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Should We Wean Patients off Vasopressors before Weaning Them off Ventilation?

Failed extubation and subsequent reintubation are independently associated with mortality and morbidity of patients under mechanical ventilation (1). This is the reason why, before starting the weaning process, one carefully waits until the patient has reached a sufficient degree of autonomy (2). Among the criteria used to ensure autonomy, it must be admitted that the absence of vasopressor infusion is one of the least solid. Although it is obvious that the patient must be sufficiently awake and positive end-expiratory pressure and FiO_2 must be low, testifying to a minimal respiratory autonomy, the need to be rid of vasopressor support before weaning from mechanical ventilation is less evident.

In many cases, the persistence of vasopressor support is accompanied by persistent dependence on the ventilator or other remaining failures, and the question of extubating the patient under vasopressors does not arise. Also, if there is ongoing myocardial ischemia or major circulatory failure, with obvious signs of tissue hypoxia, and if the doses of vasopressors are increasing, it is obvious that extubation must be avoided. The increase in oxygen consumption owing to the reactivation of the

respiratory muscles would aggravate tissue hypoxia, and extubation is clearly unreasonable in this context.

But in other cases, when the infusion of a low dose of a vasopressor is the only obstacle that remains, what justifies refraining from extubating the patient? The answer to this question is still pending.

The risk is not that extubation under vasopressors would expose the patient to weaning-induced cardiac dysfunction, even if it is a frequent cause of weaning failure (3). Indeed, this acute cardiac failure, and the frequently associated pulmonary edema, are mainly owing to unfavorable changes in the loading conditions of both ventricles during the transition to spontaneous breathing. The increase in cardiac preload owing to the inspiratory fall in intrathoracic pressure, the increase in right ventricular afterload owing to high-volume ventilation, and the increase in left ventricular afterload owing to hypertension are the main mechanisms involved (4). Then, there is no reason why the persistence of low arterial tone and the administration of a vasopressor should contribute to it. In fact, the reason one refrains from extubating a patient on a low dose of a vasopressor is simply the fear that the underlying disease that led to the intubation did not completely resolve, if there is no other clear hemodynamic reason why the patient should worsen.

In this issue of the *Journal*, Zarrabian and colleagues (pp. 1053–1063) retrospectively reviewed 6,140 adult patients in Calgary

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ICUs who were receiving vasopressors and were on mechanical ventilation (5). Of these, they focused on the 721 (11.7%) patients who were extubated while still receiving vasopressors. A multivariable competing risk model showed that extubation under vasopressors was not associated with a greater risk of being reintubated at 96 hours. However, the result differed according to the dose of vasopressor received at the time of extubation. When administered at a high dose (>0.1 $\mu\text{g}/\text{kg}/\text{min}$ of norepinephrine equivalents), the risk of being reintubated was greater than that for patients weaned off of vasopressors. On the contrary, weaning under smaller doses of vasopressor was not associated with a higher hazard of reintubation but with lower in-hospital mortality and a shorter length of stay in the ICU (5).

So, does the study answer the question perfectly? Should we change the criteria required for extubation? First, keep in mind that the main finding is that extubation under vasopressors, although not associated with a significant risk of reintubation, was associated with an increased risk of dying and a longer hospital stay. Then, the study was retrospective. Despite the considerable efforts made by the authors to attenuate this limitation, in particular through sensitivity analyses, many elements are missing concerning the context of extubation. In particular, some extubations may have been self or accidental extubations. Also, we cannot formally exclude that some patients were extubated under vasopressors in a palliative context. Apart from the dose of vasopressor, it is not known what the hemodynamic state was, whether tissue hypoxia was present or not, or whether shock was in a worsening or a deescalation phase. The authors took many precautions to justify the choice of the cut-off defining the “high” and “low” doses of vasopressors, but other thresholds could have led to different results. Finally, the study does not report what happened during the weaning trial performed before extubation. For all these reasons, it would be unreasonable, based on these results alone, to modify our practice and conclude that the extubation of patients on a low dose of a vasopressor is certainly safe.

However, the study by Zarrabian and colleagues is important. It included a huge number of patients, and the statistical analysis was well conducted, in particular, to erase the limitations owing to its retrospective nature. It confirms two observational studies of smaller size that already suggested that weaning patients under a low dose of vasopressor was safe (6, 7). Then, as the authors themselves underline, the study contributes to the certainty that there is

equipoise as to the safety of such practice. It calls for the conduct of randomized controlled studies that will definitively answer the question of whether we can and whether we should extubate patients for whom the only obstacle to doing so is the administration of a low dose of norepinephrine. ■

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