study is clinically relevant for two reasons. First, obesity is becoming a common finding in mechanically ventilated patients. Second, despite some data in support of the use of NIV among patients with obesity at high risk of extubation failure, NIV is rarely implemented after extubation (2). Although the current study does not represent a definitive trial, we believe that there are solid physiologic reasons that explain why NIV is beneficial after extubation in obesity.

In a recent ambulatory study (3) of patients with obesity and normal-range BMI, we characterized the effects of NIV on work of breathing. Our study rationale stemmed from prior observations that patients with obesity have elevated pleural pressures when mechanically ventilated and have recruitable lungs if adequate positive end-expiratory pressure (PEEP) is set to match resting pleural pressure after a recruitment maneuver (4). We found that applying noninvasive continuous positive airway pressure (CPAP) set to match pleural pressure as measured through esophageal manometry led to a dramatic reduction in work of breathing in ambulatory patients with obesity but not in patients with normal-range BMI. At baseline before CPAP initiation, patients with obesity demonstrated large inspiratory swings in pleural pressure—both for achieving airways opening as well as for VTS—representing a tremendous work of breathing in this population even outside of acute illness. CPAP matching end-expiratory pleural pressure in subjects with obesity dramatically reduced pleural pressure swings, reduced occlusion to airways opening, improved peripheral oxygen saturation, and led to a more homogeneous distribution of ventilation as observed through electrical impedance tomography.

In an intubated patient with BMI of 43 kg/m^2, we observed failure of spontaneous breathing trial when performed according to the hospital standard of care (i.e., low degrees of PEEP, 5 cm H_2O) (5). At 5 cm H_2O PEEP, esophageal manometry revealed both high amounts of end-expiratory pleural pressure and large swings during the inspiratory phase, which is expected in subjects with obesity. When PEEP was set to counterbalance the high degree of pleural pressure, a threefold reduction in inspiratory work of breathing was observed. Furthermore, the analysis of lung ventilation by electrical impedance tomography showed a more homogeneous distribution of ventilation at higher degrees of PEEP and disappearance of a Pendelluft phenomenon (6).

Taken together, these studies suggest that a titrated degree of PEEP to overcome airway occlusion and excessive work of breathing during weaning from mechanical ventilation and the application of postextubation NIV might lead to improved outcomes. Although the goal of a spontaneous breathing trial is to simulate postextubation conditions (baseline work of breathing and respiratory mechanics), NIV might help this subset of patients with obesity readapt to spontaneous breathing conditions, clear lingering anesthetics, and sit awake in the upright position. On the contrary, extubation to atmospheric pressure might promote lung derecruitment and hemodynamic derangement owing to large transthoracic pressure swings, especially in those patients who are not fully awake and/or sitting fully upright.

Although future studies should test the present hypothesis, Thille and colleagues should be complimented for demonstrating improved outcomes in this vulnerable and understudied population. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Gaetano Florio, M.D.
David A. Imber, M.D.
Lorenzo Berra, M.D.*
Massachusetts General Hospital
Boston, Massachusetts

and

Harvard Medical School
Boston, Massachusetts

*Corresponding author (e-mail: lberra@mgh.harvard.edu).

References

1. Thille AW, Coudroy R, Nay MA, Gacouin A, Decavèle M, Sonneville R, *et al.*; HIGH-WEAN Study Group and for the REVA Research Network. Beneficial effects of noninvasive ventilation after extubation in obese or overweight patients: a *post hoc* analysis of a randomized clinical trial. *Am J Respir Crit Care Med* 2022;205:440–449.
2. El-Solh AA, Aquilina A, Pineda L, Dhanvantri V, Grant B, Bouquin P. Noninvasive ventilation for prevention of post-extubation respiratory failure in obese patients. *Eur Respir J* 2006;28:588–595.
3. Florio G, De Santis Santiago RR, Fumagalli J, Imber DA, Marrazzo F, Sonny A, *et al.* Pleural pressure targeted positive airway pressure improves cardiopulmonary function in spontaneously breathing patients with obesity. *Chest* 2021;159:2373–2383.
4. De Santis Santiago R, Teggia Droghi M, Fumagalli J, Marrazzo F, Florio G, Grassi LG, *et al.* High pleural pressure prevents alveolar overdistension and hemodynamic collapse in ARDS with class III obesity. *Am J Respir Crit Care Med* 2020;203:575–584.
5. Teggia Droghi M, De Santis Santiago RR, Pinciroli R, Marrazzo F, Bittner EA, Amato MBP, *et al.* High positive end-expiratory pressure allows extubation of an obese patient. *Am J Respir Crit Care Med* 2018;198: 524–525.
6. Yoshida T, Torsani V, Gomes S, De Santis RR, Beraldo MA, Costa EL, *et al.* Spontaneous effort causes occult pendelluft during mechanical ventilation. *Am J Respir Crit Care Med* 2013;188:1420–1427.

Copyright © 2022 by the American Thoracic Society

Check for updates

Reply to Florio *et al.*

From the Authors:

In a study recently published in the *Journal* and including 623 patients at high risk of extubation failure in ICUs, we showed that prophylactic use of noninvasive ventilation (NIV) immediately after extubation significantly decreased the risk of reintubation and death in obese or overweight patients compared with high-flow nasal oxygen (1). Among obese or overweight

This article is open access and distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives License 4.0. For commercial usage and reprints, please e-mail Diane Gern (dgern@thoracic.org).

Originally Published in Press as DOI: 10.1164/rccm.202112-2776LE on February 8, 2022

patients, the rate of reintubation within the 7 days after extubation was 20% with high-flow nasal oxygen alone and only 7% with NIV ($P = 0.0002$). NIV was delivered in mean for 22 ± 9 hours within the first 48 hours with a facemask using an initial pressure support of 7.8 ± 2.4 cm H_2O and positive end-expiratory pressure (PEEP) of 5.4 ± 1.0 cm H_2O.

In their correspondence, Florio and colleagues report several studies from their research group (2–4) showing that pleural pressure can be particularly elevated in patients with severe obesity and that applying high degrees of PEEP with NIV may dramatically decrease work of breathing and subsequently favor extubation success. In their studies, the authors first measured pleural pressure using esophageal manometry and then adjusted PEEP to match this pleural pressure. As a result, PEEP exceeding 10 and even 15 cm H_2O reduced as much as possible the work of breathing. By contrast, patients with normal range of body mass index did not benefit from NIV with high PEEP in terms of work of breathing, suggesting that NIV should be specifically delivered at high PEEP in obese patients only. These physiological studies are remarkable and should have been cited in our original study to justify the beneficial effects of PEEP in obese patients. Although we are fully convinced by these findings, we would like to specify two points we consider essential. First, we showed the beneficial effects of NIV on risk of reintubation and death not only in obese but also in overweight patients. Consequently, body mass index was 32 ± 6 kg/m^2 among patients treated with NIV, which is markedly lower than that of patients included in the above-mentioned physiological studies (2, 3). Although PEEP titrated to match pleural pressure reached 12 ± 3 cm H_2O in mean, all included patients had a body mass index of at least 40 kg/m^2. The amount of PEEP even reached 18 ± 4 cm H_2O among the most obese patients with a body mass index exceeding 50 kg/m^2. As high airway pressure can promote leaks and patient–ventilator asynchrony during NIV (5), and as pleural pressure measurement to set amount of PEEP is not a daily clinical practice, we believe that PEEP of 5 cm H_2O, as in our study, suffices in most obese patients and that PEEP of more than 10 cm H_2O could be reserved for patients with morbid or super obesity. Without pleural pressure measurement, a PEEP trial of 10 cm H_2O or more may be adjusted according to patient comfort, number of leaks, exhaled V_T, and respiratory rate. Second, the other situation that may lead to adjusting high PEEP is an underlying obstructive sleep apnea syndrome. Apneas are frequent and probably underdiagnosed in ICU patients. Several studies have reported that more than half of patients admitted for acute hypercapnic respiratory failure had underlying severe sleep apnea syndrome, known or not (6, 7). Apneas are particularly frequent in obese patients and could lead to severe hypoxemia episodes and precipitate respiratory failure. Recurrent drop of pulse oximetry in obese patients after extubation may raise suspicion of underlying sleep apnea syndrome and justify increasing the PEEP to values used for treatment of sleep apnea syndrome (i.e., around 10 cm H_2O).

In conclusion, use of relatively low PEEP (i.e., around 5 cm H_2O), as in our study, seems to effectively prevent the risk of reintubation after extubation in obese or overweight patients in ICUs. However, we believe that a PEEP trial up to 10 cm H_2O or more may be beneficial in patients with morbid or super obesity or those with strong suspicion of sleep apnea syndrome. Without measurement of work of breathing, patient comfort, respiratory pattern, and number of leaks under NIV might help to judge the effectiveness of such an adjustment. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Arnaud W. Thille, M.D., Ph.D.*
Rémi Coudroy, M.D., Ph.D.
Jean-Pierre Frat, M.D., Ph.D.
Centre Hospitalier Universitaire de Poitiers
Poitiers, France

and

Université de Poitiers
Poitiers, France

Stéphanie Ragot, Pharm.D., Ph.D.
Université de Poitiers
Poitiers, France

*Corresponding author (e-mail: aw.thille@gmail.com).

References

1. Thille AW, Coudroy R, Nay MA, Gacouin A, Decavèle M, Sonneville R, *et al.*; HIGH-WEAN Study Group and for the REVA Research Network. Beneficial effects of noninvasive ventilation after extubation in obese or overweight patients: a post-hoc analysis of a randomized clinical trial. *Am J Respir Crit Care Med* 2022;205:440–449.
2. Florio G, De Santis Santiago RR, Fumagalli J, Imber DA, Marrazzo F, Sonny A, *et al.* Pleural pressure targeted positive airway pressure improves cardiopulmonary function in spontaneously breathing patients with obesity. *Chest* 2021;159:2373–2383.
3. Teggia Droghi M, De Santis Santiago RR, Pinciroli R, Marrazzo F, Bittner EA, Amato MBP, *et al.* High positive end-expiratory pressure allows extubation of an obese patient. *Am J Respir Crit Care Med* 2018;198: 524–525.
4. De Santis Santiago R, Teggia Droghi M, Fumagalli J, Marrazzo F, Florio G, Grassi LG, *et al.*; Lung Rescue Team Investigators. High pleural pressure prevents alveolar overdistension and hemodynamic collapse in ARDS with class III obesity. *Am J Respir Crit Care Med* 2020;203:575–584.
5. Vignaux L, Vargas F, Roeseler J, Tassaux D, Thille AW, Kossowsky MP, *et al.* Patient-ventilator asynchrony during non-invasive ventilation for acute respiratory failure: a multicenter study. *Intensive Care Med* 2009; 35:840–846.
6. Thille AW, Córdoba-Izquierdo A, Maitre B, Boyer L, Brochard L, Drouot X. High prevalence of sleep apnea syndrome in patients admitted to ICU for acute hypercapnic respiratory failure: a preliminary study. *Intensive Care Med* 2018;44:267–269.
7. Adler D, Pépin JL, Dupuis-Lozeron E, Espa-Cervena K, Merlet-Violet R, Muller H, *et al.* Comorbidities and subgroups of patients surviving severe acute hypercapnic respiratory failure in the intensive care unit. *Am J Respir Crit Care Med* 2017;196:200–207.

Copyright © 2022 by the American Thoracic Society