Editorial

High flow oxygen therapy and the work of breathing assessed by thickening fraction of the diaphragm (TFdi): just a side of the moon in cystic fibrosis patients?

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Cystic fibrosis (CF) is a life-limiting disorder affecting approximately 70,000 individuals worldwide. Over the past three decades, the median predicted survival rate of CF patients has critically improved thanks to therapies that better address serious complications of the disease (i.e., treatment of pulmonary infections, suppression of airway inflammation; management of airway secretions; interventions supporting the nutritional status) and to novel approaches that address the underlying cause of CF (i.e., drugs restoring CF transmembrane conductance regulator protein function) (1). However, the role of non-invasive ventilation (NIV) along the course of disease still partially belongs to a "grey" therapeutic area of intervention. Actually, NIV is used as bridge to lung transplantation (2), it is an effective airway clearance technique and is superior to low flow oxygen therapy for the treatment of nocturnal hypercapnic respiratory failure, but NIV impact on pulmonary exacerbations, CF progression and exercise capacity is unclear, still lacking long-term randomized controlled trials (3). Notably, according to the British Thoracic Society Guidelines (4), NIV is not indicated in patients with copious secretions; in clinical practice, however, NIV has become a reliable treatment of acute respiratory failure in CF, avoiding the need of invasive mechanical ventilation and its serious complications (5).

Sklar and colleagues have interestingly investigated the effect of high flow nasal-oxygen therapy (HFNT) on the work of breathing (WOB) in hypercapnic CF patients, in post-acute care. To this end, they evaluated the thickening fraction of the diaphragm (TFdi) as surrogate of WOB. The Authors found no statistically significant difference in TFdi values between conventional oxygen therapy (COT), HFNT and NIV. However, TFdi could be only a partial expression of the WOB in CF adults. The patients enrolled by Sklar and coworkers were adult and showed a severe airway obstruction at baseline (median FEV_1 0.8 L/s, median Tiffeneau 45%), then it is reasonable to argue that a rearrangement of breathing pattern in response to the increased respiratory load was already established before of the entry in the study. As reported by Bellemare (6) in a study performed on CF young adult patients with moderate impairment of pulmonary function tests, not only the diaphragm but also the inspiratory ribcage muscles give a great contribution to the inspiratory pressure development; this contribution is higher than in non-CF subjects. Indeed, the ribcage expansion in CF patients occurs without rib elevations, and this is why to safeguard the length/tension ratio of inspiratory ribcage muscles, preserving their crucial support to inspiration relative to the diaphragm. The swing of transpulmonary pressure is greater

over the lung base when the diaphragm gives the major contribution to inspiration, while during the inspiratory intercostal muscles contraction, the transpulmonary pressure swing is greater over the superior regions, resulting in an increased ventilation to upper lung zones, where the ventilation to perfusion ratio (Va/Q) is physiologically higher (7). This could explain why, in the present study, the SpO_2 does not differ between the COT and HFNT, despite the theoretical reduction of room entrainment with HFNT. Interestingly, SpO_2 and transcutaneous CO_2 do not change even between NIV and COT; there are two possible explanations: (I) complex effect of positive pressures delivered during NIV on different muscular group and on thoracic configuration in CF patients, resulting in a modest, definitive effect on Va/Q. (II) The clinical stability of patients enrolled: the authors specify that NIV settings, during the study, were left unchanged from the acute phase (few days ago); probably, the pressure delivered to the lung during the acute phase were not equally adequate after the clinical stabilization (i.e., improved pulmonary mechanic due to medical treatment), with worsening of Va/Q (i.e., increase of dead space). More than the similarity of diaphragmatic activity during HFNT and during NIV, the reduction of respiratory rate observed only during HFNT versus baseline appears more interesting. In a study performed on young adults (8), Hart and coworkers showed that in severe CF, as judged by FEV_1, there is a decrease in the dynamic lung compliance (Cl_{dyn}). This reduction causes an increase in the elastic WOB, with minimal change in the resistive WOB. Indeed, the decline in FEV_1 is associated with higher inflammatory changes and with the destruction of lung parenchyma, resulting in a severe reduction of Cl_{dyn}. As consequence, CF patients adopt a rapid shallow breathing to reduce the elastic WOB (WOB_{el}). The increase of respiratory rate worsens in turn the reduction of Cl_{dyn}: with a reduced inspiratory time, slow alveoli will receive a lower tidal volume than the fast ones, with little variations in lung volume despite high transpulmonary pressures developed by the respiratory muscles (9). HFNT could cut off this vicious circle, reversing the adoption of the rapid shallow breathing pattern.

An inclusion criterion in this study was $PtCO_2$ >40 mmHg with HCO_3 ≥32 mmol/L. In CF patients, the occurrence of chronic metabolic alkalosis is rather common. The patients enrolled were treated with diuretics or did they recently introduce diuretic therapy at home? Is it possible to suppose a transitional worsening of their metabolic alkalosis, overloading the breathing network? Could be reasonable to optimize medical therapy (i.e., acetazolamide) together with the choice of type and setting of respiratory support (NIV, HFNT)? Furthermore, the authors did not assess change in secretion characteristics during the Study, probably because of the short time of observation. Similar to positive expiratory pressure device for airway clearance and unlike to NIV, the action of HFNT is flow-dependent: this could be an attractive advantage of HFNT versus COT, because of the contemporaneous influence on gas exchange and airway clearance in the post-acute setting.

Actually, clear indications about the timing of NIV institution in CF patients are still lacking (3,10). HFNT could be an appealing support during diurnal hours in CF patients on home oxygen therapy, not so much for its direct impact on diaphragmatic pump function (probably, just a side of the moon, in the complex muscular rearrangement of breathing pattern in CF patients) but for the reduction of respiratory rate.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. 2017 Patient Registry Annual Data Report. Cystic Fibrosis Foundation. Bethesda, MD: CFF, 2017.
2. Snell G, Reed A, Stern M, Hadjiliadis D. The evolution of lung transplantation for cystic fibrosis: A 2017 update. J Cyst Fibros 2017;16:553-64.
3. Moran F, Bradley JM, Piper AJ. Non-invasive ventilation for cystic fibrosis. Cochrane Database Syst Rev 2017;2:CD002769.
4. British Thoracic Society Standards of Care Committee. Non-invasive ventilation in acute respiratory failure. Thorax 2002;57:192-211.
5. Sood N, Paradowski LJ, Yankaskas JR. Outcomes of intensive care unit care in adults with cystic fibrosis. Am J Respir Crit Care Med 2001;163:335-8.
6. Bellemare F, Jeanneret A. Sex differences in thoracic adaptation to pulmonary hyperinflation in cystic fibrosis. Eur Respir J 2007;29:98-107.
7. Derenne JP, Macklem PT, Roussos C. The respiratory

muscles: mechanics, control, and pathophysiology. Am Rev Respir Dis 1978;118:119-33.
8. Hart N, Polkey MI, Clément A, et al. Changes in pulmonary mechanics with increasing disease severity in children and young adults with cystic fibrosis. Am J Respir Crit Care Med 2002;166:61-6.
9. Woolcock AJ, Vincent NJ, Macklem PT. Frequency dependence of compliance as a test for obstruction in the small airways. J Clin Invest 1969;48:1097-106.
10. Bright-Thomas RJ, Johnson SC. What is the role of noninvasive ventilation in cystic fibrosis? Curr Opin Pulm Med 2014;20:618-22.

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