

Peer Review File

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Reviewer A

Comment: The study in the JTD profile.

Despite being a retrospective study, it involved a large number of patients. The great merit lies in the evaluation of the systemic vascular resistance index in the perioperative evaluation of patients undergoing cardiac surgery. This value is often overlooked in vital control.

Interestingly, the systemic vascular resistance index after mitral valve surgery was significantly lower than that of other surgeries ($p < 0.05$).

I missed it and, therefore, I suggest adding the importance of evaluating the systemic vascular resistance index in monitoring vasoplegia, which is a relevant problem.

Reply: Thank you very much for your insightful comments. We have reorganized the logical flow of the Introduction and Discussion sections, which seemed somewhat redundant and unfocused. We hope that you will take the time to read it.

Changes in the text: Introduction and Discussion sections.

Reviewer B

Comment 1: Drs. Umeki and Yamamoto have asked a clinically relevant question regarding the characteristics of SVR following cardiac surgery. Regretfully their summary is just too incomplete and unfocused for me to recommend publication in its' current format. I can add the following comments, questions and suggestions for improvement:

Reply 1: Thank you for your valuable and helpful suggestions. We have rewritten the entire text to address your comments on our summary. In particular, the results were expanded through statistical processing. Additionally, discussions that were somewhat redundant have been reorganized. We apologize for the fairly large number of revisions; we have explained them in detail here.

Comment 2: Abstract - As background, I would suggest that it is not that low BP is usually monitored, but rather that it is frequently encountered post-operatively. For methods, the number of patients analyzed is a result, not a method. For comparisons, you are evaluating changes over time and differences between surgical procedures. I believe this would require a 2-way ANOVA. for the results, the comparisons are not clear or precise. Overall comparisons are given as well as comparisons for random time blocks.

Reply 2: Thank you for your suggestions and insights. We have revised the Background section to state that low blood pressure is often encountered postoperatively. Furthermore, the number of cases analyzed has been presented in the Results section. Regarding statistical processing, the continuous data for each group generally stabilized at 2–4 hours postoperatively and did not change thereafter. Therefore, we did not examine the changes over time or the interactions; we only examined the significant differences among the mean

values of the data for each group for a given time period. We have tried to avoid expressions that show changes over time as much as possible; we hope that our revisions improve the clarity of the manuscript.

Changes in the text: Abstract lines 38–42, 56–58.

Comment 3: Introduction - The goal is clear, but the justification is a bit muddled. I agree that BP should be monitored and that both perfusion pressure and blood flow are important for optimal circulation distribution. Intravascular volume and resistance are mentioned, but there are no comments regarding the role of cardiac output. Other potential factors to consider are the pre-op pathology (a patient with AI is likely distinctly different than a patient with pre-operative AS), cardioplegia regimen and duration of CPB. STROBE adherence is maybe a methods or result, not an intro topic.

Reply 3: Thank you for your helpful comments. To address your concerns, we have discussed the importance of considering cardiac output during postoperative management as well as the importance of accounting for peripheral circulation. Many factors influence the systemic vascular resistance index (SVRI); these include sex, age, preoperative conditions, surgical technique, cardiopulmonary bypass (CPB) style or duration, duration of surgery, and amount of cardioplegia. However, if postoperative management is not performed taking the SVRI trend, at the very least, into account, there is a risk of unexpected hypotension due to a decrease in SVRI. Therefore, we hoped that the difference in trend based on surgical technique would prevent such risks. Finally, submission rules state that STROBE adherence must be acknowledged at the end of the Introduction section; we have thus revised it accordingly.

Changes in the text: Introduction, lines 67–82.

Comment 4: Methods. Again, the number of patients studied is a result, not a method. The "Patients" section is actually IRB/informed consent. The "Surgical procedures" is really perioperative procedure/anesthetic management. It appears there are probably 3 distinct management groups: bi-caval CPB, fem-fem bypass and off-pump CABG. CPB management for these 3 groups should probably be described individually. What is maybe more important are the post-operative management goals and protocols.

The actual data collected is not clear, in particular, the time resolution. Data seem to be in 2-hour blocks. Is the the value every 2 hours or the average of every value during that period? The statistical methods section needs significant expansion.

Reply 4: Thank you for insightful and helpful advice. The number of patients analyzed has now been mentioned in the Results section. Furthermore, the subheadings "Patients" and "Surgical procedures" have been revised to "IRB/Informed Consent" and "Perioperative procedures/anesthetic management," respectively. The CPB management groups were further divided into three groups — the total bypass, partial bypass, and off-pump groups for individual descriptions. The descriptions of the postoperative management goals and protocols have also been expanded. Data were obtained every 2 hours. As we have mentioned earlier, we did not include the presence or absence of significant differences because of time or interaction in the null hypothesis. Therefore, we used a one-way analysis of variance (ANOVA) only to compare the data of the four groups at each defined postoperative timepoint. A post-hoc analysis was performed only for data with significant differences. In the previous draft ~~paper~~, the post-hoc was based on the t-test; therefore, we have changed it to the more appropriate Tukey–Kramer test. We apologize for these misses.

Changes in the text: Methods; lines 91, 100, 116–117, 121–124, 134–141, 149–175, and 178–

182.

Comment 5: Results - The study population is not adequately characterized. Additional information regarding the demographics, pathologies, and intra-operative events is necessary. The comparisons made are not well organized and there are unclear combinations that make it all impossible to interpret. No standard deviations are provided in any of the graphical summaries. Post-operative drug use is summarized by infusion rates when the number of agents may be more relevant.

Reply 5: Thank you for your pertinent suggestions. To the extent possible, we have summarized data on aspects such as the preoperative pathology, whether it was a simple or complex surgery, plasty or replacement, AI or AS, the number of bypasses and CPB, surgical site and urgency of aortic replacement, and so on. We have also attached Table 1, which summarizes data regarding the age, sex, operative time, CPB time, and intraoperative blood loss. Because time resolution was not verified, we tried to avoid stating the results of time variation as much as possible to avoid any misunderstanding. SD was added in the form of a data table for each figure. Because catecholamines were the main three drugs used in the study, we decided to evaluate by the dose rather than by the number of drugs.

Changes in the text: Results, lines 185–234.

Comment 6: Discussion - The discussion is not well organized or focused. There is an extended discussion of post CPB vasoplegia which is outside the scope of the data. The primary points of interest and differences are not clearly emphasized.

Reply 6: Thank you for your appropriate and thought-provoking remarks. We have organized the discussion to emphasize that the purpose of the study was to remind us that a sustained decrease in the SVRI can occur after an MV surgery. Furthermore, we have simplified details of the vasoplegia syndrome. We apologize for these misses.

Changes in the text: Discussion, lines 240–288 and 295–312.