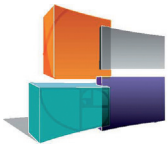
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Anaesth Crit Care Pain Med 39 (2020) 549–550



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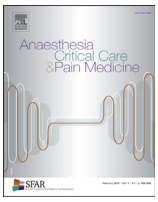

Non-invasive ventilation for acute respiratory failure (in COVID-19 patients): the non-ending story?

Since the beginning of the pandemic, the management of patients with COVID-19 associated acute respiratory failure (ARF) has rapidly evolved, based on an increasing number of reports on respiratory system mechanics, cytokines storm and ventilatory management. In this issue of *Anaesthesia Critical Care and Pain Medicine*, Mukhtar et al. reported in a letter to the editor the results of a retrospective study on non-invasive ventilation (NIV) in patients with moderate or severe ARF due to COVID-19 [1]. NIV was initiated following "predefined" criteria and an algorithm was used to detect NIV failure and initiate invasive mechanical ventilation (IMV) if required. Fifty-five patients were included and among them, 71% (n = 39) presented ARF signs requiring mechanical ventilation. From these 39 patients, NIV succeeded in 77% of cases (n = 30) and they were not intubated, while 23% (n = 9) were intubated with an in-hospital mortality rate of respectively 10% and 78%. Based on these results, authors support that NIV is feasible with a high success rate and help avoiding IMV among patients with severe COVID-19 patients.

Even if literature of the last two decades does not support NIV outside COPD exacerbation or heart failure, temptation of using NIV in ARF patients with or without COVID-19 is high, whether to decrease complications related to mechanical ventilation and sedation or to maximise IMV availability. For these reason, NIV is now advocated for patients with hypoxic respiratory failure by the World Health Organization (WHO) [2].

We strongly agree with Mukhtar et al. when they report presenting results that support the feasibility of NIV among severe COVID-19 patients. Yet, these results cannot be used to argue that NIV help avoiding IMV or reducing mortality nor any IMV related complications for several reasons: 1) study design (a retrospective small cohort without adjustment) do not allow to approach causality as a randomised trial would aim to do; 2) baseline characteristics are not comparable among groups on important parameters such as age or room-air SpO2 and 3) such assertions would require a strong reporting on the conduct of the two interventions throughout the study.

If the mortality rate of patients under NIV is low (10%) in this cohort, surrogate of a high quality of care in ICU, the reported mortality of patients under IMV (77%) seems much higher than expected. One of the first data on COVID-ARDS published was the cohort from Milano, Italy [3]. In this referral centre for COVID-19, despite multiple advanced critical care interventions and 100% patients with IMV, COVID-19 ARDS was associated with around 20% mortality at the end of the follow-up. Even if final mortality was probably higher, it seems not so far form predicted mortality according to severity at admission. In their data, an early improvement in oxygenation was interestingly associated with a greater chance of being discharged alive from the ICU. Those early oxygenated patients are likely to be those who were not intubated in further cohorts. In a recent report, we published with the *Paris-Sorbonne ECMO-COVID investigators* a mortality of 36% at day 60 in 83 very severe COVID-19 patients under ECMO with a SAPS II higher than 45 (i.e APACHE II around 22). This mortality is not different from observed mortality in non-COVID-19-ARDS [4]. Based on these observations, we may thus assume that the observed 77% mortality among NIV patients in the Mukhtar et al. study is likely to be related to an uncontrolled selection bias with extremely severe patients independent of NIV pre-intubation, but we cannot be sure that NIV failure is not responsible.

The real question is: "are COVID-19-ARDS patients different from AARDSRF patients?" We still do not know [5]. In our view, Mukhtar et al.'s paper is one more stone to limit the pendulum effect [1]. In the early beginning of the crisis, experts in the field advocate for early intubation of COVID-19 patients to avoid p-SILI and large tidal volume that may worsen ARDS [6] and to prevent nebulisation [7]. Even if the first two components play a role in the course of COVID-related ARDS, it does not justify the systematic use of IMV and its prolonged use, for which there are numerous proofs of poor outcomes. In the other hand, the true impact of mechanical ventilation is hard to measure and rely on complex questions such as, for a given patient, the real need of IMV and if required whether this patient has been intubated too late, which is a known risk of non-invasive supports. The team from Hernandez-Romieu in Atlanta recently published an interesting study on the use of high flow nasal oxygenation (HFNO) as a non-invasive respiratory support [8]. They show, in this monocentric cohort, that the delay of intubation did not interfere with mortality. With an overall mortality less than 40% in COVID-related ARDS patients, they advocate for a possible use of HFNO in COVID-ARF patients. These results are not similar to those presented by Mukhtar et al. [1] Is it related to the difference between NIV and HFNO? Comparing two monocentric cohorts with different patients, even with the same disease, is not acceptable. This crisis gives us enough confusing literature, we will not speculate on this hypothesis.

Finally, at bedside, what should we do? As usual, we treat patients and not diseases in our ICU. Nothing has changed during the COVID-19 crisis. Early intubation, deep sedation and delayed weaning from mechanical ventilation increase mortality. Non-

https://doi.org/10.1016/j.accpm.2020.08.004

invasive respiratory support may (or not) decrease the need of invasive ventilation, but please, do not listen to the sound of sirens. NIV failure kills patients, with or without COVID-19 [9]. And for those who want to use non-invasive respiratory support in ARF/ARDS patients (whether they are COVID-19 positive or not), identifying patients at risk of NIV failure, using initiation/ending algorithms and team training remain the major challenges.

Conflicts of interest

The authors have no conflict of interest to declare.

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Available online 27 August 2020