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Original Article

The effect of high-flow oxygen via tracheostomy on respiratory pattern and diaphragmatic function in patients with prolonged mechanical ventilation: A randomized, physiological, crossover study

Elena Lytra[1,2], Stelios Kokkoris[1], Ioannis Poularas[1], Dimitrios Filippiadis[3], Demosthenes Cokkinos[2], Dimitrios Exarhos[2], Spyros Zakynthinos[1], Christina Routsi[1,*]

[1] 1st Department of Intensive Care, Medical School, National and Kapodistrian University of Athens, Evangelismos Hospital, Athens, Greece
[2] Radiology Department, Evangelismos Hospital, Athens, Greece
[3] 2nd Radiology Department, Medical School, National and Kapodistrian University of Athens, Attikon Hospital, Athens, Greece

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ABSTRACT

Background: Compared to conventional oxygen devices, high-flow oxygen treatment (HFOT) through the nasal cannulae has demonstrated clinical benefits. Limited data exist on whether such effects are also present in HFOT through tracheostomy. Hence, we aimed to examine the short-term effects of HFOT through tracheostomy on diaphragmatic function and respiratory parameters in tracheostomized patients on prolonged mechanical ventilation.

Methods: A randomized, crossover, physiological study was conducted in our ICU between December 2020 and April 2021, in patients with tracheostomy and prolonged mechanical ventilation. The patients underwent a 30-min spontaneous breathing trial (SBT) and received oxygen either via T-piece or by HFOT through tracheostomy, followed by a washout period of 15-min breathing through the T-piece and receipt of 30-min oxygen with the other modality in a randomized crossover manner. At the start and end of each session, blood gasses, breathing frequency (f), and tidal volume (V_T) via a Wright's spirometer were measured, along with diaphragm ultrasonography including diaphragm excursion and diaphragmatic thickening fraction, which expressed the inspiratory muscle effort.

Results: Eleven patients were enrolled in whom 19 sessions were uneventfully completed; eight patients were studied twice on two different days with alternate sessions; and three patients were studied once. Patients were randomly assigned to start the SBT with a T-piece (n=10 sessions) or with HFOT (n=9 sessions). With HFOT, V_T and minute ventilation (V_E) significantly increased during SBT (from [465±119] mL to [549±134] mL, P <0.001 and from [12.4±4.3] L/min to [13.1±4.2] L/min, P <0.05, respectively), but they did not change significantly during SBT with T-piece (from [495±132] mL to [461±123] mL and from [12.8±4.4] mL to [12.0±4.4] mL, respectively); f/V_T decreased during HFOT (from [64±31] breaths/(min•L) to [49±24] breaths/(min•L), P <0.001), but it did not change significantly during SBT with T-piece (from [59±28] breaths/(min•L) to [64±33] breaths/(min•L)); partial pressure of arterial oxygen increased during HFOT (from [99±39] mmHg to [132±48] mmHg, P <0.001), but it decreased during SBT with T-piece (from [124±50] mmHg to [83±22] mmHg, P <0.01). In addition, with HFOT, diaphragmatic excursion increased (from [12.9±3.3] mm to [15.7±4.4] mm, P <0.001), but it did not change significantly during SBT with T-piece (from [13.4±3.3] mm to [13.6±3.3] mm). The diaphragmatic thickening fraction did not change during SBT either with T-piece or with HFOT.

Conclusion: In patients with prolonged mechanical ventilation, HFOT through tracheostomy compared with T-piece improves ventilation, pattern of breathing, and oxygenation without increasing the inspiratory muscle effort.

Trial Registration: Clinicaltrials.gov ldentifer: NCT04758910.

* Corresponding author: Christina Routsi, Department of Intensive Care, School of Medicine, National and Kapodistrian University of Athens, Evangelismos Hospital 45-47, Ipsilantou Street, Athens 10676, Greece.
E-mail address: chroutsi@med.uoa.gr (C. Routsi).

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Introduction

High-flow oxygen treatment (HFOT) is increasingly being used in everyday clinical practice in critically ill patients with hypoxemic respiratory failure. This is a respiratory support system capable of delivering a heated and humidified mixture of air and oxygen with a fraction of inspired oxygen (FiO_2) up to 1.0 at a maximum flow rate of 60 L/min.[1] HFOT is delivered via the nasal route in non-intubated patients with hypoxic respiratory failure and has emerged as an efficient technique to improve gas exchange and respiratory variables via specific mechanisms of action including, among others, generation of increased mean airway pressure and washout of the anatomical dead space.[1–5] In addition, compared to standard oxygen therapy, HFOT improves oxygenation and patient comfort after extubation and likely also prevents post-extubation respiratory failure.[6–8]

To date, little is known about whether HFOT delivered through tracheostomy offers similar beneficial effects as when delivered via the nasal route, because tracheostomy bypasses the upper-airway anatomical dead space which the nasal HFOT washes out. Thus far, published studies suggest that HFOT via tracheostomy lacks some of the physiological effects that have been demonstrated with the nasal route[9,10]; however, compared to conventional T-piece, HFOT via tracheostomy seems to improve oxygenation[11] and facilitate the ventilator weaning process.[12] These effects were only observed with 50–60 L/min of HFOT and could partially be due to inspiratory muscle unloading and breathing pattern improvement, both associated with potential respiratory assistance offered by the high-flow mixture of air and oxygen applied to the upper opening of the tracheostomy. Indeed, 50 L/min of HFOT could provide small degrees (1–2 cmH_2O) of positive airway expiratory pressure.[10] Nevertheless, because of limited existing evidence, HFOT via endotracheal tubes is not included in the official recommendations for HFOT as a respiratory support strategy.[13]

Critically ill patients with prolonged weaning from mechanical ventilation (MV) frequently require a tracheostomy; then, they usually undergo spontaneous breathing trials (SBTs) wherein oxygen is received via a T-piece or tracheostomy mask. In addition, in the context of intensive care unit (ICU)-acquired diaphragm dysfunction,[14] diaphragmatic weakness frequently contributes to weaning failure in patients with prolonged ventilator dependence[15,16] Accordingly, we undertook a physiological study aimed to assess the short-term effects of 60 L/min HFOT applied via tracheostomy on the diaphragmatic function and respiratory parameters in critically ill patients with prolonged weaning from MV. Moreover, diaphragm ultrasonography was used to assess the diaphragm muscle function. We hypothesized that 60 L/min HFOT compared to conventional oxygen therapy could improve the pattern of breathing (i.e., by decreasing the breathing frequency (f) and/or increasing the tidal volume [V_T]) and blood oxygenation without increasing the diaphragmatic muscle effort.

Methods

Study subjects

Consecutive patients admitted to our ICU between December 2020 and April 2021 requiring MV with a tracheostomy in place, owing to prolonged weaning according to the WIND study criteria,[17] i.e., patients not weaned after more than 7 days from the first separation attempt, were recruited. The enrolment criterion was the primary physicians' consideration that their patients were potentially able to succeed in an SBT lasting at least 75 min, according to previously established criteria.[6,17] The exclusion criteria were: (1) age <18 years, (2) hemodynamic instability, (3) diagnosis of neuromuscular disease, (4) pneumothorax or pleural effusion, and (5) diaphragm paresis or dysfunction prior to ICU admission. Informed consent was given by each patient or the patient's next of kin. The study protocol was approved by the Hospital Ethics Committee (reference number: 771/2019). This study was registered in ClinicalTrials.gov (NCT04758910).

Protocol

Patients were initially placed in a semirecumbent position and were ventilated in the assist-control mode with a Servo-i ventilator (Maquet, Solna, Sweden). Immediately after disconnection from the ventilator, patients underwent SBTs. A randomized, crossover design was used (Figure 1). Using a table of random numbers, sessions of SBTs through a tracheostomy were randomized into two groups. In the sessions of SBTs of the first group, patients initially underwent a 30-min SBT receiving oxygen via a T-piece followed by a washout period of 15-min breathing through the same T-piece and a 30-min trial receiving oxygen with 60 L/min of high flow. In the sessions of SBTs of the second group, patients initially underwent a 30-min trial receiving oxygen with 60 L/min of high flow followed by a 15-min washout period breathing oxygen through a T-piece and a 30-min SBT receiving oxygen with the same T-piece. A 15-minute washout period between the two SBTs of each session was deemed adequate to avoid the carryover effect. During each session, patients underwent four assessments, at the start and end of each SBT. Every assessment consisted of respiratory and hemodynamic evaluation along with right diaphragm ultrasonography. If the patient met the a priori-defined criteria of weaning failure before the end of the SBT, the assessment was made during the last minutes of the SBT. The study protocol lasted for 75 min unless the patient met the criteria of weaning failure at an earlier point in time. Patients who met these criteria returned to MV. Patients who were initially randomized to attempt a session of SBTs in the first group were evaluated the next day for eligibility to attempt a session of SBTs in the second group and vice versa.

FiO_2 with both modalities, i.e., T-piece and high flow, was initially adjusted to maintain peripheral oxygen saturation (SpO_2) between 92% and 96% and remained stable throughout each session. No intervention was made in the tracheostomy tube cuff. Conventional oxygen was administered through a T-piece circuit connected to a standard air/oxygen mixer. High-flow oxygen was delivered via tracheostomy with a gas flow rate of 60 L/min through a heated humidifier (AIRVO™ 2 system, Fisher & Paykel Healthcare, Auckland, New Zealand) with a specifically designed interface for the tracheostomy tube (OPT870, Fisher and Paykel Healthcare, Auckland, New Zealand). The temperature of the heated humidifier was set to 37 °C.

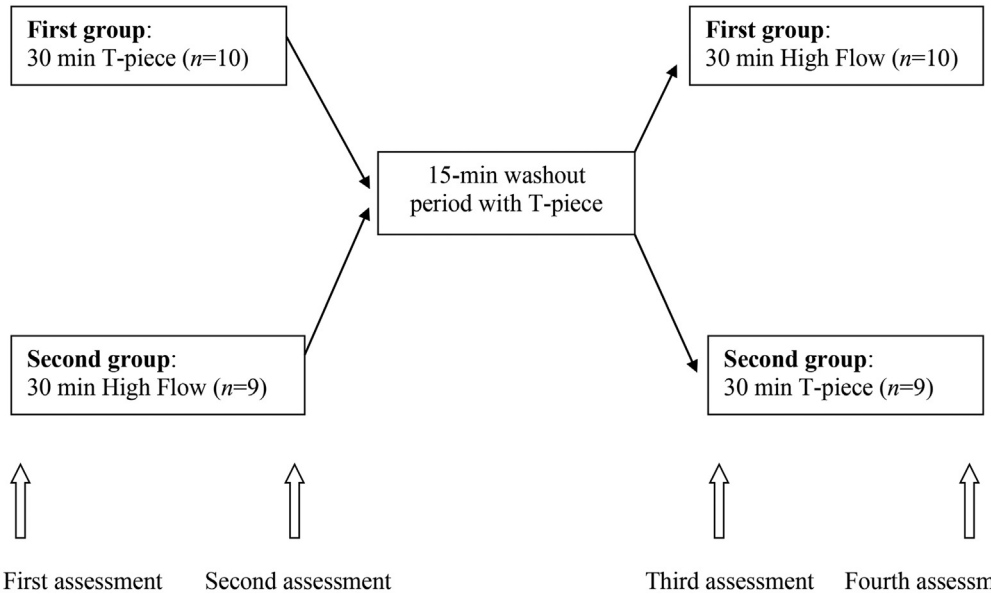

Figure 1. Study protocol. The study was undertaken according to a randomized, crossover design. After the first assessment, patients underwent a session of a 30-min spontaneous breathing trial receiving oxygen with either a T-piece or 60 L/min of high-flow through a tracheostomy, followed by a washout period of 15 min breathing spontaneously through a T-piece and a 30-min spontaneous breathing trial receiving oxygen with the other modality. At the start and end of each spontaneous breathing trial, patients underwent an assessment, which consisted of respiratory and hemodynamic evaluation along with right diaphragm ultrasonography.

Measurements

Maximum inspiratory pressure

During a temporary disconnection from the ventilator, maximum inspiratory pressure (MIP) was measured as the maximal negative excursion in airway pressure during a 20-s occlusion using a one-way valve.[18]

Hemodynamic and gas exchange parameters

Invasive systemic arterial blood pressure, heart rate, and pulsed oximetry were continuously monitored. Partial pressures of oxygen (PO_2) and carbon dioxide (PCO_2), pH, HCO_3^-, lactate, and hemoglobin oxygen saturation (SO_2) were determined from blood samples drawn from arterial and central venous lines and were immediately analyzed.

Ventilation parameters

At the start (i.e., at the second minute) and at the end of each SBT, during a temporary disconnection from the apparatus, minute ventilation (V_E) was measured with a calibrated handheld Wright's spirometer (nSpire Health Ltd, Essex, UK) through the tracheostomy tube, while the patient breathed room air spontaneously for 1 min. The average V_T was obtained by dividing V_E by f. The ratio of f to V_T, expressing the breathing pattern, was then calculated.[19]

Diaphragm ultrasonography

Diaphragm ultrasonography included excursion of the right diaphragmatic dome and thickness of the diaphragmatic zone of apposition at end-inspiration and end-expiration. The diaphragmatic thickening fraction was calculated as the difference between end-inspiratory and end-expiratory thickness divided by end-expiratory thickness and is currently considered to express diaphragmatic muscle activity/effort.[20,21] Ultrasound measurements were performed by two trained operators (E. L. and I. P.) on at least three separate breaths, and the mean measurements were reported.[20,21] A LogiQ7 (GE Healthcare, Little Chalfont, UK) equipped with a high-resolution 10-MHz linear probe and a 7.5-MHz convex phased-array probe was used.

Endpoints

The primary outcome was the breathing pattern (f/V_T). Secondary outcomes included the diaphragmatic excursion, diaphragmatic thickening fraction, and arterial PO_2.

Statistical analysis

The minimum sample size was calculated on the basis of 90% power and a two-sided 0.05 significance level (G*Power 3.0.10). The sample size capable of detecting a 10% chance of f/V_T with HFOT compared to conventional oxygen therapy via T-piece was estimated using the standard deviations obtained from our previous study.[22] The critical sample size was estimated to be 14 sessions (Figure 1). Values are presented as mean±standard deviation after testing for normal distribution (Kolmogorov–Smirnov test), and a parametric test (paired *t*-test) was used. Any correction for multiple comparisons was not applied. Because differences are not normally distributed, relationships between them were determined by the nonparametric Spearman's rank correlation coefficient (R_s). A two-tailed *P*-value of <0.05 was considered to indicate statistically significant differences.

Results

In total, 11 patients (6 male) were enrolled, of whom 19 sessions were completed uneventfully; 8 patients were studied

twice on two different days with alternate sessions, and the remaining 3 patients were studied only once. The baseline demographics and patient characteristics are detailed in Table 1. Ten sessions of SBTs were assigned to the first group and nine sessions of SBTs were assigned to the second group (Figure 1).

Study entry and post-washout

There was no significant difference in breathing pattern, arterial and central venous blood gasses, hemodynamic variables, and diaphragm ultrasonography parameters between the start of the T-piece and HFOT (Table 2). Therefore, no carryover effect on the measured parameters was observed between the entry to the first period of the study (Figure 1, first assessment) and the end of the washout period (Figure 1, third assessment), i.e., entry to the second period of the study.

Breathing pattern, gas exchange, hemodynamics, and diaphragm ultrasonography

Respiratory and hemodynamic variables along with diaphragm ultrasonography during SBTs with each modality (i.e., T-piece or HFOT) are summarized in Table 2. V_T, V_E, arterial, and central venous PO_2, diaphragmatic excursion, and diaphragmatic thickness at expiration increased, whereas f and f/V_T ratio decreased after SBTs with HFOT compared with T-piece. Diaphragmatic thickening fractions, as well as hemodynamic variables, were not different between SBTs with T-piece and HFOT.

The change of V_T after SBTs with both modalities was positively related to the change of diaphragmatic excursion (R_s=0.602,95% confidence interval [CI]: 0.336 to 0.779; P = 0.000) (Figure 2A) and inversely related to the change of f. (R_s=−0.463, 95% CI=−0.689 to −0.153; P=0.004)

Table 1
Characteristics of the studied patients.

Patient No.	Age (years)	Sex	SOFA score on ICU admission	Admission diagnosis	MIP	MV days	SBT outcome	ICU outcome
1	68	Female	9	Pneumonia, thyrotoxicosis	−30	23	Successful	Dead
2	35	Male	7	Encephalitis	−40	35	Successful	Alive
3	71	Female	9	Aortic dissection	−25	41	Successful	Alive
4	20	Female	10	Systemic lupus erythematosus, epilepsy	−45	24	Successful	Alive
5	70	Female	9	Pulmonary embolism	−50	50	Successful	Alive
6	59	Male	15	Chronic renal failure, cardiac tamponade	−30	40	Successful	Dead
7	58	Male	10	Stroke, myocardial ischemia	−28	39	Successful	Dead
8	79	Male	7	COPD	−30	21	Successful	Alive
9	74	Female	14	Aortic dissection	−27	62	Successful	Alive
10	72	Male	13	Intrabdominal sepsis	−30	39	Successful	Dead
11	75	Male	9	CABG	−28	46	Successful	Alive

CABG: Coronary artery bypass graft; COPD: Chronic obstructive pulmonary disease; ICU: Intensive care unit; MIP: Maximum inspiratory pressure; MV: Mechanical ventilation; SBT: Spontaneous breathing trial; SOFA: Sequential organ failure assessment.

Table 2
Respiratory and hemodynamic variables along with right diaphragm ultrasonography of patients at the start and end of the SBT with each modality (i.e., T-piece or HFOT).

Variables	Start of T-piece	End of T-piece	Start of HFOT	End of HFOT
V_T (mL)	495±132	461±123	465±119	549±134$^{‡, ¶}$
f (breaths/min)	27±8	27±8	27±9	24±7$^{*, ||}$
V_E (L/min)	12.8 ± 4.4	12.0 ± 4.4	12.4 ± 4.3	13.1 ± 4.2§
f/V_T (breaths/min/L)	59±28	64±33	64±31	49±24$^{‡, ||}$
FiO_2	0.51±0.05	0.51±0.05	0.51 ± 0.05	0.51 ± 0.05
PaO_2 (mmHg)	124±50	83±22†	99±39	132±48$^{*, ¶}$
SaO_2 (%)	97±3	96±3†	96±3	98±3$^{*, ||}$
$PaCO_2$ (mmHg)	38±7	36±7*	37±7	37±7
pH	7.43±0.05	7.44±0.04*	7.43±0.04	7.44±0.05
HCO_3 (mmol/L)	24.6 ± 2.2	24.6 ± 2.3	24.5 ± 2.1	24.8 ± 1.9
Lactate (mmol/L)	1.3 ± 0.5	1.3 ± 0.5	1.3 ± 0.5	1.1 ± 0.5†
PvO_2 (mmHg)	41±6	38±6‡	39±4	42±8$^{*, ||}$
SvO_2 (%)	71±9	66±10†	68±9	73±11$^{*, ||}$
$PvCO_2$ (mmHg)	42±6	41±5	42±5	42±5
Heart rate (beats/min)	85±15	84±16	83±17	84±14
Systolic blood pressure (mmHg)	138±18	134±20	136±20	137±19
Diastolic blood pressure (mmHg)	63±14	60±10	62±11	63±13
Diaphragmatic excursion (mm)	13.4 ± 3.3	13.6 ± 3.3	12.9 ± 3.3	15.7 ± 4.4$^{‡, ¶}$
Diaphragmatic thickness at inspiration (mm)	2.98±0.76	3.03±0.89	2.85±0.78	3.26±0.86‡
Diaphragmatic thickness at expiration (mm)	2.63±0.77	2.68±0.84	2.51±0.78	2.91±0.89$^{‡, §}$
Diaphragmatic thickening fraction (%)	14.5 ± 6.1	14.4 ± 6.3	15.7 ± 7.7	13.3 ± 5.9

Data are presented as mean±standard deviations.
P-values were detected by the paired *t*-test.
$^{*, †, ‡}P < 0.05$, 0.01, and 0.001, respectively, *vs.* start of the same modality.
$^{§, ||, ¶}P < 0.05$, 0.01, and 0.001, respectively, *vs.* end of T-piece.
f: Breathing frequency; FiO_2: Fraction of inspired oxygen; HFOT: High-flow oxygen treatment; $PaCO_2$: Partial pressure of arterial carbon dioxide; PaO_2: Partial pressure of arterial oxygen; $PvCO_2$: Partial pressure of central venous carbon dioxide; PvO_2: Partial pressure of central venous oxygen; SaO_2: Oxygen saturation of arterial blood; SBT: Spontaneous breathing trial; SvO_2: Oxygen saturation of central venous blood; V_E: Minute ventilation; V_T: Tidal volume.

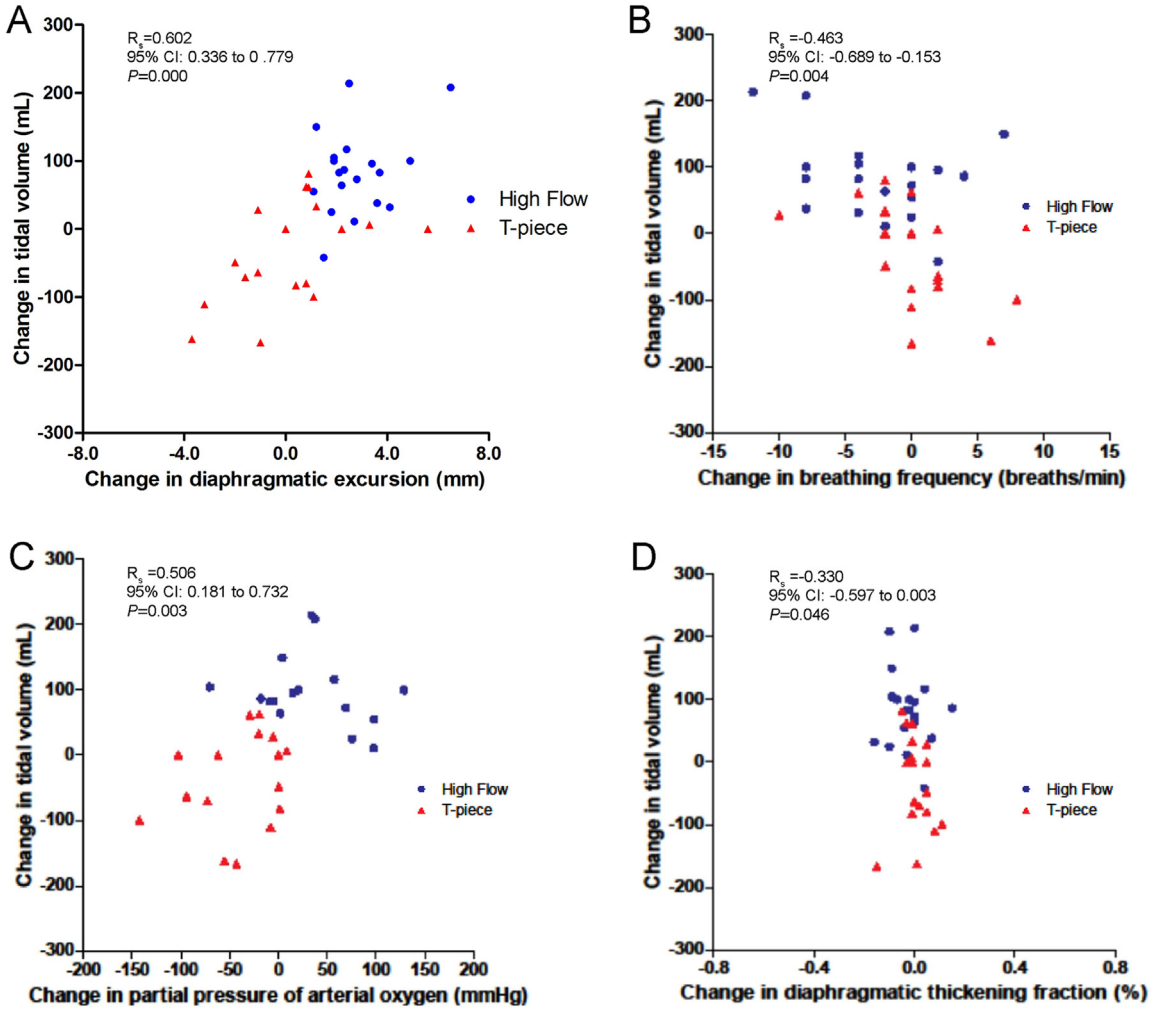

Figure 2. Relationship between the change in V_T with both modalities (i.e., high flow and T-piece). A: The change of diaphragmatic excursion (R_s=0.602, 95% CI: 0.336 to 0.779, *P*=0.000). B: The change of breathing frequency (R_s=−0.463, 95% CI: −0.689 to −0.153, *P*=0.004). C: The change of PaO_2 (R_s=0.506, 95% CI: 0.181 to 0.732, *P*=0.003). D: The change of diaphragmatic thickening fraction (R_s=−0.330, 95% CI: −0.597 to 0.003, *P*=0.046).
CI: Confidence interval; R_s: Spearman's rank correlation coefficient; PaO_2: Partial pressure of arterial oxygen; V_T: Tidal volume.

(Figure 2B). The change of V_T after SBTs with both modalities was also positively related to the change of arterial PO_2 (R_s=0.506, 95% CI: 0.181 to 0.732; *P*=0.003) (Figure 2C), and inversely but weakly related to the change of diaphragmatic thickening fraction (R_s=−0.330, 95% CI: −0.597 to 0.003; *P*=0.046) (Figure 2D).

Discussion

The main findings of this randomized, crossover, unblinded, physiological trial examining the short-term effects of HFOT on diaphragmatic function and hemodynamic and respiratory parameters in critically ill, tracheostomized patients with prolonged weaning from MV were that after a 30-min SBT receiving HFOT at the rate of 60 L/min compared with those receiving oxygen by T-piece: (1) V_T, V_E, arterial PO_2, and diaphragmatic excursion increased, whereas f and f/V_T ratio decreased; and (2) diaphragmatic thickening fraction was not different, despite V_T increase with high flow. Moreover, the change of V_T after SBTs with both modalities was positively related to the change of diaphragmatic excursion and the change of arterial PO_2, whereas it was inversely related to the change of f and the change of diaphragmatic thickening fraction.

The increase in V_T along with the increase in diaphragmatic excursion demonstrated in the present study (Figure 2A) is consistent with the earlier knowledge that diaphragm excursion, assessed by ultrasonography, is linearly and positively related to inspired lung volume.[23] An increment in V_T by HFOT at 50–60 L/min through a nasal cannula has already been shown both in post-cardiac surgical[24] and chronic obstructive pulmonary disease (COPD)[25] patients, as well as in healthy volunteers.[26] Volume was assessed by electrical impedance tomography,[24,25,27] and the V_T increase was positively related to the intensity of high flow.[27] On the contrary, no significant change in V_T measured by chest plethysmography was observed in non-intubated patients with acute respiratory failure[3] or in COPD patients recovering from an exacerbation[26] during HFOT *vs.* low-flow oxygen mask. However, both of these studies[3,26] applied HFOT at 40 L/min, possibly suggesting that the difference in the intensity of set flow compared with the above-mentioned studies[24,25,27] might have contributed to the different findings.

In the present study, V_T increase during HFOT with a concomitant decrease in respiratory frequency resulted in f/V_T decrease. Although a reduction in respiratory frequency has been reported, mainly during HFOT through the nasal route,[3,25,26] the results of studies using HFOT through a tracheostomy tube are varied. In contrast with our findings, Stripoli et al.[9] and Lersritwimanmaen et al.[28] did not report a significant difference in respiratory frequency during HFOT compared to conventional oxygen via T-piece in tracheostomized patients. In accordance with our results, Natalini et al.[10] reported that HFOT led to a slight reduction in respiratory frequency in tracheostomized patients, mainly in those with higher respiratory frequency during standard oxygen. All these studies[9,10,28] applied HFOT at 50 L/min, while our patients received HFOT at 60 L/min. Multifactorial etiology, including methodological issues and an underlying complex patient pathophysiology, might have contributed to the different findings.

Despite the widespread use of HFOT in critically ill patients, there is little information in the literature about the effect of HFOT on diaphragmatic function assessed by ultrasonography. Indeed, the effect of HFOT on diaphragmatic function has been rarely investigated even in patients with HFOT via the nasal route.[29–31] In the study by Longini et al.[29] in patients recovering from hypercapnic acute respiratory failure, the application of HFOT at 50 L/min after noninvasive ventilation interruption did not change diaphragmatic displacement, regardless of the modality of oxygen administration. On the contrary, the application of HFOT with progressively increasing intensity of set flow increased diaphragmatic excursion and lung volume, wherein the latter was measured by electrical impedance tomography in a study published only in abstract form.[31]

The diaphragmatic thickening fraction has been measured unchanged or increased during HFOT.[29,30] Indeed, the diaphragmatic thickening fraction remained unchanged during HFOT or noninvasive ventilation in a crossover trial in COPD patients recovering from an exacerbation.[29] Similarly, in ICU patients receiving HFOT through a nasal cannula, the diaphragmatic thickening fraction increased with HFOT in patients without diaphragm dysfunction, whereas it did not change with HFOT in patients with impaired diaphragm contraction (defined as diaphragmatic thickening fraction <15%).[30]

To the best of our knowledge, the present study might be the first to assess the effect of HFOT by ultrasonography on diaphragmatic function in tracheostomized patients. Diaphragmatic thickening fraction is a reliable indicator of respiratory effort in patients undergoing assisted breathing.[32] Our finding of maintaining diaphragmatic thickening fraction despite diaphragmatic excursion and V_T increase during HFOT, compared with conventional oxygenation through T-piece, indicated that HFOT improved breathing without increasing diaphragmatic effort. This likely provides indirect evidence that HFOT protects the diaphragm from excessive effort, offering a kind of mechanical support. Indeed, 50–60 L/min of HFOT could provide inspiratory assistance offered by the high flow mixture of air and oxygen applied to the upper opening of tracheostomy, also achieving small degrees (1–2 cmH_2O) of positive airway expiratory pressure.[10]

Our study has some limitations. First, we calculated V_T during a temporary disconnection from the apparatus at the start and end of each SBT by using Wright's portable spirometer to measure V_E and obtain the average V_T by dividing V_E by f. Although this disconnection lasted only 1 min, it could have influenced our findings. Although not ideal, portable spirometry is an acceptable and simple method for V_T calculation at the bedside in the presence of an endotracheal tube.[19] Other more precise techniques, such as electrical impedance tomography[24,25,27] and time-of-flight camera,[33] enabling V_T measurement under HFOT, require complex and expensive equipment and are not widely used at the bedside. Nevertheless, there are two findings in the present study, namely (1) the positive relationship of the change of V_T with the change of diaphragmatic excursion (Figure 2A), i.e., the positive relationship between two independent methods of measuring inspiratory lung volume and (2) the change in V_T under HFOT to the same direction in almost all measurements (i.e., if HFOT was the first or the second device in order) suggest that our method to calculate V_T was acceptable. Second, the duration of each intervention was short, because this study was designed to evaluate the physiological effects of HFOT via tracheostomy, and there was no intention to focus on clinical outcomes. Future studies are required to elucidate the clinical effects of HFOT via tracheostomy. Furthermore, our physiological study was not designed to test the impact of HFOT on patient's comfort. However, we can hypothesize that over a prolonged period, HFOT could better preserve the mucociliary function compared with conventional oxygen,[34] thus improving the secretion clearance and patient's comfort. Third, we were unable to measure several important respiratory parameters (e.g., end-expiratory lung volume and airway and esophageal pressures) that could have offered a more comprehensive interpretation of our results. However, the complex and invasive apparatus needed for these measurements could have modified the breathing pattern of our spontaneously breathing patients. Fourth, because we did not measure FiO_2 during conventional oxygen administration via the T-tube, actual FiO_2 secondary to room air entrainment could not be reliably concluded. Finally, the sole enrollment criterion and the basic exclusion criteria in our study facilitated the enrollment of a miscellaneous study population. Although our randomized crossover design may have partly compensated for this limitation, this enrollment impaired a deeper interpretation of our results.

Conclusions

HFOT delivered through tracheostomy compared with standard oxygen delivery through T-piece in a diverse ICU patient population with prolonged weaning from MV improves ventilation, pattern of breathing, and blood oxygenation, without increasing the inspiratory muscle effort.

Author Contribution

Elena Lytra: Writing – original draft, Data curation. **Stelios Kokkoris:** Writing – review & editing, Writing – original draft. **Ioannis Poularas:** Writing – original draft, Data curation. **Dimitrios Filippiadis:** Validation, Data curation. **Demosthenes Cokkinos:** Validation, Data curation. **Dimitrios Exarhos:** Validation. **Spyros Zakynthinos:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Christina Routsi:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization.

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Ethical Statement

The study protocol was approved by the Evangelismos Hospital Ethics Committee (reference number: 771/2019). This study was registered in ClinicalTrials.gov (NCT04758910).

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

The data sets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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