We need to predict extubation failure

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One in every three pediatric patients admitted to the PICU requires ventilatory support for a mean time of 5 days.[1] Even in the face of the clear and universally accepted benefits of mechanical ventilation (MV) applied to children with respiratory failure, the risks associated with it mean that the critical care team must constantly search for new ways to better understand the pathophysiology of this special situation and to develop indexes or parameters that may support the decision to interrupt mechanical ventilation as early as possible. The ghost of weaning failure haunts the scene, while at the same time physicians are faced with the threat of unnecessarily prolonging ventilatory support

Withdrawal from MV refers to the fast or gradual transfer of the breathing effort from the ventilator to the patient (weaning), and extubation refers to the removal of the endotracheal tube. Commonly seen as a natural continuation of weaning, extubation has its own characteristics and outcome predictors, which take into account mainly the ability to protect the airway, the management of secretions and the patency of upper airways.[2]

Fifty-five studies, totaling approximately 33,000 patients, demonstrate that 12.5% (range: 2-25%) of extubated adult patients require reintubation between 24-72 h of endotracheal tube removal.[2] Similarly, the range of extubation failure reported for the pediatric age group is very heterogeneous, varying from 4.9% to 29%.[1,3-11] The optimal rate of extubation failure in the PICU remains controversial. On the one hand, unjustified delayed extubation is associated with increased ICU length of stay, increased risk of ventilator-associated pneumonia and higher mortality. On the other hand, premature discontinuation of ventilatory support is closely linked to extubation failure and the need for reintubation, with adverse outcomes including prolonged hospital stay, higher costs, greater need for tracheotomy and, in some studies, increased mortality.[1,8,10-12] In the absence of a clear consensus on ideal extubation failure rate, clinicians must reflect about the best choice between shortening ventilatory support days or minimizing extubation failure.

The negative results of both delayed and premature extubation, and the recent information that non-invasive ventilation may be ineffective in this issue,[13] have intensified the efforts to optimize predictive factors for extubation outcome. The ability of the traditional weaning indexes (respiratory frequency, tidal volume, maximal inspiratory pressure, and frequency-to-tidal volume ratio) to discriminate between children successfully extubated and children requiring reintubation has been shown to be very poor.[4,5,8,12] Multivariate analyses indicate that premorbid status, severity of underlying illness and complications associated with reintubation do not correlate with the increased mortality attributed to extubation failure. An alternative hypothesis is the clinical deterioration taking place between the moment of extubation and the reestablishment of ventilatory support. It is in this direction that a relationship has been established between mortality and delayed reintubation.[12]

For approximately 50 years, critical care physicians treating adults have been investigating the role of Vd/Vt ratio in a variety of clinical scenarios. However, it was

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never used as an indicator to wean patients from mechanical ventilation, perhaps because measuring the Vd/Vt ratio used to be cumbersome – before the development of newer, automatized methods (such as the CO_2SMO, used by Bousso et al.[14]). Another reason, as noted by Hubble et al.,[11] could be that chronic lung disease is very common in adults, and in that case, the physician would need information on the pre-acute illness ventilatory status, making the quotient inapplicable. Conversely, most children have normal baseline pulmonary function, and consequently normal pre-injury Vd/Vt ratio.

Taking into consideration previously employed weaning indexes, and given that there is no single indicator or formula that has proven useful to predict extubation failure in children, Bousso et al.[14] conduct a prospective study using the Vd/Vt ratio as a marker of extubation readiness in mechanically ventilated children. To date, the only precedent for using Vd/Vt ratio as a predictor of extubation readiness is a prospective clinical study by Hubble et al.,[7] including 45 patients, both medical and surgical, with age between 1 week and 18 years, intubated and mechanically ventilated. If patients met the criteria for extubation according to the attending team, they were begun on a trial of pressure support and, after 20 minutes, extubated. By logistic regression analysis they established the cutoff value of Vd/Vt $\leq$ 0.5 to be an independent predictor of extubation outcome, with sensitivity and specificity of 0.75 and 0.92, respectively. The positive and the negative predictive values were 0.96 and 0.60, respectively. In addition to identifying children who will extubate successfully, they found that Vd/Vt ratio was also useful to identify those at risk of respiratory failure after extubation (a Vd/Vt $\geq$ 0.65 has a NPV of 0.8).

In the present study, Bousso et al.[14] follow a similar protocol, establishing a cut-off point of Vd/Vt $\geq$ 0.65 to detect extubation failure. Using this less specific and more sensitive cutoff point, the authors decrease the likelihood of identifying patients who will be successfully extubated (lower PPV), but they increase the likelihood of accurately selecting those at high risk of failure (higher NPV). Unlike the results in the previous study, they found no statistically significant difference between groups, with a Vd/Vt ratio of 0.62 ($\pm$ 0.17) and 0.65 ($\pm$ 0.21) for the groups with successful and failed extubation, respectively. The NPV to predict extubation failure was 41.9%, compared with 80% in the study by Hubble et al.[11]

When analyzing the circumstances that could have caused this difference in results, Bousso et al. note the mean age of 17 months in their study compared with a mean of 43 months in the Hubble study. Another important difference between the studies is the predominance of elective surgical patients, with supposedly normal lungs, in the sample studied by Hubble, while the population of Bousso comprised children with severe acute respiratory disease. Of note is the fact that at admission, more than one diagnosis was present for many children (142 diagnoses for 86 patients) making it difficult to characterize the sample. The lower PaO_2/FiO_2 at admission as an independent factor related to extubation failure, reflecting more severe injury, is coincident with previous studies.[6]

Bousso et al. remark that the difference in results could be reflecting the presence of populations with dissimilar characteristics. This is a common situation when analyzing studies conducted in South America, where there is a predominance of primary respiratory diseases[1,5,8-10,14] compared to the United States or Europe, with predominance of elective surgical patients.[4,6,11,15]

At this time, there still are no reliable criteria to predict which patients will require reintubation after tolerating a spontaneous breathing trial. Future investigations should focus on the search for factors that will allow us to determine the appropriate time for the withdrawal of sedation before weaning and extubation and to prevent respiratory infection after extubation. The early management of postextubation respiratory distress is also very important. Since non-invasive ventilation may be ineffective in this situation, invasive mechanical ventilation should be reinstituted as soon as possible.[13]

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