

Physiological comparison of high-flow oxygen via endotracheal tube and T-piece strategies during spontaneous breathing trials: a randomized crossover study

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Abstract

Background

The optimal spontaneous breathing trial (SBT) strategy remains uncertain because commonly used approaches involve distinct physiological trade-offs. Pressure support ventilation (PSV) may underestimate the respiratory load after extubation, whereas T-piece trials better reproduce unsupported breathing but may promote derecruitment and cardiopulmonary stress. High-flow oxygen (HFO) delivered via endotracheal tube has been proposed as an alternative SBT strategy, but the physiological basis for its potential clinical usefulness remains insufficiently defined.

Methods

In a randomized crossover physiological study, patients receiving mechanical ventilation for at least 24 hours and deemed ready for weaning underwent five SBT conditions: T-piece and four HFO via endotracheal tube settings combining two interfaces with different expiratory port diameters (9.8 and 6.9 mm) and two flow rates (40 and 60 L/min). Airway and esophageal pressures, respiratory variables, and electrical impedance tomography (EIT) parameters were measured during baseline mechanical ventilation and under each SBT condition. Esophageal pressure was also measured after extubation for comparison with post-extubation inspiratory effort. A complementary bench study assessed 24 simulated conditions across four interface diameters and six flow rates.

Results

Twenty patients were included in the analysis. HFO via endotracheal tube generated a flow- and diameter-dependent increase in airway pressure and end-expiratory lung volume (all $p < 0.001$ vs T-piece). While HFO with both expiratory port diameters elevated airway pressure and lung volume, downstream improvements in ventilation homogeneity and oxygenation, together with reductions in dynamic transpulmonary driving pressure and respiratory rate, occurred primarily with the smaller diameter at higher flows, indicating a pressure threshold effect. Inspiratory effort was similar across SBT conditions and comparable to post-extubation values. Bench simulations closely reproduced these flow- and diameter-dependent physiological relationships.

Conclusions

HFO via endotracheal tube produced a flow- and expiratory port diameter-dependent physiological response, linking airway pressure generation to lung-volume preservation, improved oxygenation, and lower dynamic transpulmonary driving pressure while maintaining inspiratory effort. Tracheal HFO may

therefore represent an alternative SBT strategy that preserves a post-extubation-like inspiratory workload while limiting derecruitment and dynamic lung stress during liberation from invasive ventilation.

Trial registration:

ClinicalTrials.gov (NCT06816706). Registered on 6 February 2025.

Introduction

The spontaneous breathing trial (SBT) is considered a key step during the weaning process from mechanical ventilation. Because both premature and delayed extubation are associated with adverse outcomes, SBT is widely used to assess a patient's ability to sustain spontaneous breathing after extubation [1]. Current clinical practice guidelines recommend routinely performing an SBT before extubation [2, 3].

The two most commonly applied SBT strategies are T-piece and low-level pressure support ventilation (PSV), each with distinct physiological and clinical implications [1, 4]. PSV reduces work of breathing relative to post-extubation conditions [5–7], which may contribute to false-positive SBT results. In contrast, the T-piece more closely reflects post-extubation respiratory load but may increase SBT failure and delay extubation [8, 9]. Abrupt withdrawal of positive airway pressure during T-piece trials may also expose vulnerable patients to sudden cardiopulmonary loading and alveolar derecruitment. Thus, the choice of SBT strategy is not only a methodological issue, but also a bedside decision that may influence how safely clinicians move patients from invasive support to spontaneous breathing. Recent evidence suggests that SBT strategies should be individualized according to patient-specific respiratory and clinical characteristics [10]. Alternative SBT strategies therefore require evaluation on both physiological and clinical grounds.

High-flow oxygen (HFO) via endotracheal tube has recently been proposed as a potential SBT approach [11–14]. Preliminary clinical studies suggest that HFO may be associated with higher SBT success rates and a lower risk of reintubation compared with T-piece [11–13, 15]. However, these findings are difficult to interpret without a clearer understanding of what tracheal HFO does during the trial: whether it unloads the respiratory muscles, preserves lung volume, modifies regional ventilation, or simply changes oxygen delivery. Clarifying these mechanisms is essential for defining the patients and settings in which this strategy might be clinically useful.

In this randomized crossover study, we compared the physiological effects of tracheal HFO delivered through interfaces with different expiratory port diameters and flow settings with those of T-piece during SBT. A complementary bench experiment was performed to clarify the mechanical effects of expiratory port diameter and flow rate. We hypothesized that HFO via endotracheal tube would generate flow- and interface-dependent physiological effects that could help bridge the gap between an unsupported T-piece trial and the post-extubation transition.

Methods

Clinical study

Study design and settings

This randomized crossover clinical study was conducted in four general intensive care units (ICUs) of two hospitals from May 2025 to December 2025 (Beijing Shijitan Hospital, Capital Medical University, Beijing, China and Beijing Fengtai You'anmen Hospital, Beijing, China). The Institutional Ethics Committees of both hospitals approved the study protocol (IIT2024-157-002 and KY-202505-01). The study was registered at ClinicalTrials.gov (NCT06816706). Written informed consent was obtained from all enrolled patients or their legal surrogates. The protocol and statistical analysis plan have been previously published [16].

Patients

Adult patients receiving invasive mechanical ventilation for at least 24 hours who were deemed ready for weaning were screened for inclusion. The readiness for weaning was evaluated following the currently recommended clinical guidelines [2].

Exclusion criteria included: 1) age younger than 18 years; 2) pregnancy; 3) medical history of neuromuscular diseases or phrenic nerve injury; 4) contraindications for esophageal pressure catheter insertion; 5) evidence of active air leak from the lung; 6) contraindications to electrical impedance tomography (EIT) monitoring; and 7) anticipated withdrawal of life support (details available in additional file 1).

Study procedures

After enrollment, an esophageal balloon catheter was placed in the esophagus, with proper positioning validated by the Baydur maneuver [17, 18]. Airflow, airway pressure, and esophageal pressure were continuously collected via a heated Fleisch pneumotachograph and pressure transducers. All signals were recorded simultaneously at 200 Hz using the ICU-Lab 2.5 Software Package. An EIT-dedicated belt was placed around chest and connected to the EIT monitor (PulmoVista 500; Dräger Medical, Germany). EIT data were captured at 20 Hz.

A 10-minute baseline recording was obtained using the PSV and positive end-expiratory pressure (PEEP) levels set by the responsible physician prior to inclusion. Then, each patient received five 15-minute SBTs in a computer-generated random order:

- T-piece (6 L/min);
- HFO via endotracheal tube with a 9.8 mm expiratory port (HFO-9.8) at 40 L/min;

- HFO-9.8 at 60 L/min;
- HFO via endotracheal tube with a 6.9 mm expiratory port (HFO-6.9) at 40 L/min;
- HFO-6.9 at 60 L/min.

Humidified T-piece oxygen was delivered using an air entrainment nebulizer and T-tube. HFO via endotracheal tube was delivered via the Aeonmed NeoHiF-i7 device (Beijing Aeonmed Company, Beijing, China) with the interface positioned between the endotracheal tube and the breathing circuit. Two interfaces were evaluated, with expiratory port diameters of 6.9 mm and 9.8 mm (Xiangyue Medical Ltd, Tianjin, China), defined as the minimal internal diameter at the expiratory port (additional file 1, Figure S1). For all SBT phases with tracheal HFO, FiO_2 was maintained at 0.4 and temperature at 37°C.

A 10-minute washout period with ventilator reconnection to baseline settings was implemented between phases.

Vital signs, end-tidal carbon dioxide pressure (EtCO_2) and respiratory mechanics including flow, airway pressure, esophageal pressure, and EIT data were collected during each phase (additional file 1, Figure S2). Arterial blood gas analyses were performed at the end of the following phases: T-piece, HFO-9.8 and HFO-6.9 at 60 L/min.

After completing all study procedures, participants were reconnected to the ventilator. The extubation was decided by the attending physicians, in accordance with guidelines and their clinical judgment [2].

Supplemental oxygen after extubation was determined at the clinicians' discretion. Esophageal pressure data were collected for 3 minutes after extubation when the patient's breathing condition remained stable. Details of study procedures are shown in additional file 1.

Data collection and analysis

Patient demographics and clinical characteristics were collected at study entry.

Respiratory data were analyzed from ten consecutive stable breaths recorded during the final three minutes of each study phase [7, 10]. Details of data analysis are shown in additional file 1.

Mean and peak inspiratory and expiratory airway pressure, and PEEP were recorded from the airway pressure signal. Tidal volume (V_T), respiratory rate, and minute ventilation were recorded from the flow signal. The dynamic transpulmonary driving pressure ($\Delta P_{L, \text{dyn}}$) was calculated as the difference between the maximum transpulmonary pressure (airway pressure minus esophageal pressure) and the value at the onset of inspiratory effort [18]. Inspiratory and expiratory airway resistances were derived at a standardized flow rate of 0.2 L/s [19].

The tidal swing of esophageal pressure during inspiration (ΔP_{es}) was defined as the maximal drop from the baseline at the onset of inspiration. To quantify inspiratory workload, the esophageal pressure-time

product per minute (PTPes) was computed as the time-integral of the area between the esophageal pressure curve and the estimated chest wall recoil pressure from the onset to the end of inspiration, multiplied by the respiratory rate. The pressure generated by respiratory muscles during inspiration (P_{mus}) was determined as the peak difference between the esophageal pressure and the chest wall recoil pressure. Total, elastic, and resistive work of breathing (WOB , WOB_{ela} , and WOB_{res}) were integrated utilizing the Campbell diagram framework [20, 21].

EIT data were analyzed to track regional gas distribution and lung volume variations, utilizing the T-piece phase as the baseline. Global and regional changes in end-expiratory lung volume ($\Delta EELV_{glob}$, $\Delta EELV_{dep}$, and $\Delta EELV_{non-dep}$) were estimated by multiplying the end-expiratory impedance shifts by an individual calibration ratio ($mL/\Delta Z$), derived from simultaneous tidal volume and impedance changes during stable breathing [12, 22, 23]. Furthermore, the dependent fraction of ventilation, regional tidal ventilation distribution in dependent and non-dependent lung regions (V_{Tdep} and $V_{Tnon-dep}$), center of ventilation (COV), and global inhomogeneity (GI) index were calculated to characterize lung homogeneity and ventilation distribution [24–26]

All patients were followed up until their hospital discharge, death, or 28 days post-enrollment, whichever occurred first. The weaning and extubation outcomes, post-extubation management and length of stay were collected.

Study endpoints

The primary endpoints were the mean expiratory airway pressure, PEEP, and $\Delta EELV$. The secondary endpoints included the following physiological parameters: V_T , respiratory rate, ΔP_{es} , PTPes, P_{mus} , $\Delta P_{L,dyn}$, $EtCO_2$, and SpO_2 .

Bench experiment

An 8.0-mm endotracheal tube was connected to an active lung simulator (ASL 5000, IngMar Medical, USA) to mimic spontaneous breathing. A total of 24 simulated breathing conditions were generated based on previous bench and clinical studies to represent a broad range of respiratory mechanics during SBTs, constructed by a factorial combination of two compliance levels (40 and 60 mL/cm H₂O), two airway resistance levels (10 and 20 cm H₂O s/L), three levels of inspiratory effort (P_{mus} : -5, -10, and -15 cm H₂O), and two respiratory rates (20 and 30 breaths/min), which mapped onto normal, ARDS-like, and COPD-like clinical phenotypes [10, 27, 28].

We evaluated four tracheal HFO interfaces with expiratory port diameters of 6.9 mm (HFO-6.9), 8.6 mm (HFO-8.6; Veoflo, Flexicare, Mountain Ash, United Kingdom), 9.8 mm (HFO-9.8), and 14.6 mm (HFO-14.6; OPT970 Optiflow+; Fisher & Paykel, Auckland, New Zealand), including the two interfaces used in the clinical study (additional file 1, Figure S3). Each simulation condition was tested using the four interfaces

at six flow settings (10–60 L/min), with FiO_2 set at 0.21 and temperature maintained at 37°C, yielding a total of 576 measurement segments. Flow and airway pressure were recorded through ASL software 3.6 at 512 Hz, with the last 10 breaths of each 5-minute period used for analysis. The primary outcomes of the bench study were the mean expiratory airway pressure and PEEP. The secondary outcomes included the following physiological parameters: ΔEELV , $\Delta\text{P}_{\text{L,dyn}}$, V_T , WOB, peak flow, and airway resistance. Detailed descriptions are provided in additional file 1.

Statistical analysis

Continuous variables are presented as median with interquartile range, and categorical variables are reported as counts and percentages. Comparisons across the five SBT conditions and post-extubation phase were performed using the Friedman test, with Dunn's method applied for post hoc pairwise comparisons.

For the sample size calculation of the clinical study, we employed the repeated-measures ANOVA method using mean expiratory airway pressure as the primary outcome. Since previous studies of HFO via endotracheal tube focused on clinical outcomes rather than airway pressure, no reference data were available [11, 13]. We therefore adopted a Cohen-based medium effect size of 0.25 alongside a statistical power of 0.80 and a significance level set at 0.05 to achieve adequate statistical power [29]. This yielded a required sample size of 20 subjects, calculated using G*Power version 3.1.9.7. Patients who were unable to complete all study phases were excluded. Additional patients were recruited to ensure that the final analysis included 20 subjects with complete SBTs and post-extubation datasets.

In the bench experiment, continuous variables are summarized as mean $\pm$ SD in the online supplementary table. A linear mixed-effects model was used to evaluate the effects of the HFO via endotracheal tube interface diameter, flow rate (categorical factors), and their interaction (fixed effects). The 24 simulated scenarios were modeled as random intercepts to account for variability across simulated phenotypes. Model-estimated marginal means with 95% confidence intervals were derived for graphical presentation.

Statistical analysis was performed using IBM SPSS Statistics 26.0, GraphPad Prism 9.0, and R (version 4.5.2) software. A p -value of less than 0.05 was considered statistically significant.

Results

Clinical study

Between May and December 2025, 130 mechanically ventilated patients meeting weaning readiness criteria were screened across participating ICUs. Twenty-four patients were enrolled; two failed crossover SBTs and underwent tracheostomy, and two were reintubated immediately after extubation

with the subsequent loss of post-extubation data. Thus, 20 patients were included in the final analysis (Fig. 1).

Baseline characteristics are shown in Table 1. Before enrollment, the median duration of mechanical ventilation was 6 (5–10) days. At baseline, the median pressure support was 8 (6–8) cm H₂O and PEEP was 5 (5–6) cm H₂O. The median interval from SBT completion to extubation was 24 (2–24) hours.

Table 1
Baseline characteristics of enrolled patients

Baseline characteristics	Patients (n = 20)
Age, years	66 (51–79)
Male, n (%)	10 (50%)
Body mass index, kg/m ²	23 (20–27)
APACHE II at ICU admission	16 (10–18)
Richmond Agitation Sedation Scale	0 (0–0)
Main reason for ICU admission, n (%)	8 (40%)
Septic shock	8 (40%)
Pneumonia	2 (10%)
Ischemic stroke	2 (10%)
Hemorrhagic stroke	
Endotracheal tube internal diameter, mm, n (%)	5 (25%)
7.0	11 (55%)
7.5	4 (20%)
8.0	
Baseline ventilation parameters	8 (6–8)
Pressure support, cm H ₂ O	5 (5–6)
PEEP, cm H ₂ O	
FiO ₂ of T-piece SBT, (%)	39 (37–43)
Duration of mechanical ventilation, days	7 (5–11)
Time from SBT completion to extubation, hours	24 (2–24)
Extubation failure, n (%)	1 (5%)
Post extubation oxygen management, n (%)	3 (15%)
Noninvasive ventilation	14 (70%)
Nasal HFO	3 (15%)
APACHE II: Acute Physiology and Chronic Health Evaluation II; ICU: intensive care unit; PEEP: positive end-expiratory pressure; SBT: spontaneous breathing trial; HFO: high-flow oxygen.	
Data are reported as median (interquartile range) or number (percentage).	

Baseline characteristics	Patients (n = 20)
Standard oxygenation	
Length of ICU stay, days	13 (9–17)
In-ICU mortality, n (%)	2 (10%)
APACHE II: Acute Physiology and Chronic Health Evaluation II; ICU: intensive care unit; PEEP: positive end-expiratory pressure; SBT: spontaneous breathing trial; HFO: high-flow oxygen.	
Data are reported as median (interquartile range) or number (percentage).	

Airway pressure and lung volume

Airway pressure and lung volume variables across the five study phases and PSV baseline are shown in Table 2, Table S1 (additional file 1), Table S3 (additional file 1) and Fig. 2. Airway pressure parameters differed among the five SBT study phases (all $p < 0.001$). Compared with T-piece, all tracheal HFO settings increased inspiratory and expiratory peak and mean airway pressure (all $p < 0.001$ vs T-piece).

Table 2
Airway pressure, lung volume and gas exchange across the five study phases

	T-piece	HFO – 9.8 (40 L/min)	HFO – 9.8 (60 L/min)	HFO – 6.9 (40 L/min)	HFO – 6.9 (60 L/min)	p- value
Airway pressure						
PEEP, cm H ₂ O	0.0 (0.0–0.1)	0.9 (0.8–1.0) *	1.9 (1.9–2.1) *	2.8 (2.7–3.0) *	6.0 (5.8–6.2) *	< 0.001
Peak inspiratory airway pressure, cm H ₂ O	–0.3 (–0.5––0.2)	–0.1 (–0.3–0.1) *	0.5 (0.2–0.8) *	0.3 (0.0–0.7) *	2.5 (1.8–2.8) *	< 0.001
Mean inspiratory airway pressure, cm H ₂ O	–0.1 (–0.3––0.1)	0.2 (0.1–0.4) *	1.0 (0.8–1.2) *	1.0 (0.8–1.3) *	3.5 (3.0–3.6) *	< 0.001
Peak expiratory airway pressure, cm H ₂ O	0.3 (0.2–0.3)	1.9 (1.8–2.1) *	3.2 (3.0–3.6) *	4.4 (4.1–4.7) *	8.0 (7.5–8.1) *	< 0.001
Mean expiratory airway pressure, cm H ₂ O	0.1 (0.1–0.2)	1.4 (1.2–1.5) *	2.6 (2.4–2.8) *	3.7 (3.4–4.0) *	7.2 (6.8–7.6) *	< 0.001
Lung volume and homogeneity						
V _{Tdep} , mL	186 (138–289)	183 (134–257)	191 (126–281)	192 (126–265)	216 (131–284)	0.35
V _{Tnon-dep} , mL	205 (183–279)	221 (181–305)	206 (172–304)	209 (156–254)	205 (154–254)	0.004
ΔEELV _{glob} , mL	Reference	74 (41–161) *	162 (102–278) *	240 (119–351) *	321 (261–529) *	< 0.001
HFO-9.8: HFO via endotracheal tube with a 9.8 mm expiratory port; HFO-6.9: HFO via endotracheal tube with a 6.9 mm expiratory port; PEEP: positive end-expiratory pressure; V _{Tdep} : tidal volume distending dependent regions; V _{Tnon-dep} : tidal volume distending nondependent regions; ΔEELV _{glob} : global change of end-expiratory lung volume; ΔEELV _{dep} : change of end-expiratory lung volume in dependent regions; ΔEELV _{non-dep} : change of end-expiratory lung volume in nondependent regions; COV: center of ventilation; GI index: global inhomogeneity index.						
Data are presented as median (interquartile range). <i>p</i> -values represent global differences across the five conditions determined by the Friedman test. Post hoc pairwise comparisons were performed with Dunn's correction for multiple comparisons.						
* <i>p</i> < 0.05 versus T-piece. Full pairwise comparisons are provided in Table S1 (additional file 1).						

	T-piece	HFO - 9.8 (40 L/min)	HFO - 9.8 (60 L/min)	HFO - 6.9 (40 L/min)	HFO - 6.9 (60 L/min)	<i>p</i> -value
Airway pressure						
Δ EELV _{dep} , mL	Reference	35 (19–63) *	77 (42–119) *	105 (62–174) *	161 (128–306) *	< 0.001
Δ EELV _{non-dep} , mL	Reference	40 (17–91) *	100 (46–136) *	90 (66–205) *	187 (104–287) *	< 0.001
Dependent fraction of ventilation, %	46 (38–55)	46 (34–56)	46 (33–58)	53 (37–60) *	53 (35–60) *	0.001
COV, %	48 (44–51)	47 (43–51)	48 (44–53)	48 (44–51)	48 (44–53)	0.17
GI index	0.53 (0.49–0.58)	0.51 (0.49–0.58)	0.51 (0.46–0.58)	0.51 (0.43–0.54)	0.49 (0.43–0.52) *	0.003
Gas exchange						
pH	7.43 (7.42–7.44)	–	7.42 (7.41–7.45)	–	7.42 (7.40–7.45)	0.14
PaO ₂ , mm Hg	105 (86–121)	–	109 (92–120)	–	121 (102–142) *	0.001
PaCO ₂ , mm Hg	41 (38–43)	–	40 (38–44)	–	41 (38–45)	0.11
PaO ₂ /FiO ₂ , mm Hg	268 (219–316)	–	273 (229–299)	–	303 (256–354) *	< 0.001
HFO-9.8: HFO via endotracheal tube with a 9.8 mm expiratory port; HFO-6.9: HFO via endotracheal tube with a 6.9 mm expiratory port; PEEP: positive end-expiratory pressure; V _{Tdep} : tidal volume distending dependent regions; V _{Tnon-dep} : tidal volume distending nondependent regions; Δ EELV _{glob} : global change of end-expiratory lung volume; Δ EELV _{dep} : change of end-expiratory lung volume in dependent regions; Δ EELV _{non-dep} : change of end-expiratory lung volume in nondependent regions; COV: center of ventilation; GI index: global inhomogeneity index.						
Data are presented as median (interquartile range). <i>p</i> -values represent global differences across the five conditions determined by the Friedman test. Post hoc pairwise comparisons were performed with Dunn's correction for multiple comparisons.						
* <i>p</i> < 0.05 versus T-piece. Full pairwise comparisons are provided in Table S1 (additional file 1).						

During T-piece SBT, airway pressure remained < 0.5 cm H₂O throughout the respiratory cycle. For HFO SBT, PEEP at 40 L/min was higher with HFO-6.9 than HFO-9.8 (2.8 [2.7–3.0] vs 0.9 [0.8–1.0] cm H₂O), as was the mean expiratory airway pressure (3.7 [3.4–4.0] vs 1.4 [1.2–1.5] cm H₂O). Increasing flow to 60 L/min further increased PEEP (6.0 [5.8–6.2] vs 1.9 [1.9–2.1] cm H₂O) and mean expiratory airway pressure (7.2 [6.8–7.6] vs 2.6 [2.4–2.8] cm H₂O).

Δ EELV, GI, and the dependent fraction of ventilation differed across phases ($p < 0.001$, $p = 0.003$, and $p = 0.001$, respectively), whereas COV did not. Compared with T-piece, all HFO SBTs increased global, dependent, and nondependent Δ EELV (all $p < 0.001$). HFO-6.9 increased dependent ventilation at both 40 and 60 L/min ($p = 0.015$ and $p < 0.001$), whereas HFO-9.8 had no significant effect. GI decreased only with HFO-6.9 at 60 L/min ($p = 0.03$).

Inspiratory effort

Δ Pes, PTPes, and Pmus did not differ across five SBT conditions, and Δ Pes was comparable to post-extubation values. In contrast, baseline PSV was associated with significantly lower inspiratory effort compared with all five unassisted SBT conditions and the post-extubation phase (Table 3, Tables S2–S4 in additional file 1, Fig. 3).

Table 3
Hemodynamics, respiratory variables and inspiratory effort across the five study phases

	T-piece	HFO - 9.8 (40 L/min)	HFO - 9.8 (60 L/min)	HFO - 6.9 (40 L/min)	HFO - 6.9 (60 L/min)	p-value
Hemodynamics						
Heart rate, beats/min	89 (79–101)	90 (75–104)	90 (78–103)	92 (79–105)	91 (77–103)	0.80
Mean blood pressure, mm Hg	95 (85–104)	92 (85–105)	94 (87–104)	93 (86–105)	95 (88–106)	0.42
SpO ₂ , %	99 (97–100)	99 (98–100)	99 (98–100)	99 (98–100)	99 (98–100)	0.36
Respiratory variables						
Respiratory rate, breaths/min	22 (16–27)	20 (16–26)	20 (16–27)	20 (16–25) *	19 (16–24) *	0.002
V _T , mL	421 (339–530)	438 (353–558)	423 (331–553)	423 (321–530)	429 (342–523)	0.22
Minute ventilation, L/min	9.0 (7.2–10.4)	8.7 (6.6–9.9)	8.8 (6.3–9.7)	8.5 (6.4–9.3) *	8.3 (6.1–9.5) *	< 0.001
EtCO ₂ , mm Hg	39 (32–43)	39 (32–43)	39 (32–43)	39 (32–43)	39 (32–43)	0.11
Expiratory time, s	1.66 (1.43–2.56)	1.91 (1.45–2.57)	1.85 (1.42–2.59)	1.74 (1.53–2.72)	1.98 (1.64–2.46)	0.03
Expiratory time/total respiratory time, %	64 (62–70)	65 (62–71)	65 (62–71)	65 (63–70)	67 (62–70)	0.11
HFO-9.8: HFO via endotracheal tube with a 9.8 mm expiratory port; HFO-6.9: HFO via endotracheal tube with a 6.9 mm expiratory port; V _T : tidal volume; EtCO ₂ : end-tidal carbon dioxide pressure; ΔPes: tidal swing of esophageal pressure during inspiration; PTPes: esophageal pressure time product per minute; P _{mus} : pressure generated by respiratory muscle during inspiration; ΔP _{L,dyn} : dynamic transpulmonary driving pressure; WOB: work of breathing; WOB _{res} : resistive work of breathing; WOB _{ela} : elastic work of breathing.						
Data are presented as median (interquartile range). <i>p</i> -values represent global differences across the five conditions determined by the Friedman test. Post hoc pairwise comparisons were performed with Dunn's correction for multiple comparisons.						
* <i>p</i> < 0.05 versus T-piece. Full pairwise comparisons are provided in Table S2 (additional file 1).						

	T-piece	HFO - 9.8 (40 L/min)	HFO - 9.8 (60 L/min)	HFO - 6.9 (40 L/min)	HFO - 6.9 (60 L/min)	p-value
Hemodynamics						
Peak inspiratory flow, L/s	0.63 (0.49–0.80)	0.62 (0.50–0.73)	0.61 (0.48–0.78)	0.60 (0.45–0.71)	0.57 (0.46–0.70) *	0.005
Peak expiratory flow, L/s	0.42 (0.38–0.50)	0.41 (0.35–0.45)	0.40 (0.32–0.43) *	0.35 (0.31–0.42) *	0.32 (0.27–0.37) *	< 0.001
Inspiratory airway resistance, cm H ₂ O s/L	5.1 (3.8–7.3)	6.5 (4.4–9.7)	7.1 (4.5–10.1) *	7.4 (5.4–11.6) *	7.9 (5.4–12.8) *	< 0.001
Expiratory airway resistance, cm H ₂ O s/L	6.5 (4.2–8.8)	7.8 (6.3–8.9) *	7.9 (6.4–9.7) *	9.6 (6.9–11.8) *	10.3 (8.4–13.9) *	< 0.001
Inspiratory effort						
ΔPes, cm H ₂ O	15 (11–16)	14 (10–17)	13 (10–17)	14 (10–17)	13 (10–16)	0.99
PTPes, cm H ₂ O s/min	207 (157–251)	207 (158–234)	212 (151–242)	211 (155–247)	214 (156–260)	0.31
Pmus, cm H ₂ O	17 (14–20)	17 (13–21)	16 (13–20)	16 (13–21)	15 (12–21)	0.84
ΔP _{L,dyn} , cm H ₂ O	14 (10–16)	13 (9–16)	12 (9–15) *	11 (8–14) *	9 (7–13) *	< 0.001
WOB, J/min	8.7 (7.4–11.5)	8.9 (7.2–11.0)	8.4 (6.8–12.1)	9.3 (7.2–10.7)	9.3 (6.7–10.4)	0.86
HFO-9.8: HFO via endotracheal tube with a 9.8 mm expiratory port; HFO-6.9: HFO via endotracheal tube with a 6.9 mm expiratory port; V _T : tidal volume; EtCO ₂ : end-tidal carbon dioxide pressure; ΔPes: tidal swing of esophageal pressure during inspiration; PTPes: esophageal pressure time product per minute; Pmus: pressure generated by respiratory muscle during inspiration; ΔP _{L,dyn} : dynamic transpulmonary driving pressure; WOB: work of breathing; WOB _{res} : resistive work of breathing; WOB _{ela} : elastic work of breathing.						
Data are presented as median (interquartile range). p-values represent global differences across the five conditions determined by the Friedman test. Post hoc pairwise comparisons were performed with Dunn's correction for multiple comparisons.						
* p < 0.05 versus T-piece. Full pairwise comparisons are provided in Table S2 (additional file 1).						

	T-piece	HFO – 9.8 (40 L/min)	HFO – 9.8 (60 L/min)	HFO – 6.9 (40 L/min)	HFO – 6.9 (60 L/min)	p-value
Hemodynamics						
WOB _{res} , J/min	3.9 (2.4–5.5)	3.8 (2.9–4.9)	3.9 (3.0–5.8)	4.2 (3.1–5.3)	4.1 (3.2–5.5)	0.40
WOB _{ela} , J/min	5.1 (3.9–6.5)	4.9 (4.2–5.9)	5.0 (3.7–5.9)	4.9 (3.9–5.6) *	4.8 (3.7–5.4) *	0.007
HFO-9.8: HFO via endotracheal tube with a 9.8 mm expiratory port; HFO-6.9: HFO via endotracheal tube with a 6.9 mm expiratory port; V _T : tidal volume; EtCO ₂ : end-tidal carbon dioxide pressure; ΔPes: tidal swing of esophageal pressure during inspiration; PTPes: esophageal pressure time product per minute; P _{mus} : pressure generated by respiratory muscle during inspiration; ΔP _{L,dyn} : dynamic transpulmonary driving pressure; WOB: work of breathing; WOB _{res} : resistive work of breathing; WOB _{ela} : elastic work of breathing.						
Data are presented as median (interquartile range). <i>p</i> -values represent global differences across the five conditions determined by the Friedman test. Post hoc pairwise comparisons were performed with Dunn's correction for multiple comparisons.						
* <i>p</i> < 0.05 versus T-piece. Full pairwise comparisons are provided in Table S2 (additional file 1).						

ΔP_{L,dyn} differed across SBT phases (*p* < 0.001). Compared with T-piece, HFO-9.8 at 60 L/min and HFO-6.9 at 40 and 60 L/min were associated with lower ΔP_{L,dyn} (*p* = 0.02, *p* < 0.001, and *p* < 0.001) (Table 3, Table S2 in additional file 1, Fig. 3).

WOB and WOB_{res} did not differ among study phases, whereas WOB_{ela} varied (*p* = 0.007). Compared with T-piece, HFO-6.9 at 40 and 60 L/min was associated with reduced WOB_{ela} (*p* = 0.004 and *p* = 0.001).

Hemodynamics, respiratory variables and gas exchange

Baseline respiratory and hemodynamic variables did not differ before the five SBT phases. No hemodynamic differences were observed during SBT or after extubation (Table 3, Tables S3-S5 in additional file 1).

V_T and EtCO₂ remained unchanged, whereas respiratory rate and minute ventilation varied (*p* = 0.002 and *p* < 0.001). Compared with T-piece, HFO-6.9 at 40 and 60 L/min reduced respiratory rate (*p* = 0.01 and *p* = 0.03) and slightly decreased minute ventilation (*p* = 0.04 and *p* = 0.03) without affecting EtCO₂. HFO-9.8 showed no differences versus T-piece (Table 3, Table S2 in additional file 1, Fig. 4).

Expiratory time varied slightly among study phases (*p* = 0.03), whereas its proportion within the respiratory cycle remained unchanged. Peak inspiratory and expiratory flow and airway resistance differed among SBT conditions. Compared with T-piece, HFO SBTs were associated with lower peak flows and higher airway resistance (all *p* < 0.05) (Table 3 and Table S2 in additional file 1).

Arterial oxygenation also differed across study phases ($p = 0.001$ for PaO_2 ; $p < 0.001$ for $\text{PaO}_2/\text{FiO}_2$), whereas PaCO_2 remained unchanged. Compared with T-piece, HFO-6.9 increased PaO_2 ($p = 0.007$) and improved the $\text{PaO}_2/\text{FiO}_2$ ($p < 0.001$), whereas HFO-9.8 showed no significant differences (Table 2, Table S1 in additional file 1, Fig. 4).

Bench experiment

Across simulated conditions, higher HFO flow rates and smaller expiratory port diameters were associated with reduced peak flow and V_T , increased airway resistance, elevated airway pressure and PEEP, decreased transpulmonary pressure, and increased ΔEELV . Linear mixed-effects modeling demonstrated significant main and interaction effects of flow and interface diameter across all measured parameters (all $p < 0.001$) (Table S6 in additional file 1).

PEEP and mean expiratory airway pressure increased progressively with increasing flow and decreasing expiratory port diameter (Fig. 5). Across most flow conditions, pressure levels in the bench experiment closely approximated those observed in patients.

Discussion

This study compared the physiological effects of HFO via endotracheal tube and T-piece during SBT and explored the mechanisms that may be relevant to ventilator liberation. The main findings were as follows. First, compared with T-piece, tracheal HFO increased airway pressure and end-expiratory lung volume, improved dependent ventilation and oxygenation, and modestly reduced respiratory rate. Second, the downstream benefits in ventilation homogeneity and oxygenation occurred mainly with the smaller expiratory port at higher flows, suggesting a pressure threshold effect. Third, inspiratory effort during tracheal HFO remained comparable to T-piece and closely resembled post-extubation values. Taken together, these findings indicate that tracheal HFO creates a distinct physiological condition that may preserve lung volume and reduce lung stress while maintaining a clinically meaningful test of post-extubation respiratory workload.

Physiological mechanisms of tracheal HFO during SBT

Bench simulations and clinical measurements demonstrated a flow- and expiratory port diameter-dependent physiological cascade. Consistent with Poiseuille's law, higher flows combined with smaller expiratory port diameters generated higher airway pressure [30]. This pressure effect was associated with stepwise increases in end-expiratory lung volume and a redistribution of ventilation toward dependent lung regions, consistent with recruitment of poorly ventilated units. Improved homogeneity was accompanied by lower dynamic transpulmonary driving pressure and better oxygenation at similar FiO_2 , with a modest reduction in respiratory rate.

This physiological cascade can be compared with that observed during other high-flow modalities. Nasal HFO generates flow-dependent airway pressure, increases end-expiratory lung volume, improves

oxygenation, and reduces respiratory rate [22, 31, 32]. By contrast, HFO via tracheostomy, which bypasses upper-airway resistance, produces only small increases in airway pressure and no consistent rise in end-expiratory lung volume, partly because previously studied interfaces had large expiratory port diameters (14.6 mm) with limited expiratory resistance [33–35]. In the present study, HFO via endotracheal tube with the smaller 6.9 mm expiratory port generated airway pressure and lung-volume effects approaching those reported during nasal HFO at similar flows [36, 37]. The downstream improvements were confined mainly to HFO-6.9 (additional file 1, Table S7), suggesting that a minimum pressure effect is required before recruitment-related physiological benefits emerge. While higher flows through a larger expiratory port might theoretically achieve similar airway pressure, very high flows (> 60 L/min) reduce patient comfort. Therefore, combining moderate flows with a smaller expiratory port can achieve pressure-driven benefits while preserving patient tolerance [38].

Clinical implications for ventilator liberation

Tracheal HFO during SBT may provide lung-protective benefits by mitigating excessive global lung stress. Increasing evidence suggests that the transition from supported ventilation to unsupported SBT can expose vulnerable patients to vigorous spontaneous breathing, generating large $\Delta P_{L,dyn}$ that contributes to patient self-inflicted lung injury [39, 40]. Compared with T-piece, tracheal HFO significantly reduced $\Delta P_{L,dyn}$ by increasing the inspiratory drop in airway pressure while maintaining stable esophageal pressure swings (additional file 1, Figure S2). This pattern suggests a potentially useful separation between respiratory effort and lung stress: patients continued to breathe with post-extubation-like effort, while the lung was exposed to a lower dynamic mechanical load.

Preservation of lung volume is another clinically relevant feature. Loss of end-expiratory lung volume and increased regional ventilation inhomogeneity during T-piece trials have been associated with weaning failure [41–43]. These changes may also increase stress in dependent or poorly aerated lung regions. By preserving end-expiratory lung volume and improving ventilation homogeneity, tracheal HFO may help limit derecruitment and excessive regional lung stress during SBTs. This potential benefit may be particularly relevant in patients prone to loss of aerated lung volume.

Tracheal HFO may also attenuate the abrupt cardiopulmonary transition created by T-piece trials. Sudden withdrawal of positive airway pressure can increase venous return and left ventricular afterload, potentially contributing to weaning-induced pulmonary edema in patients with limited cardiac reserve [44, 45]. The low-level, PEEP-like effect generated by tracheal HFO may smooth this transition and facilitate more gradual cardiopulmonary adaptation during ventilator liberation.

An important requirement for any SBT strategy is that it should not mask clinically relevant respiratory muscle load. PSV can unload the respiratory muscles and may underestimate the burden that patients will face after extubation [5–7]. In contrast, inspiratory effort during tracheal HFO was similar to T-piece and close to post-extubation values. Although the smaller expiratory port and higher flow increased airway resistance slightly, this was offset by recruitment-related improvements in elastic work, leaving overall inspiratory workload unchanged. There was no signal of carbon dioxide retention. These findings

suggest that tracheal HFO may preserve the diagnostic value of the SBT while adding lung-volume and oxygenation benefits. In practical terms, it may be most useful when clinicians want to avoid both excessive unloading by PSV and abrupt derecruitment during T-piece trials. As nasal HFO is commonly used immediately after extubation, this strategy may facilitate a seamless transition from invasive to post-extubation oxygen therapy with only an interface change.

Taken together, these findings support tracheal HFO as a physiologically informed SBT strategy during ventilator liberation. It combines three features typically separated across SBT methods: preservation of post-extubation-like inspiratory effort, maintenance of low-level airway pressure and lung volume, and reduction of dynamic lung stress. This physiological profile may be particularly relevant for patients vulnerable to derecruitment, cardiopulmonary intolerance, or post-extubation respiratory failure.

Limitations

Our study has several limitations. First, because some patients were unable to tolerate a tight-fitting facial mask after extubation, accurate measurements of flow, tidal volume, and derived parameters such as PTPes and WOB were not always feasible. Therefore, Δ Pes was used as a surrogate marker of inspiratory effort; this variable has been shown to correlate closely with PTPes [46]. Second, many patients in our study were extubated on the day after a successful SBT. Reliable post-extubation EIT measurements for direct comparison with SBT phases were difficult to obtain because prolonged EIT monitoring after extubation is technically challenging, with possible belt displacement, changes in posture, repeated contact-gel application, and signal artifacts [42]. Future studies may consider absolute end-expiratory lung-volume measurement techniques, such as nitrogen washout/washin, although this approach also requires a sealed interface after extubation [47]. Third, a 10-minute washout period was selected based on previous studies [7, 10]. In the present study, vital signs returned to baseline before each SBT phase, suggesting that the washout interval was sufficient to reduce carryover effects. Fourth, given the constraints of study duration, patient tolerance, and data quality control, a formal low-level PSV SBT condition was not included. The PSV baseline recorded before the study, delivered at PSV of 8 (6–8) cmH₂O and PEEP of 5 (5–6) cmH₂O, may be considered only a surrogate PSV condition. Finally, this crossover study was designed to compare short-term physiological responses within patients. Its design and sample size therefore did not permit assessment of whether different SBT strategies influence clinical outcomes. Accordingly, larger, adequately powered clinical trials are needed to determine whether the observed physiological improvements translate into better patient outcomes.

Conclusion

During SBT, HFO via endotracheal tube increased airway pressure and lung volume, improved ventilation homogeneity and oxygenation, and maintained inspiratory effort close to both T-piece and post-extubation conditions. These effects were determined by flow and expiratory port diameter, suggesting that a minimum pressure effect is needed to produce downstream physiological benefits. Tracheal HFO may therefore represent an alternative SBT strategy, preserving a post-extubation-like inspiratory workload while reducing derecruitment and dynamic lung stress during ventilator liberation. Whether

these physiological advantages improve extubation outcomes requires confirmation in adequately powered clinical trials.

Abbreviations

SBT Spontaneous breathing trial

PSV Pressure support ventilation

WOB Work of breathing

HFO High-flow oxygen

ICU Intensive care unit

EIT Electrical impedance tomography

PEEP Positive end-expiratory pressure

HFO-9.8 HFO via endotracheal tube with a 9.8 mm expiratory port

HFO-6.9 HFO via endotracheal tube with a 6.9 mm expiratory port

EtCO₂ End-tidal carbon dioxide pressure

V_T Tidal volume

$\Delta P_{L,dyn}$ Dynamic transpulmonary driving pressure

ΔP_{es} Tidal swing of esophageal pressure during inspiration

PTPes Esophageal pressure-time product per minute

P_{mus} Pressure generated by respiratory muscle during inspiration

WOB_{ela} Elastic work of breathing

WOB_{res} Resistive work of breathing

$\Delta EELV_{glob}$ Global change of end-expiratory lung volume

$\Delta EELV_{dep}$ Change of end-expiratory lung volume in dependent regions

$\Delta EELV_{non-dep}$ Change of end-expiratory lung volume in nondependent regions

V_{Tdep} Tidal volume distending dependent regions

$V_{\text{Tnon-dep}}$ Tidal volume distending nondependent regions

COV Center of ventilation

GI Global inhomogeneity

HFO-8.6 HFO via endotracheal tube with an 8.6 mm expiratory port

HFO-14.6 HFO via endotracheal tube with a 14.6 mm expiratory port

APACHE II Acute Physiology and Chronic Health Evaluation II

Declarations

Ethics approval and consent to participate

The institutional ethics committees of the two participating hospitals approved the study protocol (IIT2024-157-002 from Beijing Shijitan Hospital, Capital Medical University, Beijing, China and KY-202505-01 from Beijing Fengtai You'anmen Hospital, Beijing, China). Written informed consent was obtained from all enrolled patients or surrogates. The study was registered at ClinicalTrials.gov (NCT06816706) on 6 February 2025.

Consent for publication

Not applicable.

Competing interests

None declared.

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Author Contribution

SSX and JXZ designed the study. SSX, RZZ, JTL, and LW enrolled patients and collected data. SSX, RZZ, MXH, XA, and MYM analyzed the data and performed the statistical analysis. SSX drafted the manuscript. SSX, HLL, YFW, and JXZ reviewed the manuscript. All authors read and approved the final version of the manuscript.

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Not applicable.

Data Availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Figures

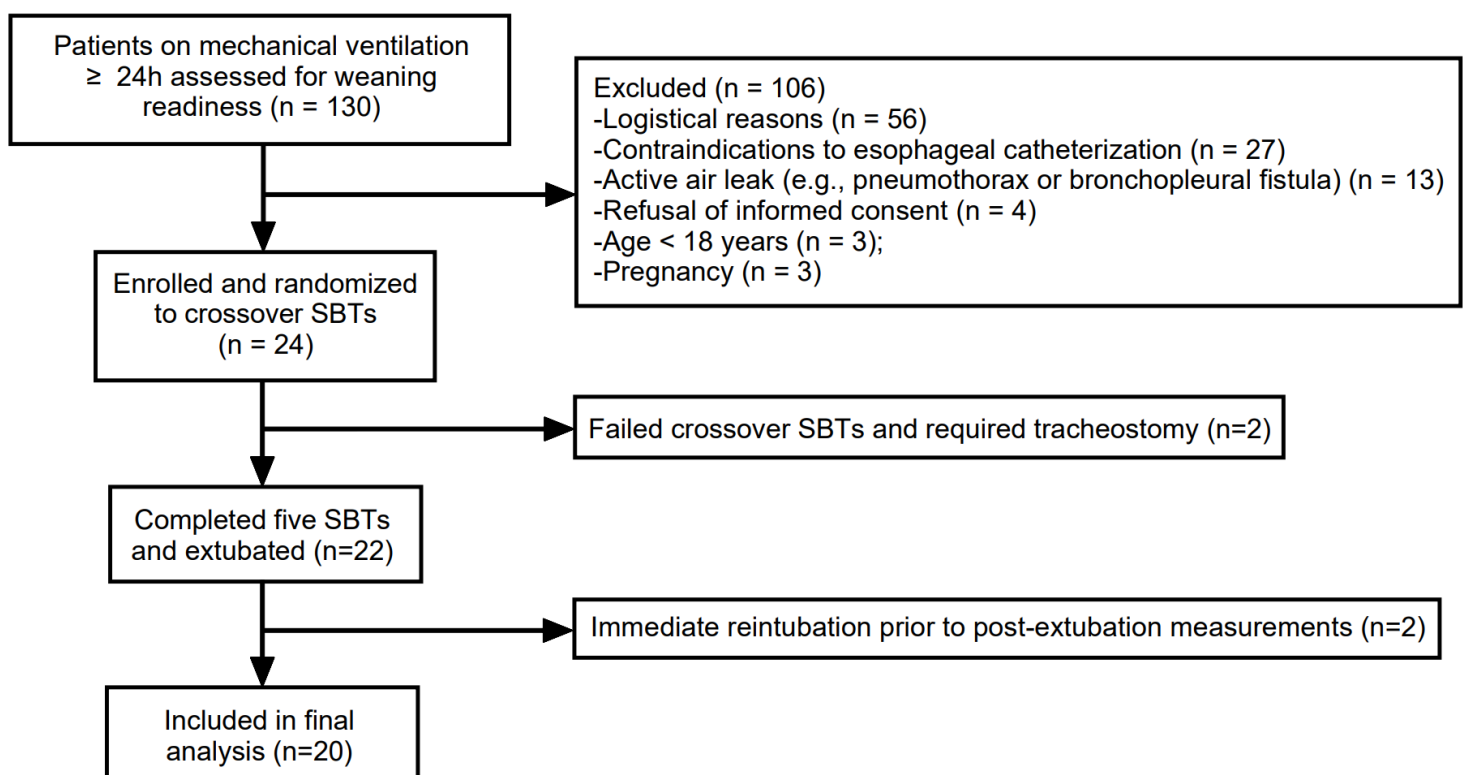


Figure 1

Flowchart of the study.

SBT: spontaneous breathing trial.

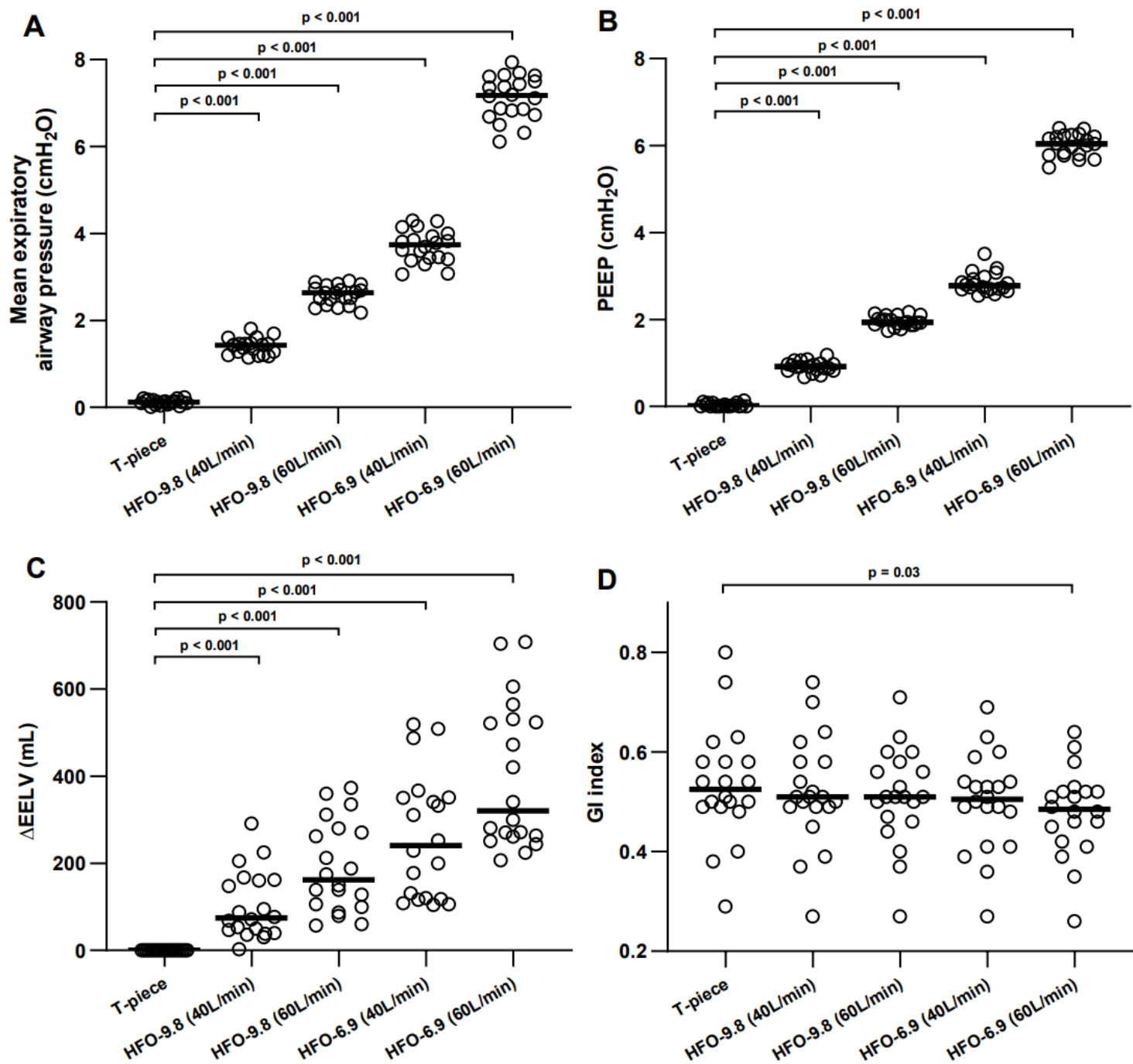


Figure 2

Airway pressure and ventilation distribution across different study phases.

Individual patient values and medians (horizontal lines) of (A) mean expiratory airway pressure, (B) positive end-expiratory pressure (PEEP), (C) change of end-expiratory lung volume (Δ EELV), and (D) global inhomogeneity (GI) index across the study phases. Overall comparisons were performed using the Friedman test. Significant pairwise comparisons versus T-piece are indicated in the figure. HFO-6.9: HFO via endotracheal tube with a 6.9 mm expiratory port; HFO-9.8: HFO via endotracheal tube with a 9.8 mm expiratory port.

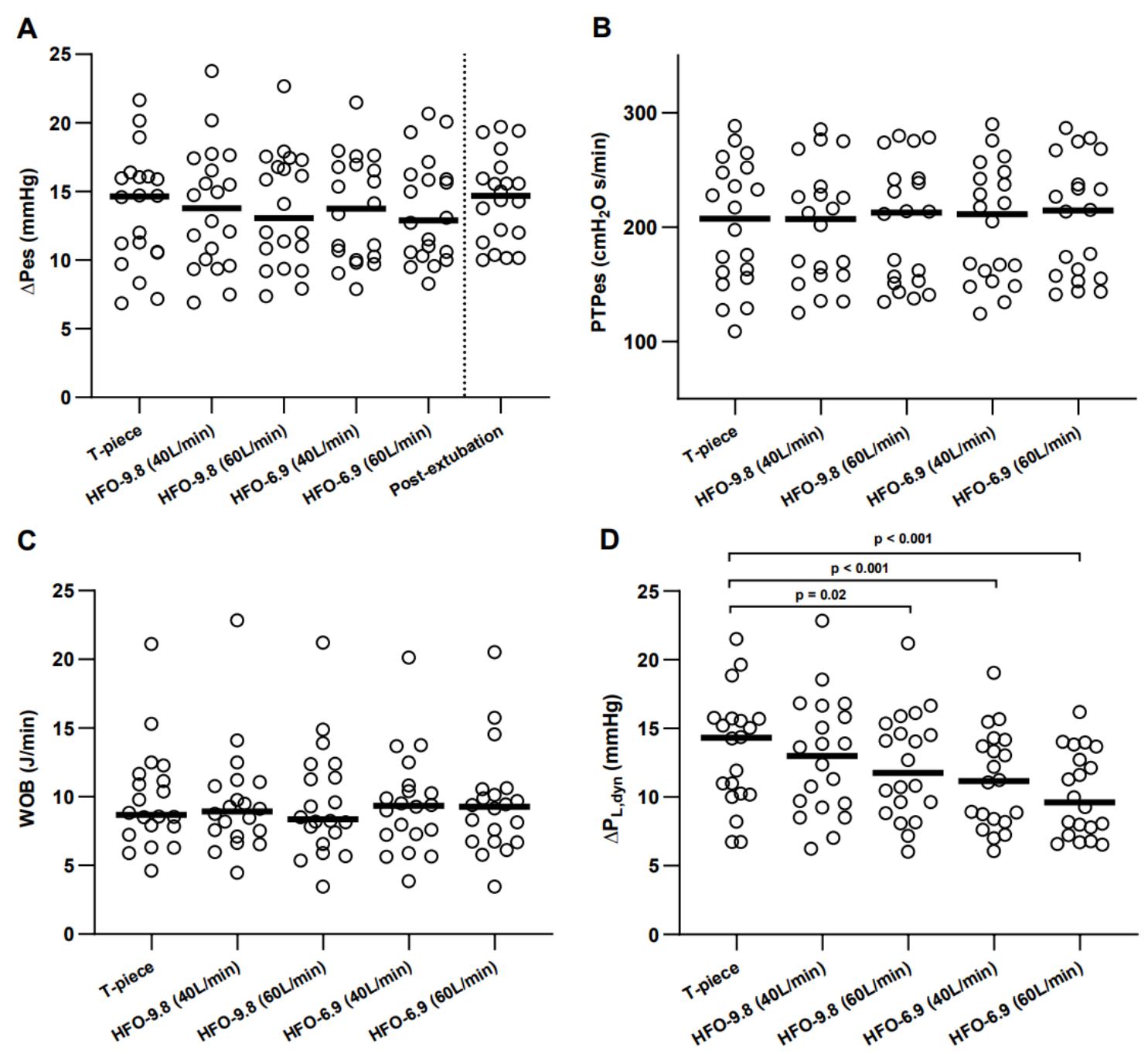


Figure 3

Inspiratory effort and lung stress across different study phases.

Individual patient values and medians (horizontal lines) of (A) tidal swing of esophageal pressure during inspiration (ΔP_{es}), (B) esophageal pressure-time product per minute (PTPes), (C) work of breathing (WOB), and (D) dynamic transpulmonary driving pressure ($\Delta P_{L,dyn}$) across the study phases. Overall comparisons were performed using the Friedman test. Significant pairwise comparisons versus T-piece are indicated in the figure. HFO-6.9: HFO via endotracheal tube with a 6.9 mm expiratory port; HFO-9.8: HFO via endotracheal tube with a 9.8 mm expiratory port.

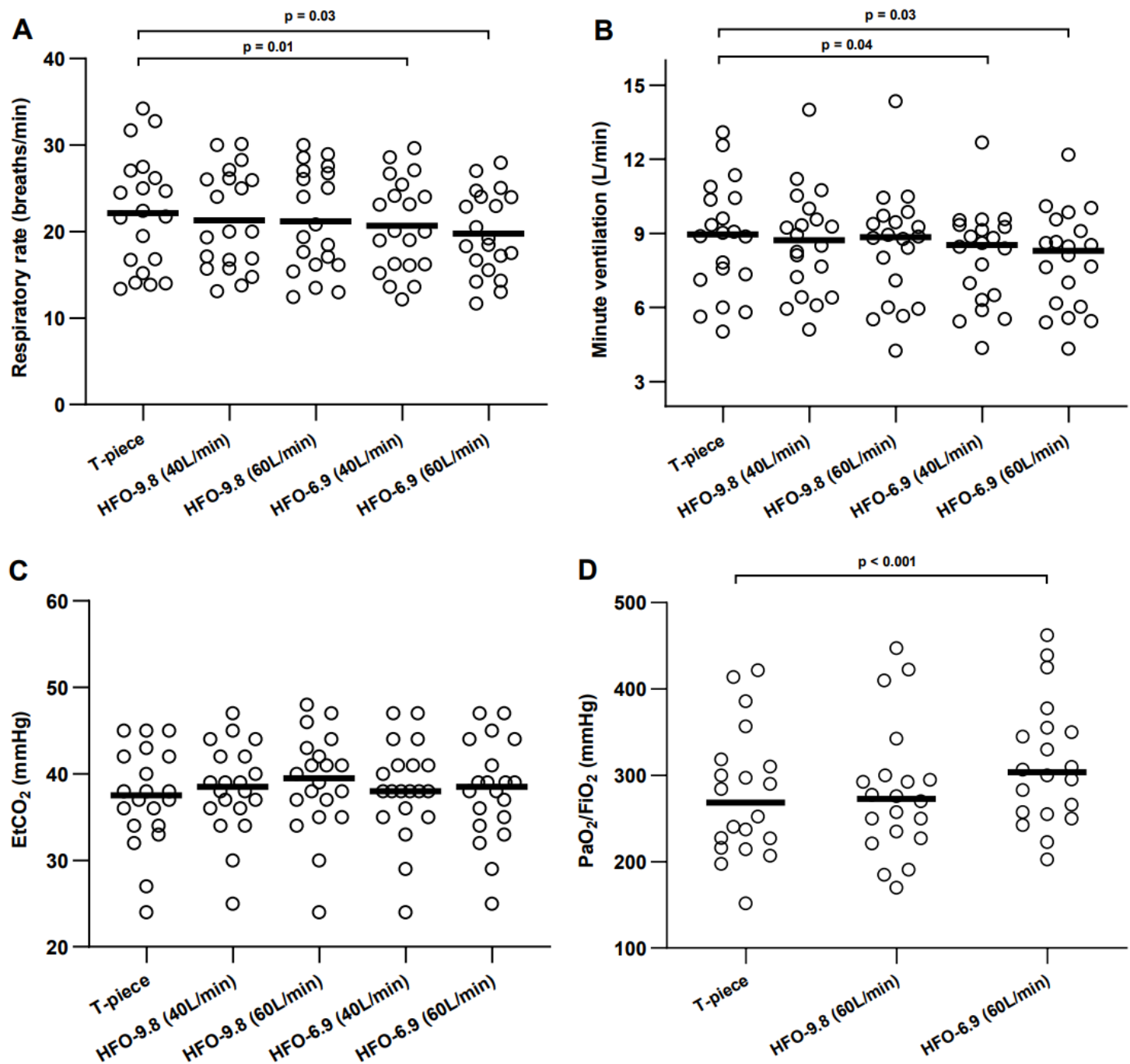


Figure 4

Respiratory rate, minute ventilation, and gas exchange across different study phases.

Individual patient values and medians (horizontal lines) of (A) respiratory rate, (B) minute ventilation, (C) end-tidal carbon dioxide pressure (EtCO₂), and (D) PaO₂/FiO₂ across the study phases. Overall comparisons were performed Friedman test. Significant pairwise comparisons versus T-piece are indicated in the figure. HFO-6.9: HFO via endotracheal tube with a 6.9 mm expiratory port; HFO-9.8: HFO via endotracheal tube with a 9.8 mm expiratory port.

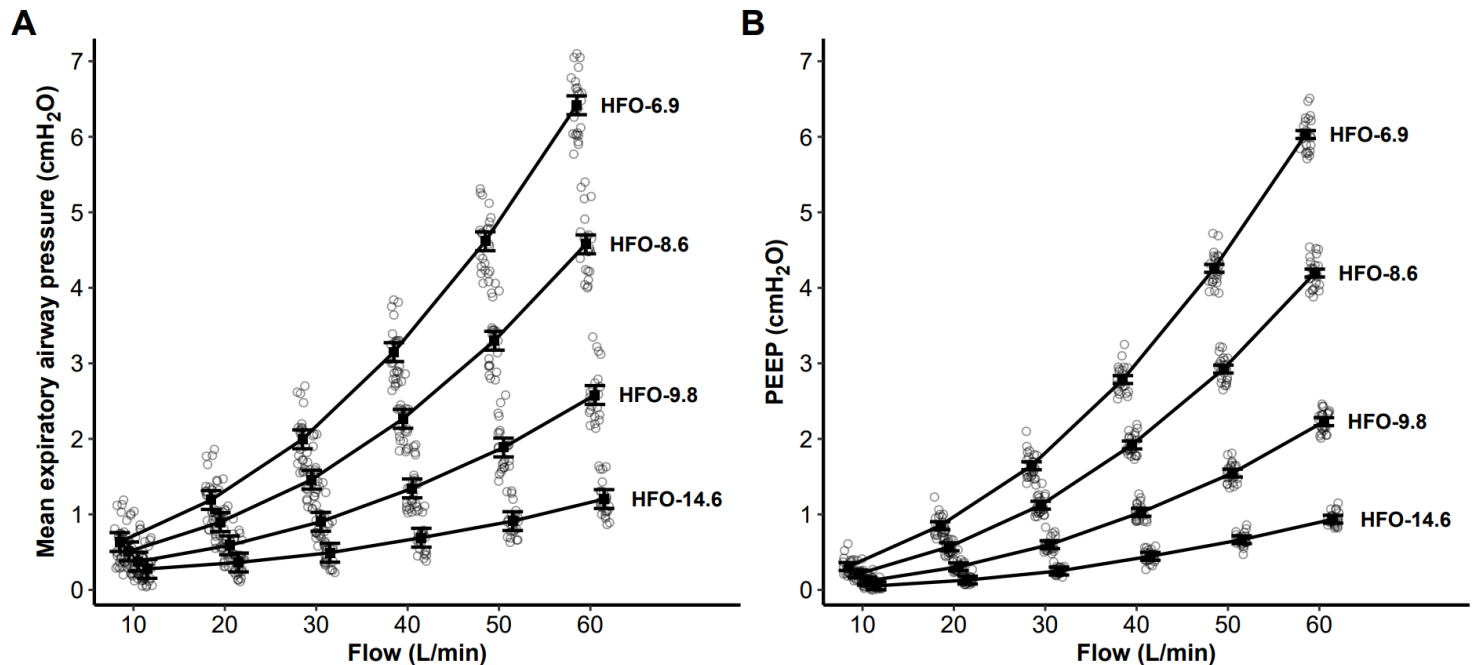


Figure 5

Effects of expiratory port diameter and flow rate in bench simulations.

Expiratory port diameter and flow rate jointly determine (A) mean expiratory airway pressure and (B) positive end-expiratory pressure (PEEP). Circles represent individual simulated data points. Squares and connecting lines indicate model-estimated marginal means derived from linear mixed-effects modeling, with error bars representing 95% confidence intervals. Flow rate, diameter, and their interaction significantly influenced both variables (all $p < 0.001$). HFO-6.9: HFO via endotracheal tube with a 6.9 mm expiratory port; HFO-8.6: HFO via endotracheal tube with an 8.6 mm expiratory port; HFO-9.8: HFO via endotracheal tube with a 9.8 mm expiratory port; HFO-14.6: HFO via endotracheal tube with a 14.6 mm expiratory port.

Supplementary Files

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