Reviewer's report

**Title:** Head CT is of limited diagnostic value in critically ill patients who remain unresponsive after discontinuation of sedation

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**Reviewer:** John Kress

**Reviewer's report:**

PEER REVIEW: Head CT is of limited diagnostic value in critically ill patients who remain unresponsive after discontinuation of sedation

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**SUMMARY**

This document represents a review of changes made to the manuscript after initial review. Specifically, we comment on the manner in which the authors addressed our concerns about the manuscript. The original review comments are below in italics, followed by new comments of the amended manuscript.

**MAJOR COMMENTS**

1. This study provides validation for the limited role of head CT in this patient population as suggested by the work of Rafanan et al. and Kress et al. Some direct comparison is made to the Kress et al. manuscript, and it is noted that the utility of head CT in this study is even lower, but there is no discussion as to why this may be the case (population, exclusion criteria, etc.).

The authors included a discussion of the differences, and allude to their exclusion of patients with focal neurological findings as a plausible explanation. This certainly begins to address our comment. We would add, however, that other reasons could also be argued, including differences in patient population (other than just coagulopathy) as well as the institutional “threshold” for ordering a CT. Additionally, Kress et al. had a higher rate of DIS across the whole
population, making a structural (as opposed to lingering sedative) cause of “non-awakening” more likely.

2. The authors state that a minority of enrolled patients undergoing head CT (8 of 42, or 19%) had a daily interruption of sedation (page 7 text and Table 4). However, different numbers are presented in Table 2 (20 of 42, or 47%), and the text on pages 8-9 suggests a third proportion (30%). Obviously, corrections are necessary to ensure accurate presentation of the data.

Corrected.

Assuming that the data demonstrate that the majority of patients undergoing CT have NOT had a daily interruption of sedation, this observation could further support the conclusions by Kress et al. that daily interruption of sedation limits utilization of such tests. However, this assertion would necessitate knowledge of the proportion of patients receiving/not receiving a daily interruption of sedation in this ICU population as a whole.

Addressed below.

3. As a continuation of point #2, many important questions are described but cannot be asked due to the limited study design. An alternative study design, such as a case-control study with a carefully selected control group (prolonged intubation with quick return to consciousness), could provide further insight. This alternative design may make it possible to evaluate the impact of sedation interruption, sedative agent, route of sedative administration, etc.

The authors discuss the limitation of their study in the discussion and conclusions section, but do not make any changes to the nature of the study presented. The discussion frames the data presented, but obviously this limitation is significant. Not addressing this limitation thus limits the impact of the data. The main conclusion is that in this medical ICU where sedation is performed with benzodiazepines and fentanyl largely without DIS, the diagnostic yield of HCT in patients who fail to awake is very low. It tells us little about the (potentially modifiable) risk factors for delayed-awakening (DIS, sedative, diagnosis, age, neurocognitive function, renal function, etc.) because we don’t know how these patients differ from patients who do wake quickly.

MINOR COMMENTS

1. Table 2 and Table 4 both report the “Type of sedation” and “Daily interruption of sedation”, although the former heading is missing data in Table 2 and the latter heading reports inconsistent data across the two tables.

Addressed.

2. The data are described with mean and standard deviation. The endpoints described, however, are often skewed, and the sample size here is relatively small. Mean and standard deviation are appropriate if the distribution has been demonstrated to be normal, but this data may be better described with median and interquartile ranges.
Addressed.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests