# High-Flow Oxygen Therapy in Tracheostomized Subjects With Prolonged Mechanical Ventilation: A Randomized Crossover Physiologic Study

Patharapan Lersritwimanmaen, Nuttapol Rittayamai, Jamsak Tscheikuna, and Laurent J Brochard

**BACKGROUND: High-flow oxygen therapy via tracheostomy (HFT) can be used in tracheostomized patients during ventilator disconnection. The physiologic effects of this technique are unknown. We hypothesized that HFT would reduce inspiratory effort and improve breathing pattern compared to conventional oxygen therapy via T-tube. This study aimed to evaluate the physiologic effects of HFT compared to conventional $O_2$ in patients with prolonged mechanical ventilation. METHODS: A randomized crossover physiologic study was conducted in adult tracheostomized patients who experienced temporary periods of ventilator disconnection. Subjects were ventilated with pressure support ventilation (PSV) for 15 min and were then randomly assigned to HFT or conventional $O_2$ via T-tube for 30 min. After a washout period, subjects were switched to the other system. Esophageal pressure ($P_{es}$), breathing frequency, blood pressure, heart rate, $S_{pO_2}$, and transcutaneously measured pressure of carbon dioxide ($P_{tcCO_2}$) were recorded. The primary outcome was inspiratory effort as determined by the simplified esophageal pressure-time product ($sPTP_{es}$). Secondary outcomes were $P_{es}$ swing, breathing frequency, heart rate, mean arterial pressure, $S_{pO_2}$, and $P_{tcCO_2}$ between groups. RESULTS: Twenty-two subjects were enrolled: $sPTP_{es}$ per minute was significantly higher with HFT and conventional $O_2$ compared to PSV (153.5 ± 97.9, 163.5 ± 111.3, and 86.8 ± 51.1 cm $H_2O$ × s/min, respectively, $P = .001$), but it was not different between HFT and conventional $O_2$ ($P = .72$). Breathing frequency increased significantly after switching from PSV to HFT and conventional $O_2$ (23 ± 4 vs 26 ± 6 and 23 ± 4 vs 27 ± 5 breaths/min, respectively, $P = .001$). $S_{pO_2}$ was higher with conventional $O_2$ compared to HFT ($P = .02$). No differences in $P_{tcCO_2}$, mean arterial pressure, or heart rate were observed between HFT and conventional $O_2$. CONCLUSIONS: Inspiratory effort and breathing frequency increased significantly during unassisted breathing compared to PSV in tracheostomized subjects, but HFT via tracheostomy provided no measurable additional physiologic benefit compared to $O_2$ therapy via T-tube.** *Key words: esophageal pressure; high-flow oxygen therapy; inspiratory effort; mechanical ventilation; tracheostomy.* [Respir Care 2021;66(5):806–813. © 2021 Daedalus Enterprises]

## Introduction

Tracheostomy is commonly performed in 10–15% of critically ill patients requiring prolonged mechanical ventilation to facilitate the weaning process,[1,2] and it has been increasingly used during the past decade.[3] A recent propensity-matched cohort study in subjects with ARDS reported that ICU and hospital length of stay were longer in those with tracheostomy.[4] While subjects with tracheostomy had the highest survival probability, there was no difference in 60-d or 90-d mortality in the subjects who survived for ≥ 5 d in the ICU, or in a propensity-matched subsample.[4] Many tracheostomized patients remain on mechanical ventilation for a substantial duration, which may increase the risk of developing complications of prolonged mechanical ventilation and increased mortality.[5-7] Increases in ICU and hospital stay also impose a large economic burden. Interventions to shorten the duration of mechanical ventilation in tracheostomized patients are, therefore, welcome.

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When tracheostomized patients are ready to wean, conventional oxygen therapy via T-tube or collar mask is often used.[6] However, many patients do not tolerate prolonged periods of disconnection and may experience increased work of breathing and desaturation. In addition, hypoxemia may occur due to variable $F_{IO_2}$ with a low-flow oxygen delivery system. Clearance of secretions is frequently a major issue, and adequate humidification of the airway may benefit the mucociliary system and reduce dryness symptom.[8-10] Therefore, optimizing patient's work of breathing, adequate humidification, and trying to improve respiratory muscle function by repeated disconnection periods may facilitate weaning in mechanically ventilated patients after tracheostomy.[11]

High-flow oxygen therapy via nasal cannula (HFNC) has been increasingly used as ventilatory support. Physiological studies in subjects with acute hypoxemic respiratory failure have demonstrated significant reduction in patient work of breathing and improved gas exchange after administration of HFNC.[12-14] HFNC may decrease the need for endotracheal intubation in patients with moderate to severe hypoxemia.[15,16] Current high-flow oxygen systems can be applied with tracheostomy tube via a dedicated interface.[17] However, the effect of high-flow oxygen via tracheostomy (HFT) is unclear and may differ from a conventional use of HFNC because the upper airway is bypassed by the tracheostomy.[18-20] We hypothesized that HFT would reduce inspiratory effort and improve breathing pattern in tracheostomized patients on prolonged mechanical ventilation. Our objectives were to compare the physiologic effects of HFT and conventional $O_2$ via T-tube in terms of inspiratory effort, breathing pattern, and hemodynamics.

## Methods

### Study Design and Population

This was a randomized, crossover, physiologic study conducted in the respiratory ICU of the Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, from July 2018 to April 2019. This study was approved by the Siriraj Institutional Review Board (#Si 322/2018) and was registered in the Thai Clinical Trial Registry (#TCTR20180612001). Written informed consent to participate was obtained from each subject or their relatives.

**QUICK LOOK**

**Current knowledge**

Conventional oxygen therapy via T-tube or collar mask is often used in tracheostomized patients who are ready to wean. High-flow oxygen can be applied with a tracheostomy tube via a dedicated interface. The physiologic effects of high-flow oxygen therapy via tracheostomy may differ from conventional high-flow oxygen via nasal cannula because the tracheostomy bypasses the upper airway.

**What this paper contributes to our knowledge**

Inspiratory effort significantly increased after switching from pressure support ventilation to unassisted breathing in tracheostomized subjects on prolonged mechanical ventilation. High-flow oxygen therapy via tracheostomy did not decrease inspiratory effort and breathing frequency compared to conventional oxygen therapy via T-tube.

We enrolled tracheostomized subjects aged 18 to 90 y who were mechanically ventilated with pressure support ventilation (PSV) with the following criteria: pressure support $\leq$ 10 cm $H_2O$, PEEP $\leq$ 8 cm $H_2O$, $F_{IO_2} \leq 0.5$, Glasgow coma score $> 8$, and able to tolerate transient periods of disconnection.[21] Patients were excluded if they met any of the following criteria under PSV: unstable hemodynamics (eg, systolic blood pressure $> 180$ or $< 90$ mm Hg, diastolic blood pressure $> 100$ or $< 60$ mm Hg, heart rate $> 140$ or $< 60$ beats/min, or any sign of poor tissue perfusion); breathing frequency $> 35$ breaths/min; $S_{pO_2} < 92\%$; severe acid/base disturbance (ie, arterial pH $< 7.3$ or $> 7.55$); contraindication for esophageal balloon catheter insertion; or pregnancy.

### Device

The Airvo 2 high-flow oxygen device (Fisher & Paykel Healthcare, Auckland, New Zealand) used in this study consists of a flow generator ($\leq$ 60 L/min), an air-oxygen blender that allows for adjustment of $F_{IO_2}$ from 21–100%, and an auto-fill MR290 heated chamber. The gas mixture at 37°C was delivered via a single-limb heated breathing tube to the patient via the Optiflow tracheostomy interface (Fisher & Paykel) (Fig. 1).

An esophageal balloon catheter (CooperSurgical, Trumbull, Connecticut) was inserted through the nose and positioned in the lower third of the esophagus. The balloon

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This study was supported by the Faculty of Medicine Siriraj Hospital, Mahidol University (grant [IO]R016131048). Dr Brochard has disclosed relationships with Covidien, Air Liquide, Philips, Sentec, Fisher & Paykel, and GE Healthcare. The other authors have disclosed no conflicts of interest.

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DOI: 10.4187/respcare.08585

was filled with 1 mL of air according to the manufacturer's instruction and connected to a pressure transducer (BIOPAC Systems, Goleta, California). The correct position of the esophageal balloon was checked by identifying cardiac artifact and applying gentle pressure on the abdomen to verify the absence of gastric pressure fluctuations; then an occlusion test was performed to confirm the position of the esophageal catheter.[22] Esophageal pressure ($P_{es}$) was recorded with an MP150 Data Acquisition System and AcqKnowledge Data Acquisition and Analysis Software (BIOPAC Systems).

### Study Protocol

Subjects were initially ventilated with PSV using their clinical settings for 15 min. We randomized subjects using a sealed opaque envelope to receive in a randomized order either HFT at a flow of 50 L/min and $F_{IO_2}$ 0.4, or conventional $O_2$ via T-tube with 100% oxygen at a flow of 10 L/min through the AQUAPAK humidification system (Teleflex, Wayne, Pennsylvania). Each intervention was applied for 30 min. Baseline PSV was then applied for 15 min during the washout period following the first intervention. The second intervention (HFT or conventional $O_2$) was applied in a crossover fashion for 30 min (Fig. 2). The cuff of the tracheostomy tube was inflated during the study intervention period to reduce the risk of aspiration of secretions above the cuff and to maximize the physiologic effects of HFT. After completion of the study protocol, the types and settings of ventilator support were decided by the attending physicians.

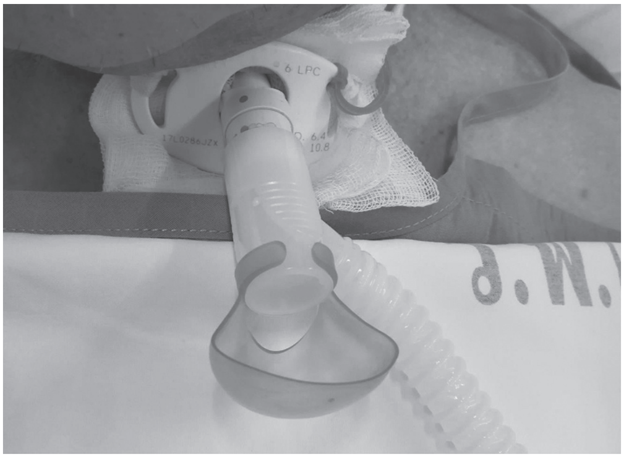

Fig. 1. Tracheostomy interface with high-flow oxygen delivery system.

### Data Collection

Baseline demographic and clinical data were collected before randomization. During the study intervention period, heart rate and breathing frequency were recorded every 5 min, and blood pressure was recorded every 15 min, including at the beginning and the end of each step. The observed values of breathing frequency, heart rate, and mean arterial pressure in the last minute of recording were reported. $S_{pO_2}$ and transcutaneously measured pressure of carbon dioxide ($P_{tcCO_2}$) were recorded continuously using a SenTec Digital Monitoring System (SenTec, Therwil, Switzerland). We continuously recorded $P_{es}$ waveforms for 5 min at the end of each step. $P_{es}$ was analyzed offline with the investigator blinded to the mode of support using the waveforms of the last 2 min of recording to calculate $P_{es}$ swing and esophageal pressure-time product ($PTP_{es}$) per breath (cm $H_2O$ × s) and per minute (cm $H_2O$ × s/min) as an index of inspiratory effort using the dedicated AcqKnowledge Data Acquisition and Analysis Software. The measurement of

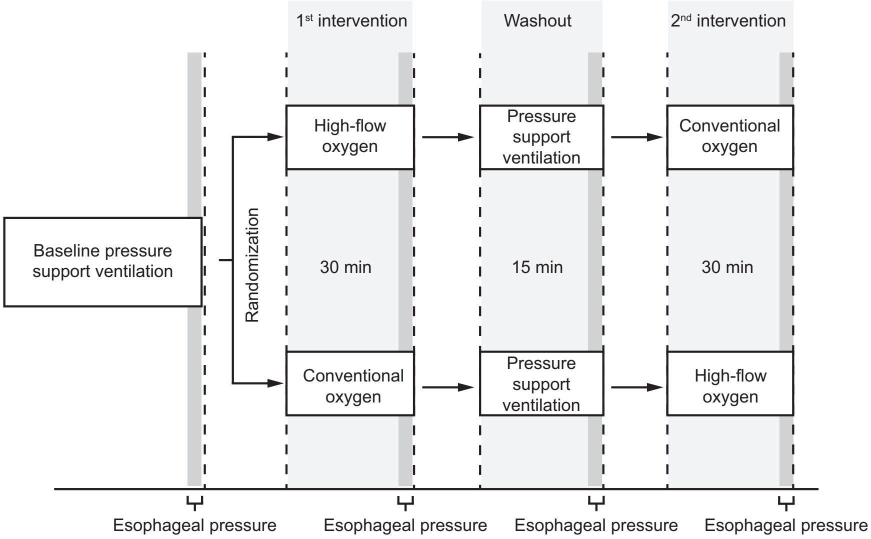

Fig. 2. Flow chart.

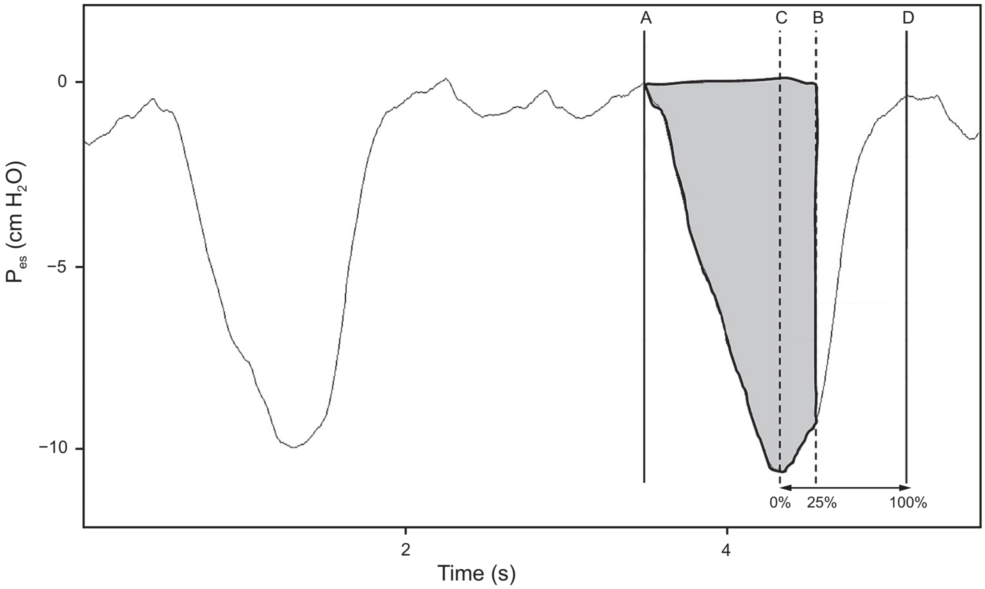

Fig. 3. Calculation of simplified esophageal pressure-time product by integrating the area under the $P_{es}$ signal (gray area). The beginning of the inspiration is the instant of the $P_{es}$ decay (A), and the end of the inspiration is the point of $P_{es}$ that elapsed 25% of time (B) from its maximum esophageal pressure deflection (C) to return to baseline (D). $P_{es}$ = esophageal pressure.

chest wall elastance would need passive ventilation and was not obtained. Moreover, determining the end of inspiration requires an air flow signal, which cannot be obtained from a pneumotachograph during HFT. Therefore, we modified the calculation of $PTP_{es}$ per breath by integrating the area under the $P_{es}$ signal from the onset of $P_{es}$ decay to the point that $P_{es}$ elapsed 25% of time from its maximum deflection to return to baseline (Fig. 3). This simplified technique has been used and reported in the previous studies,[23-25] and we refer to it in this study as the simplified $PTP_{es}$ ($sPTP_{es}$). $sPTP_{es}$ per minute was obtained by multiplying $sPTP_{es}$ per breath by breathing frequency. The average value of $P_{es}$ swing, $sPTP_{es}$ per breath, and $sPTP_{es}$ per minute were reported.

### Outcomes

The primary outcome was inspiratory effort as evaluated by $sPTP_{es}$ per minute between HFT and conventional $O_2$ via T-tube as well as between baseline PSV and each intervention. Secondary outcomes were difference in $sPTP_{es}$ per breath, $P_{es}$ swing, breathing frequency, heart rate, mean arterial pressure, $S_{pO_2}$, and $P_{tcCO_2}$ between HFT and conventional $O_2$.

### Statistical Analysis

The sample size was calculated on the basis of the previous study comparing HFNC with standard oxygen in subjects with acute hypoxemic respiratory failure[12] and an estimated decrease in $PTP_{es}$ of 30% in the HFT group. With a 2-sided significance level of .05 and power of 80%, the estimated sample size was 22 subjects.

Continuous variables are presented as mean ± SD or median (interquartile range [IQR]). Categorical variables are presented as absolute number and percentage. Normality of data distribution was tested with the Kolmogorov-Smirnov test. For normally distributed data, we used an analysis of variance (ANOVA) with repeated measures followed by a post hoc pairwise comparison. Non-normally distributed data were compared with the Friedman 2-way ANOVA by ranks with a post hoc pairwise comparison. Data were analyzed using PASW Statistics 18 (SPSS, IBM, Armonk, New York). $P < .05$ was considered statistically significant.

## Results

Twenty-two tracheostomized subjects with prolonged mechanical ventilation (mean ventilator days of 27 ± 21 d) were enrolled. The mean age was 73 ± 10 y, 15 subjects (68%) were male, and the mean Acute Physiologic and Chronic Health Evaluation (APACHE) II score was 20 ± 3. All subjects were ventilated in PSV mode at a mean pressure support level of 8 ± 1 cm $H_2O$, PEEP of 5 ± 0 cm $H_2O$, and $F_{IO_2}$ of 0.36 ± 0.06. Other baseline characteristics are detailed in Table 1.

### Inspiratory Effort

During PSV, $sPTP_{es}$ per minute was 86.8 ± 51.1 cm $H_2O$ × s/min. During conventional $O_2$ via T-tube and HFT,

Table 1. Baseline Demographic and Clinical Characteristics

| | |
|---|---|
| Age, y | 73 ± 10 |
| Male | 15 (68) |
| Body mass index, kg/$m^2$ | 21.4 ± 4.5 |
| Comorbidity | |
| Hypertension | 4 (18) |
| Diabetes mellitus | 14 (64) |
| Cardiovascular disease | 12 (55) |
| Cerebrovascular disease | 12 (55) |
| COPD | 3 (14) |
| APACHE II at enrollment | 20 ± 3 |
| Duration of mechanical ventilation before enrollment, d | 27 ± 21 |
| Inner diameter of tracheostomy tube, mm | 6.5 ± 0.2 |
| Pressure support ventilation setting | |
| Pressure support, cm $H_2O$ | 8 ± 1 |
| PEEP, cm $H_2O$ | 5 ± 0 |
| $F_{IO_2}$ | 0.36 ± 0.06 |
| Flow cycling, % | 25 ± 1 |
| Physiologic variables at enrollment | |
| Breathing frequency, breaths/min | 22 ± 6 |
| Minute ventilation, L/min | 8.8 ± 1.9 |
| Mean arterial pressure, mm Hg | 88 ± 12 |
| Heart rate, beats/min | 86 ± 17 |
| Arterial blood gas at enrollment | |
| pH | 7.44 ± 0.04 |
| $P_{aCO_2}$, mm Hg | 40.2 ± 7.1 |
| $P_{aO_2}$, mm Hg | 111.3 ± 37.0 |

Data are presented as mean ± SD or *n* (%). *N* = 22 subjects.
APACHE II = Acute Physiologic and Chronic Health Evaluation II

$sPTP_{es}$ per minute increased significantly (163.5 ± 111.3 and 153.5 ± 97.9 cm $H_2O$ × s/min, respectively) to a similar extent compared to PSV ($P = .001$). No significant difference in $sPTP_{es}$ per minute was observed between conventional $O_2$ and HFT ($P = .72$) (Fig. 4). Changes in $sPTP_{es}$ per breath and $P_{es}$ swing with conventional $O_2$ and HFT compared to PSV were also in the same direction as $sPTP_{es}$ per minute (Table 2).

### Breathing Frequency and Gas Exchange

Breathing frequency was significantly higher with conventional $O_2$ compared to PSV (27 ± 5 vs 23 ± 4 breaths/min, respectively, $P = .001$) and with HFT compared to PSV (26 ± 6 vs 23 ± 4 breaths/min, respectively, $P = .006$). There was no difference in breathing frequency between HFT versus conventional $O_2$ ($P = .90$) (Table 2). The median $S_{pO_2}$ was significantly higher with conventional $O_2$ than HFT (100% [IQR 100–100] vs 99% [IQR 99–100], respectively, $P = .02$), but no significant difference in $S_{pO_2}$ was observed between conventional $O_2$ and PSV ($P = .08$) or HFT and PSV ($P = .55$). There was no significant difference in $P_{tcCO_2}$ among PSV, conventional $O_2$, and HFT (39.5 ± 6.5 vs 39.7 ± 6.3 vs 38.0 ± 11.4 mm Hg, respectively, $P = .67$) (Table 2).

### Hemodynamics

No significant differences in mean arterial pressure were found between PSV, conventional $O_2$ via T-tube, and HFT (89 ± 13 vs 92 ± 13 vs 90 ± 11 mm Hg, respectively, $P = .10$) (Table 2). There was no significant difference in heart rate among PSV, conventional $O_2$, and HFT (86 ± 19 vs 87 ± 17 vs 87 ± 17 beats/min, respectively, $P = .55$) (Table 2).

### Adverse Events

No adverse event was observed during the study period and all subjects tolerated both interventions until the end of the study.

## Discussion

Our results indicate that inspiratory effort as determined by $sPTP_{es}$ per minute, $sPTP_{es}$ per breath, and $P_{es}$ swing and breathing frequency increased significantly after switching from mechanical ventilation with PSV to spontaneous breathing in tracheostomized subjects on prolonged mechanical ventilation. HFT did not decrease inspiratory effort or breathing frequency compared to conventional $O_2$ via T-tube. No differences were observed in $P_{tcCO_2}$, mean arterial pressure, and heart rate between conventional $O_2$ and HFT.

The benefits of HFNC in patients with acute hypoxemic respiratory failure are well established. A large randomized controlled study by Frat et al[15] reported lower 90-d mortality compared to standard oxygen and noninvasive ventilation in subjects with moderate to severe hypoxemic respiratory failure. In addition, a recent meta-analysis reported that HFNC may decrease the need for endotracheal intubation and escalation of oxygen therapy in subjects with moderate to severe hypoxemia.[16] However, high-flow oxygen in these clinical studies was applied with nasal cannula. High-flow oxygen can also be used with tracheostomy tube via a dedicated interface,[17] although data regarding physiologic effects and clinical outcomes are limited.[18-20]

We found no significant difference in inspiratory effort as determined by $sPTP_{es}$ per minute, $sPTP_{es}$ per breath, and $P_{es}$ swing between HFT and conventional $O_2$ via T-tube. A study by Corley et al[18] compared HFT at 50 L/min with conventional $O_2$ via T-tube at 15 L/min in 20 tracheostomized subjects who were weaned from mechanical ventilation in randomized crossover fashion. They reported significant improvement in oxygenation with HFT as determined by $S_{pO_2}/F_{IO_2}$, but no differences in breathing

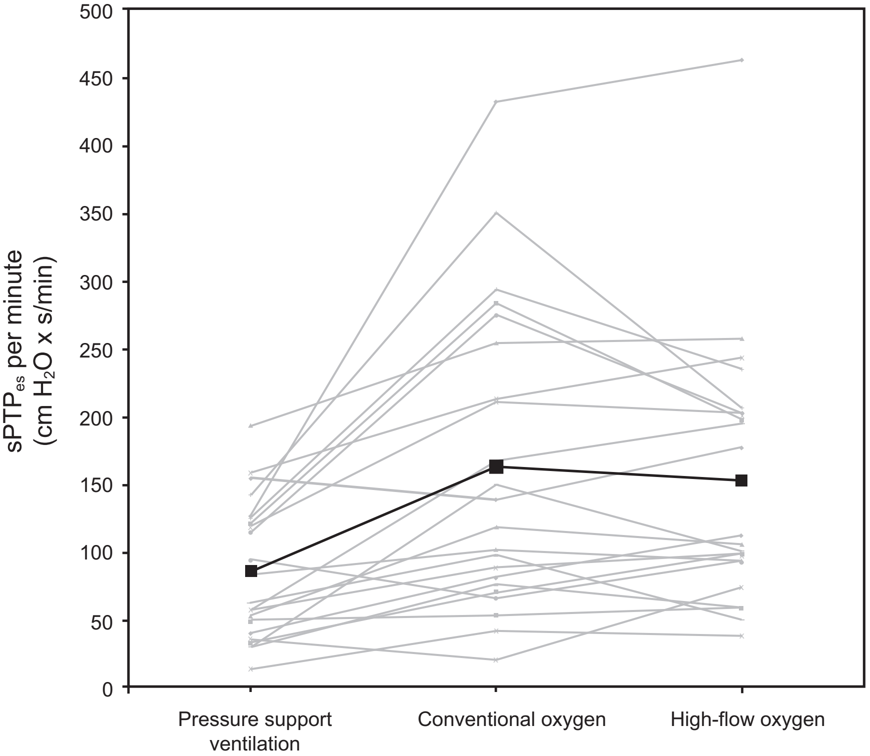

Fig. 4. Individual data and mean value of simplified esophageal pressure-time product ($sPTP_{es}$) per minute during pressure support ventilation, conventional oxygen therapy, and high-flow oxygen via tracheostomy.

Table 2. $sPTP_{es}$, $P_{es}$ Swing, Respiratory Variables, and Hemodynamic Variables During Ventilation

| Variables | PSV | Conventional $O_2$ | HFT | *P* |
|---|---|---|---|---|
| $sPTP_{es}$ per minute, cm $H_2O$ × s/min | 86.8 ± 51.1 | 163.5 ± 111.3* | 153.5 ± 97.9* | .001 |
| $sPTP_{es}$ per breath, cm $H_2O$×s | 3.8 ± 2.4 | 6.6 ± 4.4* | 6.1 ± 3.8* | < .001 |
| $P_{es}$ swing, cm $H_2O$ | 5.2 ± 2.7 | 9.2 ± 5.6* | 8.8 ± 4.8* | < .001 |
| Breathing frequency, breaths/min | 23 ± 4 | 27 ± 5* | 26 ± 6* | .001 |
| $S_{pO_2}$, % | 100 (98–100) | 100 (100–100)† | 99 (99–100) | .004 |
| $P_{tcCO_2}$, mm Hg | 39.5 ± 6.5 | 39.7 ± 6.3 | 38.0 ± 11.4 | .67 |
| Heart rate, beats/min | 86 ± 19 | 87 ± 17 | 87 ± 17 | .55 |
| Mean arterial pressure, mm Hg | 89 ± 13 | 92 ± 13 | 90 ± 11 | .10 |

Data are presented as mean ± SD or median (interquartile range).
*$P < .05$ compared with PSV.
†$P < .05$ compared with HFT.
$sPTP_{es}$ = simplified esophageal pressure-time product
$P_{es}$ = esophageal pressure
PSV = pressure support ventilation
HFT = high-flow oxygen via tracheostomy
$P_{tcCO_2}$ = transcutaneously measured partial pressure of carbon dioxide

frequency, end-tidal $CO_2$, end-expiratory lung volume, or heart rate between the 2 groups. The duration of each intervention was short (ie, only 20 min), and the effect on inspiratory effort was not investigated. Our findings are consistent with a recent prospective crossover study by Stripoli et al,[19] who compared conventional $O_2$ via T-tube at a flow of 10 L/min to HFT with a gas flow of 50 L/min) via tracheostomy cannula in 14 tracheostomized subjects at high risk for weaning failure. The authors reported no difference in neuro-ventilatory drive as determined by electrical activity of the diaphragm, the pressure-time product of inspiratory muscles calculated from the electrical activity of the diaphragm, breathing frequency, and gas exchange between conventional $O_2$ and HFT. The effect of HFT on inspiratory effort observed in our study and in the study by Stripoli et al[19] contrasts with the expectation that HFT might alleviate inspiratory effort and breathing pattern in tracheostomized patients. Physiological studies in subjects with acute hypoxemic respiratory failure reported significant reduction in inspiratory effort with HFNC.[12,13,26,27] The physiologic benefit of HFNC to reduce inspiratory effort can be explained by mechanisms not present in tracheostomized patients, such as generation of positive airway pressure by high flow of gas, alteration of airway resistance, and washing out of the oropharyngeal dead space.[28-30] Bypassing the normal respiratory passage with tracheostomy may diminish the physiologic effects of HFT compared to HFNC.[31] Natalini et al[20] evaluated the effect of high-flow oxygen therapy via tracheostomy with different flows (10, 30, and 50 L/min) compared to standard oxygen in 26 tracheostomized subjects. They found a small increase in peak and mean expiratory pressure with HFT, and HFT at a flow of 50 L/min was needed to increase the peak tracheal expiratory pressure to 1.8 cm $H_2O$. Moreover, compared to HFT, Natalini et al[20] reported significantly higher peak tracheal expiratory pressure with HFNC in 5 subjects who underwent tracheostomy decannulation (1.8 vs 5.1 cm $H_2O$, respectively). The findings from that study support the different physiologic effect of HFT on positive airway pressure from HFNC. In addition, the dedicated HFT connector to the tracheostomy tube, which has a large outlet for exhaled air, may also affect the physiologic change as compared to the narrow space surrounding the nostrils when using HFNC. Moreover, the high flow of gas might not reach deeper into the tracheal lumen because of flow delivery outside of the trachea through a large outlet of tracheostomy interface. However, some patients might benefit from the effect of heat and humidification that may improve patient comfort and alleviate inspiratory effort, thus it should be tested in the future studies.

We noted a significant increase in breathing frequency from PSV to noninvasive respiratory support. In addition, there was a trend toward increased breathing frequency between conventional $O_2$ via T-tube and HFT, but the difference was not statistically significant. This finding was similar to previous studies, but comparison with the baseline value has not been reported.[18,19] In contrast, we observed lower $S_{pO_2}$ with HFT compared to conventional $O_2$. This discordance might be explained by the higher $F_{IO_2}$ in the conventional $O_2$ group because we used a fixed flow of oxygen via T-tube; however, this difference might not be clinically important.

Our study has limitations. First, the duration of each intervention was short. Second, we did not measure $F_{IO_2}$ during conventional $O_2$ via T-tube due to technical limitations; therefore actual $F_{IO_2}$ secondary to room air entrainment cannot be reliably concluded. Third, the simple eligibility criteria for inclusion in our study facilitated the enrollment of a diverse study population; however, our randomized crossover design may compensate for this limitation. Finally, this study was designed to evaluate the physiologic effects of HFT via tracheostomy, and there was no focus on clinical outcomes. Future study is needed to elucidate the clinical effects of HFT via tracheostomy.

## Conclusions

Inspiratory effort and breathing frequency significantly increase during unassisted breathing in tracheostomized subjects compared to those treated with PSV. HFT provides no measurable additional benefit on inspiratory effort as determined by $sPTP_{es}$, breathing pattern, and hemodynamics compared to conventional $O_2$ via T-tube.

### ACKNOWLEDGMENTS

The authors thank Pattranan Vaidyakula (Division of Respiratory Diseases and Tuberculosis, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand) for her assistance in identifying and recruiting the subjects; as well as Khemajira Karaketklang (Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand) and Suthipol Udompunthurak (Clinical Epidemiology Unit, Research Department, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand) for their assistance with statistical analysis.

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