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LETTER

Determining Risk Factors of Postoperative Delirium in Patients Undergoing Liver Transplantation [Letter]

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Dear editor

In the recent article of Chen et al[1] determining the risk factors for postoperative delirium (POD) in patients undergoing liver transplantation, the multivariate logistic regression analysis showed that preoperative ammonia ≥46 μmol/L, Model for End-Stage Liver Disease score ≥15, hepatic encephalopathy, anhepatic period, and aspartate aminotransferase at the first postoperative day were the independent risk factors for POD. The findings of this study have potential clinical implications, but there are several issues in methodology that need further clarification.

First, the authors describe that two doctors independently diagnosed POD using the Confusion Assessment Method for the ICU. It was unclear whether all of POD assessments were performed in the ICU. In fact, this tool should be used daily on all patients admitted to the ICU even if they are mechanically ventilated. For non-ventilated patients in the surgical ward, the Confusion Assessment Method is more appropriate tool for POD evaluation.[2] Most importantly, the readers were not provided with the duration of POD assessment and definitions of POD. The 2018 newest recommendations for neurocognitive change associated with anesthesia and surgery suggest reporting on the occurrence of POD during hospital stay up to 1 week after surgery or until discharge and require that definitions of POD must meet the diagnostic criteria of delirium in the DSM-5.[3] We are concerned that the use of inappropriate assessment tool, non-recognized diagnostic criteria and a short assessment time to define POD would have confounded the incidence of POD reported in this study.

Second, regarding statistical analysis, the authors stated that the univariate factors with a $P<0.1$ were included in the multivariate analysis. However, the detailed results of univariate analysis were not provided. In fact, establishment of a multivariate model includes three steps: a) initial comparison of demographic and perioperative variables between patients with and without POD, as described in Tables 1 to 4 of Chen et al article;[1] b) incorporation of the variables with statistical significance in initial comparison, defined as $P<0.05$, into the univariate analysis to examine multicollinearity among candidate independent factors; c) inclusion of the variables with large P values ($P<0.1$ or 0.2) in the univariate analysis into the multivariate model to identify the independent risk factors of POD, with their P-values, adjusted odds ratios and 95% confidence intervals.[4] Due to the lack of

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multicollinearity among candidate independent variables by the univariate analysis, their results of the multivariate logistic regression analysis would be subject to bias. Furthermore, another potential bias in the study by Chen et al[1] is the large number of variables studied in relation to the number of subjects included. In this case, the model built by them is probably highly overfitted.

Third, this study demonstrated that median onset and duration of POD were 2 days (Q25, Q75; 1, 3) and 5 days (Q25, Q75; 3, 7), respectively. We are very interested in knowing why other complications besides POD in early postoperative period were not observed at the same time and taken into the multivariate model for adjustment of confounders. It has been shown that early postoperative sepsis, intra-abdominal infection, renal failure, and reintubation are significantly associated with an increased risk of POD after liver transplantation.[5,6] We argue that not taking postoperative factors associated with POD into the model would further have distorted with the inferences of the multivariate analysis when determining the independent risk factors of POD in this study.

Finally, this study assessed the contribution of POD to postoperative outcomes including intubation time, length of ICU or hospital stay and medical cost. Because there were significant differences between patients with and without POD in many demographic and perioperative variables affecting postoperative outcomes, however, directly comparing postoperative outcomes between them only has a limited clinical value. To determine real contribution of POD to postoperative outcomes, the authors should apply the multivariate analysis to adjust patients' demographic and perioperative data and control selection biases.

We believe that addressing the above issues will further improve transparency of this study and avoid any misinterpretation of their findings.

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Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this communication.

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