the PIF/PEF model as peak inspiratory flow gave a better approximation. Lung compliance was included in all 3 models with a positive coefficient and suggests that low compliance lungs assist in creating an expiratory flow bias. Proximal inspiratory pressure and V_T were also factors included in some of the regression models, but their co-efficients were small and inconsistent in direction of effect. Expiratory time was included in the model for PIF − PEF with a positive co-efficient and suggests that shorter expiratory times assist in creating an expiratory flow bias.

Achievement of Flow Bias Thresholds

The comparison of the flow bias achieved during manual hyperinflation with previously published flow bias thresholds is shown in Table 5. For the normal lung compliance setting, no expiratory flow bias threshold was exceeded when an inspiratory time of 1 s was used, and most expiratory flow bias thresholds were not met with an inspiratory time of 2 s (with the exception of the MIF − MEF <−7.9 L achieved in only 1 case). An inspiratory time of 3 s achieved criterion success of 76% of cases on average, being more likely to achieve the expiratory flow bias thresholds of PIF/PEF <0.9 and MIF − MEF <−7.9 L (100%) rather than PIF − PEF <−17 L/min (63%) and <−22 L/min (33%). Lower compliance settings achieved the expiratory flow bias thresholds more often than the normal compliance lung settings. Like the normal compliance lung setting, the average success rate was minimal (5%) when inspiratory time was 1 s and considerable (99%) when inspiratory time was 3 s. However, unlike the normal compliance setting, the average success was seen in a larger proportion (58%) of manual hyperinflation attempts when inspiratory time was 2 s with a similar pattern of

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Table 1. Pairwise Comparisons of Inspiratory Time (1, 2, and 3 s) for the Normal Compliance Setting Experiments

Variable	T_I Target = 1 s	T_I Target = 2 s	T_I Target = 3 s	Mean Difference (1 s vs 2 s)	*P*	Mean Difference (1 s vs 3 s)	*P*	Mean Difference (2 s vs 3 s)	*P*
V_T, mL	1,357.00 ± 13.64	1,344.30 ± 9.50	1,370.63 ± 18.05	−12.7	.02	13.63	.009	26.33	<.001
T_I experiment, s	0.93 ± 0.06	2.03 ± 0.09	2.98 ± 0.12	1.10	<.001	2.05	<.001	0.95	<.001
T_{IH}, s	0.06 ± 0.03	0.58 ± 0.09	0.72 ± 0.15	0.51	<.001	.65	<.001	0.14	<.001
T_E, s	2.21 ± 0.12	2.86 ± 0.22	2.80 ± 0.23	0.65	<.001	.59	<.001	−0.06	.27
PIP, cm H_2O	47.42 ± 5.67	27.33 ± 1.61	17.51 ± 1.50	−20.09	<.001	–29.91	0.005	9.82	<.001
MIF, L/min	43.31 ± 2.60	19.65 ± 0.91	13.60 ± 0.63	−23.66	<.001	–29.71	<.001	−6.05	<.001
PIF, L/min	134.87 ± 9.94	94.22 ± 14.70	65.40 ± 4.52	−40.65	<.001	–69.47	<.001	−28.82	<.001
MEF, L/min	−18.11 ± 0.99	−13.90 ± 1.00	−14.48 ± 1.18	4.21	<.001	3.78	<.001	−0.58	.11
PEF, L/min	−92.16 ± 1.64	−81.02 ± 31.89	−85.20 ± 2.42	11.14	.001	6.96	.042	−4.18	.22
PIF/PEF	1.46 ± 0.11	1.08 ± 0.17	0.77 ± 0.06	−0.38	<.001	−0.70	<.001	−0.32	<.001
PIF − PEF, L/min	42.70 ± 10.11	7.35 ± 14.67	−19.81 ± 5.39	−35.35	<.001	−62.510	<.001	−27.16	<.001
MIF − MEF, L/min	25.20 ± 2.85	5.75 ± 1.28	−0.88 ± 1.28	−19.45	<.001	−26.08	<.001	−6.63	<.001

Values are mean ± SD.
T_I = inspiratory time
V_T = tidal volume
T_{IH} = inspiratory hold time
T_E = expiratory time
PIP = peak inspiratory pressure
MIF = mean inspiratory flow
PIF = peak inspiratory flow
MEF = mean expiratory flow
PEF = peak expiratory flow
PIF/PEF = ratio of peak inspiratory flow to peak expiratory flow
PIF − PEF = peak inspiratory flow to peak expiratory flow difference
MIF − MEF = mean inspiratory flow to mean expiratory flow difference

Table 2. Pairwise Comparisons of Inspiratory Time (1, 2, and 3 s) for the Low Compliance Setting Experiments

Variable	T_I Target = 1 s	T_I Target = 2 s	T_I Target = 3 s	Mean Difference (1 s vs 2 s)	*P*	Mean Difference (1 vs 3 s)	*P*	Mean Difference (2 s vs 3 s)	*P*
VT, mL	1,420.13 ± 27.16	1,414.43 ± 23.49	1,434.67 ± 22.63	−5.7	.27	14.53	.005	20.23	<.001
T_I experiment, s	1.05 ± 0.08	1.91 ± 0.12	2.94 ± 0.11	0.865	<.001	1.90	<.001	1.03	<.001
TIH, s	0.11 ± 0.04	0.56 ± 0.10	0.86 ± 0.17	0.46	<.001	0.76	<.001	0.30	<.001
TE, s	1.79 ± 0.10	2.46 ± 0.23	2.18 ± 0.29	0.67	<.001	0.38	<.001	−0.29	<.001
PIP, cm H_2O	56.25 ± 7.48	40.02 ± 2.33	37.05 ± 0.45	−16.23	<.001	−19.20	<.001	−2.98	.005
MIF, L/min	40.59 ± 3.66	21.98 ± 1.55	14.44 ± 0.64	−18.61	<.001	−26.15	<.001	−7.54	<.001
PIF, L/min	133.21 ± 15.23	102.66 ± 6.05	77.21 ± 4.61	−30.56	<.001	−56.007	<.001	−25.45	<.001
MEF, L/min	−23.44 ± 1.18	−17.00 ± 1.53	−19.66 ± 2.08	6.44	<.001	3.63	<.001	−2.66	<.001
PEF, L/min	−124.29 ± 1.22	−120.35 ± 1.53	−126.20 ± 2.16	3.94	.25	−1.90	.58	−5.84	.09
PIF/PEF	1.07 ± 0.12	0.85 ± 0.05	0.61 ± 0.04	−0.22	<.001	−0.46	<.001	−0.24	<.001
PIF − PEF, L/min	8.92 ± 14.68	−17.70 ± 6.32	−48.99 ± 5.56	−26.62	<.001	−57.91	<.001	−31.29	<.001
MIF − MEF, L/min	17.15 ± 4.02	4.98 ± 2.20	−5.22 ± 2.51	−12.17	<.001	−22.37	<.001	−10.20	<.001

Values are mean ± SD.
T_I = inspiratory time
V_T = tidal volume
T_{IH} = inspiratory hold time
T_E = expiratory time
PIP = peak inspiratory pressure
MIF = mean inspiratory flow
PIF = peak inspiratory flow
MEF = mean expiratory flow
PEF = peak expiratory flow
PIF/PEF = ratio of peak inspiratory flow to peak expiratory flow
PIF − PEF = peak inspiratory flow to peak expiratory flow difference
MIF − MEF = mean inspiratory flow to mean expiratory flow difference

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Table 3. Pairwise Comparisons of Normal and Low Compliance Setting by Inspiratory Time (1, 2, and 3 s)

Variable	Mean Difference (T_I Target = 1 s)*	*P*	Mean Difference (T_I Target = 2 s)*	*P*	Mean Difference (T_I Target = 3 s)*	*P*
V_T, mL	−63.13	<.001	−70.13	<.001	−64.03	<.001
T_I experiment, s	−0.12	<.001	0.12	<.001	.04	.17
T_{IH}, s	−0.04	.12	0.02	.61	−1.47	<.001
T_E, s	0.42	<.001	0.40	<.001	.62	<.001
PIP, cm H_2O)	−8.83	<.001	−12.69	<.001	−19.54	<.001
MIF, L/min	2.72	<.001	−2.33	<.001	−0.84	.11
PIF, L/min	1.65	.53	−8.43	.002	−11.81	<.001
MEF, L/min	5.32	<.001	3.10	<.001	5.18	<.001
PEF, L/min	32.13	<.001	39.33	<.001	40.99	<.001
PIF/PEF	0.39	<.001	0.23	<.001	0.16	<.001
PIF − PEF, L/min	33.78	<.001	25.05	<.001	29.18	<.001
MIF − MEF, L/min	9.04	<.001	0.77	.24	4.38	<.001

Values are mean ± SD. * Mean difference is calculated by taking the mean normal compliance result minus the mean low compliance result.
T_I = inspiratory time
V_T = tidal volume
T_{IH} = inspiratory hold time
T_E = expiratory time
PIP = peak inspiratory pressure
MIF = mean inspiratory flow
PIF = peak inspiratory flow
MEF = mean expiratory flow
PEF = peak expiratory flow
PIF/PEF = ratio of peak inspiratory flow to peak expiratory flow
PIF − PEF = peak inspiratory flow to peak expiratory flow difference
MIF − MEF = mean inspiratory flow to mean expiratory flow difference

Table 4. Regression Model for Measures of Flow Bias

Variable	Coefficients	*P*
PIF/PEF		
PIF (L/min)	0.010	<.001
PIP (cm H_2O)	−0.002	.006
V_T (mL)	0.000	.001
C_L (L/cm H_2O)	0.887	<.001
Constant	0.326	<.07
PIF − PEF (L/min)		
T_I experiment (s)	−16.85	<.001
C_L (L/cm H_2O)	139.40	<.001
PIP (cm H_2O)	1.34	<.001
T_E (s)	12.44	<.001
Constant	−100.00	<.001
MIF − MEF (L/min)		
T_I experiment (s)	−12.71	<.001
V_T (mL)	0.05	<.001
C_L (L/cm H_2O)	25.58	<.001
Constant	−42.45	.002

PIF/PEF = ratio of peak inspiratory flow to peak expiratory flow
PIF = peak inspiratory flow
PIP = peak inspiratory pressure
V_T = tidal volume
C_L = lung compliance
PIF − PEF = peak inspiratory flow to peak expiratory flow difference
T_I = inspiratory time
T_E = expiratory time
MIF − MEF = mean inspiratory flow to mean expiratory rate difference

being more likely to achieve the expiratory flow bias thresholds of PIF/PEF <0.9 (70%) and MIF − MEF <−7.9 L (67%) rather than PIF − PEF < −17 L/min (53%) and <−22 L/min (30%).

Discussion

The main findings of our bench study suggest that a prolonged inspiratory time of 3 s may be required to generate an expiratory flow bias in a patient with normal compliant lungs, and at least 2 s may be required in a patient with lower compliance. This agrees with a recent bench study that achieved similar expiratory flow bias thresholds with 2 s of inspiratory time and ideally 3 s of inspiratory time using pressure-controlled ventilator hyperinflation.[32]

Although manual hyperinflation may be commonly delivered with short inspiratory times,[6,7,18] there may be additional factors that facilitate mucus movement under these conditions. It is likely that alterations in V_T,[32] airway resistance and airway pressure,[17] manual hyperinflation circuit design,[23-26] and inclusion of an inspiratory hold[17] may also interact with the expiratory flow bias and alter whether the expiratory flow bias thresholds can be exceeded. Furthermore, gravity,[21] mucus layer thickness and consistency,[19] and patient expiratory effort probably interact with the expiratory flow bias generated and impact mucus

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Table 5. Influence of Lung Compliance and Inspiratory Time on Success in Achieving Flow Bias Thresholds During Manual Hyperinflation

Lung Compliance	Inspiratory Time, s	Flow Bias Threshold	Flow Bias Threshold Exceeded?, *n* (%)		P*	Flow Bias Threshold Exceeded?, Group Mean (%)	
			Yes	No		Yes	No
Normal	1	PIF/PEF < 0.9	0 (0)	30 (100)	<.001	0	100
		PIF − PEF <−17 L	0 (0)	30 (100)	<.001		
		PIF − PEF <−22 L	0 (0)	30 (100)	<.001		
		MIF − MEF < −7.9 L	0 (0)	30 (100)	<.001		
	2	PIF/PEF < 0.9	0 (0)	30 (100)	<.001	1	99
		PIF − PEF < −17 L	0 (0)	30 (100)	<.001		
		PIF − PEF < −22 L	0 (0)	30 (100)	<.001		
		MIF − MEF < −7.9L	1 (3)	29 (9)	<.001		
	3	PIF/PEF < 0.9	30 (100)	0 (0)	<.001	76	24
		PIF − PEF < −17 L	19 (63)	11 (33)	<.001		
		PIF −PEF < −22 L	12 (37)	18 (60)	<.001		
		MIF −MEF < −7.9 L	30 (100)	0 (0)	<.001		
Low	1	PIF/PEF < 0.9	3 (10)	27 (90)	<.001	30	70
		PIF − PEF < −17 L	2 (7)	28 (93)	<.001		
		PIF − PEF < −22 L	1 (3)	29 (96)	<.001		
		MIF − MEF < −7.9 L	0 (0)	30 (100)	<.001		
	2	PIF/PEF <0.9	23 (70)	7 (23)	<.001	58	32
		PIF − PEF <−17L	16 (53)	14 (47)	<.001		
		PIF − PEF <−22 L	10 (30)	20 (67)	<.001		
		MIF − MEF <−7.9L	20 (67)	10 (30)	<.001		
	3	PIF/PEF <0.9	30 (100)	0 (0)	<.001	100	0
		PIF − PEF <−17 L	30 (100)	0 (0)	<.001		
		PIF − PEF <−22 L	30 (100)	0 (0)	<.001		
		MIF − MEF <−7.9 L	28 (93)	2 (7)	<.001		

* Statistical significance of distribution from chi-square analysis.

movement. The combination of manual hyperinflation together with expiratory rib cage compressions may accelerate the weaning process and ICU discharge.[33]

The use of V_T values of <1.4 L may be able to generate sufficient expiratory flow bias during manual hyperinflation, but this was not the focus of this investigation. A recent bench study using ventilator hyperinflation demonstrated that V_T values of 1 L rather than 1.5 L may be more effective in achieving similar expiratory flow bias thresholds.[32] In this study, the delivery of V_T to 1.4 L was standardized to control for this as a variable. This volume was selected based on previous work that suggests that it is the V_T commonly generated during clinical practice.[11] In one regression model (MIF − MEF) only a small positive coefficient of 0.05 (Table 4) was found, suggesting that smaller V_T values may increase the expiratory flow bias by only a very small amount.

Of note, the peak inspiratory pressures generated during manual hyperinflation in our study exceeded the traditional safety recommendation of < 40 cm H_2O when a 1 s inspiratory time was used (independent of lung compliance settings), which leads to concern about its potential to cause barotrauma.[34] However, these safety recommendations for manual hyperinflation are based on the mechanical ventilation literature. The dose of manual hyperinflation is comparatively much shorter than the period of mechanical ventilation. It remains to be investigated whether a dosage of manual hyperinflation where proximal airway pressures exceed, for example, 40 cm H_2O increases the risk of acute lung injury/ARDS. The potential risks with manual hyperinflation require further investigation as one recent skills laboratory study found that the majority of ICU nurse participants performed manual hyperinflation with an inspiratory time of < 1 s.[27]

There are several important limitations of our study that should be acknowledged. The use of a bench model cannot capture the complexity of the human lungs, especially if they are altered by pathology. The airways in the bench model were of a single consistent diameter and rigid as compared with human airways. We did not utilize any mucus simulant in our study, so the flow bias achieved in this study and its impact on mucus movement were not examined. Gravity plays a significant role in mucus movement and possibly more so than expiratory flow bias.[21] Expiratory rib cage compressions during manual hyperinflation can also increase peak expiratory flow generated and may facilitate mucus clearance.[35,36] Gravity and expiratory rib cage compressions should be investigated further in the context of the flow bias generated by manual hyperinflation in bench and animal models. Furthermore, in the patient population, the patient may assist expiration with increased expiratory muscle activity during manual hyperinflation, and this may have the effect of increasing the peak expiratory flow and expiratory flow bias generated. Patient tolerance to a 2–3 s inspiration should also be considered in terms of synchrony with manual ventilation, airway pressures generated, and potential impact on hemodynamic function. The effect of patient expiratory effort on expiratory flow bias during manual hyperinflation may explain why a recent human study found that manual hyperinflation was able to achieve a mean PIF/PEF = 0.63 which was <0.9 in 76% of cases despite a mean inspiratory time = 1.45 s.[16]

The impact on mucus movement through different flow bias thresholds during manual hyperinflation has not yet been directly investigated in human subjects. The relative importance of one flow bias threshold over another is unclear and should be investigated further. In particular, the threshold of MIF − MEF < −7.9 L/min is based on the delivery of mechanical ventilation in intubated swine for 30 min at flows much lower than those achieved during the shorter applications of manual hyperinflation.[20]

Conclusions

Our study is the first to examine the effect of inspiratory time and lung compliance on the expiratory flow bias generated by manual hyperinflation in a bench model. Inspiratory times of at least 3 s for normal compliance lungs and at least 2 s for lower compliance lungs appear to be necessary to achieve expiratory flow bias thresholds the majority of the time in a bench model. Inspiratory times shorter than this may be ineffective for mucus movement and may lead to excessive peak inspiratory pressures and increase risks for barotrauma. The verification of these findings on the movement of mucus simulant during manual hyperinflation in a bench and/or animal model should be further investigated.

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