Awake Prone Positioning in COVID-19: Signal or Noise?

To the Editor} In their nonrandomized controlled trial of awake prone positioning (APP) in patients hospitalized with COVID-19, Dr Qian and colleagues\(^1\) describe the short-term potential harm from APP that was no longer apparent by day 28. This potential for harm needs to be explained and reconciled with contrasting evidence of benefit demonstrated in our larger meta-trial\(^2\) and further confirmed in a recent meta-analysis that included more than 4000 patients, approximately 2000 of whom were included in randomized clinical trials.\(^3\)

First, the authors’ speculation that APP could have obscured the natural progression of disease by transiently improving oxygenation, with resulting delay in life-saving therapies, is not supported by their data.\(^1\) Their data did not show any improvement in oxygenation—the maximum fraction of inspired oxygen was consistently higher in the APP group from day 1 through 5. Indeed, as the authors noted, “more patients in the intervention group received mechanical ventilation during the first 5 days, suggesting no delay in time to intubation with the use of prone positioning.”\(^1\)

Second, the overall 28-day mortality rate in the trial by Dr Qian and colleagues\(^1\) is comparable to that reported in our meta-trial (22.3% vs 22.2%\(^2\)), despite significantly lower disease severity in the former and more than 40% of patients discharged by day 5. Contrasting this high mortality with a low cumulative incidence of intubation (12.1% vs 36.4% in our trial\(^2\)) suggests that a high proportion of patients died without being intubated. Did those patients have do not intubate or do not resuscitate (DNI/DNR) orders and were not offered intubation before dying? If so, these patients who were not eligible for intubation in the first place could not have been harmed by any hypothetical delays.

Finally, the median duration of APP in the intervention group was 4.2 hours per day (IQR, 1.8-6.7 h/d)\(^1\), which is likely insufficient. Durations of less than 8 hours per day are associated with a high risk of failure.\(^2,4\)

We theorize that the surprising signal of potential harm reported by Dr Qian and colleagues\(^1\) is best explained by some baseline imbalance between groups, likely related to DNI/DNR status, with more deaths without intubation occurring in the APP group. To explore this possibility, we request that the authors provide the number of patients who died without intubation in each study group of the trial.

Ivan Pavlov, MD
Miguel Ibarra-Estrada, MD
Stephan Ehrmann, MD, PhD

Author Affiliations: Department of Emergency Medicine, Hôpital de Verdun, Montreal, Quebec, Canada (Pavlov); Unidad de Terapia Intensiva, Hospital Civil Fray Antonio Alcalde, Guadalajara, Jalisco, Mexico (Ibarra-Estrada); CHRU Tours, Médecine Intensive Réanimation, CIC INSERM 1415, CRICs-TriggerSep FCRIN Research Network, Tours, France (Ehrmann); INSERM, Centre d’Etude des Pathologies Respiratoires, U1100, Université de Tours, Tours, France (Ehrmann).

Corresponding Author: Ivan Pavlov, MD, Department of Emergency Medicine, Hôpital de Verdun, 4000 Boulevard LaSalle, Montreal, QC H4G 2A3, Canada (ivan.pavlov.md@gmail.com).

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