RESPONSE TO LETTER TO THE EDITOR

Response to “Pay Attention to Blood Pressure and Oxygen Supply for Neurocritically Ill Patients: Each Pathology Deserves a Specific Treatment”

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We thank Schmitt and colleagues for their valuable viewpoints on our recent paper on the association of oxygen and blood pressure with outcome in neurocritically ill patients [1]. We agree that the study population is heterogeneous, with multiple types of brain injury populations (traumatic brain injury [TBI], ischemic stroke, intracranial hemorrhage, subarachnoid hemorrhage [SAH], and cardiac arrest [CA]). The pathophysiology and mechanisms underlying the initial brain injury are different, but similarities in disease mechanisms and mechanisms underlying the actual neuronal cell death do exist [2]. Local or global reduction in cerebral blood flow, possible ischemia, and metabolic changes occur after brain hemorrhage, hypoxic-ischemic brain injury, and traumatic brain injury. Inflammation as well as swelling and tissue edema are associated with all neuronal injury types. Neuronal tissue vulnerability to secondary injuries is increased in all of the conditions. Hypotension will reduce brain perfusion irrespective of the cause of autoregulation dysfunction. Also note the very loosely specified blood pressure targets recommended for these different conditions: TBI (systolic blood pressure [SBP] > 100 mmHg), CA (mean arterial pressure [MAP] > 65 mmHg and SBP > 90 mmHg), and SAH

(SBP < 160 mmHg) all refer to a similar blood pressure range [1]. The oxygen demand can vary between patients but is likely heterogeneous between the individuals irrespective of their brain injury type. The actual partial pressure of arterial oxygen blood peripheral oxygen saturation targets are not specified for any of these conditions; SpO₂ targets are specified only for ischemic stroke (> 94%) and CA (94–98%). There is no clear evidence that these cohorts would need very different treatment targets during the initial care. Indeed, avoiding hypoxia and hypotension are likely to be important in all these patient types. When planning the analysis, we decided to study the brain injury population as a whole and complement the analysis with relevant subgroup assessments. In these analyses with the performed sensitivity analysis separating the different diagnosis cohorts with logistic regression analysis and local regression curves, we found the results to be consistent with those obtained from the analysis of the whole study population.

As stated by Schmitt and colleagues, PaO₂ and MAP are not the only measures to determine brain tissue oxygenation. For example arterial CO₂, intracranial pressure, and blood hemoglobin concentration are all factors in oxygen delivery to the brain [3]. Nevertheless, MAP is a major determinant of cerebral perfusion pressure, and there is evidence that increasing PaO₂, regardless of already 100% O₂-saturated blood hemoglobin, increases partial pressure of brain oxygen (PbO₂) [4]. Similar findings have been found when manipulating oxygen in patients with cardiac arrest. Our registry only contained certain discrete values of MAP (the worst value recorded during the initial 24 h in the intensive care unit) and PaO₂

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(the value associated with the lowest P/F ratio) available, and instead of exact measures the values should be seen as surrogates to categorize patients into groups based on their hemodynamic and oxygenation conditions. Altogether, we agree that our study has limitations; for example, actual measurements of intracranial pressure, arterial CO₂, and PbO₂ would have been of great value, but unfortunately these important variables are not routinely collected in the registry. Importantly, we agree that a study such as this can only find associations between variables and therefore causative mechanisms can only be speculated. There is no doubt that further studies incorporating more refined measures of brain oxygenation are required in patients with different types of brain injury [5].

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Conflicts of Interest

None.

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