Postextubation Respiratory Support: One More Piece to the Puzzle

Extubation failure is defined as the need for mechanical ventilation within days after planned extubation, and it occurs in 10–20% of critically ill patients (1). Importantly, extubation failure is independently associated with longer ventilation duration, longer ICU and hospital length of stay, and higher mortality. As several causes may contribute to extubation failure (indeed some of them may even coexist in the same patient), the study of the pathophysiology of extubation failure is still challenging. In this scenario, different noninvasive supportive therapies could be used to decrease the rate of extubation failure.

High-flow nasal cannula (HFNC) has various effects that could be of interest after extubation (2). Compared with conventional oxygen, it increases dead-space washout, improves secretion clearance using heated humidification, and generates a certain degree of positive airway pressure, increasing the end-expiratory lung volume and decreasing expiratory diaphragm loading. It is also associated with better oxygenation and decreased respiratory rate and inspiratory effort (3). Consistent with these physiological benefits, one previous study showed that HFNC use immediately after extubation decreased reintubation rate within the first 72 hours after extubation compared with low-flow oxygen delivery applied continuously through a nasal cannula or a nonrebreather facemask (4). Compared with low-flow oxygen devices, a Venturi mask delivers higher flows of gas admixture. However, in a previous physiological study comparing the use of HFNC with that of a Venturi mask, HFNC was also associated with improved oxygenation, lower respiratory rate, and better comfort (5). Whether these physiological benefits were associated with improved clinical outcomes was uncertain.

In this issue of the *Journal*, Maggiore and colleagues (pp. 1452–1462) report the results of a randomized trial assessing whether HFNC after extubation decreased the reintubation rate within 72 hours in critically ill patients among those who succeeded to a spontaneous breathing trial but presented hypoxemia within the first 120 minutes after extubation; the results were compared with those obtained with Venturi mask oxygen (6). Interestingly, prespecified criteria for both reintubation and the need for noninvasive ventilation (NIV) were used, and the use of these criteria was blindly revised a posteriori by three independent experts. No differences in the need for reintubation at 72 hours and at 28 days were observed. However, patients randomized to be supported with the Venturi mask after extubation more frequently needed to be rescued with NIV because of the presence of tachypnea and respiratory distress.

A previous study showed that HFNC was superior to low-flow oxygen in preventing extubation failure (4). The question was, therefore, once again on the table: is HFNC superior to conventional oxygen in preventing reintubation? One main difference between the two studies is that in the present study, Venturi masks were used in the control group. Compared with low-flow oxygen, a Venturi mask allows higher flow delivery while achieving higher oxygen concentrations. Moreover, HFNC treatment was applied for shorter periods of time, and the use of rescue NIV was allowed in those patients with worsening postextubation respiratory failure. Indeed, the results of the present study are consistent with those observed in the PROPER (Protocolized Postextubation Respiratory Support to Prevent Reintubation: A Randomized Clinical Trial) trial (7), which also suggested that postextubation HFNC did not reduce the rate of reintubation under these circumstances. However, if considering a composite outcome of escalation of treatment that encompasses the use of NIV and the need for reintubation, it is possible that the results of both studies would have been similar, and HFNC may be considered superior to conventional oxygen in terms of preventing escalation of treatment after a scheduled extubation.

Recent NIV guidelines suggest the use of NIV to prevent postextubation respiratory failure in high-risk patients for reintubation (8). However, they do not suggest the use of NIV for overt postextubation respiratory failure (8), and it may even be harmful and increase ICU mortality because of delayed intubation (9). Moreover, compared with HFNC, the use of NIV is associated with increased patient discomfort and increased workload for healthcare personnel. These results may be especially relevant in the context of different situations with high medical demand and shortage of ventilators, such as the recent coronavirus disease (COVID-19) pandemic. Importantly, the results of the present study showed that NIV used by an experienced team may prevent the need for reintubation in almost the half of these patients. Unfortunately, no data about differences in ICU length of stay or mortality of those patients who finally needed to be intubated were reported.

Another difference is that, in the present study, the Venturi mask was used despite low-flow oxygen. The Venturi mask used with a F_{IO_2} at a treatment initiation of 36% should correspond to total gas outflow exceeding 30 L/min. However, different physiological effects have been observed between high-flow oxygen therapy through tracheostomy and HFNC (10), suggesting that the effects of high flow also depend on the interface that is used. Indeed, the intubation rates in the Venturi mask group were similar to those observed in the low-flow group in the study by Hernandez and colleagues (4) (11% vs. 12%). Therefore, it is unlikely that this could lead to significant differences in intubation rates. The differences were, in fact, in the HFNC group (14% vs. 5%). Other differences may explain this result. First, HFNC was not used as a preventive strategy immediately after extubation, and patients were randomized if they presented a certain

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degree of hypoxemia within the first 120 minutes after extubation. Second, conservative positive end-expiratory pressure criteria were used to attempt a spontaneous breathing test ($Pa_{O_2}/FI_{O_2} > 150$ with positive end-expiratory pressure ≤ 5 cm H_2O), leading to a low reintubation rate secondary to hypoxemia. These differences may limit the potential benefit of using HFNC to prevent extubation failure in some critically ill patients.

Finally, it is worth noting that although there was no benefit of any of the supportive therapies compared in the study, it does not necessary mean that no patients will benefit from the intervention (11). The results presented in randomized controlled clinical trials represent the average treatment effect, which is the mean of all individual treatment effects observed in each patient. Thus, clinical physiological assessments at the bedside could be used as predictive enrichment tools to design targeted clinical trials to assess the effectiveness of different noninvasive supportive therapies or even their combined use. Indeed, in some patients, the combination of different therapies may be associated with better outcomes (12).

In summary, extubation failure pathophysiology is complex, and different mechanisms could be in play in a single patient at the same time. Identifying potential causes of extubation failure is crucial to initiate the type of noninvasive supportive therapy that could be most beneficial to each patient. Moreover, the use of different noninvasive supportive therapies, or the combination of some of them, according to their physiological benefits and different clinical situations, may be a pragmatic approach to address any clinical situation of potential extubation failure at the bedside. ■

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Oriol Roca, M.D., Ph.D.
Parc Taulí Hospital Universitari
Sabadell, Spain

Ciber Enfermedades Respiratorias (CIBERES)
Madrid, Spain
and
Universitat Autònoma de Barcelona
Bellaterra, Spain

Lluís Blanch, M.D., Ph.D.
Parc Taulí Hospital Universitari
Sabadell, Spain
and
Ciber Enfermedades Respiratorias (CIBERES)
Madrid, Spain

Gonzalo Hernández, M.D., Ph.D.
Toledo University Hospital
Toledo, Spain

ORCID ID: 0000-0003-3841-4551 (O.R.).

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