The importance of timing for the spontaneous breathing trial

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Weaning intubated patients from mechanical ventilation may be defined as the transition from total ventilatory support to spontaneous breathing, sometimes performed abruptly, sometimes gradually (1). Worldwide, millions of patients are intubated each year for various purposes. The numerically most important situation refers to the so-called "anaesthesiologic" patient, who is scheduled for a surgical procedure, and tracheal intubation is performed for a short period of mechanical ventilation with the expectation of subsequent smooth extubation. This would correspond to a quick and abrupt separation. Unlike the "anaesthesiologic" patient, those in the Intensive Care Unit (ICU) principally get ventilator support for lung failure (altered lung parenchima), inappropriate respiratory mechanics due to a neuromuscular affection, severely compromised hemodynamics or mental dysfunction (2). In this case, mechanical ventilation is sustained until a (partial) reversal of the causative process implying ventilatory support has been achieved. Obviously some of these patients will need to be managed with a relatively gradual separation. However, it is still common belief that the separation should always be gradual, which is not justified. In addition, the assessment of the degree of reversal of the causative process is often based on subjective grounds, with a frequent natural tendency for clinicians to keep their patients on the 'safe' side, i.e., considering them as not being ready for separation. Unfortunately, the clinical course of an ICU-patient may be complicated by the so-called critical illness polyneuromyopathy (3), dysfunction of the diaphragm (3), intravascular catheter-related infections, acute renal failure, delirium or ventilator associated pulmonary infection, all of them eventually prolonging the ventilator support (4). In some reports, weaning accounts for more than 40% of the total ventilation period (2,5-7). Although fast and secure discontinuation of mechanical ventilation is always the primary goal, immature or excessively postponed extubation quite often take place, giving rice to adverse consequences (8-10). For this reason, a number of objective tests have been proposed to help with this difficult medical decision process.

According to a classification suggested by a combined North-American/European task force, liberation from mechanical ventilation may be categorized into three groups: simple, difficult and prolonged weaning (1). This stratification, though simplistic, represents a useful instrument to better describe and compare epidemiological characteristics and clinical outcomes. The first group—simple weaning—includes patients who tolerate the initial spontaneous breathing trial (SBT) and are consecutively extubated with success. In clinical practice it is very important to continuously observe and evaluate patients, in order to detect the appropriate moment for the SBT, best carried out as a T-tube trial (meaning disconnection of the patient from the ventilator) or on low-level inspiratory pressure support (11). One or more trial failures define difficult and prolonged weaning, respectively; characteristic features of these two groups and their management are detailed elsewhere (11). According to a recent epidemiologic study on weaning outcome, about 60% of patients have a simple weaning process of less than 24 hours (12). As the results of most trials on weaning will be heavily influenced by this group, they do not necessarily apply to more challenging patients.

This editorial commentary will deal with simple weaning by commenting a recent *JAMA* paper that compares two different SBT techniques: a "physiologic" (mimicking well spontaneous breathing) but prolonged 2-hour T-tube SBT or a "supported" 30-minute SBT (low-level inspiratory pressure support ventilation leading to decreased work of breathing) (13). This study on 1,153 "ready-to-wean" patients is the largest ever performed randomized clinical trial on different SBT procedures. Subirà and co-workers found that a 30-minute PSV-SBT (supported breathing) resulted in a significantly higher 72-hour successful extubation rate than a unsupported 2-hour T-piece SBT (82.3% *vs* 74.0%; P=0.001). Once extubated, extubation failure rate was similar in the two groups. Beyond expectation, hospital and 90-day mortality (but not ICU mortality) were significantly higher in the T-tube group, a finding that cannot be readily explained, as the two groups did not differ significantly neither in baseline characteristics nor in all captured secondary, exploratory, and post hoc outcomes.

As for any test in medicine, the results of the SBT must be interpreted based on the pre-test probability of weaning. Thus, let's now emphasize some strengths and flaws of this paper. The most important message deriving from Subirà's work is the definitive confirmation of already known facts, i.e., that the 30-min PSV-technique is an adequate initial SBT for correctly identifying patients with a very high probability of success in extubation. In fact, various previous clinical trials have actually shown similar successful extubation rates when directly comparing either the technique or the duration of the SBT (14-16). Another laudable aspect of this research is the authors' attempt to record the patients' subjective condition, confirming previous work that showed a correlation between extubation success and the patients' personal perception of autonomous breathing at the end of the SBT (17).

On the other hand, some important limitations deserve to be discussed, namely the process of patient selection in general, and a positive bias towards the less demanding PSV-SBT in patients with a high pre-test probability. First, the very nature of a good diagnostic test lies in its capacity of accurately distinguishing between true positive and true negative outcomes (avoiding the negative ones), but its results are highly dependent of the conditions of application (prevalence of the condition tested). For simple weaning this discriminative power is required at the soonest possible time point, in order to evade delayed weaning. In Subirà's trial, most patients (88%) had a successful initial SBT, and to be frank, similar results were also achieved in older trials (7,16). This would be close to the situation of the so-called anaesthesiologic patient described above. Yet, if not all the ICU patients in the study corresponded to the so-called "anaesthesiologic" group, one might rightly question whether some patients had not to be considered for extubation at an earlier time point. In the ICU one might expect to have a much lower rate of SBT success, indicating much earlier screening. The relatively high median PaO_2/FiO_2 ratio after the successful SBT in both groups suggests, that many patients were probably quite above the minimal respiratory inclusion criteria (SaO_2 >90% with FiO_2 ≤0.4, respiratory rate <35/min, spontaneous tidal volume >5 mL/kg, respiratory rate/tidal volume <100/min per liter, and maximal inspiratory pressure >15 cmH_2O). Moreover, when the pre-test probability of successful separation from the ventilator is so high (here almost 90%!), the SBT will implicitly loose some of its predictive performance and produce more false negative results, namely predicting failure in patients who could have been separated. Conversely, the risk of false positive results (predicting success in a patient who cannot be separated) is almost non-existent when around 90% of the patients are ready for separation (18). By directly comparing - in this "ready to extubate" study population - a very challenging stress-test with a less laborious and shorter technique, the risk of false negative results was indeed increased in the 2-hour T-tube SBT and minimized in the 30 minutes PSV arm (19,20). The positive result in favor of the short trial could therefore have been anticipated by Bayes' theorem (18).

Second, according to the study protocol attending physicians had to decide on the extubation strategy (whether to reconnect the patient to the ventilator for 1 hour before extubation and whether to administer noninvasive ventilation or high-flownasal cannula after extubation). Although this decision was taken before randomization, more prophylactic noninvasive ventilation or high-flow nasal cannula oxygen therapy after extubation was delivered to the PSV arm (25% *vs.* 19%; P=0.01). This difference, while not significant, may still have affected the primary outcome, i.e., successful extubation. Clinical signs of respiratory fatigue occurred with similar frequency in both groups. However, apart from the abovementioned prophylactic measures, treatment of postextubation respiratory failure was not further protocolized (use of bronchial toilette after extubation), as well as there is no mention of the tube diameter; both of them could have been potentially confounding factors. Finally, we wonder why median ICU and hospital length-of-stay were unaffected by the weaning technique, although PSV led to a significantly higher extubation success.

In conclusion, for daily practice the initial SBT has to be performed at the soonest possible moment in order to avert delayed extubation and correspondent adverse events. And exactly for this setting, when the discriminative capacity of the SBT is extremely important, we don't get any real answer from Subirâ's trial. Clinicians should monitor the percentage of successful initial SBT in their center. They should be concerned when values higher than 75% are obtained (18). Thus, awaiting further studies, we still privilege a 30-min T-tube strategy (or zero pressure assistance on the ventilator) (20) for most patients as the initial weaning trial.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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