IL-18 and SC5b-9 for predicting neurocognitive dysfunction after cardiopulmonary bypass

Editor—Dichotomization of quantitative measures can result in loss of information about individual differences, loss of effect size and power in the case of bivariate relationships, spurious statistical significance and overestimation, and can potentially overlook non-linear relationships, or less reliable measurements. Unfortunately, Kumar and colleagues2 have dichotomized the results of the cognitive tests using an arbitrary definition of one standard deviation (SD). The cognitive measurements and the biological measures of inflammation are all continuous variables and as such, linear rather than logistic regression analysis should have been used.3

Another limitation of their analytical approach is that they have used nine cognitive tests. This will lead to an increased possibility of statistical significance being found by chance when none exist. A robust approach, as their group has done previously, would have been to create dimensionless z scores for each test and then summed them to give a single measure of cognition.4 5 This could have then been used as the outcome variable in the linear regression analysis to determine any association with IL18 or SC5b-9.

A lack of robust statistical methodology in research examining cognitive decrements associated with heart surgery has clouded the area. It is important that authors use appropriate methods and that reviewers and editors reject papers that do not.

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Editor—We are grateful for the opportunity to respond to the comments made by Dr Alston about our study.2 We would like to point out that the use of 1 SD in two or more of the nine neurocognitive tests to define neurocognitive dysfunction is not an arbitrary one. The 1 SD rule (one standard deviation decline on two or more tasks) and the 20–20 rule (20% decline on 20% tasks) are the two most commonly applied means of examining postoperative cognitive dysfunction after coronary artery bypass graft surgery.6 Conflicting reports exist in literature regarding the sensitivity and specificity of these two rules.7 8

As regards the use of nine cognitive tests in our study, we chose to include the core tests from the recommendations of the ‘Statement of consensus on assessment of neurobehavioral outcomes after cardiac surgery’.9 These were the same battery of tests used in our earlier study.3 We would also like to point out that we did not make use of z scores in our previous study.

We do agree with the observation that a continuous variable such as a composite z score rather than a binary ‘impairment/no impairment’ outcome would have been more sensitive. We also accept that evidence has emerged since the completion of our study that there is a potential for false positives with the 1 SD rule10 and with increasing number of tests in the battery.11 We feel that our study, in spite of any potential limitations, will stimulate interest in the role of IL-18, a key pro-inflammatory cytokine, in neurocognitive dysfunction after cardiac surgery.

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Editor—We read with interest the comment of Dr Wrench concerning the incidence of side-effects associated with the preoperative use of clonidine to reduce sevoflurane-induced emergence agitation. However, we do not agree with his statement that there was an increased incidence of postoperative hypotension and bradycardia. First, the incidence of postoperative hypotension and bradycardia was not significantly different between the clonidine 4 mg kg\(^{-1}\) group and the midazolam groups. Suggesting that this difference might become significant in a more powerful study is speculative, in particular in relation to bradycardia which was 1/20 patients in the clonidine 4 mg kg\(^{-1}\) group and 0/20 patients in the midazolam group. Secondly, only the 4 µg kg\(^{-1}\) dose of clonidine was effective in reducing sevoflurane-induced emergence agitation. In comparison with the 2 µg kg\(^{-1}\) dose, the incidence of postoperative hypotension (5/20 in each group) or bradycardia (3/20 in the 2 µg kg\(^{-1}\) dose and 1/20 in the 4 µg kg\(^{-1}\) dose) was not increased. Thirdly, episodes of hypotension or bradycardia did not require treatment in any of the children. After leaving the recovery room, all the children had an uneventful postoperative course. We therefore believe that in comparison with midazolam, clonidine 4 µg kg\(^{-1}\) reduced sevoflurane emergence agitation without increasing clinically relevant postoperative side-effects.

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Editor—We thank Dr Abbas and Brull for their interest in our recent article.\(^1\) They suggest that we have reported