Short-Term Effect of Intermittent Intrapulmonary Deflation on Air Trapping in Patients With COPD

Juliana Ribeiro Fonseca Franco de Macedo, Gregory Reychler, Giuseppe Liistro, and William Poncin

BACKGROUND: Intermittent intrapulmonary deflation is an airway clearance technique that generates negative pressure during expiratory phases. This technology is intended to reduce air trapping by delaying the onset of air-flow limitation during exhalation. The objective of this study was to compare the short-term effect of intermittent intrapulmonary deflation versus positive expiratory pressure (PEP) therapy on trapped gas volume and vital capacity (VC) in patients with COPD. METHODS: We designed a randomized crossover study in which the participants with COPD received a 20-min session of both intermittent intrapulmonary deflation and PEP therapy on separate days and in random order. Lung volumes were measured via body plethysmography and helium dilution techniques, and spirometric outcomes were reviewed before and after each therapy. The trapped gas volume was estimated via functional residual capacity (FRC), residual volume (RV), and by the difference between FRC obtained through body plethysmography and helium dilution. Each participant also performed 3 VC maneuvers, from total lung capacity to RV with both devices. RESULTS: Twenty participants with COPD (mean ± SD ages 67 ± 8 y; FEV_1 48.1 ± 17.0%) were recruited. There was no difference between the devices in FRC or trapped gas volume. However, the RV decreased more during intermittent intrapulmonary deflation compared with PEP. The intermittent intrapulmonary deflation mobilized a larger expiratory volume than PEP during the VC maneuver (mean difference 389 mL, 95% CI 128–650 mL; *P* = .003). CONCLUSIONS: The RV decreased after intermittent intrapulmonary deflation compared with PEP, but this effect was not captured by other estimates of hyperinflation. Although the expiratory volume obtained during the VC maneuver with intermittent intrapulmonary deflation was greater than that obtained with PEP, the clinical importance as well as the long-term effects remain to be determined. (ClinicalTrials.gov registration NCT04157972.)

Key words: intermittent intrapulmonary deflation; lung hyperinflation; chronic obstructive pulmonary disease; positive expiratory pressure; airway clearance technique. [Respir Care 0;0(0):1–•. © 2023 Daedalus Enterprises]

Introduction

Air trapping is a hallmark feature of COPD.[1] It is defined as the presence of an excessive volume of gas in the lungs.[2] To reduce air trapping, positive expiratory pressure (PEP) therapy is often used.[3-5] The PEP technique requires active exhalation against a predefined resistance.[3-5] The induced physiologic effects have been referred to as a reduced pressure drop across the airway wall, which limits airway collapse.[4-6] However, breathing against an expiratory resistance may be difficult to tolerate in patients with severe COPD because their respiratory muscles are already exposed to high resistive loads due to airway obstruction.[4]

In response to the drawbacks of techniques that require active exhalation, new technologies are being developed, one example of which is intermittent intrapulmonary deflation, designed to aid the elimination of bronchial secretions during relaxed expiration.[7] Briefly, after a slow inspiration, the patient inserts the mouthpiece into the mouth and activates intermittent intrapulmonary deflation by using a remote control. This triggers the device to generate intermittent negative pressure, interrupted at a frequency of 12 Hz during the expiratory phase, thereby generating consecutive low-frequency vibrations.[7]

Moreover, the lung deflation is performed passively. Because of the passive and relaxed expiration required by

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the device, intermittent intrapulmonary deflation is intended to delay the onset of early bronchial collapse in patients with obstructive lung diseases. Therefore, the aim of this study was to assess changes in trapped gas volume, in the lung function, and in dyspnea after one 20-min session of intermittent intrapulmonary deflation or PEP therapy in the participants with COPD. We also assessed the expiratory volume mobilized during a standard vital capacity (VC) maneuver with both devices.

Methods

Participants

Participants with COPD who met the following inclusion criteria were recruited: being in a stable state (no exacerbation in the previous 3 weeks),[8] presenting moderate-to-severe COPD according to the Global Initiative for Chronic Obstructive Lung Disease criteria,[9] and having no previous experience with intermittent intrapulmonary deflation or PEP therapy. Exclusion criteria were severe cardiac comorbidities (ie, recent heart attack, unstable angina, uncontrolled rhythm disorders, and unstable cardiac failure) or neuromuscular disorders. The participants were recruited at the Clinique Universitaires Saint-Luc, Brussels, Belgium.

Study Design

This was a randomized crossover study (Fig. 1). The participants performed, in a randomized order, on separate days, either intermittent intrapulmonary deflation by using the Simeox device (PhysioAssist, Aix-en-Provence, France) or PEP (Pari-PEP systems II, Pari, Starnberg, Germany) therapy, for 20 min. Allocation concealment was performed by using sequentially numbered sealed opaque envelopes prepared by an independent researcher not involved in the trial. The investigators opened the envelope only after the consent form had been signed by the participant. All included participants provided written informed consent to participate in the study. The study was carried out in accordance with the Helsinki Declaration and approved by Comité d'Éthique Hospitalo-Facultaire Saint-Luc (UCL B403201940373) and is registered in ClinicalTrials.gov (NCT04157972).

Familiarization with intermittent intrapulmonary deflation and with PEP were performed in visit 1. Familiarization with intermittent intrapulmonary deflation was controlled by the performance indicator included on the device. The familiarization period was tailored to each participant and was considered correctly performed once the participant switched at least 2 of 5 green LEDs (performance indicator present on the intermittent intrapulmonary deflation device) over 3 consecutive expirations. The PEP familiarization was indicated by maintaining an expiratory pressure between 5 and 10 cm H_2O over a series of 10 consecutive expirations. The pressure was monitored with a manometer connected to the PEP device. After the familiarization period, 3 reproducible VC maneuvers were register for each condition.

QUICK LOOK

Current knowledge

Air trapping leads to disabling symptoms, such as exercise limitation and dyspnea, in patients with COPD. Therapies that involve active exhalation against a predefined resistance have been referred to prevent premature airway closure. Breathing against an expiratory resistance may be difficult to tolerate in patients with severe COPD. The intermittent pulmonary deflation technique produces an intermittent intrapulmonary air deflation in the bronchial tree during a relaxed expiration.

What this paper contributes to our knowledge

The intermittent intrapulmonary deflation mobilized a larger expiratory volume compared with PEP in patients with COPD. After a single session, intermittent intrapulmonary deflation reduces the residual volume, which reflects hyperinflation, but this effect was not captured by other estimates of hyperinflation.

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The study was performed at Cliniques Universitaires Saint-Luc, Avenue Hippocrate, 10–1200 - Brussels, Belgium.

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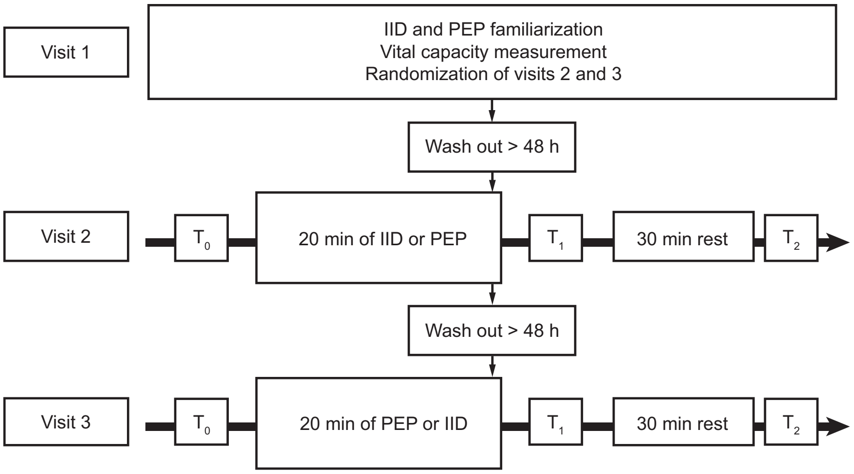

Fig. 1. Study design. PEP = positive expiratory pressure; IID = intermittent intra pulmonary deflation; T_0 = dyspnea and lung volume measurements taken before performing the devices; T_1 = dyspnea and lung volume measurements taken immediately after performing the devices; T_2 = dyspnea and lung volume measurements taken after a resting time of 30 min.

Instructions and Session Description

The immediate effect of intermittent intrapulmonary deflation was assessed via the change in VC during intermittent intrapulmonary deflation as well as during PEP VC and during a standard slow VC (SVC) maneuver. The VC measurements were performed by asking the participants to inhale maximally, insert the mouthpiece into the mouth, seal lips around the mouthpiece, and exhale slowly and evenly for as long as possible. With intermittent intrapulmonary deflation, the participants inhaled maximally, inserted the mouthpiece into the mouth, activated the device, and passively exhaled through the mouthpiece, driven by the deflation generated by the device, up to the maximum tolerated by the participant. With PEP, the participants inhaled maximally and exhaled for as long as possible while maintaining an expiratory pressure between 5 and 10 cm H_2O.

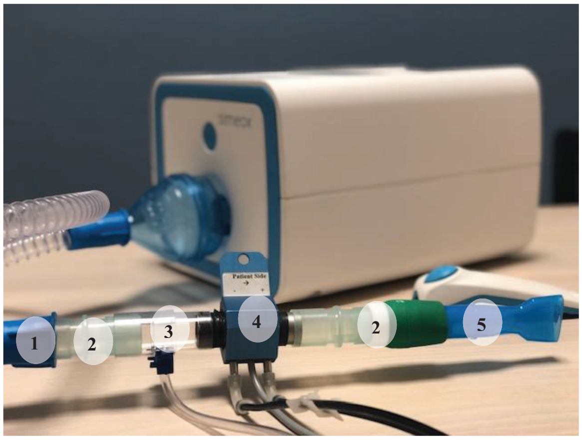

Fig. 2. The intermittent pulmonary deflation technique (IID) system assembly: 1. IID tube; 2. connections; 3. pressure transducer; 4. pneumotachograph; 5. IID mouthpiece.

Flow and pressure were measured by using a pneumotachograph, previously calibrated (Biopac System UIM 10°C, Santa Barbara, California), connected to an MP100 (MP150 System and AcqKnowledge software, version 3.7.3, Biopac Systems) and a pressure transducer (Biopac Systems TSD 160A) placed in series with both devices (Fig. 2). The highest volume of 3 reproducible maneuvers (<150 mL difference between extremes) was reported for each condition.[10] A rest period of at least 5 min was observed between the measurements. The VC values obtained during intermittent intrapulmonary deflation, during PEP, and during a standard SVC maneuver, that is, without any device, were compared.

The 20-min therapy session with intermittent intrapulmonary deflation consisted of inspirations at tidal volume and passive exhalations through the device to the maximum tolerated by the participant. The 20-min session therapy with PEP consisted of inspirations at tidal volume, followed by exhalation through the PEP device while maintaining an expiratory pressure between 5 and 10 cm H_2O. Rest periods were allowed when performing the therapy with the devices: with intermittent intrapulmonary deflation, a rest period was imposed after each program cycle of 10 expirations, and, with regard to PEP therapy, rest periods were allowed after cycles of 10 expirations.

Measurements and Outcomes

The following measurements were taken at baseline: anthropometric data (age, sex, height, weight), smoking status, pack-years, and lung function outcomes. The lung diffusing capacity of carbon monoxide (D_{LCO}) outcomes were obtained from the participants' medical records and

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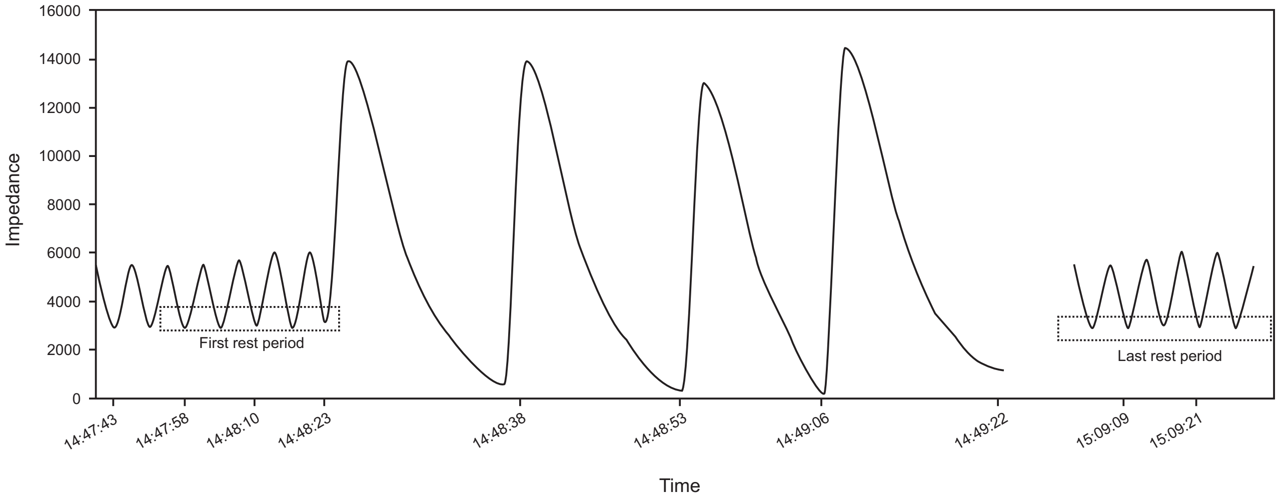

Fig. 3. Illustration of electrical impedance tomography (EIT) waveform during impedance recording in the first rest period (which corresponds to the minimum end-expiratory value of 5 tidal volumes before performing the device) and last rest period (which corresponds to the minimum end-expiratory value of 5 tidal volumes after performing the device). Time represents the hour:minutes:second measures taken in this example participant.

correlated with the lung volumes and capacities. Lung volumes via body plethysmography and helium dilution techniques, were performed at baseline (T_0), immediately after one 20-min session (T_1), and 30-min after the completion of each technique (T_2). FVC was also performed at T_0. All these tests were completed according to the American Thoracic Society/European Respiratory Society guidelines.[10] The recorded outcomes used to analyze the short-term effect of intermittent intrapulmonary deflation were (i) changes in trapped gas estimated via the functional residual capacity (FRC) obtained through body plethysmography (plethysmography FRC) and helium dilution (helium FRC), and by the difference between the 2 FRC measurements (plethysmography FRC – helium FRC); (ii) changes in residual volume (RV), total lung capacity, specific airway resistance, and specific airway conductance; and (iii) changes in dyspnea when using the Borg scale.[12]

We also analyzed the almost-immediate effect of intermittent intrapulmonary deflation by measuring the ventilation changes by using electrical impedance tomography (PulmoVista 500, Dräger Medical, Lübeck, Germany).[13-16] Electrical impedance tomography monitors lung ventilation continuously and noninvasively by generating cross-sectional images of the lung by using a 16-electrode belt placed between the fourth and fifth intercostal space.[13,14] We assessed the differences in end-expiratory lung impedance, which reflect changes in end-expiratory lung volume.[17] To do this, we averaged the minimum end-expiratory impedance values of 5 consecutive breaths before (denominated the first rest period) and after running each device (denominated the last rest period); an example is shown in Figure 3. The differences in end-expiratory lung impedance was registered during the 20-min session with both devices.

Statistics

The sample size needed was based on plethysmography FRC as the primary end point, which reflects air trapping. When assuming a 0.3 L difference in pre-post plethysmography FRC variation between the 2 groups and when assuming an SD of ±0.45 L,[18] 20 patients with COPD were needed to achieve an 80% power with an α risk set at 0.05. When considering a 20% dropout rate, we aimed to recruit 25 subjects. The Shapiro-Wilk test was used to test the normality of the data. Data are reported as mean ± SD or median (interquartile range [IQR]), depending on the normality of the distribution. Within-group pairwise comparisons were assessed by using the Student paired *t* test or the Wilcoxon signed rank test, as appropriate.

Comparisons between groups were calculated by using the Student unpaired *t* test or the Mann-Whitney test, as appropriate. Two-way analysis of variance with repeated measures was used to assess the change in outcomes over time within each device. Time (T_0, T_1, and T_2) and devices (intermittent intrapulmonary deflation and PEP) were treated as within-subject factors. The Bonferroni method was used for post hoc comparisons. The Friedman test was used when data violated the assumptions necessary to run the analysis of variance with repeated measures. Correlation coefficients were calculated to establish whether there was a correlation between the D_{LCO} and the lung volumes and capacities. $P < .05$ was considered statistically significant. All analyses were performed by using SPSS v.27 (IBM SPSS Statistics, Armonk, NY). The carry-over effect was tested by using the *t* test, which is considered not significantly different when $P > .05$.[19] In this study, no carry-over effect was detected ($P = .79$).

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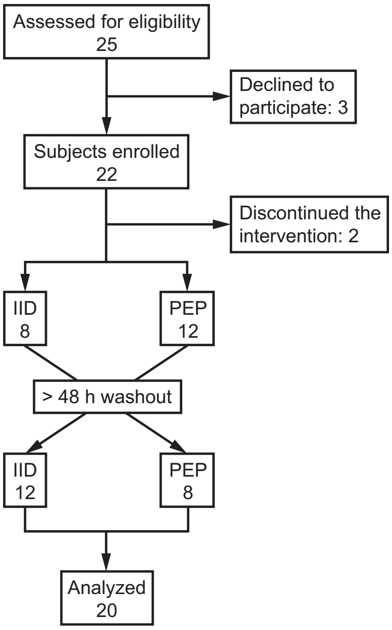

Fig. 4. Flow chart. PEP = positive expiratory pressure, IID = intermittent intrapulmonary deflation

Results

From the 25 eligible participants, 22 agreed to participate and were subsequently randomized. During the study duration, 2 participants discontinued the intervention for reasons deemed unrelated to the trial (pulmonary exacerbation, *n* = 1; surgical procedure for urological troubles, *n* = 1). Thus, 20 participants remained in the final analysis (Fig. 4). Demographic and lung function data of the study participants are detailed in Table 1. The short-term effect of change in lung capacities and volumes, specific airway resistance, specific airway conductance, and dyspnea between the different time points and between groups are displayed in Table 2.

Table 1: Baseline Characteristics of the Study Population

Characteristic	Results
Men/women, *n*	13/7
Age, y	66.7 ± 8.0
BMI, kg/m^2	26.2 ± 5.1
Pack-years	38.3 ± 17.3
FEV$_1$, L	1.36 ± 0.6
FEV$_1$ % predicted	48.1 ± 17.0
FVC, L	3.20 ± 1.1
FVC % predicted	86.9 ± 23.7
FEV$_1$/FVC	55.3 ± 13.4
RV/TLC (quotient)	0.57 ± 0.1
RV/TLC % predicted	136.3 ± 31.9
GOLD, *n* (%)	
II	8 (40)
III	10 (50)
IV	2 (10)
D$_{LCO}$ % predicted	39.4 ± 14.5

Data are mean ± SD unless otherwise indicated.
BMI = body mass index
RV = residual volume
TLC = total lung capacity
GOLD = Global Initiative for Chronic Obstructive Lung Disease
D$_{LCO}$ = diffusing capacity of carbon monoxide

There were no between-group differences in the change in plethysmography FRC between T_0 and T_1 (intermittent intrapulmonary deflation, mean ± SD 0.03 ± 0.30; PEP, 0.02 ± 0.32; $P = .45$). When considering the different time points (T_0, T_1, T_2), there was no main effect for device in any outcome. In addition, we only found an interaction between time and device for plethysmography RV. Bonferroni-adjusted comparisons for simple main effect analysis showed that plethysmography RV was smaller in T_2 during intermittent intrapulmonary deflation compared with PEP therapy (mean difference −0.355 L, 95% CI −0.696 to −0.015; $P = .042$). No correlation was found among the D$_{LCO}$, dyspnea, and lung volumes and capacities.

With regard to the almost-immediate effect, there was no significant change during intermittent intrapulmonary deflation ($P = .21$) or the PEP therapy ($P = .63$) (Fig. 5). The immediate effects of intermittent intrapulmonary deflation in expiratory volume and in expiratory flow and pressure are shown in Table 3. The volume mobilized in the VC during intermittent intrapulmonary deflation was 389 mL higher than during the PEP VC maneuver (95% CI 128–650; $P = .003$) and 186 mL higher than during the SVC maneuver (95% CI 9–364; $P = .038$). The volume mobilized in PEP VC was 0.202 mL lower than during the SVC maneuver (95% CI −0.356 to −0.049; $P = .008$). Expiratory flow in the VC during intermittent intrapulmonary deflation was 0.326 L/min higher versus in PEP VC (median [IQR] 0.67 [0.58–1.75] L/min vs 0.34 [0.24–0.48] L/min; $P = .008$). The expiratory flow in PEP VC was 1.243 L/min lower versus in SVC (median [IQR] 0.34 [0.24–0.48] L/min vs 1.59 [0.99–1.89] L/min; $P < .001$). Expiratory pressure differed strongly between the maneuvers. With the VC during intermittent intrapulmonary deflation, the expiratory pressure was –57.30 cm H_2O lower versus in PEP VC (median [IQR] −49.59 [–43.20 to −58.30] cm H_2O vs 8.31 [6.95–9.05] cm H_2O; $P = .008$) and –49.95 cm H_2O versus in SVC (median [IQR] –49.59 [–43.20 to –58.30] cm H_2O vs 0.36 [0.17–0.61] cm H_2O; $P < .001$). The expiratory pressure was 7.95 cm H_2O higher in PEP VC versus with SVC (median [IQR] 8.31 [6.95–9.05] cm H_2O vs 0.36 [0.17–0.61] cm H_2O; $P = .008$).

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Table 2: Change in Lung Capacities and Volumes, Specific Airway Conductance and Resistance, and Dyspnea

Parameter	Time			*P*		
				Within-Subjects		Interaction (time × device)
	T_0	T_1	T_2	Time	Device	
Plethysmography FRC				.71	.18	.25
IID	4.80 ± 1.15	4.75 ± 1.23	4.76 ± 1.25			
PEP	4.87 ± 1.11	4.88 ± 1.24	4.95 ± 1.30			
Helium FRC				.68	.85	.33
IID	4.31 ± 1.00	4.43 ± 1.07	4.33 ± 1.12			
PEP	4.41 ± 1.06	4.30 ± 0.94	4.30 ± 1.00			
Plethysmography FRC – helium FRC				.02	.32	.12
IID	0.86 ± 0.62	0.23 ±0.64	0.35 ± 0.54			
PEP	0.61 ± 0.73	0.50 ± 0.72	0.58 ±0.65			
Plethysmography RV				.35	.10	.007
IID	3.97 ± 1.09	3.76 ± 1.10	3.72 ± 1.09			
PEP	4.00 ± 1.06	3.94 ± 1.18	4.08 ± 1.26			
Helium RV				.42	.69	.76
IID	3.04 ± 0.82	3.19 ± 0.83	3.15 ± 0.99			
PEP	3.16 ± 0.94	3.21 ± 0.84	3.16 ± 0.90			
RV/TLC, %				.66	.57	.61
IID	126.17 ± 30.52	125.79 ± 28.91	126.18 ± 29.21			
PEP	127.83 ± 32.27	125.98 ± 30.82	126.98 ± 30.11			
RV/TLC, Quotient				.51	.88	.14
IID	0.56 ± 0.17	0.54 ± 0.21	0.54 ± 0.18			
PEP	0.56 ± 0.09	0.55 ± 0.10	0.56 ± 0.11			
Plethysmography TLC				.52	.96	.26
IID	7.21 ± 1.43	7.14 ± 1.45	7.08 ± 1.42			
PEP	7.16 ± 1.44	7.11 ±1.50	7.24 ± 1.62			
Helium TLC				.80	.40	.96
IID	6.39 ± 1.46	6.46 ± 1.24	6.41 ± 1.47			
PEP	6.35 ± 1.31	6.37 ± 1.32	6.33 ± 1.12			
Specific R_{aw}				.15	.23	.39
IID	36.98 ± 15.33	37.33 ± 17.28	38.24 ± 17.03			
PEP	39.87 ± 21.87	41.54 ± 26.22	46.55 ± 36.32			
sG_{aw}				.65	.66	.97
IID	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01			
PEP	0.03 ± 0.02	0.03 ± 0.02	0.03 ± 0.02			
Dyspnea				.12	.87	.14
IID	1.25 ± 1.50	2.07 ± 1.67	1.10 ± 1.24			
PEP	0.67 ± 1.10	1.17 ± 1.26	0.85 ± 1.21			

Data are reported as the mean ± SD.

T_0 = data acquired before performing the devices

T_1 = data acquired immediately after performing the devices (during the use of PEP or IID)

T_2 = data acquired after a resting time of 30 min

Plethysmography FRC = functional residual capacity obtained through whole-body plethysmography

IID = intermittent intrapulmonary deflation

PEP = positive expiratory pressure

Helium FRC = functional residual capacity obtained through helium dilution

Plethysmography RV = residual volume obtained through whole-body plethysmography

Helium RV = residual volume obtained through helium dilution

RV = residual volume

TLC = total lung capacity

Plethysmography TLC = total lung capacity obtained through whole-body plethysmography

Helium TLC = total lung capacity obtained through helium dilution

specific R_{aw} = specific airway resistance

sG_{aw} = specific airway conductance

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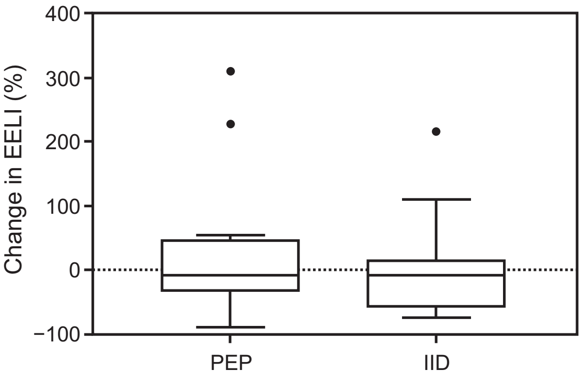

Fig. 5. Results of recruitment differences in end-expiratory lung impedance (ΔEELI) expressed by impedance change between the first and last rest period with both devices. Impedance values are expressed as arbitrary units.

Discussion

The aim of this study was to compare the short-term effect of intermittent intrapulmonary deflation versus PEP therapy on trapped gas volume and VC in the participants with COPD. The results did not show differences between devices in FRC or trapped gas volume. However, the plethysmography RV decreased more with intermittent intrapulmonary deflation compared with PEP after a 20-min session. With regard to the immediate effects of both techniques on VC, the results showed a greater mean expiratory volume and flow but lower airway pressure with intermittent intrapulmonary deflation compared with PEP.

The trapped gas volume occurs due to expiratory air-flow limitation in patients with COPD.[2] In turn, air-flow limitation is caused by an association of small airway disease and parenchymal destruction (emphysema) that, associated with chronic inflammation, leads to structural changes, narrowing of the small airways, and decreased lung elastic recoil.[2,9] Expiration is driven by the pressure gradient from alveolar pressure to atmospheric pressure at the airway opening.[20,21] During quiet expiration, the alveolar pressure is only determined by the elastic recoil forces of the rib cage and lungs.[20,22] Below the FRC, the expiration becomes active, which involves the active use of expiratory muscles, which thus increases pleural pressure.[20,22] Because this pressure also acts on the airways, the "equal pressure point," which occurs when the pressure inside the airways is equal to the intrapleural pressure, occurs very early at some point in their airways and expiratory flow limitation may occur.[21-23] In patients with obstructive lung disease, in which airway resistance and bronchial wall compliance are increased, the increase in expiratory pressure may lead to early airway collapse and air trapping,[20] even during quiet expiration, in which the onset of flow limitation causes its collapse by dynamic compression.[22,23] This collapse decreases the capacity of the airways to remain open during expiration and further deflation of the lung is limited.[9] As a result, the FRC of patients with COPD is higher than in healthy individuals.

The intermittent intrapulmonary deflation acts during relaxed exhalation by generating intermittent intrapulmonary air deflation at a frequency of 12 Hz, similar to that of the vibrating cilia of the bronchial epithelium.[24] The gas flowing through the airway is not only determined by the resistance of these bronchi but also by the pressure gradient. This implies that expiratory flows should also represent the pressures developed by the expiratory muscles.[21] Owing to the slow and passive expiratory flow intermittently interrupted with intermittent intrapulmonary deflation, we hypothesized that the device minimizes the expiratory pressure required to empty the lungs. Therefore, early airway collapse should be delayed, which may explain the greater VC observed under intermittent intrapulmonary deflation condition when compared with the PEP device. With PEP therapy, patients are instructed to

Table 3: Comparison of Expiratory Volume, Expiratory Flow, and Pressure During the IID Device, During the PEP Device, and SVC During Standard Maneuver

Parameter	SVC	IID VC	PEP VC	*P*	*P*, Pairwise Comparison		
					IID VC vs PEP VC	IID VC vs SVC	PEP VC vs SVC
Expiratory volume, L	3.09 ± 0.88	3.27 ± 0.87	2.89 ± 0.75	.001	.003	.038	.008
Expiratory flow, L/min	1.59 (0.99–1.89)	0.67 (0.58–1.75)	0.34 (0.24–0.48)	<.001	.008	.14	<.001
Expiratory pressure, cm H_2O	0.36 (0.17–0.61)	−49.59 (−43.20 to −58.30)	8.31 (6.95–9.05)	<.001	.008	<.001	.008

Data are reported as the mean ± SD or median (interquartile range).
IID = intermittent intrapulmonary deflation
PEP = positive expiratory pressure
VC = vital capacity
IID VC = maximum expiratory volume mobilized during intermittent intrapulmonary deflation
SVC = slow vital capacity during standard maneuvers
PEP VC = maximum expiratory volume mobilized during PEP

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exhale against a resistance created in a device, which generates increased PEP.

Some researchers demonstrated that the increased pressure in the airway may move the equal pressure point to more central and stable airways, decreasing the risk of airway closure.[25,26] To achieve these effects, the breathing pattern and strength of the expiratory muscles have an important influence on the success of PEP therapy.[4] In this study, the VC observed under intermittent intrapulmonary deflation and the standard SVC were greater when compared with the PEP device. Our hypothesis is that the possible presence of expiratory muscle weakness in the participants may have contributed to the fact that the expiratory volume found under the PEP device condition was lower when compared with intermittent intrapulmonary deflation and with the standard SVC. Due to the passive expiration required during the use of intermittent intrapulmonary deflation, the influence of the expiratory muscles is eliminated, and, during an active expiration without the device, the expiratory muscles do not need to overcome the additional overload imposed by the PEP device.

Although the plethysmography RV decreased more during intermittent intrapulmonary deflation compared with PEP therapy after a 20-min session, other outcomes, such as FRC and total lung capacity, that also reflect trapped gas volume were not impacted by either device.[2,27] A review published in 2019 with 97 trials concluded that PEP reduces hyperinflation.[26] Although the PEP level was similar to the one we used in our study, PEP therapy was conducted over a longer period. Conversely, our study aimed to investigate the immediate effect after a single 20-min session. This may explain the lack of effects of PEP therapy on hyperinflation in our study. The natural history of the development of lung hyperinflation in COPD indicates that RV is the first volume component to increase, which reflects increased airway closure. FRC increases as a consequence of increased airway resistance and closure. This reflects the effects of flow limitation and alteration in static mechanics, and eventually total lung capacity increases as lung compliance increases, which results in reduced lung recoil.[2,27] All the subjects in this study had an increased RV, 75% also presented an increase in FRC, and 40% presented an increase in total lung capacity. Our hypothesis is that, during intermittent intrapulmonary deflation, the effect of increased RV is minimized due to the increased airway closure mentioned above and the passive expiration required by intermittent intrapulmonary deflation. However, intermittent intrapulmonary deflation has no effect on lung compliance and, therefore, no impact on total lung capacity.

Regardless of the device used, specific airway resistance and specific airway conductance were not modified in our cohort of subjects with COPD. Both specific resistance and conductance are influenced, among other things, by the pressure and flow into the airway.[28,29] Other trials evaluated the effects of PEP on airway resistance and conductance by using a similar protocol and population.[30-32] One of these trials found a different result.[32] The researchers evaluated the acute effects of an oscillatory PEP (Flutter VRP1, VarioRaw SA, Switzerland) on airway resistance in patients with COPD. A significant decrease in airway resistance was shown after a 20-min session of PEP therapy. The researchers considered that this effect could be related to the mobilization of bronchial secretions and to maintaining patent airways. In this study, the PEP device used was not equipped with an oscillatory system and the presence of lung hypersecretion was not evaluated, which may have contributed to the difference in the results. No short-term effect was found on dyspnea after using either device. This result is in accordance with the literature.[33-36] A positive impact on dyspnea was demonstrated in some trials[37,38] as a consequence of decreased lung hyperinflation, but all of these trials used a long-term protocol.

It is known that the D_{LCO} is reduced in most patients with COPD in the presence of emphysema due to irreversible destruction of the gas-exchanging surfaces of the lung.[28] We hypothesized that patients with lower D_{LCO} (ie, presenting higher abnormalities in gas-exchanging surfaces) would respond differently to intermittent intrapulmonary deflation or to PEP therapies than would patients with higher D_{LCO}. However, no correlation was found between D_{LCO} and any of the lung volumes and capacities analyzed. Some studies investigated the effect of PEP devices on D_{LCO} changes;[37,39,40] among which, 2 studies found an increase in D_{LCO} after performing PEP compared with a control group.[39,40] In 1 study, the population was composed of subjects with cystic fibrosis who are younger than our sample (mean age, 22 years old).[40] In the other study, the protocol consisted of 4 weeks of treatment instead a single session as in the current study; the researchers also combined PEP with the forced expiratory technique.[39]

No change was found in the differences in end-expiratory lung impedance between the first rest period and last rest period in either group. One study assessed the short-term effects of PEP and incentive spirometry on lung recruitment in subjects admitted for endocrinological surgical procedure after surgery that involved anesthesia, all the participants were free of pulmonary diseases.[13] Although the authors used a similar PEP device, the indication as well as the population and the resistance used in the PEP device were different. In that study, the objective was to increase the FRC, whereas, in the current study, it was to reduce hyperinflation. When analyzing the rest phases, the researchers also did not observe differences. Furthermore, they compared the PEP and incentive spirometry short-term effect in recruitment and showed that both devices improved recruitment.[13] This comparison could not be performed in the current study because intermittent intrapulmonary deflation and the PEP therapy were used on different days, which

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makes the reference values of impedance different and, therefore, not comparable. In this study, we assessed the immediate effect of intermittent intrapulmonary deflation on selected markers of COPD in 1 session. Future studies are therefore necessary to assess the mid- to long-term effect of intermittent intrapulmonary deflation by expanding the therapy over several consecutive days or weeks. Accordingly, the impact of intermittent intrapulmonary deflation on other relevant health-related outcomes, such as, among other things, quality of life, physical activity, exercise tolerance, rescue inhaler use, pulmonary exacerbation, should be determined.

This study had some limitations that must be considered when interpreting the results. Our protocol was designed to analyze the short-term effects of intermittent intrapulmonary deflation and PEP techniques after 1 single session, and so, it is not possible to evaluate the impact of these results in the daily life of these patients. The minimum clinically important difference for static volumes is unknown in this condition and settings. The absence of subgroups of patients according to disease phenotype (those more affected by emphysema or chronic bronchitis) did not allow us to verify whether intermittent intrapulmonary deflation behaves differently in these individuals. Although the trapped gas reduced with regard to the RV, it was not observed in other parameters that reflected hyperinflation.

Conclusions

The VC obtained during intermittent intrapulmonary deflation was greater than that obtained with the PEP therapy. The RV decreased with intermittent intrapulmonary deflation compared with PEP, but this effect was not captured by other estimates of hyperinflation. The clinical importance as well as the long-term effects remain to be determined.

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REFERENCES

1. Gagnon P, Guenette JA, Langer D, Laviolette L, Mainguy V, Maltais F, et al. Pathogenesis of hyperinflation in chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis 2014;9:187-201.
2. O'Donnell DE, Laveneziana P. Physiology and consequences of lung hyperinflation in COPD. Eur Respir Rev 2006;15(100):61-67.
3. Fagevik Olsen M, Westerdahl E. Positive expiratory pressure in patients with chronic obstructive pulmonary disease–a systematic review. Respiration 2009;77(1):110-118.
4. Fagevik Olsén M, Lannefors L, Westerdahl E. Positive expiratory pressure - common clinical applications and physiological effects. Respir Med 2015;109(3):297-307.
5. Clini E. Positive expiratory pressure techniques in respiratory patients: old evidence and new insights. Breathe 2009;6(2):153-159.
6. Myers TR. Positive expiratory pressure and oscillatory positive expiratory pressure therapies. Respir Care 2007;52(10):1308-1326; discussion 1327.
7. Walicka-Serzysko K, Postek M, Jeneralska N, Cichocka A, Milczewska J, Sands D. ePS3.09 The effect of chest physiotherapy with the Simeox airway clearance technology in the treatment of cystic fibrosis pulmonary exacerbation - open-label study. J Cystic Fibrosis 2019;18:S46-S47.
8. Bonnevie T, Elkins M, Paumier C, Medrinal C, Combret Y, Patout M, et al. Nasal high flow for stable patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. COPD 2019;16(5-6):368-377.
9. Agusti A, Beasley R, Celli BR, Chen R, Criner G, Halpin D, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2022.
10. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al; ATS/ERS Task Force. Standardisation of lung function testing. Eur Respir J 2005;26(2):319-338.
11. Wanger J, Clausen JL, Coates A, Pedersen OF, Brusasco V, Burgos F, et al. Standardisation of the measurement of lung volumes. Eur Respir J 2005;26(3):511-522.
12. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14(5):377-381.
13. Reychler G, Uribe Rodriguez V, Hickmann CE, Tombal B, Laterre PF, Feyaerts A, Roeseler J. Incentive spirometry and positive expiratory pressure improve ventilation and recruitment in postoperative recovery: a randomized crossover study. Physiother Theory Pract 2019;35(3):199-205.
14. Lobo B, Hermosa C, Abella A, Gordo F. Electrical impedance tomography. Ann Transl Med 2018;6(2):26.
15. Milne S, Huvanandana J, Nguyen C, Duncan JM, Chapman DG, Tonga KO, et al. Time-based pulmonary features from electrical impedance tomography demonstrate ventilation heterogeneity in chronic obstructive pulmonary disease. J Appl Physiol (1985) 2019;127(5):1441-1452.
16. Zhang C, Dai M, Liu W, Bai X, Wu J, Xu C, et al. Global and regional degree of obstruction determined by electrical impedance tomography in patients with obstructive ventilatory defect. PloS One 2018;13(12):e0209473.
17. Hinz J, Hahn G, Neumann P, Sydow M, Mohrenweiser P, Hellige G, Burchardi H. End-expiratory lung impedance change enables bedside monitoring of end-expiratory lung volume change. Intensive Care Med 2003;29(1):37-43.
18. O'Donnell DE, Hernandez P, Kaplan A, Aaron S, Bourbeau J, Marciniuk D, et al. Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease - 2008 update - highlights for primary care. Can Respir J 2008;15 Suppl A(Suppl A):1A-8A.
19. Cleophas TJ. Carryover effects in clinical research. In: Cleophas TJ, ed. Human Experimentation: Methodologic Issues Fundamental to Clinical Trials. Dordrecht: Springer Netherlands; 1999:25-36.
20. Sherwood L. Human Physiology. 3rd edition. Louvain-la-Neuve, Belgium, Deboeck 2015;3:590.
21. Zach MS. The physiology of forced expiration. Paediatr Respir Rev 2000;1(1):36-39.
22. West JB. Pulmonary Pathophysiology. 8th ed. Williams and Wilkins, Baltimore, 1978:227.
23. Reychler G, Roeseler J, Delguste P. Kinésithérapie Respiratoire. 3th ed. Respiratory Physiotherapy: Paris. Elsevier Masson; 2009:384.
24. Giovannetti P, Morin L, Lafforgue O, Poncet S, Favier J, Reynaud-Gaubert M. SIMETOL study: evaluation of the tolerance and efficacy of an innovative Simeox-assisted bronchial drainage procedure

RESPIRATORY CARE Paper in Press. Published on February 21, 2023 as DOI: 10.4187/respcare.10398

in cystic fibrosis as an alternative to conventional conventional respiratory physiotherapy. Revue Des Maladies Respiratoires 2019;36: A22.

25. Groth S, Stafanger G, Dirksen H, Andersen JB, Falk M, Kelstrup M. Positive expiratory pressure (PEP-mask) physiotherapy improves ventilation and reduces volume of trapped gas in cystic fibrosis. Bull Eur Physiopathol Respir 1985;21(4):339-343.
26. Liverani B, Nava S, Polastri M. An integrative review on the positive expiratory pressure (PEP)-bottle therapy for patients with pulmonary diseases. Physiother Res Int 2020;25(1):e1823.
27. Rossi A, Aisanov Z, Avdeev S, Di Maria G, Donner CF, Izquierdo JL, et al. Mechanisms, assessment and therapeutic implications of lung hyperinflation in COPD. Respir Med 2015;109(7):785-802.
28. Gibson GJ. Clinical Tests of Respiratory Function: Raven Press; London. 1984:334.
29. Pereira CAC, Moreira MAF. Plethysmography - airway resistance. J Pneumol; 28:139-150.
30. van Hengstum M, Festen J, Beurskens C, Hankel M, van den Broek W, Buijs W, Corstens F. The effect of positive expiratory pressure versus forced expiration technique on tracheobronchial clearance in chronic bronchitics. Scand J Gastroenterol Suppl 1988;143:114-118.
31. van Winden CM, Visser A, Hop W, Sterk PJ, Beckers S, de Jongste JC. Effects of flutter and PEP mask physiotherapy on symptoms and lung function in children with cystic fibrosis. Eur Respir J 1998;12 (1):143-147.
32. Gastaldi AC, Paredi P, Talwar A, Meah S, Barnes PJ, Usmani OS. Oscillating positive expiratory pressure on respiratory resistance in chronic obstructive pulmonary disease with a small amount of secretion: a randomized clinical trial. Medicine (Baltimore) 2015;94(42):e1845.
33. Gass R, Merola P, Monteiro MB, Cardoso DM, Paiva DN, Teixeira PJ, et al. Effects of expiratory positive airway pressure on exercise tolerance, dynamic hyperinflation, and dyspnea in COPD. Respir Care 2017;62(10):1298-1306.
34. Cardoso DM, Gass R, Sbruzzi G, Berton DC, Knorst MM. Effect of the expiratory positive airway pressure on dynamic hyperinflation and exercise capacity in patients with COPD: a meta-analysis. Sci Rep 2020;10(1):13292.
35. Nicolini A, Merliak F, Barlascini C. Use of positive expiratory pressure during six minute walk test: results in patients with moderate to severe chronic obstructive pulmonary disease. Multidiscip Respir Med 2013;8(1):19.
36. Ubolsakka-Jones C, Pongpanit K, Boonsawat W, Jones DA. Positive expiratory pressure breathing speeds recovery of postexercise dyspnea in chronic obstructive pulmonary disease. Physiother Res Int 2019;24 (1):e1750.
37. Nicolini A, Mascardi V, Grecchi B, Ferrari-Bravo M, Banfi P, Barlascini C. Comparison of effectiveness of temporary positive expiratory pressure versus oscillatory positive expiratory pressure in severe COPD patients. Clin Respir J 2018;12(3):1274-1282.
38. Nicolini A, Mollar E, Grecchi B, Landucci N. Comparison of intermittent positive pressure breathing and temporary positive expiratory pressure in patients with severe chronic obstructive pulmonary disease. Arch Bronconeumol 2014;50(1):18-24.
39. Su C-L, Chiang L-L, Chiang T-Y, Yu C-T, Kuo H-P, Lin H-C. Domiciliary positive expiratory pressure improves pulmonary function and exercise capacity in patients with chronic obstructive pulmonary disease. J Formos Med Assoc 2007;106(3):204-211.
40. Radtke T, Böni L, Bohnacker P, Maggi-Beba M, Fischer P, Kriemler S, et al. Acute effects of combined exercise and oscillatory positive expiratory pressure therapy on sputum properties and lung diffusing capacity in cystic fibrosis: a randomized, controlled, crossover trial. BMC Pulm Med 2018;18(1):99.