

Peer Review File

Article information: <http://dx.doi.org/10.21037/jtd-21-644>

Reviewer A

Comment 1: It is quite rare we deal with POH after cardiac surgery in my experience. Most patients complain wound pain after cardiac surgery, therefore, usually most patients take any kind of painkillers in postoperative period. As a matter of course, those analgesic drugs will relieve headaches in like manner even if patients have POH. If a lot of patients have taken painkillers, it is difficult to evaluate the incidence of POH after HVS. The authors should present how many patients used analgesic drugs for wound pain. Besides, the authors should present the pain control protocol in your hospital.

Reply 1: Thank you for your valuable feedback. Postoperative headache has been ignored for various reasons. However, the incidence of postoperative headache is high according to our clinical observation. As you have said, *“most patients complain wound pain after cardiac surgery and usually most patients take any kind of painkillers in postoperative period. As a matter of course, those analgesic drugs will relieve headaches in like manner even if patients have POH.”* We believe this is one of the common reasons why the development of headache is ignored or covered. Probably unlike your treatment regimen, patients after cardiac surgery do not routinely use analgesics in our hospital. We only use short-acting analgesics to solve pain problems when patients really need them. Of course, there is no denying that some patients also complain wound pain in our hospital. However, in our clinical experience, language-comforting and short-acting analgesics are sufficient to address these problems in most cases and do not affect observations of other indicators. We cannot deny that the use of short-acting drugs may lead to underestimation of the true incidence of POH, but it may be difficult to solve this problem at this stage. In our analysis, only about 17.6% of patients (677 cases) had taken painkillers at least once

for wound pain or other causes before the development of POH and the incidence of POH in these patients was 28.7%. The other 82.4% of patients (3,176 cases) had not taken pain medication before the development of POH and the corresponding incidence of POH was 27.3%. We performed a chi-square test and found that the statistical difference was not significant ($P = 0.473$). This means that whether painkillers were taken for other reasons may not have much effect on the detection rate of POH. We have added this part as advised in our text (Results section) (see Page 11, line 157).

Changes in the text: Short-acting analgesics were used for postoperative pain control in our hospital. In this study, about 17.6% of patients had taken painkillers at least once for wound pain or other causes before the development of POH and the incidence of POH in these patients was 28.7%. The other 82.4% of patients had not taken pain medication before the development of POH and the corresponding incidence was 27.3%. No significant difference was found between groups ($P = 0.473$), indicating that the use of painkillers may not have much effect on the detection rate of POH.

Comment 2: The authors should present the approach of HVS whether sternotomy or MICS, because postoperative course is quite different between two approaches.

Reply 2: Thank you for your kind suggestion. We are very sorry for our failure to make it clear before. We have previously written in the article that all included patients underwent open HVS in the Abstract (Methods section, Page 3, line 30) and Methods section (“Study population”, Page 7, line 80). This meant that all the procedures were carried out by sternotomy and cardiopulmonary bypass. We have added some sentences to make it clear in the “Results Section” (see Page 10, line 141).

Changes in the text: All patients underwent sternotomy and cardiopulmonary bypass.

Comment 3: The authors mentioned that “the mortality of patients with POH was significantly higher than that of patients without POH”, but the multivariate analysis for mortality using POH as one of the variables should be done to prove the association with mortality. Because as the authors mentioned, “significantly higher rates of postoperative pneumonia, reintubation and tracheotomy, and longer postoperative durations of mechanical ventilation, ICU and hospital stay were observed in patients with POH”. Obviously, these factors are associated with perioperative mortality, so to say cofounders.

Reply 3: Thanks for your comments. We didn’t describe this aspect much because it is not the main focus of our study. The aim of this study was to identify independent risk factors for POH and to develop a risk prediction model. Mortality is only used as a descriptive result in this study, not the focus of our analysis. The mortality of patients with POH was significantly higher than that of patients without POH (4.3% versus 2.4%, OR = 1.872, $P = 0.001$). Other adverse outcomes were also significantly different between groups. These are sufficient to indicate that POH is closely related to various postoperative adverse events and thus early prediction of POH means a lot. We believe that a univariate analysis is enough to achieve our objective. Analyzing independent risk factors for mortality is meaningful, but it is not the content of our study. We hold that a multivariate analysis for mortality is unnecessary and inappropriate in this study. Anyway, thank you very much for your advice. If possible, we hope to be able to study this issue carefully when appropriate in future work.

Comment 4: The authors used the STROBE statement checklist, but TRIPOD statement for prediction model study is better for your work.

Reply 4: Thank you for your kind suggestion. There is no doubt that TRIPOD statement is appropriate for prediction model study and we strongly agree with you. But we cannot choose this statement because it is not on the shortlist of this magazine. All the Reporting Checklists available on the official website of the magazine are listed below. After selection, we believe that “STROBE checklist” is relatively suitable for our work.

Study Type	Guideline*	Download Checklist (reformatted for the journal)
Randomized controlled trial	CONSORT (CONsolidated Standards Of Reporting Trials)	CONSORT Checklist
Nonrandomized design	TREND (Transparent Reporting of Evaluations with Nonrandomized Designs)	TREND Checklist
Observational studies in Epidemiology	STROBE (STrengthening the Reporting of Observational studies in Epidemiology)	STROBE Checklist
Diagnostic accuracy study	STARD (STAndards for Reporting of Diagnostic Accuracy Studies)	STARD Checklist
Systematic review or meta-analysis	PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)	PRISMA Checklist
Animal research	ARRIVE Guidelines	ARRIVE Checklist
Clinical practice guideline	RIGHT Guidelines	RIHGT Checklist

Comment 5: In table 1, if the authors willing to present the balance of two groups (training set and validation set), SMD might be better than p value.

Reply 5: Thank you for your comments. To our knowledge, the *P* value has usually been used to compare the balance between two groups in the literature. SMD is suitable for continuous variables, but not for categorical variables. Therefore, using SMD may not be appropriate in this study as there are some categorical variables.

Reviewer B

Comment 1: Congratulations. Lateral thinking and important subject and safety issue for patients after HVS. Well presented and easy to understand.

Reply 1: Thank you for your comments. Your encouragement is a great affirmation of our work. We will try to make more valuable and meaningful research in future work. Thank you!

Reviewer C

Comment 1: You did not mention some details about the pathologies for the patients treated (aortic valve stenosis, mitral valve stenosis or regurgitation, etc) and also there were no mention about the procedures performed whether patients are having multi valvular heart surgery versus single valve and whether you did valve repairs or replacements and whether you used mechanical vs biological prosthesis, since we are

discussing an issue related to heart valve surgery, so I think that is an important issue to mention. But all in all I think you did a good work.

Reply 1: Thank you for your valuable feedback. We have added this part as advised in the Results section (see Page 10, line 141). We think it is very helpful to improve the quality of our paper. Thank you!

Changes in the text: All patients underwent sternotomy and cardiopulmonary bypass, in which 59.8% underwent single-valve surgery. Approximately 63.6% of patients underwent mitral valve surgery and more than half underwent aortic valve surgery. About two-thirds of mitral valve surgery and a quarter of aortic valve surgery were repair procedures. In patients undergoing valve replacement surgery, about two-fifths used biological prosthesis. Regarding the valvular pathologies, stenosis accounted for about one-third of mitral valve diseases and about one-fifth of aortic valve diseases.