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Effect of high flow nasal cannula versus conventional nasal cannula oxygen therapy in patients undergoing endobronchial ultrasound-guided transbronchial needle aspiration

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Abstract

Patients undergoing endobronchial ultrasound-guided fine needle aspiration may have multiple comorbidities, contributing to higher risks of hypoxia and adverse events, such as arrhythmias. The current study compared the efficacy of two oxygenation modalities: the high flow nasal cannula (HFNC) *vs.* conventional oxygen therapy (CNC). Patients were randomized to either the HFNC or the CNC arm. HFNC and CNC were initiated and escalated as per predefined protocols. The number of desaturation events [fall in saturation of peripheral oxygen (SpO_2) by 3% from the baseline] and change in levels of transcutaneous CO_2 ($tcCO_2$) from baseline were noted. Subgroup analysis was done in patients with cardiopulmonary comorbidities and in patients with SpO_2<97%. A total of 122 patients were randomized. Overall, there was no significant difference in the number of desaturation events and change in $tcCO_2$ levels; however, in patients with cardiopulmonary comorbidities (obstructive sleep apnea, heart diseases, and stable chronic obstructive airway disease), 50% in the HFNC arm had no desaturation compared to 11.7% in the CNC arm (p=0.007). 41.17% of patients in the HFNC arm had a rise in $tcCO_2$ levels, compared to 36.11% of patients in the CNC arm (p>0.5). In patients with SpO_2<97%, 48.88% in the HFNC arm had no desaturations compared to 14.70% in the CNC arm (p=0.001); there was no statistical difference in the rise in $tcCO_2$. Hence, HFNC would be a better modality for oxygenation in patients with a high risk of hypoxia without increasing the risk of hypercapnia.

Key words: bronchoscopy methods, endoscopic ultrasound-guided fine needle aspiration methods, hypercapnia, lymphadenopathy pathology, comorbidity.

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Introduction

Endobronchial ultrasound-guided transbronchial fine needle aspiration (EBUS-TBNA) is a standard procedure for real-time sampling of mediastinal and hilar lymph nodes and parabronchial lung masses [1]. Like bronchoscopy, ventilation is impaired during EBUS due to multiple factors, including the diameter of the EBUS scope, depth, and duration of sedation. The plausible mechanisms are the effect on ventilation-perfusion and increased airway resistance due to the device's presence in the airway [2]. These factors contribute to hypoxemia, particularly in patients with cardiopulmonary comorbidities [obesity, obstructive sleep apnea (OSA), diffuse parenchymal lung disease, chronic obstructive pulmonary disease (COPD), and heart failure], leading to increased risk of arrhythmias, which can have an adverse effect on health outcomes.

The Indian Guidelines for EBUS-TBNA recommend the use of oxygen supplementation *via* common oxygen delivery devices (nasal prongs/nasopharyngeal catheter), along with pulse oximetry monitoring as a routine practice [3].

However, conventional oxygen therapy (COT) systems have a variable fraction of inspired oxygen concentration (FiO_2) concentration dependent on the patient's breathing pattern [4], heightening the risk of intra- and post-procedural hypoxemia and subsequent arrhythmias. In addition, COPD is a frequent comorbidity in this patient group. COPD patients have a risk of carbon dioxide (CO_2) retention when given supplemental oxygen, especially under sedation, prompting exploration of alternative modalities for better oxygenation control.

High flow nasal cannula (HFNC) oxygen therapy offers both clinical (*e.g.*, patient comfort and ease of use) and physiological benefits (*e.g.*, high oxygenation, alveolar recruitment, humidification and heating, increased secretion clearance, reduction of dead space), potentially mitigating lung function deterioration and avoiding the need for endotracheal intubation [5,6].

Sharma *et al.* conducted a triple-arm randomized trial compar-

ing HFNC, COT, and non-invasive ventilation (NIV) in stable COPD patients undergoing fiberoptic bronchoscopy [7]. They found that saturation of oxygen in peripheral capillary [saturation of peripheral oxygen (SpO_2)] nadirs during bronchoscopy was significantly lower with COT (87.03) compared to HFNC (95.57) and NIV (97.04). A meta-analysis by Roy *et al.* showed HFNC reduced desaturation events during bronchoscopy (RR 0.34) [8].

Studies specific to the use of HFNC in EBUS-TBNA are limited. Ucar *et al.* reported fewer desaturations below 90% with HFNC (5 out of 85) compared to COT (26 out of 85) ($p<0.0001$), with no data on CO2 levels [9]. Takakuwa *et al.* demonstrated HFNC's efficacy in preventing hypoxemia during EBUS fine needle aspiration cytology (FNAC), noting fewer desaturations (25% *vs*. 68.42% in COT, $p<0.005$) and similar trends in transcutaneous CO2 [10]. Irfan *et al.* found a significant saturation drop difference between HFNC and COT ($p<0.001$) but no CO2 differences [11]. Douglas *et al.* reported no statistically significant benefit with HFNC in reducing desaturation in EBUS [12]. However, most of these studies did not include patients with preexisting cardiopulmonary comorbidities.

The current study aims to investigate the effectiveness of HFNC compared to COT in reducing desaturation events and preventing a rise in transcutaneous CO_2 ($tcCO_2$) levels during the EBUS-TBNA procedure.

Materials and Methods

Study settings

This study was conducted in the tertiary care university hospital in the Department of Pulmonology, Critical Care and Sleep Medicine, New Delhi, over 18 months (2022-2024).

Study design

The current study was a single-center, double-arm study. The primary objective was the number of desaturations (defined as a fall in SpO_2 of 3% from baseline) during the EBUS FNA procedure. The secondary outcome was change in $tcCO_2$ levels from baseline. The study was initiated after approval from the Ethics and Research Committees [S. No. IEC/VMMC/SJH/Thesis/9/2022/CC-14] dated 6/10/2022

Participants

All patients over 18 years of age with mediastinal lesions measuring more than 0.5 cm in short axis were enrolled. Tracheostomy patients and pregnant females were excluded.

Randomization

After taking the informed written consent, the patients were randomized using tamper-proof sealed envelopes and allocated to either the HFNC arm (group 1) or the conventional nasal cannula (CNC) arm (group 2). The randomization sequence was computer-generated by an independent expert and kept at the study site in sealed opaque envelopes opened just before the procedure. The research staff was not blinded.

Intervention

Pre-procedure vitals [heart rate (HR), blood pressure (BP), SpO_2, $TcCO_2$) were documented.

- Patients allocated to the CNC arm: patients were started at an O_2 flow rate of 2 L/min, and O_2 was increased in increments of 1 L/min till patients' SpO_2>90%
- Patients allocated to the HFNC arm: patients were started at a flow rate of 30 L/min, FiO_2 28%, and FiO_2 was increased in increments of 4% till the patients' SpO_2>90%.

The procedure was initiated after ensuring pre-procedure SpO_2 levels of >90%. We used EBUS Olympus BF - UC 180 F bronchoscope with EUME1 ultrasound processor (Olympus, Japan) for the procedure, with a working channel of 2.2 mm and a diameter of 6.3 mm. EBUS FNAC was carried out under local anesthesia (using 2% lignocaine spray to the vocal cords and the tracheobronchial tree) and moderate sedation with midazolam, targeting a Richmond Agitation Sedation Scale (RASS) level of 0 to -1. Airway was sequentially screened for lymph nodes at the following stations: 7, 4R, 2R, 4L, 2L, 10R, 10L, and 11s, 11i, and 11L. The treating intensivist targeted the largest lymph node, and three needle aspirates (each with ten passes) were made using a 21 G needle (Olympus, Japan). Glass slide-fixed smears and cell blocks were prepared. Aspirates were also processed for microbiological investigations, including staining for *Mycobacterium tuberculosis* smear, Xpert Mtb-RIF test, and Mycobacterial liquid cultures. The sample was sent for staining for cytological examination. Vital monitoring was done: HR, BP, SpO_2, and $tcCO_2$.

In the event of desaturation during the procedure: in patients with a nasal cannula, FiO_2 was increased by 1 L/min, observed for 10 seconds; if SpO_2 was still below 90%, FiO_2 was increased by another 1 L/min, till we got SpO_2>90%. In patients with HFNC, FiO_2 was increased by 4% and flow by 5 L/min; observed for 10 seconds; if SpO_2 is still below 90%, FiO_2 was increased by 4% and flow by 5 L/min till we got SpO_2>90%.

The number of desaturations (defined as a fall of 3% from baseline) was noted. At the end of the procedure, $tcCO_2$ levels were reported. The patient was assessed in the recovery room for 1 hour post-procedure and then discharged. Per our hospital protocol, all patients were followed up for 1 month for a clinical radiological response after the procedure.

Data collection

Baseline demographics and clinical symptoms were noted along with comorbidities such as OSA (included patients who were already diagnosed with OSA), heart disease (diagnosed heart failure with preserved ejection fraction, heart failure with reduced ejection fraction, valvular heart disease), and diagnosed COPD (stable on management with inhaled bronchodilators). Detailed history and clinical examination were done, including the history of fever, chest symptoms, and any other systemic complaints. Patients underwent hematological examination (routine blood investigations and coagulation parameters where indicated). $tcCO_2$ levels were recorded at the start and end of the procedure. The number of desaturations (defined as a fall of 3% from baseline) was noted during the procedure.

Statistical analysis

Concerning a previous study by Ucar *et al.* [9], the sample size was estimated using a finite population formula to be 61. The demographic and procedural details were noted in Microsoft Excel, and patient reports and procedural videos were also stored in the department's system. Statistical analyses were performed using the Stata 16 package (StataCorp, 2019. Stata Statistical Software: Release 16) (StataCorp LLC, College Station, TX, USA). Categorical variables

were summarised as numbers (percentages), while quantitative variables were as mean (standard deviation) or median (interquartile range). The Chi-squared test was used to compare categorical variables. Freeman-Halton's extension of Fisher's exact test was used for a 2×3 contingency table with any cell column less than 5.

Further subgroup analysis was done by characterizing patients as per the underlying cardiopulmonary comorbidity, which included patients with OSA (including patients who were already diagnosed with OSA), heart disease (diagnosed heart failure with preserved ejection fraction, heart failure with reduced ejection fraction, valvular heart disease), and diagnosed COPD (stable on management with inhaled bronchodilators).

Patients were also characterized as per baseline SpO2 at the start of the procedure: ≥97% and <97%.

Results

A total of 132 patients were screened. Baseline demographics of randomized patients are given in Table 1. All patients were given sedation to achieve RASS -1 for the entire duration of the procedure, which was initiated with 1 mg of midazolam and 50 mcg of fentanyl. An additional dose of 1 mg midazolam was required in 9 patients in the CNC group and 7 in the HFNC group to achieve RASS -1.

The frequency of lymph nodes sampled is mentioned in *Supplementary Table 1 and Supplementary Figure 1*. The majority of patients had a single site sampled during the procedure, with the subcarinal lymph node station as the most commonly sampled EBUS station (75.40% in HFNC and 77.04% in CNC), followed by the right paratracheal (52.45% in HFNC group and 40.98% in CNC group). The least sampled site was the right upper paratracheal (4.91% in HFNC and 3.27% in CNC) (*Supplementary Table 2*).

Primary outcome

A fall of 3% from baseline SpO_2 was counted as an individual desaturation (Table 2). There was no statistical difference in the two groups concerning the number of episodes of fall in SpO_2 by 3% from baseline. The median (range) in the HFNC group was 2 (0-6) *vs.* 2 (0-10) in the CNC arm (p=0.26).

Secondary outcomes

The ordered waterfall plot shows the change in $tcCO_2$ [$tcCO_2$ end – $tcCO_2$ start] levels from the baseline for each group. Most patients had no change in their baseline CO_2 levels - 57.37% in the HFNC group compared to 62.29% in the CNC group (*Supplementary Figure 2*). However, this was not found to be statistically significant (p=0.57). A further subgroup analysis was done in patients with cardiopulmonary comorbidities (COPD, preexisting heart diseases, and OSA):

i. Patients with cardiopulmonary comorbidities: 50% of patients in the HFNC group had no desaturations (compared to baseline), compared to 11.47% of patients in the CNC arm. This was found

Table 1. Baseline demographic data of patients in the high-flow nasal cannula and conventional nasal cannula groups.

Characteristics	HFNC (n=61)	CNC (n=61)
Age (in years)	50.57±17.05	47.57±15.28
Male sex, n (%)	36 (59)	32 (52.5)
BMI (kg/m²)	24.43±3.42	24.185±3.42
Baseline SpO_2	94.98±2.26	96.46±1.82
STOP BANG, n (%)		
0-2	39 (63.93)	46 (75.40)
3-4	11 (18.03)	6 (9.83)
5-8	11 (18.03)	9 (14.75)
Patients with cardiopulmonary comorbidities, n (%)		
No risk factors	17 (27.86)	13 (21.31)
COPD	20 (32.78)	17 (27.86)
Heart Disease	11 (18.03)	11 (18.03)
OSA	12 (19.67)	14 (22.95)

HFNC, high flow nasal cannula; CNC, conventional nasal cannula; BMI, body mass index; SpO_2, saturation of peripheral oxygen; COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnea.

Table 2. Comparison between the number of patients with desaturations (fall of 3% from baseline SpO_2 values) and change of transcutaneous CO_2 levels from baseline between the conventional nasal cannula group and high flow nasal cannula group.

	HFNC (n=61), n (%)	CNC (n=61), n (%)	p
Number of patients with desaturations (fall of 3% from baseline)			
Zero	25 (40.98)	17 (27.86)	
1-3	25 (40.98)	28 (45.90)	0.26
≥4	11 (18.03)	16 (26.22)	
Change in baseline of transcutaneous CO_2 levels			
No increase from the baseline	35 (57.37)	38 (62.29)	0.57
Increase from baseline	26 (42.62)	23 (37.70)	

HFNC, high flow nasal cannula; CNC, conventional nasal cannula; SpO_2, saturation of peripheral oxygen; FiO_2, fraction of inspired oxygen concentration; CO_2, carbon dioxide.

to be statistically significant. (p=0.01) (Table 3). Although 41.17% of patients in the HFNC arm and 36.11% of patients in the CNC arm had a rise in $tcCO_2$ at the end of the procedure, this was not found to be statistically significant (p=0.66) (Table 3).

ii) A subgroup analysis was done between two groups with baseline SpO_2 < 97%.

A total of 45 patients (73.77% of patients from the baseline group) in the HFNC arm and 34 patients (55.73% of patients from the baseline group) in the CNC arm had SpO_2 less than 97%. 48.88% of patients in the HFNC arm had no desaturation from baseline compared to 14.7% of patients in the CNC arm. This was found to be statistically significant (Table 4). 18 (40%) patients in the HFNC arm had increased $tcCO_2$ levels from baseline *vs.* 15 (44.11%) patients in the CNC arm. However, this was not found to be statistically significant. (p=0.123) (Table 4).

Discussion

The study included 122 patients who required the EBUS-guided sampling of lymph nodes and masses for their diagnosis and disease management. The frequency of lymph nodes sampled is mentioned in *Supplementary Table 1* and *Supplementary Figure 1*. Most patients had a single site sampled during the procedure, with the subcarinal lymph node station being the most commonly sampled EBUS station.

The sample size in the current study is comparable to the number of patients in the study by Ucar *et al.,* where they randomized 85 patients in each arm [9]. Irfan *et al*. randomized 20 patients in each arm [11]. Takakuwa *et al*. had 12 patients in the HFNC arm compared to 19 historical cohorts [10]. Douglas *et al*. had 30 patients in each arm [12].

The protocol for initiation of the CNC and HFNC arm varied between studies. In our study, patients enrolled in the nasal cannula group were started on an oxygen flow rate of 2 L/min. Other authors had higher flow rates at the beginning of the procedure. Ucar *et al.* gave a nasal cannula at 5 L/min [9], and Douglas *et al.* started with 10 L/min *via* bite block [12]. In the current study, patients in the HFNC arm were started at 28% FiO_2 and a flow rate of 30 L/min. The 28% mark was chosen to make both arms comparable at baseline. Takakuwa *et al.* initiated HFNC at 30% FiO_2 and 40L/min flow [10]. Ucar *et al.* started patients on 35 L/min and FiO_2 40% [9]. Irfan *et al.* started the patients on HFNC at FiO_2 100% with 30 L/min flow during the preparation period, and the flow was increased to 70 L/min at the start of the procedure [11]. Douglas *et al.* also gave 100% FiO_2; the flow rate was variable and kept between 30-70% depending on patient comfort [12]. Compared to all the above studies, the present study had the lowest FiO_2 and flow at initiation.

The protocol for escalation of HFNC and CNC also varied in the literature. For the HFNC group, after desaturation, Douglas *et al.* intervened by increasing flow in the HFNC arm to 70 L/min [12]; Takauwa *et al.* allowed increments of 10% FiO_2 to keep SpO_2 above 90%. Ucar *et al.* and Irfan *et al.* did not increase the flow rates or FiO_2 and noted the number of desaturations [9,11]. In our patients, FiO_2 was increased by 4% sequentially till SpO_2>90%. In the CNC arm, we increased flow by 1 L/min sequentially till SpO_2>90%. Douglas *et al.* increased the flow *via* block bite to 15 L/min in the event of desaturation [12]. A study by Takakuwa *et al.* used a histor-

Table 3. Comparison between the number of patients with desaturations (fall of 3% from baseline SpO_2 values) and change of transcutaneous CO_2 levels from baseline between the conventional nasal cannula group and high flow nasal cannula group in a subgroup of patients with cardiopulmonary comorbidity

	HFNC (n=34), n (%)	CNC (n=36), n (%)	p
Number of patients with desaturation (fall of 3% from baseline), n (%)			
No desaturations	17 (50)	7 (11.47)	0.007
Desaturations present	17 (50)	29 (80.55)	
1-3	8 (13.11)	19 (31.14)	
≥4	9 (14.75)	10 (16.39)	
Change in baseline of transcutaneous CO_2 levels			
No change	20 (58.82)	23 (63.88)	0.66
Increase from baseline	14 (41.17)	13 (36.11)	

HFNC, high flow nasal cannula; CNC, conventional nasal cannula; SpO_2, saturation of peripheral oxygen; FiO2, fraction of inspired oxygen concentration; CO^2, carbon dioxide.

Table 4. Comparison between the number of patients with desaturations (fall of 3% from baseline SpO_2 values), number of patients with desaturations below 90% (lasting 10 seconds), fraction of inspired oxygen concentration at the end of the procedure and change of transcutaneous CO_2 levels from baseline between the conventional nasal cannula group and high flow nasal cannula group in the subgroup of patients with SpO_2 <97%.

	HFNC (n=45), n (%)	CNC (n=34), n (%)	p
Desaturations (fall below 3% from baseline)			
No desaturation	22 (48.88)	5 (14.70)	0.001
Desaturations present	23 (51.11)	29 (85.29)	
Change in baseline of transcutaneous CO_2 levels			
No change	27 (60.00)	19 (55.88)	0.71
Increase from baseline	18 (40.00)	15 (44.11)	

HFNC, high flow nasal cannula; CNC, conventional nasal cannula; SpO_2, saturation of peripheral oxygen; FiO_2, fraction of inspired oxygen concentration; CO_2, carbon dioxide.

ical cohort of patients on CNC undergoing EBUS FNA and noted only the number of desaturations [10].

The definition of desaturation varied between studies. The present study defined desaturations as a fall from the patient's baseline of 3%. Ucar *et al.* and Douglas *et al.* defined desaturation as SpO_2<90% [9,12]. Irfan *et al.* and Takakuwa *et al.* noted the lowest SpO_2 during the procedure from baseline [10,11]. There was no significant difference between the HFNC arm and the CNC arm in the number of desaturations, with a fall of 3% from baseline in our study, although the range of desaturations was less in the HFNC arm. Douglas *et al*. also found no significant difference but found an absolute reduction of 21%, a relative risk reduction of 40%, and a number needed to treat of 4.7 [12]. Irfan *et al.* found that the difference in a drop in oxygen saturation compared to baseline between the two groups was significant [11]. The number of desaturations in the CNC arm ranged between 6 and 8 *vs.* 0-2 in the HFNC arm. There was a difference of 7.7% between the two groups. Only 5% of patients in the HFNC arm had desaturation to <90% during the procedure compared to 55% in the CNC arm. Takakuwa *et al.* found that 68.42% of patients in the CNC group had desaturation below 90% compared to 25% of patients in the HFNC arm [10]. Also, the lowest SpO_2 was 77% in the CNC arm compared to 84% in the HFNC arm. This was found to be statistically significant. They also noticed that even after increasing FiO_2, the hypoxia duration was longer in the CNC arm. Ucar *et al.* also had significantly fewer desaturations in the HFNC group (5 in HFNC *vs.* 26 in CNC) [9]. SpO_2 at the end of the procedure was significantly higher in the HFNC group.

The nonsignificant difference in desaturation in our study could have been due to comparatively lower FiO_2 and flows in HFNC, and also attributable to lighter sedation used in our studies. It may be possible that higher sedation may have predisposed patients to more desaturations in nasal cannula arms in the above studies. In a study by Douglas *et al.*, patients were on maximum FiO_2 already [12]. The effect on desaturations due to higher sedation may have been overshadowed by the use of higher FiO_2 and flows used in all previous studies. Also, our study included a much more comprehensive range of patients, with significant numbers of patients with cardiorespiratory comorbidity and SpO_2<94%.

Only two previous studies studied changes in CO_2 levels with oxygenation modality. Irfan *et al.* noted that the venous and $EtCO_2$ levels during the procedure were similar in both arms and venous pCO_2 levels seen 1 hour post-procedure were also identical [11]. Takakuwa *et al.* [10], like us, used a transcutaneous CO_2 monitor. He found the mean of the highest pCO_2 in 12 patients in the HFNC arm to be 39 mm Hg. Takakuwa *et al.* assessed the peak cutaneous CO_2 levels [10], whereas our study assessed the change in transcutaneous CO_2 levels during the procedure, categorizing them as an increase from baseline or no increase in the baseline. Change in CO2 level was deemed an essential outcome in patients with COPD and OSA, specifically when higher FiO_2 delivery devices may ameliorate the hypoxic drive. In our study, although more patients in the HFNC group had an increase in $tcCO_2$ compared to CNC, this was not statistically significant.

Subgroup analysis of patients with cardiorespiratory abnormality

Patients with underlying cardiopulmonary comorbidities (COPD, OSA, and heart failure) were deemed to have a high risk for hypoxia. Also, these patients were believed to respond more acutely to hypoxia due to low reserve and were at higher risk of arrhythmias due to hypoxia. These patients have traditionally been excluded from clinical trials. In our study, 12 patients in the HFNC arm had OSA compared to 14 patients in the CNC arm. Twenty patients in the HFNC arm and 17 patients in the CNC arm had COPD, and 11 patients in both HFNC & CNC arms had heart disease. Takakuwa *et al.* only had two patients with prior cardiorespiratory comorbidity in both arms, and these patients had lower baseline SpO_2 than the other groups [10]. None of them were screened for OSA. Ucar *et al.* only considered coronary artery disease and hypertension comorbidity during baseline [9], which were well-controlled, and excluded patients with a body mass index >30. In the study by Irfan *et al*. [11], 52.5% of patients had lung cancer, along with five patients with sarcoidosis. Douglas *et al.* had a comparable number of patients with obstructive airway disease, malignancy [12], OHS, or OSA in both arms. However, none of the studies specifically analyzed the effect of oxygenation modality in these high-risk patients. Thus, the current study is the first with a significant proportion of patients deemed at high risk of hypoxia. The current study found significantly lower desaturations in patients randomized to the HFNC arm than in the CNC arm. In the subgroup analysis of patients with SpO_2<97%.

No patient had SpO_2 <97% in the HFNC arm in the study by Takakuwa *et al*. [10]. Only one patient in the CNC arm had a baseline SpO_2 of 96%. No other research has performed an analysis based on baseline SpO_2 levels. We stratified patients based on baseline SpO_2 and found significantly lower desaturations in the HFNC arm.

Thus, our study is the first to precisely assess the utility of these oxygenation delivery devices in high-risk populations, as most patients are denied the procedure, citing high risk and potential for landing in respiratory failure post-procedure. HFNC can also provide better oxygenation in hypoxic patients requiring EBUS procedures. The study's limitations were that it was single-center, the procedure duration was not noted, the effect on yield or patient or operator comfort was not evaluated, and a cost analysis was not done.

Conclusions

The HFNC is an effective oxygenation modality to prevent hypoxia in high-risk patients undergoing endobronchial ultrasound-guided fine needle aspiration of mediastinal lymph nodes and masses. Future studies may be needed to confirm its cost-effectiveness.

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Online supplementary material:

Supplementary Table 1. Total number of sites sampled and corresponding stations sampled

Supplementary Table 2. Radiographic findings on computed tomography scans for patients.

Supplementary Figure 1. Number of sites sampled and the number of times each lymph node station sampled. HFNC, high flow nasal cannula; CNC, conventional nasal cannula.

Supplementary Figure 2. a) Ordered waterfall plot of change in transcutaneous CO_2 as compared to baseline in patients with high-flow nasal cannula; b) ordered waterfall plot of change in transcutaneous CO_2 as compared to baseline in patients with conventional nasal cannula.

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Informed consent: informed consent obtained from patient prior to procedure.

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Availability of data and materials: data and materials are available from the corresponding author upon request.