

Weaning from Mechanical Ventilation

Have We, so Far, Missed a Crucial Point?

Giacomo Grasselli, M.D., Giacomo Bellani, M.D., Ph.D.

FUNCTIONAL impairment of respiratory muscles is considered one of the determinants of difficult weaning from the ventilator,¹ which results in prolonged mechanical ventilation and is associated with worse patient outcome.² Patients requiring invasive ventilation are exquisitely prone to the development of respiratory muscle dysfunction (including ventilator-induced diaphragmatic dysfunction), which is worsened by a number of concomitant factors like sepsis, electrolyte imbalance, malnutrition, and administration of aminoglycosides, steroids, and neuromuscular blockers. Most of the studies tackling this issue were focused on the dysfunction of inspiratory muscles, mostly the diaphragm. At variance, very few studies aimed at assessing the role of expiratory muscles.

In healthy subjects at rest, expiration is a passive process: when the inspiratory muscles relax at the end of inhalation, the elastic recoil of the lung tissue (*i.e.*, the “release” of the elastic energy stored during lung inflation) generates a positive pressure gradient between the alveoli and the atmosphere, causing the outflow of air. Although expiration is usually passive, it can become an active process involving the contraction of muscles with expiratory activity, in particular abdominal muscles (which push the diaphragm upward, reducing the volume of the chest cavity) and internal intercostal muscles (which pull the ribs downward, compressing the rib cage). This happens during forced breathing and in some pathologic conditions characterized by airways obstruction (like asthma or chronic obstructive pulmonary disease). On one hand, recruitment of expiratory muscles may facilitate the subsequent inspiration and limit hyperinflation; on



“...[E]xpiratory muscle recruitment significantly contributes to the total respiratory effort of the patient during weaning from mechanical ventilation.”

the other hand, it may result in a significant increase in the oxygen consumption of respiratory muscles (*i.e.*, in the work of breathing). Another mechanism acting to limit hyperinflation in the presence of airway obstruction is the persistence of diaphragm contraction during exhalation: this diaphragmatic “tonic activity” has been described in different experimental models and might contribute to stabilize peripheral airways and prevent expiratory lung collapse.

In the current issue of *ANESTHESIOLOGY*, Doorduyn *et al.*³ report the results of an interesting study exploring the role of expiratory muscle recruitment and electrical diaphragmatic postinspiratory activity in patients undergoing a weaning trial after at least 3 days of mechanical ventilation. The spontaneous breathing trial was performed with a T-tube (no positive end-expiratory pressure) for at least 60 min. Patients were instrumented with a modified nasogastric tube equipped with an esophageal and a gastric balloon and with microelectrodes for diaphragm electromyography recording, underlining the potential for electromyography as a monitoring tool,^{4,5} irrespective of the application of neurally adjusted ventilatory assist. Expiratory muscle recruitment was computed as the pressure–time product of gastric pressure, and tonic activity of the diaphragm was expressed as a percentage of the peak inspiratory diaphragm electromyography activity during the last quartile of neural expiration. As expected, patients who failed weaning (*i.e.*, those who failed the spontaneous breathing trial or required reintubation within 48 h from extubation) had a higher rapid shallow breathing index, a higher inspiratory electrical activity of the diaphragm, and a significantly lower neuromechanical efficiency of diaphragm contraction (indicative

Image: J. P. Rathmell.

Corresponding article on page 490.

Accepted for publication May 29, 2018. From the Department of Anesthesiology, Intensive Care and Emergency, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy (G.G.); Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy (G.G.); Department of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy (G.B.); and Department of Emergency and Intensive Care, San Gerardo Hospital, Monza, Italy (G.B.).

Copyright © 2018, the American Society of Anesthesiologists, Inc. Wolters Kluwer Health, Inc. All Rights Reserved. *Anesthesiology* 2018; 129:394-5

of an impaired force-generating capacity of the diaphragm per unit of electrical activity). Weaning-failure patients also presented a significant increase in expiratory gastric pressure and the contribution of expiratory muscles to the total pressure-time product increased from 13% in the weaning-success group to 24% in the weaning-failure group.

These findings indicate that recruitment of expiratory muscles is increased in patients failing weaning from mechanical ventilation and account for a significant proportion of the total energy expenditure of respiratory muscles. On the contrary, tonic diaphragmatic activity was not different between the two patient subgroups. However, this finding is not unexpected because tonic contraction of the diaphragm during expiration seems to play a meaningful role in specific patient subgroups (*e.g.*, neonates) or in particular experimental settings (*e.g.*, as a means to prevent derecruitment⁶), whereas its relevance in adult subjects with acute or chronic respiratory failure remains to be demonstrated.

The study by Doorduyn *et al.*³ highlights the concept that expiratory muscle recruitment significantly contributes to the total respiratory effort of the patient during weaning from mechanical ventilation. From the findings of the present article, it is unknown whether the presence of expiratory activity is only “associated” with weaning failure, for example in patients with worst respiratory system mechanics, or whether it is a factor also contributing to weaning failure, for example by increasing oxygen consumption.⁷ In addition, this study underlines the importance of monitoring the work of breathing and respiratory mechanics in patients failing a weaning attempt to identify the mechanisms contributing to the failure and to drive the therapeutic approach.⁸

The experimental setup implemented in the study patients is relatively complex, requiring the simultaneous acquisition of esophageal and gastric pressure signals and of diaphragm electromyography. Hence, an adequate knowledge and level of experience are necessary to obtain reliable and reproducible data, to integrate the information, and to apply them at the bedside. The development of noninvasive techniques based on surface electromyography⁹ of both inspiratory and expiratory muscles may represent a significant advance in this respect, although signal interference and electrical crosstalks might arise as relevant technical limitations. Doorduyn *et al.*³ should be congratulated for performing such a complex, elegant study and for dragging our attention to an issue that should receive

more attention in daily clinical practice and become the object of further scrutiny in research.

Competing Interests

The authors are not supported by, nor maintain any financial interest in, any commercial activity that may be associated with the topic of this article.

Correspondence

Address correspondence to Dr. Bellani: giacomo.bellani1@unimib.it

References

1. Perren A, Brochard L: Managing the apparent and hidden difficulties of weaning from mechanical ventilation. *Intensive Care Med* 2013; 39:1885–95
2. Goligher EC, Dres M, Fan E, Rubenfeld GD, Scales DC, Herridge MS, Vorona S, Sklar MC, Rittayamai N, Lanys A, Murray A, Brace D, Urrea C, Reid WD, Tomlinson G, Slutsky AS, Kavanagh BP, Brochard LJ, Ferguson ND: Mechanical ventilation-induced diaphragm atrophy strongly impacts clinical outcomes. *Am J Respir Crit Care Med* 2018; 197:204–13
3. Doorduyn J, Roesthuis LH, Jansen D, van der Hoeven JG, van Hees HWH, Heunks LMA: Respiratory muscle effort during expiration in successful and failed weaning from mechanical ventilation. *ANESTHESIOLOGY* 2018; 129:490–501
4. Bellani G, Mauri T, Coppadoro A, Grasselli G, Patroniti N, Spadaro S, Sala V, Foti G, Pesenti A: Estimation of patient's inspiratory effort from the electrical activity of the diaphragm. *Crit Care Med* 2013; 41:1483–91
5. Bellani G, Coppadoro A, Patroniti N, Turella M, Arrigoni Marocco S, Grasselli G, Mauri T, Pesenti A: Clinical assessment of auto-positive end-expiratory pressure by diaphragmatic electrical activity during pressure support and neurally adjusted ventilatory assist. *ANESTHESIOLOGY* 2014; 121:563–71
6. Pellegrini M, Hedenstierna G, Roneus A, Segelsjö M, Larsson A, Perchiazzi G: The diaphragm acts as a brake during expiration to prevent lung collapse. *Am J Respir Crit Care Med* 2017; 195:1608–16
7. Bellani G, Foti G, Spagnoli E, Milan M, Zanella A, Greco M, Patroniti N, Pesenti A: Increase of oxygen consumption during a progressive decrease of ventilatory support is lower in patients failing the trial in comparison with those who succeed. *ANESTHESIOLOGY* 2010; 113:378–85
8. Silva S, Ait Aissa D, Cocquet P, Hoarau L, Ruiz J, Ferre F, Rousset D, Mora M, Mari A, Fourcade O, Riu B, Jaber S, Bataille B: Combined thoracic ultrasound assessment during a successful weaning trial predicts postextubation distress. *ANESTHESIOLOGY* 2017; 127:666–74
9. Schmidt M, Kindler F, Gottfried SB, Raux M, Hug F, Similowski T, Demoule A: Dyspnea and surface inspiratory electromyograms in mechanically ventilated patients. *Intensive Care Med* 2013; 39:1368–76