Effects of High Flow Nasal Cannula on the Coordination between Swallowing and Breathing in Postextubation Patients, a Randomized Crossover Study

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Abstract

Background: Timing of swallows in relation to respiratory phases is associated with aspiration events. Oxygen therapy possibly affects the timing of swallows, which may alter airway protective mechanisms.

Objectives: To compare the coordination between swallowing and respiration during water infusion in post-extubation patients using high flow nasal oxygen (HFNO) with the coordination in those using low flow nasal oxygen (LFNO).

Methods: We conducted a randomized controlled crossover study in post-extubation patients. The patients extubated within 48 hours were randomly assigned into two groups, namely HFNO and LFNO. The eligible patients in each group received either HFNO with FiO2 35%, flow 50 LPM and temperature 34˚C or LFNO 5 LPM for 5 minutes. The coordination between swallowing and respiration was observed during continuous infusion of 10 ml of water in one minute for three times. Respiratory phases and swallowing were monitored using ECG-derived respiratory signals and submental EMG, respectively. The swallowing frequency and timing of swallows in relation to respiratory phases were recorded. The coordination between swallowing and respiration was classified into 4 patterns, namely I-E, I-E, E-I and E-I swallows. (I; inspiration and E; expiration) Subsequently, after the 5 minute washout period, the patients were switched to receive the other type of oxygen therapy with the same procedure. Wilcoxon Signed Ranks Test was used for statistical analysis.

Results: A total of 22 patients with the mean age of 55.8 years were enrolled into the study. The major indication for invasive mechanical ventilation was pneumonia with the median duration of endotracheal intubation of 2.5 days. The median of total swallowing numbers (three minutes) were 18.5 in the HFNO period and 21 in the LFNO period (p = 0.158). The most common swallowing pattern was E swallow. The patients using HFNO had higher numbers of E-swallow pattern (74.3% in HFNO vs 67.6% in LFNO; p = 0.048) and lower numbers of I-swallow pattern (14.3% in HFNO vs 23.1% in LFNO; p = 0.044). The numbers of other swallowing patterns were not different between 2 groups.

Conclusions: Compared with LFNO, HFNO significantly increased the E-swallow and decreased the I- swallow in post-extubation patients. The findings indicated that HFNO might reduce the risk of aspiration during the post-extubation period.

Background

High flow nasal oxygen therapy (HFNO) brings several physiological benefits that differ from conventional low flow nasal oxygen therapy (LFNO). HFNO provides positive end expiratory pressure (PEEP), constant fraction of inspired oxygen, pharyngeal dead-space washout and also improves mucocilliary clearance. This oxygen delivery system has been increasingly used in clinical practice, especially in postextubation patients.¹

Patients who had at least one of the following factors: older than 65 years, Acute Physiology and Chronic Health Evaluation II score higher than 12 points on extubation date, body mass index higher than 30 Kg/m², inadequate secretion management, difficult or prolonged weaning, and more than one comorbidities, including heart failure as primary indication for mechanical ventilation, moderate to severe chronic obstructive pulmonary disease, airway patency problems or prolonged mechanical ventilation, were at high risk for extubation failure.² In these patients, HFNO was not inferior to noninvasive ventilation for prevention of postextubation respiratory failure and reintubation. Moreover, Hernandez et al.³ demonstrated that HFNO significantly decreased the reintubation rate within 72 hours after extubation in patients at low risk for extubation failure, compared with LFNO.

One of the important advantages of HFNO in postextubation patients is allowance for patients to eat and drink orally without interruption of therapy. However, there is a lack of evidence supporting the safety of HFNO regarding to the risk of aspiration during oral intake.

During the postextubation period, the risk of aspiration increases due to several conditions such as postextubation dysphagia, incoordination between swallowing and breathing, and feeding intolerance.

The incidence of postextubation dysphagia varies from 3 to 62% and this condition shares the common risk factors with postextubation respiratory failure, such as advanced age, prolonged intubation and preexisting congestive heart failure. Moreover, postextubation dysphagia leads to aspiration pneumonia, prolonged hospitalization, increased cost of medical treatment and mortality.⁴
According to the coordination between swallowing and respiration, breathing ceases briefly during swallowing by inhibition of respiration at neural control centers in the brainstem and closure of the upper airway. In healthy adults, swallowing usually begins during the expiration and then respiration resumes with continuation of expiration after swallowing. Thus, the most common pattern of swallowing-breathing relationship is exhale–swallow–exhale or E swallow, followed by inhale–swallow–exhale or I-E swallow, which regards as one of the airway protective mechanisms. (Fig. 1) In addition, the alteration of this coordination, namely inhale–swallow–inhale or I swallow, and exhale–swallow–inhale or E-I swallow, also appears with the lower percentages in the healthy adults.

From the previous studies, the incidence of aspiration was associated with the increase in percentages of I and E-I swallows, which commonly occurred in elderly and patients with cerebrovascular, Parkinson's and chronic obstructive pulmonary diseases. Although many studies have investigated the alteration of swallowing and breathing coordination in many populations, the information in the postextubation patients remains limited.

Few studies examined the effect of airway pressure on the swallowing and breathing coordination. Samson et al. demonstrated that bronchopulmonary receptor stimulation by nasal continuous positive airway pressure (nCPAP) in lamps reduced the frequency of swallowing and altered the patterns of swallowing-breathing relationship during continuous water infusion. The changes in this relationship during continuous infusion under nCPAP, particularly a decrease in swallowing during inspiration (I and E-I swallows), might decrease the risk of aspiration.

In addition, Hori et al. demonstrated the effect of bi-level positive airway pressure (BiPAP) on the coordination between respiration and swallowing in 22 healthy volunteers. They found that the occurrence rate of inspiration after swallow was greater in those with BiPAP, compared with the control and CPAP conditions.

Corley et al. showed that HFNO increased end expiratory lung volume and airway pressure. Therefore, HFNO might stimulate the bronchopulmonary receptor and change timing of swallowing in relation to respiratory phases.

In recent years, researchers have become increasingly interested in the effect of HFNO on the swallowing function. However, there was the only research investigating in the healthy population.

Sanuki et al. demonstrated that HFNO reduced the swallowing latency time in healthy volunteers. Nevertheless, the timing of swallowing during continuous infusion of water for one minute was not different between HFNO and LFNO periods.

Up to our knowledge, no study had looked specifically at the effect of HFNO on the relationship of swallowing and breathing during the postextubation period. The present study was firstly designed to compare the swallowing-breathing coordination during continuous water infusion between HFNO and LFNO therapy in the postextubation patients.

**Methods**

Our study was the prospective, randomized, interventional, 2 x 2 crossover study. We carried out the trial in the medical inpatient department and medical intensive care unit at King Chulalongkorn Memorial Hospital, Bangkok, Thailand between June 2019 and February 2020. The protocol was approved by the institutional review board of the Faculty of Medicine, Chulalongkorn University. This study was funded by Ratchadapiseksompotch Fund, Faculty of Medicine, Chulalongkorn University, the grant number RA63/018

**Patients**

We enrolled the patients at the age of 18 – 80 years, who were intubated for more than 48 hours and extubated within 48 hours, able to maintain adequate oxygen saturation (SpO2 ≥ 95%) by using low flow oxygen cannula 1-5 LPM, had stable vital signs, and passed the modified swallowing test with the score of more than 3 points. We excluded patients who were poor cooperative or refused to participate in the study, had contraindication for enteral feeding, cerebrovascular disease or muscle weakness, head and neck cancer, structural abnormalities or history of surgery within oral cavity or pharyngeal area, previous diagnosis of dysphagia, skin lesions which interfered with submental EMG monitoring and had automated implantable cardioverter-defibrillator (AICD) or permanent pacemaker.

To screen the eligible patients, the modified water swallowing test was performed by asking the postextubation patients to swallow 3 ml of water and then swallow their own saliva at least 2 times. We observed the failure of swallowing, choking and/or changes in breathing, or wet hoarseness. The worst swallowing activity was evaluated and recorded as the final result. The score of more than 3 points was defined as passing the test.
Equipment and techniques

We applied HFNO (OptiflowTM, Fisher and Paykel healthcare) to our patients. Muscle activity (bilateral suprahylid muscles) during swallowing was measured by using two surface electrodes that attached to the skin at a submental region. Respiratory phases were monitored using ECG-derived respiratory signals and electromyography (EMG) of respiratory muscles, including bilateral sternocleidomastoid muscles, 2nd intercostal muscles and diaphragm. The continuous infusion of water was performed by using a 50 ml syringe, infusion pump and extension tube with the length of 42 inches. The distal tip of the extension tube was placed on the retromolar gingiva.

Study protocol

After informed consent, the eligible patients were assigned into two groups by block of four randomization. The patients in each group were in the upright position and applied either HFNO or LFNO for 5 minutes. The HFNO setting was a flow rate at 50 LPM, temperature 34 °C and adjustable FiO₂ to maintain SpO₂ at least 95%, while the LFNO setting was a flow rate at 5 LPM to maintain SpO₂ at least 95%. Subsequently, we asked the patients to swallow the 10 ml continuous water infusion within one minute. The continuous water swallowing test was repeated for three times. The frequency of swallows and timing of swallowing in relation to respiratory phases, classified into 4 patterns, namely I; Inhale-swallow-inhale, E; Exhale-swallow-Exhale, I-E; Inhale-swallow-Exhale and E-I; Exhale-swallow-Inhale, were recorded. The respiratory phases were monitored by ECG-derived respiratory signals and EMG of respiratory muscles. Blood pressure, heart rate and oxygen saturation were also monitored. After completion of the first period, LFNO with an adjustable flow rate of 1-5 LPM to achieve SpO2 at least 95% was provided during the 5-minute washout period. Then, the second period was started. The patients were switched to receive the other type of oxygen therapy and the same procedure was performed. (Figure 2)

During the swallowing test, if the signs of aspiration, including cough, choking, breathlessness, decrease in SpO₂ by more than 2% or vital sign changes presented, the test would be immediately stopped and the patients would be rescued with the aspiration treatment protocol.

End points

The primary endpoint was the effects of high flow nasal oxygen on the coordination between swallowing and breathing in the postextubation patients, compared with conventional low flow nasal oxygen.

The secondary endpoint was factors that might affect the coordination between swallowing and breathing in the postextubation patients, such as age, sex, comorbidities and duration of intubation.

Statistical analysis

The calculated sample size was 22, which provided 80% power at 0.05 level of significance. The continuous data were expressed as mean ± SD or median [Q1, Q3]. The categorical data were expressed as numbers or percentages. The baseline characteristics of the patients receiving HFNO and LFNO were compared using chi-square or independent t-test or Wilcoxon signed ranks test. The patterns of the relationship between swallowing and breathing were expressed as percentages of each swallowing pattern to total numbers of swallows (using mean values of three swallowing tests during the HFNO and LFNO periods). The differences of these percentages between the HFNO and LFNO periods were compared by Wilcoxon signed ranks test. Additionally, chi-square and independent t-test or Wilcoxon signed ranks test were used to evaluate the factors that might affect the coordination between swallowing and respiration. P-value of < 0.05 was accepted as statistically significant.

Results

A total of 40 patients met the inclusion criteria but 16 of them were excluded due to delirium, poor cooperation, contraindication for enteral feeding, head and neck cancer, prior diagnosis with dysphagia and refusing to participate in the study. Twenty-four patients (16 males and 8 females) were enrolled into our study and assigned into 2 groups. (Fig. 3) One patient from each group dropped out during the test due to intolerance to high flow oxygen. Therefore, there were 22 patients who completed the study. Baseline characteristics were shown in table 1. The mean age of the eligible patients was 55.8 ± 12.21 years. The majority of them had the underlying disease of hypertension (50%) or diabetes mellitus (40.9%). The most common indication for invasive mechanical ventilation was pneumonia,
followed by congestive heart failure, with the median duration of endotracheal intubation of 2.5 days. The median APACHE II score on the study date was 6.

The median frequencies of total swallowing numbers (three minutes) were 18.5 in the HFNO period and 21 in the LFNO period (\(p = 0.158\)). The mean expiratory time in one minute during the swallowing test was significant longer in HFNO period (41.48 ± 3.99 in HFNO vs 39.21 ± 2.9 in LFNO, \(p < 0.001\)). However, the respiratory rate during the swallowing test was not different (19.5[17, 21] in HFNO vs 20[18, 24] in LFNO, \(p = 0.068\)). (Table 2)

For the swallowing-breathing coordination, we calculated each swallowing pattern in percentages to the total swallows. The most common swallowing pattern in both HFNO and LFNO periods was the exhale-swallow-exhale pattern (E-swallow), followed by the inhale-swallow-inhale pattern (I-swallow). The patients using HFNO had higher percentage of the E-swallow pattern (74.3% in HFNO vs 67.6% in LFNO; \(p = 0.048\)) and lower percentage of the I-swallow pattern (14.3% in HFNO vs 23.1% in LFNO; \(p = 0.044\)). (Fig. 4) The numbers of other swallowing patterns were not different between 2 groups. We analyzed the favourable swallowing patterns (E and I-E swallows) and the unfavourable swallowing patterns (I and E-I swallows) and found that the favourable pattern was higher while using HFNO. (Fig. 5)

For the secondary outcomes, we determined the factors that might affect the swallowing-breathing coordination by using the median values of the percentage of each swallowing pattern as the cut-off values to separate the patients into 2 subgroups and analyzing parameters possibly associated with the presence of each swallowing pattern.

In the subgroup analysis, the older age (61.73 vs 50 years; \(p = 0.020\)) was associated with the presence of higher percentage of the E-swallow pattern (Table 3). Except for the age previously mentioned, there were no factors related to the higher percentages of each swallowing pattern.

**Discussion**

Our study demonstrated the effect of HFNO on the coordination of swallowing and breathing in the postextubation patients. During the HFNO period, there were the higher percentage of the E-swallow pattern and lower percentage of the I-swallow pattern, compared with the LFNO period. However, regardless of the type of oxygen therapy, the E-swallow pattern was the predominant swallowing and breathing relationship in the postextubation patients. In addition, only the greater age affected the presence of the E-swallow pattern.

Application of HFNO promoted the synchronization between swallowing and breathing during the postextubation period. There were several reasons explaining these findings.

Firstly, our study showed that HFNO lengthened the expiratory time, as a result the probability of swallowing during the expiratory phase increased. Thus, HFNO significantly increased the E-swallow pattern and the breathing resumption with expiration after swallowing helped protect the airways from aspiration.

Secondly, Thawanapong S and Kongpolprom N demonstrated that HFNO shortened the mean swallowing latency time in the postextubation patients.\(^{13}\) The swallowing latency time was time from the swallowing onset (time when the patients were asked to swallow) to the onset of the first wave in surface electromyography. The longer latency time was associated with aspiration\(^{14}\), so the decreased latency time from HFNO might reflect the more effective and synchronized swallowing. However, our study could not demonstrate the swallowing latency time due to the different technique of the swallowing test.

Lastly, the subglottic pressure could stabilize the pharyngeal structure or stimulate airway mechanoreceptors, which influenced the swallowing efficiency.\(^{19}\) The previous studies showed that the reduction of subglottic pressure prolonged duration of pharyngeal contraction in the healthy subjects.\(^{16}\) Additionally, in tracheostomized patients, the decreased subglottic pressure slowed the pharyngeal transit time, possibly leading to accumulation of pharyngeal residue and aspiration.\(^{17,18}\) In contrast, HFNO provided positive airway pressure\(^{15}\), which increased the subglottic pressure and might enhance the swallowing efficiency.

However, the increased percentage of the E-swallow pattern during the HFNO period in our study was inconsistent with a previous study. Sanuki et al.\(^{10}\) demonstrated the swallowing-breathing patterns were not affected by the 3 different flow rates (15, 30 and 45 LPM) of HFNO in the healthy volunteers. It might be explained by the different populations. We conducted the study in the postextubation patients, who might benefit from the high flow oxygen physiology. The postextubation patients generally had more work of breathing,
worse respiratory mechanics and higher respiratory rate than the healthy volunteers. HFNO could recruit alveoli and increase effective ventilation, which minimized work of breathing and respiratory rate during the postextubation period.\textsuperscript{12} Although our study showed no difference in respiratory rates between HFNO and LFNO, the improvement of respiratory physiology might result in breathing comfort and swallowing facilitation. For these reasons, the coordination of swallowing and breathing improved while using HFNO.

Moreover, our study demonstrated the majority of the swallowing-breathing pattern was the E swallow, followed by the I swallow, while Sanuki et al.\textsuperscript{10} demonstrated the most common pattern was the E swallow, followed by the I-swallow-E in the healthy volunteers. The higher presence of the I swallow in our study might be from the illness associated with changes in breathing patterns. It was supported by a previous study. Roxann Diez Gross et al.\textsuperscript{21} showed an increase in the I swallow in chronic obstructive pulmonary disease, which possibly resulted from dynamic hyperinflation.

Earlier studies demonstrated that the swallowing and respiration relationship was altered by aging. There were high occurrences of swallowing during inspiration in the elderly. Bonnie martin harris et al.\textsuperscript{20} reported that in healthy adults, the mean age for the E-swallow was 56 years while the mean age for the I swallow and E-I swallow was 68 years. In contrast, our study found that the more advanced age was associated with the higher percentage of the E swallow. This finding might result from the difference of the population and study protocol. In our study, the severity of illness might more influence the swallowing coordination than aging. In addition, we performed the continuous water swallowing test, while Bonnie martin harris et al. performed the bolus swallowing test. Therefore, the result could not be directly compared.

Our study had some limitations. The continuous water infusion was used to test the swallowing-breathing coordination and the recruited patients had to pass the modified swallowing test. Thus, our findings could not apply to a food bolus and the patients with dysphagia.

**Conclusions**

This was the first study demonstrating the provision of HFNO during the postextubation period increased the E-swallow and decreased the I-swallow, compared with LFNO. These findings pointed out that HFNO improved the swallowing-breathing coordination in the postextubation patients and possibly reduced the risk of aspiration. Further research is needed to confirm our results.

**Declarations**

**Ethics approval and consent to participate**

The protocol was approved by the institutional review board of the Faculty of Medicine, Chulalongkorn University. (Approval certificate no. 143/62)

Informed consent was obtained from the patients or their nearest relatives.

**Consent for publication**

not applicable

**Availability of data and materials**

All data generated or analysed during this study are included in this published article and its supplementary information files.

**Competing interests**

The authors declare no competing interests.

**Funding**
Authors' contributions

Both PR and NK contributed the conception and design of this study. PR contributed to the acquisition of data. PR and NK analyzed and interpreted the data. PR drafted the manuscript. NK contributed to its critical revision. Both PR and NK approved the final version submitted for publication and take responsibility for the statements made in the published article.

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References

1. Corrado TA, Iskandar G, Pelaia G, Abdalla K, Navalesi P. A High-flow nasal oxygen therapy in intensive care and anaesthesia. Br J Anaesth. 2018;120(1):18e27.
2. Gonzalo Hernández C, Vaquero L, Colinas R, Cuena. Paloma González et.al. Effect of Postextubation High-Flow Nasal Cannula vs Noninvasive Ventilation on Reintubation and Postextubation Respiratory Failure in High-Risk Patients. A Randomized Clinical Trial. JAMA. 2016;316(15):1565–74.
3. Hernandez G, Vaquero C, Gonzalez P, Subira C, Frutos-Vivar F, Rialp G, et al. Effect of Postextubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Reintubation in Low-Risk Patients: A Randomized Clinical Trial. JAMA. 2016;315(13):1354–61.
4. Rassameehiran S, Klimjit S, Mankongpaisamrung C, Rakvit A. Postextubation Dysphagia. Proc (Bayl Univ Med Cent). 2015;28(1):18–20.
5. Koichiro Matsuoa JB, Palmer. Coordination of Mastication, Swallowing and Breathing. Jpn Dent Sci Rev. 2009;45(1):31–40.
6. Gross RD, Atwood CW Jr, Ross SB, Eichhorn KA, Olszewski JW, Doyle PJ. The coordination of breathing and swallowing in Parkinson’s disease. Dysphagia. 2008;23:136–45.
7. Nathalie Samson B, Roy A, Ouimet, François Moreau-Bussière, D, Dorion et al. Origins of the inhibiting effects of nasal CPAP on nonnutritive swallowing in newborn lambs. Prospective cohort study. J Appl Physiol. 2008;105:1083–1090.
8. Ryuji Hori M, Isaka K, Oonishi. Toru Yabe and Yoshitaka Oku. Coordination between respiration and swallowing during non-invasive positive pressure ventilation. Respirology. 2016;21:1062–7.
9. Corley A, Caruana LR, Barnett AG, Tronstad Ø, Fraser JF. Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. Prospective cohort study. Br J Anaesth. 2011;107(6):998–1004.
10. Sanuki T, Mishima G, Kiriishi K, Watanabe T, Okayasu I, Kawai M, et al. Effect of nasal high-flow oxygen therapy on the swallowing reflex: an in vivo volunteer study. Clin Oral Investig. 2017;21(3):915–20.
11. Wakasugi YTH, Hattori F, Motohashi Y, Nakane A, Goto S, et al. Screening test for silent aspiration at the bedside. Dysphagia. 2008;23(4):364–70.
12. Rittayamai N, Tscheikuna J, Rujiwit P. High-flow nasal oxygen cannula versus conventional oxygen therapy after endotracheal extubation: a randomized cross over physiologic study. Respir Care. 2014;59:485e90.
13. Thawanaphong S, Kitisonprayoonkul W, Pongpipatpaiboon K, Kongpolprom N. Electromyographicswallowingstudyduringhigh flow oxygen therapy compared with low flow oxygen therapy in post-extubated patients European Respiratory Journal 2019; 54: Suppl. 63, PA4021.
14. Kobayashi HSK, Sasaki H. Aging Effects on Swallowing Reflex. Chest. 1997;111(5):1466.
15. Hori R, Ishida R, Isaka M, Nakamura T, Oku Y. Effects of noninvasive ventilation on the coordination between breathing and swallowing in patients with chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2019;14:1485–94.
16. Gross RD, Atwood CW Jr, Grayhack JP, Shaiman S. Lung volume effects on pharyngeal swallowing physiology. J Appl Physiol. 2003;95(6):2211–7. doi:10.1152/japplphysiol.00316.2003.

17. Dettelbach MA, Gross RD, Mahlmann J, Eibling DE. Effect of the passy-muir valve on aspiration in patients with tracheostomy. Head Neck. 1995;17(4):297–302. doi:10.1002/(ISSN)1097-0347.

18. Logemann JA, Pauloski BR, Colangelo L. Light digital occlusion of the tracheostomy tube: a pilot study of effects on aspiration and biomechanics of the swallow. Head Neck. 1998;20(1):52–7. doi:10.1002/(ISSN)1097-0347.

19. Eibling DE, Gross RD. Subglottic air pressure: a key component of swallowing efficiency. Ann Otol Rhinol Laryngol. 1996;105(4):253–8. doi:10.1177/000348949610500401.

20. Harris BM, Michel MartinBBrodsky,Y, Walters CLFord,B, Heffner J. Breathing and swallowing dynamics across the adult lifespan. Arch otolaryngol head neck surg. 2005;131:762–70.

21. Gross R, Atwood C, Ross S, Olszewski J, Eichorn K. The Coordination of Breathing and Swallowing in Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2009;179:559–65.

### Tables

#### Table 1: Baseline characteristics of study population

| Baseline characteristics of study population (n=22) |       |
|-----------------------------------------------|-------|
| Age (years), mean ± SD                        | 55.86 ± 12.21 |
| Sex : Male, n (%)                             | 15 (68.2%) |
| BMI (Kg/m²), mean ± SD                        | 22.3 ± 4.41 |

| Indication for mechanical ventilation, n (%)  |       |
|-----------------------------------------------|-------|
| Pneumonia                                     | 9 (41%) |
| Congestive heart failure                      | 4 (18%) |
| Alteration of consciousness                   | 4 (18%) |
| Lactic acidosis                               | 3 (14%) |
| Asthmatic attack                              | 1 (4.5%) |
| COPD with acute exacerbation                  | 1 (4.5%) |

| APACHE II score on study date, median [Q1,Q3] | 6 [4,7.75] |

| Endotracheal tube intubation duration (days), median[Q1,Q3] | 2.5 [2.5,7.5] |

| Mechanical ventilation duration (days), median [Q1,Q3] | 2.5 [2.5,5.5] |

| Comorbidities, n (%) |       |
|---------------------|-------|
| Hypertension        | 11 (50%) |
| DM type 2           | 9 (40.9%) |
| Dyslipidemia        | 7 (31.8%) |
| Chronic kidney disease | 6 (27.3%) |
| Ischemic heart disease | 1 (4.5%) |

| History of sedative drugs use, n (%) |       |
|-------------------------------------|-------|
| Fentanyl                            | 11 (50%) |
| Midazolam                           | 4 (18.2%) |
| Propofol                            | 1 (4.5%) |
| None                                | 6 (27%) |

| History of neuromuscular blockade use, n (%) | 1 (4.5%) |
| Outcomes                                      | Total patients (n=22) | p-value |
|----------------------------------------------|-----------------------|---------|
|                                              | HFNO                  | LFNO    |         |
| Respiratory rate (rpm), median [Q1,Q3]       | 19.5 [17, 21]         | 20 [18, 24] | 0.068   |
| Expiratory time within 1 minute (sec), mean ± SD | 41.48 ± 3.99         | 39.21 ± 2.9 | <0.001* |
| Total swallowing numbers*, median [Q1,Q3]    | 18.5 [15, 22]         | 21 [17, 24] | 0.158   |

**Swallowing-breathing coordination, median [Q1,Q3]**

|                                          | HFNO                  | LFNO    |         |
|------------------------------------------|-----------------------|---------|---------|
| I swallow (number)                       | 2.5 [1, 4]            | 4 [3, 6] | 0.002*  |
| I swallow (%)                            | 14.35 [6.7, 22.2]     | 23.1 [10.7, 28.5] | 0.044*  |
| E swallow (number)                       | 14 [9, 21]            | 13.5 [11, 19] | 0.452   |
| E swallow (%)                            | 74.3 [65.9, 86.7]     | 67.6 [55.6, 81] | 0.048*  |
| I-E swallow (number)                     | 0.5 [0, 2]            | 1 [0, 2] | 0.292   |
| I-E swallow (%)                          | 1.1 [0, 8.3]          | 6.1 [0, 9.3] | 0.384   |
| E-I swallow (number)                     | 1 [0, 2]              | 1 [0, 2] | 0.886   |
| E-I swallow (%)                          | 7.5 [0, 10.5]         | 4.5 [0, 9.5] | 0.943   |

*Total swallowing numbers : summation of three swallowing tests
I swallow : inhale – swallow – inhale
E swallow : exhale – swallow – exhale
I-E swallow : inhale – swallow – exhale
E-I swallow : exhale – swallow - inhale

**Table 3: Secondary outcomes; Exhale-swallow-Exhale (E-swallow) pattern**
### Variables

| Variables               | Total (n=22) | HFNO (n=22) | LFNO (n=22) |
|-------------------------|--------------|-------------|-------------|
| Age (yr), mean ± SD    | 50±10.79     | 49.89±12.22 | 55.45±12.86 |
| E <=68% (n=11)         | 61.73±11.01  | 60±10.78    | 56.27±12.15 |
| E >68% (n=11)          |              | 0.020*      |             |
| Male, n (%)            | 8 (72.7%)    | 6 (66.7%)   | 8 (72.7%)   |
| Female, n (%)          | 3 (27.3%)    | 4 (36.4%)   | 4 (36.4%)   |
| BMI (Kg/m²), mean ± SD | 20.4 ± 2.38  | 20.01 ± 2.72| 21.61 ± 4.06|
| Comorbidities, n (%)   |              |             |             |
| HT                     | 3 (27.3%)    | 3 (33.3%)   | 5 (45.5%)   |
| DM                     | 3 (27.3%)    | 3 (33.3%)   | 4 (36.4%)   |
| DLP                    | 3 (27.3%)    | 3 (33.3%)   | 3 (27.3%)   |
| CKD                    | 3 (27.3%)    | 3 (33.3%)   | 4 (36.4%)   |
| IHD                    | 0 (0%)       | 1 (9.1%)    | 1 (9.1%)    |
| APACHE II, mean ± SD   | 5.55 ± 2.66  | 5.89 ± 2.67 | 6.55 ± 3.42 |
| ETT duration (days), median | 3 [2, 4] | 2 [2, 6] | 3 [2, 4] |
| Sedation, n (%)        |              |             |             |
| Fentanyl               | 6 (54.5%)    | 6 (66.7%)   | 6 (54.5%)   |
| Midazolm               | 3 (27.3%)    | 3 (33.3%)   | 2 (18.2%)   |
| Propofol               | 1 (9.1%)     | 1 (11.1%)   | 1 (9.1%)    |

**Figures**

**Figure 1**

Swallowing and breathing coordination patterns This figure demonstrates 4 patterns of the swallowing and breathing coordination, namely E-swallow: swallow during the expiratory phase, I-E swallow: swallows occurring in the inspiratory phase and followed by the
expiratory phase, I-swallow: swallow during the inspiratory phase, and E-I swallow: swallows occurring in the expiratory phase and followed by the inspiratory phase.

Figure 2

The study protocol MWST; modified water swallowing test, EMG; electromyography, HFNC; high flow nasal cannula and LFNC; low flow nasal cannula

Figure 3

Flow of participants
Figure 4

Comparison of percentages of each swallowing pattern to total swallows between the HFNO vs LFNO period.

Figure 5
The summation of two unfavourable patterns (I and E-I swallows) and two favourable patterns (E and I-E swallows), compared between the HFNO vs LFNO period