Author's response to reviews

Title: Risk Factors for Early Postoperative Cognitive Dysfunction after Non-Coronary Bypass Surgery in Chinese Population

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Author's response to reviews: see over
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Title: Risk factors for early postoperative cognitive dysfunction after Non-Coronary-Artery-Bypass-Graft Cardiovascular surgery in a Chinese Han population

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Author’s response to reviews:
1. Why not choose ISPOCD’s methods, but choose MMSE?

Re: Thanks for your review on this point. It is known that ISPOCD’s methods were sensitive neuropsychological tests, but might be influenced by culture. In our current research, most of the patients were poor educated. In other words, it was difficult to finish the neuropsychological test with ISPOCD’s method. In fact, we took about half an hour to explain the test minutes for every patient and the family to explanation. MMSE was another way used to examine the POCD. We thought that the MMSE test was suitable for the research.

2. POCD is common in elderly patients, many studies have shown that the POCD incidence of elderly patients is about 20-30%. I confused that the incidence of POCD are really 33% in population who’s average age are 41.7 years. Please provide the 176 patients with preoperative and postoperative MMSE scores.

Re: Patients in our study underwent non-CABG surgery were poor educated, which might influence the results and lead to the relative high incidence of POCD. For the details of the MMSE score of each patient, please see the attachment.
3. Please provide proof that statistical professionals conducted this article statistical.

Re: our research protocol and the whole process of the research were under the supervision of a statistician, named Xiaofei Ye. We had provided the proof of the statistics for our manuscript. Please see the attachment.

4. In Table1 and Table3, ASA(#/#/#)#HYHA(#/#/#/#) Shows no specific classification.

Re: we feel apologized for our missing data in table 1 and 3. We have modified the table and filled all the blanks. We wish our revised version is much more acceptable.

5. Exclusion criteria should refer to ISPOCD.

Re: We revised the description of exclusion criteria refer to ISPOCD.

6. Please reduce the description content of anesthesia and surgical, do a detailed description of the process of evaluation and diagnosis POCD.

Re: The description of anesthesia and surgery was shortened. The process of evaluation POCD was revised in much more details.

7. Authors elucidated that patients developed POCD were older than those who did not. Is there any difference in the incidence of POCD in each age group (such as age of 60-70, 71-80 and over81), Please define these data.

For CABG is excluded, the patients who were included in the study were younger than who were excluded. There were only a few patients whose age was over 60. There were insufficient data for advanced age group analysis.

8. If you have any data concerning to the incidence of POCD after CABG surgery without using CPB. Please add those as the baseline data without relation to aortic cross-clamp procedure.

It was reported in a meta-analysis that POCD after OPCAB was significantly less severe in the early postoperative period compared with that observed after CABG over this time period. It was implicated that early POCD may be associated with the occurrence of microemboli generated during cardiopulmonary bypass.

9. How about the long-term outcome in POCD?

Re: It was reported that long-term outcome postoperative cognitive dysfunction correlates significantly with decreasing activity of daily living, which suggests that patients with postoperative cognitive dysfunction need more assistance with everyday actions than before surgery. Our research protocol was first designed to identify the risk factors of POCD during 5 days after surgery, but not the long-term outcome. Further studies were needed to answer
10. Is there the occurrence of chronic cognitive impairment?

Re: It was reported in the meta-analysis study that POCD after CABG beyond 5 years was up to 42% of patients. However, our current study was not designed to illustrate this issue. Further studies were warranted to define the question.

11. Do you have any suggestion or advice to cardiovascular surgeons?

Re: It was found that fewer grafts were performed in the OPCAB group than in the CABG group, requiring less manipulation and, potentially, reducing the risk of an inflammatory response. This might explain why the occurrence of early stage POCD was greater in the CABG group than in the OPCAB group. For reducing the incidence of early stage POCD, it is suggested that surgeon do less work as much as possible.

12. The word “non-CABG cardiovascular surgery” is too long, so I feel the word “non-coronary bypass surgery” may be suitable.

Re: Thanks for your opinion on this point. Our study was originally designed for cardiovascular surgery. I agree with you that the word “non-coronary bypass surgery” is suitable.

13. Author did the study in one hospital or center and selected only 176 patients, no matter what the result is, it is not appropriate to derived it to Chinese Han population.

Re: Thanks for your opinion on this point. Our study was a prospective observational study to identify the risk factors in these patients. It was conducted in a teaching hospital. We do accept that using word “Han population” was inappropriate. We did not use these words in our revised version and discuss this limitation in our discussion.

14. There are minor Chinese way of expressions and grammatical mistakes to be corrected.

Re: we do feel awkward for our poor written English. We have revised our manuscript and made an extensive modification to it. We hope the revised version is much more acceptable.

15. Since the word “tumor” described with aortic surgery, please clarify that means cardiac tumor or aortic aneurysm.

Re: Here the word “tumor” means cardiac tumor, we have revised it in our new version for a much more clear description.

16. In table 3, please clarify if the following data is correct

Sufentanil dose( μg) 1.6 ± 1.0 2.2 ± 1.1  P#0.002
Re: Thanks for your careful review on it. We made some errors in Table 3. We have corrected it in the new version.

17. In table 3, ASA showed significant difference, but author did not include it in multivariate analysis, please explain the reason why?

Re: Thanks for your opinion on it. We reviewed our data in SPSS again to identify whether we did the right analysis. We found that when applying the logistic regression backward model, SPSS automatic removed the data step by step. According to the record of the software, ASA was removed in step 4. That’s why ASA level was not listed in the final table.

18. The MMSE examination was designed as a screening tool. It is inappropriate to use this as an assessment for cognition when defining POCD.

Re: The MMSE has been used to determine gross cognitive changes as in Alzheimer’s dementia. Despite some failings, the MMSE is still used as the only measure of cognitive function in studies of post-anaesthetic outcome. To obviate the use of crude measures of cognitive dysfunction, more accurate assessments have been made using cognitive test batteries to examine a number of cognitive domains. While assessing a broad number of domains is believed to be important to determine the extent of functional impairment, and possibly infer mechanisms of action of POCD, utilizing multiple measures introduces further problem. First increasing the number of tests increases the time required for testing. The amount of testing that patients will tolerate is limited by their ill-health and anxiety, and may magnify the role of confounding factors such as fatigue and motivation. And finally, even if the duration of assessment is kept to a minimum, the use of multiple increases the probability of false positive classifications which would inflate the reported incidence of POCD. In a Chinese study, more time and more tests could increases the probability of false positive classification more likely, for relative poor education and corporation.

19. Appropriate cognitive batteries for POCD are well described in the literature. They generally involve about 7 or 8 tests covering a variety of cognitive domains. Generally POCD is defined as $z < 1.96$ SD below controls on 2 or a composite score of cognition. The test must be administered by trained individuals under the strict control of an experienced neuropsychologist with experience in psychometrics. If the authors wish to move away from conventional definitions of POCD they need to justify this.

Re: It was selected by some researchers if $z < 1.96$SD. In some anesthesiology study about POCD after cardiac surgery, 1.0 SD has been also accepted.

20. Testing 3 to 5 days after surgery is very early and likely to measure residual drug effects, the effect of hospitalization etc. Generally 6-7 days is the earliest one would attempt this and in reality 3 month testing out of hospital is considered most useful.
Re: It was considered that the early POCD is in the first week after surgery. For study on early POCD, it was not included 3 month testing. Long term POCD is considered most useful. Some researchers also take 3 to 5 days after surgery for evaluation and was considered suitable for the detection of early POCD.

21. Intra-operative hypotension and multiple micro embolization are responsible for POCD is not correct; the cause remains unknown.

Re: The mechanism of POCD after cardiac surgery remains unknown. But it was revealed that some factors may contribute to the POCD. There were some study suggested that intra-operative hypotension and multiple micro embolization are reasons for POCD development.

22. The multiple risk factors are also erroneous; the only constant is age and years of education or IQ.

Re: Although there were limited studies, it was reported that some other factors were risk except constant risk factors of age and years of education and IQ.

23. The mixing of 3 muscle relaxants is bad anesthesia and likely to lead to potentiation of relaxant’s.

Re: “Vecuronium” was a spelling mistake. It was revised by “rocuronium”.

24. The aim is to measure incidence of POCD but the wrong tool has been used, so one cannot regard the 33% incidence as reflecting the true situation.

Re: Both statistical and conceptual issues associated with determination of what constitutes clinically significant change. A battery of neuropsychologic tests will provide more details on POCD but more false positive likely. For the poor education and corporation, a battery of test might be inefficient and more false.

25. CBP is now considered to be a minor player. Off pump surgery has been shown to lead to the same incidence for POCD both in large prospective controlled trials and in meta-analysis.

Re: In a recent meta-analysis, it was revealed that early POCD after OPCAB was significantly less severe in the early postoperative period compared with that observed after CABG over this time period.