



HHS Public Access

Author manuscript

Crit Care Med. Author manuscript; available in PMC 2023 February 01.

Published in final edited form as:

Crit Care Med. 2022 February 01; 50(2): e215–e216. doi:10.1097/CCM.0000000000005388.

Letter to the Editor: Hemoglobin level on admission is less important

Julián N. Acosta, MD¹, Audrey C. Leasure, BS¹, Kevin N. Sheth, MD¹, Guido J. Falcone, MD, ScD, MPH¹

¹Division of Neurocritical Care and Emergency Neurology, Department of Neurology, Yale School of Medicine, New Haven, CT, USA.

Keywords

hemoglobin; intracranial hemorrhage; neurological outcome; red blood cell transfusion

To the Editor,

We would like to thank Ye and colleagues for their thoughtful letter to the Editor in connection to our study evaluating the relationship between admission hemoglobin (Hb) levels and neurological outcome in patients with spontaneous intracranial hemorrhage (ICH).¹ Our colleagues raised important points, including that baseline Hb levels do not represent the longitudinal change in Hb across the entire admission, an exposure that may be more relevant than baseline levels, and the futile and potentially harmful role of red blood cell (RBC) transfusions in these patients.

We agree with our colleagues that a single admission value of Hb levels does not reflect its longitudinal evolution. However, we argue that the role of baseline and longitudinal Hb levels in ICH outcome constitute two different questions. We decided to focus on baseline Hb as the exposure of interest for several reasons. First, baseline Hb levels are almost always available in both clinical trials and observational studies, facilitating the evaluation of the question at hand in multiple populations while maximizing statistical power. Second, the focus on baseline Hb allows the evaluation of a narrowly defined exposure, with very specific implications in terms of opportunities for prognosis and intervention. Third, the focus on admission Hb values provide a unique opportunity for prognostic categorization early in the course of the disease, when important goals of care conversations take place. While questions pertaining to longitudinal Hb levels would certainly add important information to this line of research, the study design required to tackle this question is entirely different, requiring a standardized approach to the ascertainment of Hb levels on

Corresponding author: Guido J. Falcone, MD, ScD, MPH, Department of Neurology, Yale School of Medicine, 20 York Street, LLCI 10th Floor. New Haven, CT, USA, 06520, guido.falcone@yale.edu.

Copyright Form Disclosure: Drs. Acosta, Leasure, and Sheth received support for article research from the National Institutes of Health (NIH). Dr. Acosta received support for article research from the American Heart Association (AHA). Dr. Sheth's institution received funding from the NIH, the AMA, Hyperfine, Biogen, Alva, Astrocyte, and Bard. Dr. Falcone has disclosed that he does not have any potential conflicts of interest.

multiple occasions during the admission and appropriate capturing of the interventions (transfusions) triggered by their fluctuations.

We also agree with Ye and colleagues that the focus on baseline Hb levels may introduces bias. It is conceivable that the associations we describe may not represent a true underlying causal association. However, as we point out in the discussion, even in this setting the reported associations still have important value from a prognostication and/or risk stratification perspective. Along these lines, we note that when using specific biomarkers for this purpose, powerful statistical associations point to important risk predictors irrespective of whether they recapitulate true causal associations.

While we recognize that the lack of information on RBC transfusions during hospitalization is a limitation of our work, we respectfully disagree with the authors that the existing evidence indicates that this intervention is futile or potentially harmful in ICH. The clinical trial and two observational studies cited in the letter focused on traumatic brain injury and their conclusions cannot be directly extrapolated to ICH due to the significant pathophysiological differences between these two diseases. As an example, a small retrospective study found that RBC transfusions was associated with lower 30-day mortality in ICH patients.² In addition, the association between transfusions and poor outcomes in some observational studies³ could represent confounding by indication,⁴ where the association reflects the poor clinical status of the patients receiving the intervention of interest.

References

1. Ye T, Du K. Letter to the Editor: Hemoglobin level on admission is less important. *Crit Care Med.* 2021.
2. Sheth KN, Gilson AJ, Chang Y, et al. Packed red blood cell transfusion and decreased mortality in intracerebral hemorrhage. *Neurosurgery.* 2011;68(5):1286–1292. [PubMed: 21307801]
3. Roh DJ, Carvalho Poyraz F, Magid-Bernstein J, et al. Red Blood Cell Transfusions and Outcomes After Intracerebral Hemorrhage. *J Stroke Cerebrovasc Dis.* 2020;29(12):1–8.
4. Kyriacou DN, Lewis RJ. Confounding by Indication in Clinical Research. *JAMA.* 2016;316(17):1818–1819. [PubMed: 27802529]