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Gravity-induced ischemia in the brain-and prone positioning for COVID-19 patients breathing spontaneously

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Letter to the Editor

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Dear Editor:

A group of Tunisian investigators recently explored whether the early application of prone positioning can improve severe hypoxemia and respiratory failure in coronavirus disease 2019 (COVID-19) patients with spontaneous breathing—through a prospective observational study of patients admitted to the intensive care unit (ICU). After studying 21 subject-patients and 17 control-patients, who underwent prone positioning within 6 hours following ICU admission, they reported affirmatively in *Acute and Critical Care* [1] that yes, early prone positioning can improve severe hypoxemia—and significantly so.

But there was still a problem. The resolution of hypoxemia resulted in no change in the rate of mortality, or in the need for mechanical ventilation. How can that be possible? If ventilation/perfusion ratios are improving significantly throughout the lungs, and measured respiratory parameters are improving, why are patients still dying at the same rate? The answer may lie not in the lungs, but elsewhere. The Tunisian Investigators, in designing this study, made use of gravitational considerations within the lungs. In prone positioning, the beneficial changes in ventilation/perfusion ratios are based largely on gravity. But no one made use of gravitational considerations within the brain—even as concurrent reports [2,3] from 2021 have suggested their importance.

In the article, "Impact of prone position on outcomes of COVID-19 patients with spontaneous breathing" [1] all of 21 subject-patients were placed in prone position for 2 to 4 hours (as tolerated by the patient) followed by 2 hours of supine positioning during the day, and placed in prone position at night, when possible. "Gravitational ischemia in the brain" results from the mass effect of one part of the brain upon another in a gravitational field [2,3]. In any given head position, the top half of the brain (farthest from the center of the earth) is sitting on the bottom half as a weight-burden. In healthy individuals, head and body positions are roughly vertical for 16 hours a day, and then roughly horizontal for 8 hours at night during sleep. Ischemia, which may form on the bottom layers, is reversible in its early stages [2,3].

Gravitational ischemia in the brain may potentially be largely preventable by frequently changing the head tilt—just as ischemic skin breakdown, bed sores, and decubitus ulcers are currently prevented by frequent changes in general body positioning, focused on the effects of gravity. It might have been reasonably hoped that alternating between supine and prone positioning "rotisserie-style" would significantly relieve gravitational ischemia in the brain; but research results, like those of the Tunisian Investigators, suggest that this may not always happen—at least not in brainstem vital centers.

Part of the answer to this apparent discrepancy may be revealed by a group of British investigators who recently reported [4] that "positional brain shift," the sagging of the brain under the effect of gravity, is significant, relative to the specific geometric coordinates generated by magnetic resonance imaging (MRI) for the purpose of guiding stereotactic surgery. If the guiding coordinates are generated by an MRI done in supine position, the brain will move slightly away from those coordinates, if the patient is placed into a different position for surgery. This was confirmed by studying 11 health young adult volunteers, who were specifically moved from supine position to prone, and back again [4]. The head and body rotation studied by the British investigators was essentially identical to that utilized by the Tunisian investigators in their study.

The British investigators concluded that slight non-uniform brain shifting due to differences in head orientation can lead to a significant discrepancy between the planned and the actual location of surgical targets [4]. Additionally, strain analysis in their study revealed local variations in compressibility within the brain. When horizontally rotating from prone position back to supine, the anterior regions showed expansion (with changes in both volume and shape), and the posterior regions showed compression, mostly dominated by changes in shape [4].

Given its low stiffness, brain tissue shifts occur within the cranial vault under the influence of gravity, due to changes in head orientation even in normal healthy individuals without any surgical intervention [4]. The British investigators thus found that in repositioning young healthy adults from prone position to supine, the posterior fossa is compressed. This movement has a potential to compress brainstem autonomic nuclei, predisposing to ischemia formation there.

Data from the Tunisian investigators [1] and the British investigators [4], taken together, suggests that upright head position (or at least partially upright) may be required to relieve gravitational ischemia in the brainstem autonomic nuclei. Intermittently elevating the patient's head by 30° may be helpful—and it may also decrease intra-cranial pressure.

However, intra-cranial pressure is relatively independent of gravity in this closed system. Similarly, in an open system, at the peak of Mont Blanc (15,771 feet or 4,807 meters), in the Alps, the atmospheric pressure is about half of what it is at sea level —yet a ball-point pen, if dropped, still falls to the ground at nearly the same speed—under the influence of gravity [2].

A group of Norwegian investigators [5] recently reported on a cohort of healthy volunteers in whom they studied sleep deprivation, a condition during which the top half of the brain has been sitting on the bottom half for too long—possibly resulting in excessive gravitational ischemia. They used novel brain MRI techniques to examine the white matter microstructure of subjects compared to a control group.

The Norwegian investigators found significant white matter changes during sleep deprivation compared to during a normal sleep/wake cycle—which they considered to represent changes in axonal diffusivity [2,5].

Autoregulation is a mechanism by which cerebral blood flow is maintained—primarily through regional vasoconstriction and vasodilation within the brain. It does not respond well to physical barriers such as intravascular clot or extravascular mass lesion. Gravity behaves as an extravascular mass lesion because it forces extravascular skull or brain tissue to push against the external walls of the blood vessels.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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