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Spyros D. Mentzelopoulos
Sotiris Malachias
Stelios Kokkoris
Charis Roussos
Spyros G. Zakynthinos

Comparison of high-frequency oscillation and tracheal gas insufflation versus standard high-frequency oscillation at two levels of tracheal pressure

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S. D. Mentzelopoulos · S. Malachias · S. Kokkoris · C. Roussos · S. G. Zakynthinos
First Department of Intensive Care Medicine, University of Athens Medical School, Athens, Greece

S. D. Mentzelopoulos (✉)
Evangelismos General Hospital,
45-47 Ipsilandou Street,
10675 Athens, Greece
e-mail: sdm@hol.gr;
sdmentzelopoulos@yahoo.com
Tel.: +30-6977-465832
Fax: +30-210-3218493

Abstract *Purpose:* In acute respiratory distress syndrome (ARDS), combined high-frequency oscillation (HFO) and tracheal gas insufflation (TGI) may improve oxygenation through a TGI-induced increase in mean tracheal pressure (P_{tr}). We compared standard HFO and HFO-TGI matched for P_{tr}, in order to determine whether TGI affects gas exchange independently from P_{tr}. *Methods:* We conducted a prospective, randomized, crossover, physiological study in a 37-bed intensive care unit. Twenty-two patients with early acute lung injury (ALI) or ARDS were enrolled. On day 1, patients were ventilated with HFO, without (60 min) and combined with TGI (60 min) in random order. HFO/HFO-TGI sessions were repeated in inverse order within 7 h. HFO/HFO-TGI mean airway pressure (P_{aw}) was titrated to a P_{tr} that was either equal to (low P_{aw}) or 3 cmH_2O higher than (high P_{aw}) the P_{tr} of the preceding conventional mechanical ventilation. On day 2, the protocol was repeated at the alternative P_{tr} level relative to day 1. *Results:* Gas exchange and hemodynamics were determined before, during, and after HFO/HFO-TGI sessions. HFO-TGI-high P_{aw} versus HFO-high P_{aw} resulted in significantly higher PaO_2/inspired O_2 fraction (FiO_2) [mean ± standard error of the mean (SEM): 281.6 ± 15.1 versus 199.0 ± 15.0 mmHg; mean increase: 42%; $P < 0.001$]. HFO-TGI-low P_{aw}, versus HFO-low P_{aw}, resulted in significantly higher PaO_2/FiO_2 (222.8 ± 14.6 versus 141.3 ± 8.7 mmHg; mean increase: 58%; $P < 0.001$). $PaCO_2$ was significantly lower during HFO-TGI-high P_{aw} versus HFO-high P_{aw} (45.3 ± 1.6 versus 53.7 ± 1.9 mmHg; mean decrease: 16%; $P = 0.037$). *Conclusions:* At the same P_{tr} level, HFO-TGI results in superior gas exchange compared with HFO.

Keywords Respiratory distress syndrome · Adult · Respiration · Artificial · High-frequency ventilation · Thoracic wall compliance · Pulmonary gas exchange

Introduction

In acute respiratory distress syndrome (ARDS), addition of tracheal gas insufflation (TGI) to high-frequency oscillation (HFO) improves gas exchange [1, 2]. TGI may increase carinal pressure and promote lung recruitment [1, 2], improve the washout of the anatomical dead space [2, 3], and augment HFO-dependent, distal gas transport [1–3]. TGI flow of 6.0 L min^{-1} increases mean tracheal pressure (P_{tr}), even if a cuff leak is used [1]. During

standard HFO, P_{tr} increases after a simple clockwise turn of the ventilator's mean airway pressure (P_{aw}) valve [1]. This may obviate any need for TGI.

We determined the effect of adding TGI to HFO on gas exchange independently from P_{tr}. We compared standard HFO and HFO-TGI matched for a higher and a lower, clinically relevant P_{tr} level [higher P_{tr} level = 3 cmH_2O above P_{tr} of preceding conventional mechanical ventilation (CMV); lower P_{tr} level = P_{tr} of preceding CMV; see Electronic Supplementary Material (ESM)]. The rationale for additionally varying P_{tr} was high-pressure-associated recruitment of dependent and well-perfused lung regions. This may improve ventilation–perfusion matching and promote TGI-enhanced distal gas transport [1]. A possible, TGI-related oxygenation improvement [1] could be greater at higher P_{tr} versus lower P_{tr}. Also, a higher P_{tr} could increase physiological dead space, thus altering the effect of TGI on CO_2 removal [1]. Consequently, potential differences in gas exchange between HFO and HFO-TGI could depend on P_{tr} level.

Methods

Patients

Institutional approval and informed, written next-of-kin consent were obtained. Patients had early (onset within ≤72 h) acute lung injury or ARDS [4]: PaO_2/FiO_2 <250 mmHg with positive end-expiratory pressure (PEEP) ≥8 cmH_2O for >12 h. Eligibility criteria, sedation, analgesia, neuromuscular blockade, and patient monitoring are detailed in the ESM. Patients received lung-protective CMV; PEEP and FiO_2 were set in concordance with the ARDSnet protocol (ESM).

Study design

A randomized, crossover design was adopted. Figure 1 illustrates the study protocol. Additional details are provided in the ESM.

Baseline CMV period

Tracheal tube correct positioning and patency were confirmed, and anesthesia and paralysis were induced. Within 15–20 min post enrollment, blood gases and respiratory compliance were determined. Subsequently, two 4.8-cm-long circuit adapters with side-arms were introduced in between the connector of the tracheal tube and the Y-piece of the breathing circuit (associated equipment dead-space increase = 12.5 mL). A rigid-wall TGI catheter [inner diameter (ID) = 1.0 mm, outer diameter = 2.0 mm] was passed through the proximal adapter. The tip of the TGI catheter reached the tip of the tracheal tube. A second catheter was passed through the distal adapter to monitor P_{tr}. The tip of the pressure-measuring catheter was placed at 2.0 cm beyond the tip of the tracheal tube. The adapter/catheter system was maintained in place during the study intervention periods (Fig. 1). Following recruitment and 55 min of CMV, physiologic measurements were conducted (Fig. 1).

HFO strategies

The Sensormedics 3100B ventilator was connected to the proximal adapter. The TGI catheter was connected to a gas-mixing flowmeter for precise control of the composition of the TGI O_2/air mixture. The TGI gas was not humidified, because the use of TGI was intermittent and brief [1]. High-frequency ventilator settings were: $FiO_2 = FiO_2$ of the preceding CMV, bias flow = 40 L/min, frequency (f) = 3.5 Hz, pressure amplitude (ΔP) = 90 cmH_2O, and inspiratory-to-expiratory time (I:E) ratio = 1:2 (inspiratory time ~0.1 s). On HFO initiation, a recruitment maneuver was performed, a cuff leak of 4–5 cmH_2O was placed, and P_{aw} was titrated to the prespecified P_{tr} level (Fig. 1). For HFO-TGI initiation, the recruitment maneuver was repeated, the cuff leak was placed, TGI ($FiO_2 = FiO_2$ of preceding CMV; flow = 50% of immediately preceding CMV minute ventilation) was added to HFO, and P_{aw} was titrated to the prespecified P_{tr} level (Fig. 1) [1]. During HFO/HFO-TGI, f and ΔP were to be maintained unchanged unless $PaCO_2$ and pHa could not be kept within ±20 mmHg of the preceding CMV $PaCO_2$ and >7.15, respectively. Within 55–60 min following HFO/HFO-TGI initiation, physiologic measurements were conducted (Fig. 1).

CMV periods following HFO/HFO-TGI

After 120 min of HFO/HFO-TGI, patients were returned to pre-HFO CMV. Within 55–60 min thereafter, physiologic measurements were repeated and the adapters/catheters system was removed (Fig. 1).

Mean esophageal pressure (P_{es})

In the last five patients, we measured P_{es} as an indicator of lung volume (ESM).

Statistical analysis

According to an a priori power analysis, 22 patients were required for a = 0.048 and power = 0.86. Physiological data were compared using repeated-measures analysis of variance (ANOVA), followed by the Tukey test.

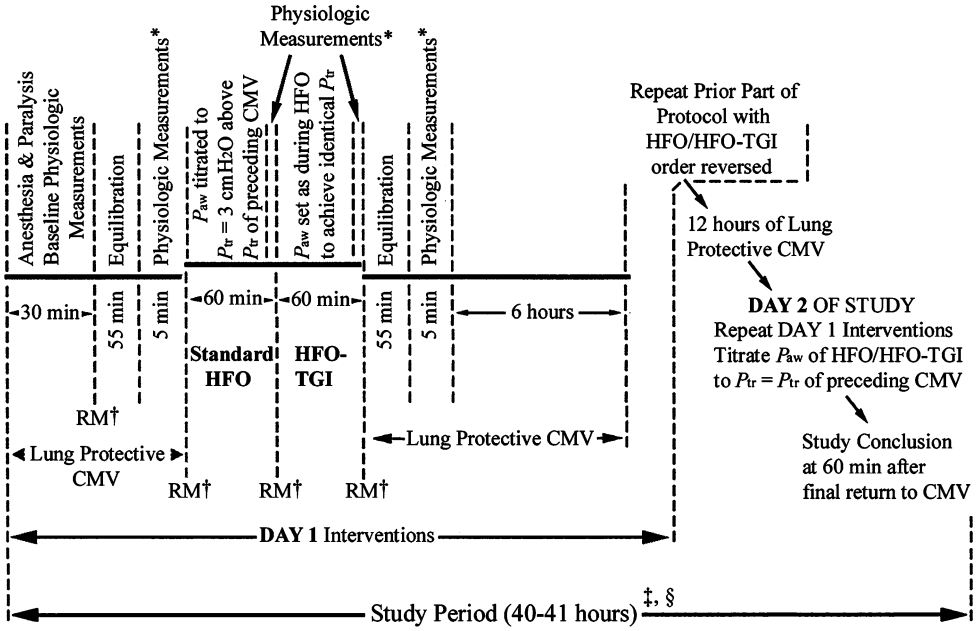

Fig. 1 Schematic representation of the study protocol. *CMV* conventional mechanical ventilation, *RM* recruitment maneuver, *HFO* high-frequency oscillation, *TGI* tracheal gas insufflation, P_{aw} mean airway pressure, P_{tr} mean tracheal pressure. * Comprised hemodynamics, gas exchange (arterial and central-venous blood gases), and respiratory mechanics during CMV, and hemodynamics and gas exchange during HFO/HFO-TGI. † Comprised application of continuous positive airway pressure of 45 cmH_2O for 40 s. ‡ For day 1, use of a P_{aw} that was either "high" (i.e., titrated to a P_{tr} that was 3 cmH_2O higher relative to the P_{tr} of the preceding CMV) or "low" (i.e., titrated to a P_{tr} equal to the P_{tr} of the preceding CMV) was randomized (www.randomizer.org); if day 1 P_{aw} was "high," day 2 P_{aw} was low, and vice versa; this was done to control for the possible effect of disease evolution on our measurements. § During each day, the order of standard HFO and HFO-TGI was initially randomized and then reversed during the "repeat protocol"; this was done to control for any potential influence of the first HFO/HFO-TGI sessions on gas-exchange results obtained during the immediately subsequent HFO-TGI/HFO sessions

Table 1 Patient characteristics and baseline ventilatory settings (volume-assist control mode with square-wave inspiratory flow)

Age (years)	56.3 ± 3.6
Sex (male/female)	17/5
Body mass index (kg/m^2)	25.8 ± 1.0
Simplified Acute Physiology Score II[a]	43.7 ± 2.1
Murray score[b]	3.1 ± 0.1
PaO_2/inspired O_2 fraction (mmHg)[b]	124.8 ± 10.4
Inspired O_2 fraction[b, c]	0.72 ± 0.03
$PaCO_2$ (mmHg)[b]	52.0 ± 3.1
Positive end-expiratory pressure (cmH_2O)[b]	13.4 ± 0.5
Tidal volume (L)/(mL/kg PBW)[b, d]	0.48 ± 0.01/6.3 ± 0.1
Plateau airway pressure (cmH_2O)[b]	32.6 ± 1.2
Mean airway pressure (cmH_2O)[b]	22.4 ± 0.6
Oxygenation index[b]	21.3 ± 2.3
Time from ALI/ARDS diagnosis (h)[e]	29.1 ± 3.1
Pulmonary ALI/ARDS, no./total no. (%)	17/22 (77.2)
Survival to hospital discharge, no./total no. (%)	12/22 (54.5)

Values are mean ± SEM unless otherwise specified. For males, PBW was calculated as 50 + [height(cm) − 152.4] × 0.91; for females as 45.5 + [height(cm) − 152.4] × 0.91

PBW predicted body weight, *ALI* acute lung injury, *ARDS* acute respiratory distress syndrome, *ID* inner diameter of tracheal tube (mm)

[a] Determined within 12 h prior to study enrollment

[b] Recorded/determined within 15–20 min after study enrollment

[c] On study enrollment, inspired O_2 fraction was reduced from 0.76 ± 0.03 to 0.72 ± 0.03 (see also Electronic Supplementary Material), which was maintained during study day 1 and then reduced to 0.71 ± 0.03 on study day 2

[d] Kept at ≤6.0 mL kg^{-1} PBW if plateau pressure exceeded 30 cmH_2O

[e] Refers to the time interval between establishment of ALI/ARDS diagnosis and study enrollment

Table 2 Ventilatory parameters and respiratory compliance during the study period

Ventilatory strategy	V_T (L)	RR/min[a]	PEEP[a] (cmH_2O)	*P*maxaw[a] (cmH_2O)	P^a_{aw} (cmH_2O)	PEEPtot[b] (cmH_2O)	P_2aw[b] (cmH_2O)
CMV pre-high	0.48 ± 0.01	27.5 ± 0.6	13.0 ± 0.4	47.4 ± 1.2	22.5 ± 0.5	15.3 ± 0.4	32.3 ± 0.8
HFO-high P_{aw}	NA	NA	NA	NA	31.9 ± 0.4*	NA	NA
HFO-TGI-high P_{aw}	NA	NA	NA	NA	31.0 ± 0.4*	NA	NA
CMV post-high	0.48 ± 0.01	27.4 ± 0.6	13.0 ± 0.4	46.8 ± 1.2	22.1 ± 0.5†	15.3 ± 0.4	31.8 ± 0.9
CMV pre-low	0.47 ± 0.01	28.1 ± 0.6	12.4 ± 0.4	47.2 ± 1.2	21.9 ± 0.5†	14.1 ± 0.3	31.6 ± 0.4
HFO-low P_{aw}	NA	NA	NA	NA	27.9 ± 0.4 *, †	NA	NA
HFO-TGI-low P_{aw}	NA	NA	NA	NA	26.2 ± 0.4 *, †	NA	NA
CMV post-low	0.47 ± 0.01	28.1 ± 0.6	12.4 ± 0.4	46.2 ± 1.2	21.6 ± 0.5 †, ‡	14.0 ± 0.4	31.0 ± 0.4

Ventilatory strategy	*C*rs (mL/cmH_2O)	*P*tr[c] (cmH_2O)	*P*maxtr[c] (cmH_2O)	*P*mintr[c] (cmH_2O)	*P*es[d] (cmH_2O)	ΔP[a] (cmH_2O)	TGI (L/min)
CMV pre-high	30.8 ± 1.8	23.0 ± 0.5	44.6 ± 1.2	13.8 ± 0.3	18.2 ± 0.6	NA	NA
HFO-high P_{aw}	NA	26.0 ± 0.5*	41.5 ± 1.2	18.2 ± 0.7*	17.5 ± 0.6	88.7 ± 1.3	NA
HFO-TGI-high P_{aw}	NA	26.0 ± 0.4*	39.2 ± 1.1*	19.5 ± 0.7*	20.8 ± 0.7	88.0 ± 1.2	6.7 ± 0.1
CMV post-high	33.0 ± 2.4	22.5 ± 0.5†	43.9 ± 1.2	13.6 ± 0.3†	18.2 ± 1.1	NA	NA
CMV pre-low	29.7 ± 1.8	22.5 ± 0.4†	44.4 ± 1.2#	12.8 ± 0.3†	17.7 ± 0.8	NA	NA
HFO-low P_{aw}	NA	22.0 ± 0.4†	36.5 ± 1.1*	14.7 ± 0.7†	14.9 ± 0.7#	87.3 ± 1.2	NA
HFO-TGI-low P_{aw}	NA	22.3 ± 0.5†	33.8 ± 1.2*, †	16.5 ± 0.6*, †	17.7 ± 0.7	88.3 ± 1.3	6.7 ± 0.1
CMV post-low	30.5 ± 1.9	22.0 ± 0.5†	43.3 ± 1.2‡	12.8 ± 0.3†, ¶	18.0 ± 1.4	NA	NA

Values are mean ± SEM

CMV conventional mechanical ventilation, *HFO* high-frequency oscillation, *TGI* tracheal gas insufflation, *CMV pre-/post-high* CMV preceding/following HFO-/HFO-TGI-high P_{aw}, *CMV pre-/post-low* CMV preceding/following HFO-/HFO-TGI-low P_{aw}, V_T tidal volume, *RR* respiratory rate of conventional ventilator, *Pmaxaw* peak airway pressure, *PEEP* positive end-expiratory pressure, *PEEPtot* total PEEP, *P_2aw* end-inspiratory plateau airway pressure, *Crs* respiratory system compliance, P_{aw} mean airway pressure, P_{tr} mean tracheal pressure, *Pmaxtr* maximal (peak) tracheal pressure, *Pmintr* minimal (or trough) tracheal pressure, *Pes* mean esophageal pressure, *ΔP* oscillatory pressure amplitude, *NA* not applicable

[a] Variable values were recorded as displayed by the ventilators over 3-min periods, which corresponded to time points of physiologic measurements (see also Fig. 1); recorded values were first averaged and then analyzed

[b] Variable values determined from averaged, computer-stored rapid airway occlusion data; end-expiratory/inspiratory airway occlusions were performed in duplicate during the first min of the 5-min-lasting physiologic measurements performed during CMV (see also Fig. 1)

[c] Variable values are averaged, computer-stored data collected over 3-min periods, which corresponded to time points of physiologic measurements (see also Fig. 1)

[d] Determined concurrently with P_{tr} in the last five patients (see also "Methods" and Electronic Supplementary Material). Oscillation frequency and bias flow were always kept at 3.5 Hz and 40 L/min, respectively

* $P < 0.05$ versus preceding CMV; † $P < 0.05$ versus both HFO-high P_{aw} and HFO-TGI-high P_{aw}; ‡ $P < 0.05$ versus both HFO-low P_{aw} and HFO-TGI-low P_{aw}; # $P < 0.05$ versus HFO-TGI-high P_{aw}; ¶ $P < 0.05$ versus HFO-TGI-low P_{aw}

Significance was set at $P < 0.05$. Data are reported as mean ± SEM.

Results

Twenty-two patients were enrolled within a 4-month period (Table 1; ESM). The effect of the catheters on the inspiratory resistance of the tracheal tube (mean increase: 41%) is detailed in the ESM.

Ventilatory variables

Data are presented in Table 2. A lower (by 1–2 cmH_2O) P_{aw} was required during HFO-TGI versus standard HFO to achieve the prespecified P_{tr} levels; the corresponding average peak tracheal pressure was also lower (by 2.3–2.7 cmH_2O), whereas the average minimal (trough) pressure was 1.3–1.8 cmH_2O higher, suggesting a TGI-induced PEEP effect [1, 2]; in five patients, P_{es} was 1.6–4.7 cmH_2O higher, indicating a TGI-induced increase in mean lung volume of ~68–139 mL (ESM). P_{tr} was ~4 cmH_2O higher during HFO/HFO-TGI-high P_{aw} versus HFO/HFO-TGI-low P_{aw}, because the reference P_{tr} of the preceding CMV (Fig. 1) exhibited a variation of ~1 cmH_2O.

Gas exchange

PaO_2/FiO_2 was higher during HFO-TGI-high P_{aw} versus HFO-high P_{aw} (281.6 ± 15.1 versus 199.0 ± 15.0 mmHg; mean increase: 42%; $P < 0.001$), and during HFO-TGI-low P_{aw} versus HFO-low P_{aw} (222.8 ± 14.6 versus 141.3 ± 8.7 mmHg; mean increase: 58%; $P < 0.001$) (Fig. 2). $PaCO_2$ was lower during HFO-TGI-high P_{aw} versus HFO-high P_{aw} (45.3 ± 1.6 versus 53.7 ± 1.9 mmHg; mean decrease: 16%; $P = 0.037$), and exhibited a trend toward

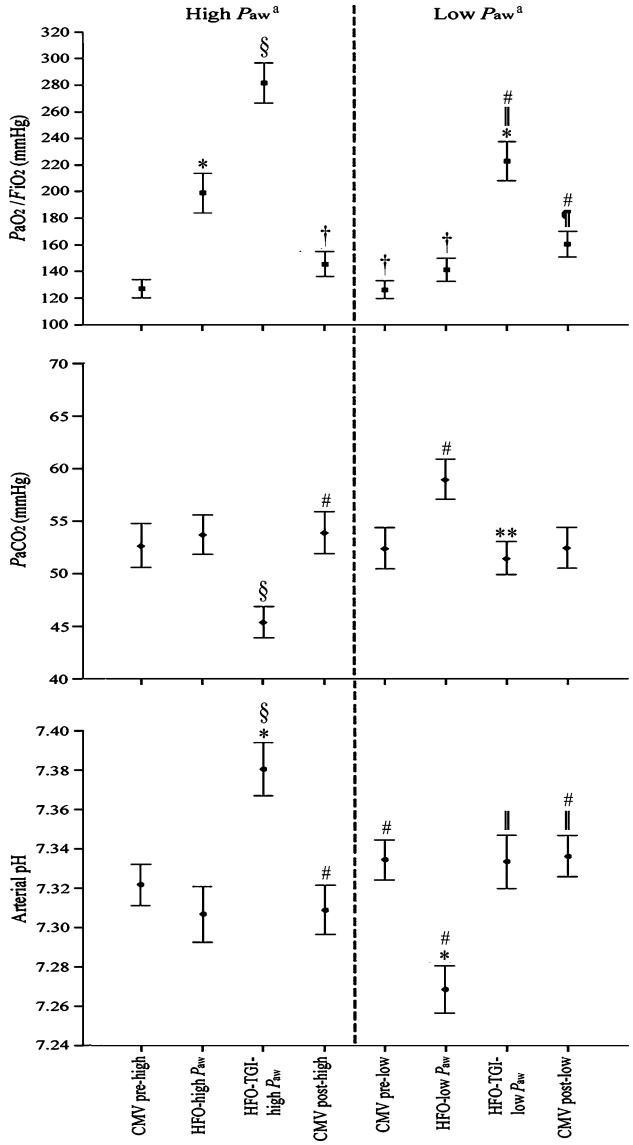

Fig. 2 Results on gas exchange. *FiO_2* inspired O_2 fraction, *CMV* conventional mechanical ventilation, *HFO* high-frequency oscillation, *TGI* tracheal gas insufflation, *P_{aw}* mean airway pressure, *CMV pre-/post-high* CMV preceding/following HFO-/HFO-TGI-high P_{aw}, *CMV pre-/post-low* CMV preceding/following HFO-/HFO-TGI-low P_{aw}. *Filled squares diamonds*, and *circles* represent mean value, and *bars* represent standard error of the mean. [a] Refers to the titration of P_{aw} of HFO/HFO-TGI to either a higher (high P_{aw}) or lower (low P_{aw}) level of mean tracheal pressure (see also "Methods" and Fig. 1). $^{*}P < 0.05$ versus preceding CMV. $^{\dagger}P < 0.05$ versus both HFO-high P_{aw} and HFO-TGI-high P_{aw}. $^{\S}P < 0.05$ versus HFO-high P_{aw}. $^{\#}P < 0.05$ versus HFO-TGI-high P_{aw}. $^{\|}P < 0.05$ versus HFO-low P_{aw}. $^{\P}P < 0.05$ versus HFO-TGI-low P_{aw}. $^{**}P = 0.09$ versus HFO-low P_{aw}

a lower value during HFO-TGI-low P_{aw} versus HFO-low P_{aw} (51.4 ± 1.7 versus 60.0 ± 1.9 mmHg; mean decrease: 14%; $P = 0.09$). At both P_{tr} levels, pHa was higher during HFO-TGI versus HFO ($P < 0.001$) (Fig. 2). In five patients, the increase in PaO_2/FiO_2 and decrease in $PaCO_2$ from HFO to HFO-TGI correlated with the estimated concomitant increase in mean lung volume ($r^2 = 0.58$–0.71, $P \leq 0.011$; ESM, Fig. E5).

Hemodynamics and CO_2 elimination

Ventilatory technique did not affect hemodynamics; shunt fraction was lowest during HFO-TGI-high P_{aw} (Table 3). During CMV and HFO/HFO-TGI, determinants of metabolic rate (e.g., temperature), medication (e.g., vasopressors/inotropes), oxygen consumption, respiratory quotient, cardiac index, and central-venous CO_2 concentration remained stable (Table 3; ESM), indicating stable CO_2 production and delivery rate to the lungs. Consequently, changes in $PaCO_2$ reflected changes in CO_2 elimination efficiency.

Discussion

HFO-TGI versus HFO resulted in higher PaO_2/FiO_2 (at both P_{tr} levels) and lower $PaCO_2$ (at the higher P_{tr} level). HFO-TGI-induced, proportional blood-gas improvements were comparable between the employed P_{tr} levels. These results imply enhanced lung recruitment and/or gas transport, and alveolar ventilation during HFO-TGI [1, 2, 5].

TGI impedes the opposite-directed expiratory flow, thus exerting a PEEP effect [3]; this explains the higher trough tracheal pressure, despite a lower P_{aw} setting (Table 2). TGI-induced PEEP should increase expiratory lung volume and driving (i.e., alveolar) pressure, with consequent higher expiratory flow and less expiratory airway narrowing or closure [6, 7]. In five patients, the estimated TGI-induced increases in mean lung volume were explanatory of 58–71% of the TGI-induced improvements in gas exchange at both P_{tr} levels. This suggests that lung recruitment is a major mechanism of TGI action. An increase in lung volume augments the axial wall tension of collapsed airways and facilitates their reopening [8], and decreases the diffusional resistance to gas exchange [1].

Preceding imaging studies [9, 10] showed that, at $f \leq 6$ Hz, there is preferential distribution of ventilation in dependent and basal lung regions. Gas streams created by oscillatory flows tend to travel with minimal directional change, favoring lung base filling, since the branching angles of basal airways are less acute [11]. As steady flows behave similarly [12], the addition of TGI to HFO should further enhance lung base aeration, and ventilation–perfusion matching, since the vertical perfusion gradient is maintained during HFO [13]. Basal lung aeration is augmented as HFO tidal volume (V_T) and corresponding pressure swings increase [9]. Our f and ΔP settings correspond to V_T of ~200 mL [14]. The average,

Table 3 Hemodynamics, central-venous oxygen saturation, and shunt fraction

Ventilatory strategy	Heart rate (beats/min)	MAP (mmHg)	CVP (mmHg)	Cardiac index (L min^{-1} m^{-2})	$ScvO_2$ (%)	Shunt fraction	VO_2I (L min^{-1} m^{-2})
CMV pre-high	101 ± 3	83 ± 2	15 ± 1	4.1 ± 0.2	74.3 ± 1.3	0.37 ± 0.02	0.14 ± 0.01
HFO-high P_{aw}	100 ± 3	87 ± 2	15 ± 1	4.3 ± 0.2	78.6 ± 1.8	0.34 ± 0.01	0.13 ± 0.01
HFO-TGI-high P_{aw}	102 ± 4	85 ± 2	15 ± 1	4.3 ± 0.2	78.4 ± 1.9	0.28 ± 0.02*	0.14 ± 0.01
CMV post-high	102 ± 4	82 ± 2	15 ± 1	4.5 ± 0.2	75.7 ± 1.5	0.36 ± 0.02[#]	0.14 ± 0.01
CMV pre-low	102 ± 3	82 ± 2	14 ± 1	4.1 ± 0.2	72.9 ± 1.1	0.34 ± 0.02	0.14 ± 0.01
HFO-low P_{aw}	98 ± 4	89 ± 2	15 ± 1	4.4 ± 0.2	78.7 ± 1.7	0.38 ± 0.02[#]	0.13 ± 0.01
HFO-TGI-low P_{aw}	101 ± 4	87 ± 3	15 ± 1	4.4 ± 0.2	79.8 ± 1.8*	0.32 ± 0.02	0.13 ± 0.01
CMV post-low	101 ± 3	83 ± 2	14 ± 1	4.1 ± 0.2	72.9 ± 1.1[¶]	0.31 ± 0.02	0.14 ± 0.01

Values are mean ± SEM. For the computation of shunt fraction, we used blood-gas values obtained from central-venous blood
CMV conventional mechanical ventilation, *HFO* high-frequency oscillation, *TGI* tracheal gas insufflation, P_{aw} mean airway pressure, *CMV pre-/post-high* CMV preceding/following HFO-/HFO-TGI-high P_{aw}, *CMV pre-/post-low* CMV preceding/following HFO-/HFO-TGI-low P_{aw}, *MAP* mean arterial pressure, *CVP* central venous pressure, *CI* cardiac index, VO_2I O_2 consumption index, $ScvO_2$ central-venous oxygen saturation
* $P < 0.05$ versus preceding CMV; [#] $P < 0.05$ versus HFO-TGI-high P_{aw}; [¶] $P < 0.05$ versus HFO-TGI-low P_{aw}

TGI-induced increase in V_T was ~11 mL (~5%) (see ESM, Appendix II). TGI may have also acted as an "additional, high-velocity bias flow bypassing the resistance of the tracheal tube and augmenting the effect of a relatively large V_T on CO_2 elimination" [15].

The calculated mean molecule velocity of the TGI gas at the tip of the TGI catheter was 142.7 m/s, as opposed to an HFO mean inspiratory velocity of ~35.3 m/s at the tip of a tracheal tube with ID of 8.5 mm (ESM, Appendix II). During inspiration, the TGI jet stream may increase the difference between inspiratory and expiratory velocity profiles, and enhance convective gas exchange [16]. The high jet stream velocity implies short dead-space transit time and contribution to direct alveolar ventilation [17]. In the convection–diffusion zones, TGI flow may augment the asymmetry in inspiratory velocity profiles, promote the radial mixing and gas exchange with the expired alveolar gas, and enhance the airway bifurcation phenomenon [17]. The relative importance of the mechanisms of TGI action during HFO warrants further study.

Limitations

Limitations of routine, long-term TGI include absence of commercially available equipment, and possible tracheal mucosal damage, retention and inspissation of secretions, hemodynamic compromise, pneumothorax, and gas embolism [1, 3]. Humidification of TGI gas and cuff leak during HFO-TGI are essential [18]. We excluded patients with 7.5–8.0-mm ID orotracheal tubes, because the two catheters would raise inspiratory tube resistance to >20 cmH_2O/L/s (ESM). For long-term TGI, we employ just one catheter, causing an increase in inspiratory tube resistance of <20%, and administer humidified TGI gas [18; ESM].

Clinical implications

When added to CMV, TGI improves CO_2 clearance, increases total PEEP, and enables reduction of V_T and driving pressures [19, 20]. This may facilitate lung protection in ARDS patients with poor tolerance to hypercapnia due to brain edema, or concurrent metabolic acidosis [19, 20]. In such clinical scenarios, HFO-TGI may prove superior to standard HFO.

Targeting gas-exchange improvements through increases in P_{aw} or V_T may accentuate ventilator-associated lung injury. However, HFO-TGI-low P_{aw} versus HFO-high P_{aw} resulted in similar gas exchange (Fig. 2) at lower ventilator-applied lung distending pressure(s), i.e., P_{aw} and P_{tr} (Table 2).

Conclusion

At equal P_{tr} level, HFO-TGI results in superior gas exchange compared with HFO.

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