

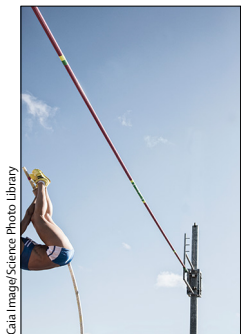


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Prone positioning in non-intubated patients with COVID-19: raising the bar



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As the COVID-19 pandemic has put severe stress and strain on the capacity of hospitals around the world, concerted efforts have been made to evaluate therapeutics aimed at preventing the need for mechanical ventilation. The dissemination of information about potential therapeutic options through various media platforms has been swift and unprecedented. Although the goal of sharing through non-traditional channels might be to accelerate the implementation of therapeutic approaches, some of this information is low-quality evidence that has not been peer-reviewed and is subject to bias. Should reservations about the adoption of potentially beneficial interventions be relaxed in the context of a pandemic? What threshold of evidence is needed for simple, apparently safe, low-technology, or low-cost interventions in the absence of effective treatments?

In *The Lancet Respiratory Medicine*, Anna Coppo and colleagues report on the feasibility and physiological effects of prone positioning in non-intubated patients with COVID-19.¹ Prone positioning has previously been shown to improve mortality in mechanically ventilated patients with moderate-to-severe acute respiratory distress syndrome (ARDS).² The mortality benefit was not observed in patients with mild ARDS, despite improving oxygenation. However, oxygenation is often one of the most important variables in decision making surrounding intubation, so the implications of potentially improving oxygenation in non-intubated patients are important. In theory, prone positioning in non-intubated patients could prevent the need for intubation, and so avoid the risks of harm associated with a stay in the intensive care unit (ICU), such as ventilator-induced lung injury.

Several reports in the past couple months have assessed the feasibility and effectiveness of prone positioning in awake, non-intubated patients with COVID-19.^{3,4} The study by Coppo and colleagues is one of the largest studies of this intervention during the pandemic and we commend the authors for doing this important study in difficult circumstances in an effort to contribute to the evidence base.¹ Between March 20 and April 9, 2020, the study group enrolled 56 patients, of whom 44 (79%) were male and the mean age was 57.4 years (SD 7.4). Prone positioning for

at least 3 h was feasible in 47 patients (83.9% [95% CI 71.7–92.4]). A significant improvement in oxygenation was found from supine to prone positioning; however, this improvement was not sustained in half of the patients after resupination. Furthermore, no difference in rates of intubation was seen in those who maintained oxygenation (responders) compared with those who did not (non-responders). Given these relatively modest results, what should clinicians do about prone positioning in awake, non-intubated patients with COVID-19 moving forwards?

The adoption of therapies has not always mirrored the quality of the evidence. For instance, despite the accumulation of high-quality data showing benefit, lung-protective ventilation has not been consistently adopted in the ICU.⁵ Conversely, activated protein C was rapidly adopted for the treatment of severe sepsis after publication of the PROWESS study,⁶ but was subsequently found to have no benefit and was removed from the market.⁷ Many factors affect decision making by physicians outside the pandemic setting, such as perceptions of treatment risks and benefits (evidence, physiology), contextual factors (ease, cost), and characteristics of the physician (early vs later adopters of evidence). Not unlike the sentiments surrounding COVID-19, the desperate need for a treatment for sepsis, given the high mortality, might have contributed to the rapid adoption of activated protein C after publication of the PROWESS trial in 2001.

The desperation associated with pandemic pressures—with many lives at stake and a surfeit of anecdotes and opinion on social media and other outlets—might affect clinical decision making, leading to the use of therapeutics for which evidence is lacking. To complicate matters, ample evidence exists within critical care of difficulties associated with the de-adoption of practices after a subsequent accumulation of negative studies.⁸ Hence, we argue that physicians must resist the temptation to sweep aside the scientific rigour required to evaluate a new therapy. Does the combination of pandemic pressures and availability, simplicity, or apparent safety of a therapy justify lowering the threshold for adoption? We understand

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the allure of using a potentially beneficial intervention with seemingly low risks. However, many critical care interventions that make physiological sense have failed to translate into improved patient-centred outcomes when assessed in randomised controlled trials. Indeed, many ARDS trials have shown that oxygenation improvements do not translate to survival benefits.^{9,10}

Prone positioning in non-intubated patients might be beneficial; however, many important questions remain. For instance, does prone positioning prevent intubation and harms associated with invasive mechanical ventilation, or simply delay intubation (with potentially worse outcomes)? Who are the ideal candidates? What is the optimal dose? What are the safety concerns? A systematic approach is needed, through observational studies and randomised controlled trials—building on the physiological findings of Coppo and colleagues¹—to address these questions. By lowering the bar for adoption of prone positioning in the pandemic setting, we could be rapidly disseminating an intervention that might not be useful and could potentially be harmful.

We recognise that important differences exist between adopting an intervention as a rescue manoeuvre in centres that are overstretched and lowering the bar as part of routine practice. The rapid adoption of prone positioning in non-intubated patients with COVID-19—despite data from decades of work in ARDS suggesting no benefit in mild cases—seems to be an example of a confluence of powerful anecdotes, amplified by both social media and traditional data sources, supported by a desperation to improve outcomes. Importantly, despite the high numbers of patients with COVID-19 admitted to their hospital, Coppo and colleagues were able to do a prospective feasibility cohort study of prone positioning in awake, non-intubated patients. We look forward to

the results of ongoing studies of non-intubated prone positioning in patients with COVID-19 (NCT04383613, NCT04350723). We also encourage all health-care workers who have adopted protocols out of necessity to publish their experience so that the medical community can learn from them.

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Managing unexplained chronic cough in adults: what are the unmet needs?



Gibson and colleagues¹ defined an unexplained chronic cough in adults as a cough that persists longer than 8 weeks and remains unexplained after investigation and supervised therapeutic trials done according to best-practice guidelines in an adherent patient. The authors further specified that the cough could remain

unexplained because chronic cough had no diagnosable cause, a putative diagnosis was made but it was refractory to treatment, or the cause of the cough was not diagnosable and remained refractory to treatments. The authors stressed the importance of addressing two clinical needs that must be met to improve the poor

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