Establishing a predictive nomogram for postoperative delirium: Methodology is critical

To the editor,

We read with interest the recent article by Zhang et al [1] establishing a predictive nomogram for postoperative delirium (POD) in elderly patients undergoing hip fracture surgery. Based on the results of multivariate logistic regression analyses with the backward method, a POD risk prediction model was formed in this study. Given that POD is a common postoperative complication associated with adverse events and outcomes including functional decline, prolonged stay of hospital, and increased risks of institutionalization, morbidity and mortality in the elderly patients with hip fracture surgery [2], their findings have potential implications. Other than the limitations described by authors in discussion section, however, we noted several methodological issues in this study that were not well addressed.

First, regarding inclusion criteria, it was unclear whether study subjects included the elderly patients undergoing emergency hip surgery. The available evidence shows that incidence of POD is significantly increased after emergency hip surgery compared to elective hip surgery [3]. This study only provided methods of anesthesia, such as general anesthesia, spinal anesthesia and nerve block, but did not include and compare the perioperative medication uses between patients with and without POD. It has been demonstrated that intraoperative ketamine and opioids, postoperative benzodiazepines and ketamine are significantly associated with an increased risk POD after total knee and hip arthroplasty [4], while intraoperative dexmedetomidine can significantly reduce the incidence of POD in the elderly patients undergoing hip fracture surgery [5]. Recently, it is appealed that when developing a POD risk prediction model, perioperative medications, especially POD-inducing medications, should be used as potential predictors for statistical adjustment because of the modifiable nature of medication use and their possible impacts on other risk factors included commonly in the models, such as cognition function [6]. Furthermore, postoperative adverse events and complications were also not included in their models. Actually, postoperative anemia and blood transfusions, postoperative complications including urinary tract infection and pneumonia, and inadequate postoperative pain control have been significantly associated with an increased risk of POD after noncardiac surgery [7–9]. We are concerned that not taking the above known risk factors into their models would have distorted with the inferences of multivariate regression analyses for the risk factors of POD and their adjusted odds ratios in this study.

Second, to identify independent risk factors of POD, only variables achieving a significance of $P < 0.05$ in the univariate regression analyses were selected for multivariate regression analyses in this study. It is recommended that after multicollinearity among candidate independent variables is examined by univariate regression analyses, all variables with large *P*-values ($P < 0.2$) should be included into the multivariate regression model [10]. Thus, the method that the authors constructed the multivariate regression models would have missed some useful variables for prediction of POD, such as advanced age, diabetes, anemia, preoperative dependent functional status, complexity of surgery, and others [2,3].

Finally, an ideal risk prediction model demonstrates good calibration and discrimination. The POD risk prediction model established in this study only has a C-index of 0.67 (95% CI 0.62-0.72), though the calibration test shows a good concordance between predicted and actual probabilities. It is generally believed that model discrimination is considered adequate when the c-index exceeds 0.7 and strong when the c-index exceeds 0.8 [10]. Thus, their POD risk prediction model may not be ideal because of a moderate discrimination ability.

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