RESPIRATORY CARE Paper in Press. Published on October 20, 2020 as DOI: 10.4187/respcare.08145

Mechanical Insufflation-Exsufflation With Oscillations in Amyotrophic Lateral Sclerosis With Home Ventilation via Tracheostomy

Jesus Sancho, Enric Burés, Santos Ferrer, Carolina Lahosa, Jaime Signes-Costa, and Emilio Servera

BACKGROUND: Mechanical insufflation-exsufflation (MI-E) applied via tracheostomy tubes in patients with amyotrophic lateral sclerosis (ALS) who are on home mechanical ventilation via tracheostomy is an effective procedure for respiratory secretion management. Nonetheless, tenacious secretions may remain and increase the risk of respiratory infections. The aim of this study was to determine whether adding oscillations to MI-E could reduce the rate of respiratory infections and the need for bronchoscopy to remove secretions in patients with ALS on home mechanical ventilation via tracheostomy. METHODS: This was a 2-y, prospective, crossover study. Subjects were treated with conventional MI-E and MI-E with oscillations for 2 alternate 6-month periods. Data were collected on episodes of respiratory infections, hospital admission, and number of bronchoscopy procedures. RESULTS: In the 19 ALS subjects enrolled, the median (interquartile range [IQR]) number of acute respiratory infections per subject was 1.0 (0.5–2.0) in the MI-E period and 0.0 (0.0–2.0) in the MI-E plus oscillations period ($P = .92$). The median (IQR) number of hospital stays was 0.0 (0.0–1.0) in the MI-E period and 0.0 (0.0–1.0) in the MI-E plus oscillations period ($P = .80$). The median (IQR) number of bronchoscopies per subject was 0.0 (0.0–1.0) in MI-E period and 0.0 (0.0–0.5) in the MI-E plus oscillations period ($P = .26$). MI-E plus oscillations treatment had no impact on the risk of respiratory infections (odds ratio 3.71, 95% CI 0.81–16.84, $P = .09$) or the need for bronchoscopy (odds ratio 2.70, 95% CI 0.44–16.68, $P = .29$). CONCLUSIONS: Adding oscillations to MI-E therapy in subjects with ALS on home mechanical ventilation via tracheostomy did not decrease the risk of respiratory infections, hospital admission, or need for bronchoscopy. *Key words: amyotrophic lateral sclerosis; respiratory secretions; respiratory failure; long-term mechanical ventilation; tracheostomy; mechanical insufflation-exsufflation.* [Respir Care 0;0(0):1–●. © 0 Daedalus Enterprises]

Introduction

Noninvasive respiratory muscle aids, such as noninvasive ventilation and assisted coughing techniques, can prolong survival in patients with amyotrophic lateral sclerosis (ALS).[1] However, in those with severe bulbar dysfunction, noninvasive muscle aids may become ineffective, and a tracheostomy may be necessary for life support in patients who accept the procedure.[2,3] Home mechanical ventilation via tracheostomy provides adequate ventilation and direct access to respiratory secretions, prolonging life in these patients, particularly for those who exhibit severe bulbar

Drs Sancho and Ferrer are affiliated with the Respiratory Care Unit, Respiratory Medicine Department, Hospital Clínico Universitario, Valencia, Spain. Drs Sancho, Burés, Ferrer, Lahosa, Signes-Costa, and Servera are affiliated with the Research Group for Respiratory Problems in Neuromuscular Diseases, INCLIVA Health Research Institute, Valencia, Spain. Drs Sancho, Ferrer, Burés, Lahosa, and Signes-Costa are affiliated with the Respiratory Medicine Department, Hospital Clínico Universitario, Valencia, Spain. Dr Servera is affiliated with the Physical Medicine Department, Universitat de València, Valencia, Spain.

Enric Burés is supported by a grant from INCLIVA Health Research Institute, sponsored by Philips-Respironics. The other authors have disclosed no conflicts of interest.

Correspondence: Jesus Sancho MD PhD, Respiratory Care Unit, Respiratory Medicine Service, Hospital Clínico Universitario, Valencia, Spain. Avd Blasco Ibañez 17, 46010 Valencia, Spain. E-mail: jesus.sancho@uv.es.

DOI: 10.4187/respcare.08145

RESPIRATORY CARE Paper in Press. Published on October 20, 2020 as DOI: 10.4187/respcare.08145

dysfunction.[3] Nevertheless, the number of patients with ALS treated with home mechanical ventilation via tracheostomy is low, and this treatment is usually reserved for those who do not respond to noninvasive respiratory management.[3]

Mechanical insufflation-exsufflation (MI-E) applied directly through tracheostomy tubes is a safe and effective procedure to manage respiratory secretions in patients with ALS on home mechanical ventilation via tracheostomy.[4] Conventional secretion management using transtracheal suctioning with a catheter fails to reach the left main bronchus in > 90% of cases, and peripheral secretions are not directly removed.[5] In this regard, MI-E has greater efficacy than suctioning in removing respiratory secretions and improving ventilator and mechanical parameters.[4] Patients also suffer less discomfort with MI-E than with conventional catheter suctioning.[4] Nevertheless, respiratory infections are the main cause of hospital admission and death in patients with ALS on home ventilation via tracheostomy.[3,6] Furthermore, tenacious secretions and mucus plugs leading to the obstruction of airways or tracheostomy tubes are a complication in tracheostomized patients.[7]

Some current generation MI-E devices now include a feature that enables mechanically assisted coughing to be combined with oscillatory vibrations during insufflation or exsufflation, or during both cycles.[8] The aim is to loosen thick secretions from the bronchial wall and thus facilitate their clearance, avoid the need for bronchoscopy, and lower the risk of respiratory infections. Theoretically, this provides a peripheral airway clearance technique using oscillation to mobilize secretions, complementing the role of MI-E as a central airway clearance technique.[9] Data proving the effectiveness of this combination in patients with ALS and tracheostomy are lacking. This study aims to evaluate the effectiveness of adding oscillations to MI-E in reducing the rate of respiratory infections and the need for bronchoscopy to remove thick secretions in patients with ALS on home mechanical ventilation via tracheostomy.

QUICK LOOK

Current knowledge

Mechanical insufflation-exsufflation applied directly through tracheostomy tubes is a safe and effective procedure to manage respiratory secretions in patients with ALS on home invasive mechanical ventilation. Despite the proven usefulness of the technique, tenacious secretions and mucus plugs are a common complication, and respiratory infections are the main cause of hospital admission and death in this patient population.

What this paper contributes to our knowledge

Adding oscillations to mechanical insufflation-exsufflation for the management of respiratory secretions in subjects with ALS on home mechanical ventilation via tracheostomy did not decrease the number of acute respiratory infections, hospital admissions due to chest infections, or bronchoscopies for thick secretions or mucus plug removal.

Methods

A 2-y, prospective, crossover study was performed in a respiratory care unit located in a university hospital to compare the use of conventional MI-E via tracheotomy and MI-E with oscillations in clinically stable subjects with ALS (diagnosed according to the revised El Escorial criteria[10]) who were receiving home invasive mechanical ventilation via tracheostomy. Consecutive patients with ALS on home invasive mechanical ventilation managed at our respiratory care unit were included in the study. Prior to the method tested in this study, home tracheostomy ventilation was provided with a portable volume-cycled ventilator in assist-control mode and respiratory secretions were managed at home by conventional MI-E, applied by well-trained caregivers.[3] In all subjects, to avoid tenacious secretions, humidification was provided with a heated humidifier connected to the ventilator circuit, proximal to the ventilator, along with proper hydration; saline instillation was not performed. Exclusion criteria were refusal to participate in the study, presence of bronchial disease (eg, asthma, COPD, bronchiectasis) or a contraindication to the use of MI-E (eg, antecedent of barotrauma, undrained neumothorax, pulmonary bullae).[3,4] Informed consent was obtained, and the protocol was approved by the hospital's ethics committee.

Subjects were randomized with a random number generated by a computer to determine which mode would be applied first in each case. For one group, during the first 6 consecutive months, respiratory secretions were managed with conventional MI-E (E70, Philips-Respironics, Murrysville, Pennsylvania) via a tracheostomy tube at home or during hospital admission if necessary; in the following 6 months, secretions were managed with MI-E plus oscillations. For the other group, this procedure was reversed (ie, they received MI-E plus oscillations first).

The appropriate form of MI-E was applied by trained caregivers 3 times a day and as needed on detection of S_{pO_2} < 95%, an increase in peak inspiratory pressure of 5 cm H_2O from baseline values[4] as measured with the home ventilators, or when subjects noted a sensation of retained secretions. Every MI-E session consisted of 6–8 cycles using an insufflation pressure of +40 cm H_2O, an exsufflation pressure of –40 cm H_2O, an insufflation-exsufflation time of 0.67 s and a pause of 1 s. When oscillations were applied, a frequency of 15 Hz and an amplitude of 10 cm

RESPIRATORY CARE Paper in Press. Published on October 20, 2020 as DOI: 10.4187/respcare.08145

H_2O was set. The frequencies and amplitudes chosen are within the range found to be most effective in techniques using high-frequency oscillations for mucus removal and are similar to those used in previous studies.[8,11-13] Every MI-E session was followed by superficial airway suctioning with a conventional catheter connected to a portable home aspiration device (V7, Hersill, Madrid, Spain).

Caregivers were able to contact the respiratory care unit by telephone or e-mail. Follow-up telephone calls were made every 15 d, and hospital visits were scheduled every 3 months. The numbers of lower respiratory tract infections, hospital admissions for acute respiratory tract infections, outcomes of hospitalization, and bronchoscopies to remove respiratory secretions were recorded.

A respiratory tract infection was defined as an increased amount or purulence of respiratory secretions accompanied by fever, dyspnea, thoracic sounds, or chest discomfort.[14] In addition to medical treatment, MI-E session frequency was increased as needed during these acute chest episodes. In cases of clinical deterioration, hospital referrals were encouraged based on recommendations by the primary care physician or the respiratory care unit staff following caregiver contact via e-mail or telephone. Criteria for hospitalization at the respiratory care unit during acute episodes were need for intensive MI-E (ie, $>$ 4 sessions per hour), need for intravenous medication, presence of persistent dyspnea despite adequate home management, failure to remove mucus with mechanically assisted coughing techniques at home, or $S_{pO_2} < 90\%$ despite appropriate home management. The diagnosis of pneumonia was based on the identification of a new pulmonary infiltrate on a chest radiograph upon admission to hospital and signs and symptoms of a lower respiratory tract infection.[14] Indications for bronchoscopy were established by the attending pulmonologist at hospital admission or during the in-patient stay according to the presence of specified criteria, and despite the application of MI-E with increasing set insufflation-exsufflation pressures (pressures were increased by 10 cm H_2O, both in insufflation and exufflation, up to $\pm$ 60 cm H_2O, if sessions with MI-E were not effective): persistent drop in S_{pO_2}, maintained peak inspiratory pressures values $>$ 30 cm H_2O, or difficulty passing the suction catheter.

Statistical Analysis

Binary and categorical variables were summarized using frequency counts and percentages. Continuous distributed variables were expressed as median and interquartile range (IQR). Data comparisons were performed using a paired data Wilcoxon test. Dichotomous variables were compared using the chi-square test. Poisson regression was performed to compare the number of respiratory infections, hospitalizations due to respiratory infection, and bronchoscopies performed for mucus removal under each treatment modality and to confirm the results from the Wilcoxon test. Logistic regression analysis was performed to evaluate whether adding oscillations to MI-E contributed to decreasing the risk of respiratory infections and the need for bronchoscopy for tenacious secretions and mucus plug removal. Statistical significance was set at $P < .05$.

Results

During the study period, no subject managed in the respiratory care unit declined to participate in the study. A total of 19 subjects with ALS on home invasive mechanical ventilation via tracheostomy were enrolled (Table 1). Median (IQR) age was 67 (56–76) y, and 7 (36.8%) subjects were male. Time from ALS diagnosis was 20 (9–59) months, and time from tracheostomy was 8 (2–39) months. Nine subjects (47.4%) had bulbar onset disease. All subjects were on full-time, invasive mechanical ventilation using volume control continuous mandatory ventilation without supplemental oxygen and received enteral feeding via percutaneous endoscopic gastrostomy. All subjects had the same cuffed tracheostomy tube (Shiley 6LPC, Covidien/Medtronic, Dublin, Ireland). Four subjects used mechanical ventilation through tracheostomy tube with a deflated cuff, but in these subjects the cuff was inflated to 30 cm H_2O during MI-E sessions.

Eleven subjects were randomly assigned to receive MI-E first, while 8 were assigned to receive MI-E plus oscillations first, and the respiratory secretion management mode was switched after 6 months. Although there were no subject complaints with either modality, 1 subject who started the protocol with MI-E plus oscillations refused to switch to the conventional MI-E device after 6 months due to the greater comfort experienced with MI-E with oscillations. Neither MI-E nor MI-E plus oscillations caused side effects.

During the 6-month follow-up period, there were 17 respiratory infection episodes during MI-E (3 of which were pneumonia) and 13 episodes (1 was pneumonia) during MI-E plus oscillations. Median (IQR) acute respiratory infections per subject were 1.0 (0.5–2.0) during the MI-E period and 0.0 (0.0–2.0) during the MI-E plus oscillations period ($P = .92$). The odds ratio obtained for respiratory tract infection within 6 months was 3.71 (95% CI 0.81–16.84, $P = .09$). There were 8 hospital admissions due to respiratory infection during the MI-E period and 6 during the MI-E plus oscillations period, with median (IQR) per subject of 0.0 (0.0–1.0) versus 0.0 (0.0–1.0), respectively, ($P = .80$). Bronchoscopy was performed in 5 subjects (a total of 8 times) to remove thick secretions or mucus plugs during the MI-E period and in 2 subjects during the MI-E plus oscillations period (a total of 6 times) ($P = .27$). The median (IQR) number of bronchoscopies per subject was 0.0 (0.0–1.0) during the MI-E period and 0.0 (0.0–0.5) during the MI-E plus oscillations period ($P = .26$). The odds ratio of the need for bronchoscopy to remove

RESPIRATORY CARE Paper in Press. Published on October 20, 2020 as DOI: 10.4187/respcare.08145

Table 1. Demographic and Clinical Characteristics of Subjects

Subjects, *n*	19
Gender (male/female)	7/12
Age, y	67 (56–76)
ALS onset (spinal/bulbar)	10/9
Time from ALS onset, months	31 (21–68)
Time from ALS diagnosis, months	2 (9–59)
Time from tracheostomy performance, months	8 (2–39)
Gastrostomy (yes/no)	19/0
ALSFRS-R at study inclusion	8 (7–10)
Ventilatory parameters*	
Tidal volume, mL	75 (70–85)
Back-up breathing frequency, breaths/min	15 (14–16)
Peak inspiratory pressure, cm H_2O	10.0 (17–18)
S_{pO_2} in stable condition, %	97 (97–98)
P_{tcCO_2} in stable condition, mm Hg	40.0 (38–41)

Summary data are presented as median (interquartile range). Peak inspiratory pressure, S_{pO_2}, and P_{tcCO_2} values represent the average value of a measurement performed over 30 min in stable medical condition during the hospital medical visit.
* Volume-cycled continuous mandatory ventilation mode.
ALS = amyotrophic lateral sclerosis
ALSFRS-R = Revised Amyotrophic Lateral Sclerosis Functional Rating score
P_{tcCO_2} = transcutaneously measured partial pressure of CO_2

respiratory secretions was 2.70 (95% CI 0.44–16.68, $P = .28$). No statistical differences were found in the Poisson regression for respiratory tract infections ($P = .51$), hospital admissions ($P = .59$), or bronchoscopies for mucus removal ($P = .23$).

Discussion

Our results indicate that oscillations added to MI-E for management of respiratory secretions in subjects with ALS on home invasive mechanical ventilation via tracheostomy do not decrease the number of acute respiratory infections, hospital admissions due to chest infections, or the number of bronchoscopies for thick secretion or mucus plug removal.

Patients receiving long-term home invasive mechanical ventilation via tracheostomy tend to experience increased production and decreased mobilization of respiratory secretions. Contributing factors are the fact that the tracheostomy tube represents a foreign body irritating tracheal tissue and inducing an inflammatory response, reduced mucociliary clearance, and cough effectiveness is greatly decreased in patients with ALS who require a tracheostomy.[15] Moreover, mechanical ventilation through tracheostomy tubes bypasses the upper airway, eliminating the humidifying, warming, and filtering function of the upper airway.[15] These factors lead to increased mucus volume and consistency and consequently the risk of retained secretions, mucus plugs, and respiratory infections, indicating the vital need for effective respiratory secretion management in patients with ALS on home invasive mechanical ventilation via tracheostomy. MI-E is often used to manage respiratory secretions in patients with long-term invasive ventilation, as tracheal suctioning with a conventional catheter is limited to secretions of proximal airways and is associated with traumatic lesions of the mucosa, poor tolerance, pain, and possible respiratory and hemodynamic adverse events.[4] MI-E is more effective in eliminating airway secretions than tracheal suctioning. S_{pO_2}, peak inspiratory pressure, mean airway pressure, and work of breathing improve significantly with MI-E sessions.[4,16] Subjects have reported MI-E to be more effective and more comfortable than suctioning, and different studies have reported on the safety of MI-E in subjects with ALS on long-term home invasive mechanical ventilation via tracheostomy.[3,4] However, some studies report mucus plugging, sometimes requiring bronchoscopy, despite the use of MI-E with tracheostomy tubes.[7] This is the motivation behind adding oscillations to MI-E to manage tenacious secretions and prevent mucus plug formation.

Additional techniques for mucus removal have been utilized in patients with invasive mechanical ventilation via tracheostomy, such as lung volume recruitment or techniques using high-frequency oscillations, such as high-frequency chest wall oscillations or intrapulmonary percussive ventilation.[7] Bidiwala et al[17] reported similar results regarding high-frequency airway clearance techniques in 8 pediatric subjects receiving long-term invasive mechanical ventilation via tracheostomy. Intrapulmonary percussive ventilation decreased the number of lower respiratory tract infections and the number of hospitalizations compared to high-frequency chest wall oscillations. However, in a study performed in a weaning center that included 46 tracheostomized subjects, Clini et al[18] reported no differences in the number of subjects needing bronchoscopy for mucus removal compared to those who received conventional chest physiotherapy or intrapulmonary percussive ventilation.

Although we chose frequencies and amplitudes within the most effective range in techniques using high-frequency oscillations for mucus removal,[11,12] our results indicate that, in comparison to conventional MI-E, adding oscillations in our subjects with ALS on home invasive mechanical ventilation via tracheostomy failed to decrease the number of bronchoscopies required to remove thick secretions or mucus plugs, and the rate of respiratory infections remained unchanged. In a previous report,[13] we noted that oscillations added to MI-E in non-tracheostomized subjects with ALS produced no significant benefit regarding required invasive procedures, chest infections, hospitalizations, or survival compared with conventional MI-E. These results of noninvasive use of MI-E were attributed to the interaction of bulbar dysfunction with the oscillations. Thus, when MI-E is applied through a tracheostomy tube, thus avoiding upper airway interaction, one would expect the results to improve by adding oscillations. However, our results show no

RESPIRATORY CARE Paper in Press. Published on October 20, 2020 as DOI: 10.4187/respcare.08145

differences in variables associated with secretion management by adding oscillations to MI-E.

The main limitation of our research was the small sample size, which necessitated the use of a crossover study design instead of a prospective randomized controlled trial, and limited statistical power. A post hoc analysis for the main study objective (ie, the need for bronchoscopy), accounting for the sample size, showed a power of 62.3%. However, it should be noted that the number of patients with ALS treated with invasive mechanical ventilation via tracheostomy is low,[3,6,19] and this was a single-center study. Another limitation of the study is that oscillations were used in all subjects; in addition, oscillations were applied both in exsufflation and insufflation with a single value for the frequency, although the values for frequency and amplitude are in the range of those found to be more effective in techniques using high-frequency oscillations for mucus removal.[11,12] More bench studies and clinical trials with large sample sizes are necessary to determine whether individualized values for oscillation amplitude and frequency could increase the effectiveness of MI-E through a tracheostomy tube. Additional potential study limitations are seasonal variations in the incidence of respiratory infections and the possibility that one of the MI-E protocols was not used during the winter months, when respiratory infections in the general population are more common. However, in our historical cohort of subjects with ALS on home invasive mechanical ventilation via tracheostomy, the seasonal effect on the incidence of respiratory infections was not relevant; the majority of our subjects were colonized by Gram-negative bacteria, and when a respiratory infection occurred, it was caused by these bacteria without a predominance in a certain period of the year.[3]

Conclusions

Our results suggest that adding oscillations to MI-E therapy applied through tracheostomy tubes in subjects with ALS does not improve performance compared to MI-E alone. In our ALS cohort on home invasive mechanical ventilation via tracheostomy, MI-E plus oscillations failed to reduce the number of bronchoscopies required to remove tenacious respiratory secretions, and the risk of acute respiratory infections and hospital admissions remained the same.

REFERENCES

1. Burkhardt C, Neuwirth C, Sommacal A, Andersen PM, Weber M. Is survival improved by the use of NIV and PEG in amyotrophic lateral sclerosis (ALS)? A post-mortem study of 80 ALS patients. PLoS One 2017;12(5):e0177555.
2. Sancho J, Martínez D, Bures E, Díaz JL, Ponz A, Servera E. Bulbar impairment score and survival of stable amyotrophic lateral sclerosis after noninvasive ventilation initiation. ERJ Open Res 2018;4 (2):00159-2017.
3. Sancho J, Servera E, Díaz JL, Bañuls P, Marín J. Home tracheotomy mechanical ventilation in patients with amyotrophic lateral sclerosis: causes, complications and 1-year survival. Thorax 2011;66(11):948-952.
4. Sancho J, Servera E, Vergara P, Marin J. Mechanical insufflation-exsufflation vs. tracheal suctioning via tracheostomy tubes for patients with amyotrophic lateral sclerosis: a pilot study. Am J Phys Med Rehabil 2003;82(10):750-753.
5. Chatwin M, Toussaint M, Gonçalves MR, Sheers N, Mellies U, Gonzáles-Bermejo J, et al. Airway clearance techniques in neuromuscular disorders: a state of the art review. Respir Med 2018;136(3):98-110.
6. Chio A, Calvo A, Ghiglione P, Mazzini L, Mutani R, Mora G, PARALS. Tracheostomy in amyotrophic lateral sclerosis: a 10-year population-based study in Italy. J Neurol Neurosurg Psychiatry 2010;81(10):1141-1143.
7. Rose L, Adhikari NK, Poon J, Leasa D, McKim DA. Cough augmentation techniques in critically ill: a Canadian national survey. Respir Care 2016;61(10):1360-1368.
8. Sancho J, Bures E, de la Asunción S, Servera E. Effect of high-frequency oscillations on peak cough flows generated by mechanical in-exsufflation in medically stable subjects with amyotrophic lateral sclerosis. Respir Care 2016;61(8):1051-1058.
9. Toussaint M, Chatwin M, Gonzales J, Berlowitz DJ, Toussaint M, Chatwin M, ENMC Respiratory Therapy Consortium. 228th ENMC International Workshop: airway clearance techniques in neuromuscular disorders. Naarden, The Netherlands. Neuromuscul Disord 2018;28(3):289-298.
10. Brooks BR, Miller RG, Swash M, Munsat TL, World Federation of Neurology Research Group on Motor Neuron Diseases. El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord 2000;1 (5):293-299.
11. Gross D, Zidulka A, O'Brien C, Wight D, Fraser R, Rosenthal L, et al. Peripheral mucociliary clearance with high-frequency chest wall compression. J Appl Physiol 1985;58(4):1157-1163.
12. King M, Phillips DM, Zidulka A, Chang HK. Tracheal mucus clearance in high-frequency: chest wall versus mouth oscillation. Am Rev Respir Dis 1984;130(5):703-706.
13. Sancho J, Burés E, Ferrer S, Bondía E, Servera E. Usefulness of oscillations added to mechanical in-exsufflation in amyotrophic lateral sclerosis. Respir Care 2020;65(5):596-602.
14. Woodhead M, Blasi F, Ewig S, Garau J, Huchon G, Ieven M, et al. Guidelines for the management of adult lower respiratory tract infections. Clin Microbiol Infect 2011;17(Suppl 6):E1-E59.
15. Ntoumenopoulos G, Hammond N, Watts NR, Thompson K, Hanlon G, Paratz JD, et al. Secretion clearance strategies in Australian and New Zealand intensive care units. Aust Crit Care 2018;31(4):191-196.
16. Nunes L. D C, Rizzetti DA, Neves D, Vieira FN, Kutchak FM, Wiggers GA, et al. Mechanical insufflation/exsufflation improves respiratory mechanics in critical care: randomized crossover trial. Respir Physiol Neurobiol 2019;266:115-120.
17. Bidiwala A, Volpe L, Halaby C, Fazzari M, Valsamis C, Pirzada M. A comparison of high-frequency chest wall oscillation and intrapulmonary percussive ventilation for airway clearance in pediatric patients with tracheostomy. Postgrad Med 2017;129(2):276-282.
18. Clini EM, Antoni FD, Vitacca M, Crisafulli E, Paneroni M, Chezzi-Silva S, et al. Intrapulmonary percussive ventilation in tracheostomized patients: a randomized controlled trial. Intensive Care Med 2006;32(12):1994-2001.
19. Ceriana P, Surbone S, Segagni D, Schreiber A, Arlucci A. Decision-making for tracheostomy in amyotrophic lateral sclerosis (ALS): a retrospective study. Amyotroph Lateral Scler Frontotemporal Degener 2017;18(7-8):492-497.

RESPIRATORY CARE Paper in Press. Published on October 20, 2020 as DOI: 10.4187/respcare.08145