Author’s response to reviews

Title: Neurological Complications After Cardiac Surgery: A Retrospective Case-control Study of Risk Factors and Outcome

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To

Editors in Chief of:

Journal of Cardiothoracic Surgery
Dear Prof Vipin Zamvar and Prof David Taggart,

Thank you for the review of our manuscript entitled “Neurological Complications After Cardiac Surgery: A Retrospective Case-control Study of Risk Factors and Outcome (JCTS-D-18-00262)” submitted for publication in the Journal of Cardiothoracic Surgery.

We have carefully revised the manuscript according to the #2 reviewer’s comments (corrections in bold).

Our responses to the comments are below

English language was carefully revisited.

With these changes and corrections we hope that the manuscript can now be accepted as it stands.

All authors have read and approved the revised manuscript.

The authors state that:

(1) there has been no duplicate publication or submission elsewhere;
(2) all authors have read and approved the manuscript;
(3) subject to acceptance, authors will transfer copyright to the Publisher;
(4) there is no ethical problem or conflict of interest.

We thank you in advance for your interest in this submission.

Warmest regards,

Giuseppe M Raffa
The paper could be strengthened by consideration of the following:

Reviewer Comments:

Reviewer #1: The contents of the article is difficult to understand. Too many bias may be included and the important predictors lost.

- Response: We thank you Dr. Jong Bum Choi for the time he spent reading the manuscript. All the bias and the limitations are well acknowledged by the authors however, please consider the multidisciplinary approach to the complex topic of neurological complications after cardiac surgery. Radiologists (F.A, R.M., A.L.; who first designed the protocol), neurologist (V.L.R), cardiac surgeons (G.M.R, M.P), anesthesiologists (G.O., A.A.) and statistician (F.T.) have been deeply involved in this project try to giving their contributions at the best. The major findings of our retrospective analysis and clearly stated in the manuscript were that 1) neurological complications can occur in patients with bilateral internal carotid artery (ICA) stenosis of less than 50%, that must be considered as marker of systemic atherosclerosis (identifying an high risk population for atherosclerosis of ascending aorta and embolisms) 2) The absence of damage on brain CT scan/magnetic resonance in patients with neurological complications is a prognostic indicator of prolonged hospitalization and high risk of mortality. To the best of our knowledge, these findings were never reported in the literature.

Reviewer #2: I would like to thank all authors for the work they presented. From my perspective, a few issues need to be clarify:

1. First is to discuss the issue of imaging diagnosis. This study only refers to the time after surgery until the imaging diagnosis. However, the important thing that I want to emphasize is the time from onset of symptoms to the time of diagnostic imaging. Because it will involve the detection of lesions in the image, especially in the 37 patients with major stroke patients (including 35 patients with ischemic stroke and 2 patients with hemorrhage stroke).

- Response: We thank you Dr. Khang Dang Cao for this comments. We do agree and the “Brain Imaging Protocol and Analysis” section has been expanded and this issue clarified (page 5 and 6, line 133-135).

Similarly, in the 54 patients with TIA (including delirium/psychosis/convulsion), are there any patients who are actually infarcted but unable to perform MRI? (e.g after mechanical valve operation or metallic implants, pacemakers). Instead of undergoing an MRI brain imaging,
patient was given 64-section CT scan but early or minor injuries were missed and therefore classified as TIA.

- Response: We thank you for this comments. The risk of this bias has been mitigated in the “Brain Imaging Protocol and Analysis” section (page 5 and 6, line 132-136).

2. Second, internal carotid artery stenosis is considered to increase the risk of postoperative neurological complications. The problem that has not been considered here is that the mechanism of ICA stenosis encompasses two major mechanisms: artery to artery (thrombosis from proximal segment to distal segment) or hypoperfusion (causing border zone infarcts - watershed infarction - should be noted in cardiac surgery) but this has not been mentioned until the imaging diagnosis is performed later. It would be better if it was described previously in MRI or CT. Because it will closely relate to the intraoperation parameters as the operative variables mentioned in Table 1 (Surgical Details - page 9).

- Response: We thank you for this comments. The mechanism of neuro-damage in patients with ICA stenosis has been added to the discussion (page 9, line 215-218) and furthermore the relation between bilateral ICA stenosis, atherosclerosis and embolism have been added to the discussion (page 9, line 227-230).

3. The third problem is MRI was done on a 1.5 Tesla, but in the protocol, there was no MRA for examining intracranial arterial system, and CT was done on a 64-section CT with contrast (some cases) without referring to the problem of cerebrovascular tree on CTA. Therefore, the risk of stroke is not adequately researched, while the means are quite feasible.

- Response: We thank Dr. Khang Dang Cao for this comments and we acknowledge this important issue that has been now addressed in the limitations of the article (page 11, line 276-278). Further, we decide to add a paragraph on pro and cons of CT and MRI in detection of neurologic complication after cardiac surgery (page 10, line 246-254).