Author’s response to reviews

Title: Six-years survival and predictors of mortality after CABG using cold vs. warm blood cardioplegia in elective and emergent settings

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Author’s response to reviews: see over
Six-years survival and predictors of mortality after CABG using cold vs. warm blood cardioplegia in elective and emergent settings

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Category: Original Article

Version: 1, Date: 24 August 2015
Reviewer 1: Mudassir Iqbal Iqbal Dar

Version: 1 Date: 30 August 2015
Reviewer 2: Hiroshi Yamamoto

The Authors thank the Reviewers and the Associate Editor for their time and effort. Their valuable comments and suggestions were thoughtfully considered and incorporated in the manuscript. The Authors hope that the manuscript is now strengthen and will be of high interest for the Reader of the Journal of Cardiothoracic Surgery.

Reviewer 1 Comments for the Author.

Reviewer’s Comment 1.
In Methods, Patients, line 10, 176 patients recieving ICC versus 506 reveiving IWC, there are 23 patients are missing there is no explanation about it

Author’s response 1:
Indeed, after matching a total of 13 patients (not 23) had to be further excluded from the subsequent analysis. The reason for that was missing variables of interest despite initial availability of parameters that the matching was based on (gender, ejection fraction and age).
As requested the explanation was amended in the methods section.

Reviewer’s Comment 2:
In Results, 3rd para line 2, i think need to write platelets units used or transfused.

Author’s response 2:
As requested it is changed in the manuscript.

Reviewer’s Comment 3:
In Results 3rd para line 10 'need for IABP' is already mentioned before therefore, no need to write again.

Author’s response 3:
Thank you for this comment, we agree that there is no need for mentioning ‘IABP’ again. As suggested it is corrected in the manuscript.
Reviewer 2 Comments for the Author:
In the present study comparing the effectiveness of intermittent cold blood cardioplegia (ICC) with that of intermittent warm blood cardioplegia (IWC), the authors demonstrated using data from 695 CABG patients (176 and 506 patients receiving ICC and IWC, respectively) that IWC has effective myocardia protection, regardless the urgency of the operation, in terms of 30-day mortality and perioperative myocardia protection after surgery.

Reviewer’s Comment 1.
The authors should describe the number of operators and how do they decided which cardioplegia (ICC or IWC) was chosen before surgery, because of avoiding a patient-selection bias. Are there any criteria determining the type of cardioplegia?

Author’s response 1:
Over the study period a total of 8 surgeons were performing elective and emergent CABG. Whereas 3 surgeons were advocates of Buckberg cardioplegia (ICC), other 5 surgeons were proponents of Calafiore cardioplegia (IWC). There were no surgeons who had used both types of cardioplegia dependent on clinical factors. Also, as it is a retrospective analysis, the choice of cardioplegia could not be influenced. This information was added to the Methods section.

Reviewer’s Comment 2.
The authors should describe the presence or absence of topical cooling in the ICC group, and they should specify the temperature and dose of “hot shot” (terminal warm cardioplegia).

Author’s response 2:
In the ICC group the body temperature was routinely cooled down to 34°C. According to our institutional policy there was no additional topical cooling. Despite recommendations by the Buckberg protocol warm terminal reperfusion (‘hot shot’) was not infused prior to aortic unclamping in our center. This information was amended in the Methods section.

Reviewer’s Comment 3.
The authors should describe the composition of crystalloid Buckberg solution in the method section. I think this is very important to understand the influence of ionic concentration difference between the ICC and IWC groups on the results.

Author’s response 3:
In terms of cardioplegia protocol the so called „cold induction” and „cold reinfusion” Buckberg cardioplegia is normally used in our centre. The components are supplied separately in two bottles (400mL and 100mL) and are first mixed when needed. The induction cardioplegia solution contains 400 mL of high potassium concentration with KCl 34 mmol, THAM 17.45 mmol and NaCl 16.12 mmol. Following substances are added from the second 100 mL bottle: citric acid 0.45 mmol x H2O, sodium citrate 2.60 mmol x 2 H2O, sodium hydrogen phosphate 0.47 mmol x 2 H2O and glucose 92.42 mmol x H2O. For the reinfusion cardioplegia there are also two bottles with the following composition: 400mL low potassium concentration of KCl 16.90 mmol, THAM 18.30 mmol and NaCl16.90 mmol. As with induction cardioplegia, additional substances are added from the 100 mL bottle: citric acid 0.48 mmol, sodium citrate 2.73 mmol, sodium hydrogen phosphate 0.49 mmol and glucose 96.93 mmol. This concentrated solution is diluted in a ratio 1:4 with blood to provide oxygen, the desired pH and osmolarity. The cardioplegic induction solution with the high potassium
concentration is then delivered over 4 minutes to initiate cardiac arrest whereas the following reinfusion solution with the lower potassium concentration is delivered over 2 minutes to maintain the cardiac arrest every 15-20 min. These informations were added to the Methods section of the manuscript.

Reviewer’s Comment 4.
The authors should specify the lowest body (e.g., rectal) temperature in CPB in both cardioplegia groups. Was there a difference in CPB blood or body temperature between the two groups?

Author’s response 4:
Thank you very much for this important point. According to our institutional policy the body temperature using IWC was maintained between 36°C and 37°C rectally whereas in cases of using ICC patients the body temperature was always cooled down to 34°C.
This information was added to the Methods section of the manuscript.

Reviewer’s Comment 5.
As shown in Table 3, in the emergent CABG cases, the 30-day mortality was 9 patients (5.1%) and 21 patients (4.2%) in the ICC and IWC groups, respectively, and in the elective CABG cases, it was 0 patients (0%) and 10 patients (2.0%) in the ICC and IWC groups, respectively. The authors should describe the cause of deaths of those 40 patients, for example, heart failure (low output syndrome), cerebrovascular events or other organ failures.

Author’s response 5:
Thank you very much for this comment. In the IWC and ICC emergent CABG group 8 patients vs. 5 patients died after acute myocardial infarction with postcardiotomy ECMO, 2 of them had cerebrovascular events, 4 patients vs. 1 patient died due to severe sepsis with multiorgan failure, 2 patients vs 0 patients with mesenterial ischemia and laparotomy, 1 patients vs. 0 patients with LV and LA thrombus in association with heparin induced thrombocytopenia and 6 patients vs. 3 patients died postoperatively after CPR due to electromechanical dissociation and low-output syndrome, respectively. On the other hand, in the IWC and ICC elective CABG group 3 patients vs. 0 patients died after pericardial tamponade or pulmonary emboli with postcardiotomy ECMO, 3 patients vs. 0 patients died due to severe sepsis and multiorgan failure, 1 patient vs 0 patients after mesenterial ischemia and laparotomy in association with sepsis and 3 patients vs. 0 patients postoperatively after CPR due to electromechanical dissociation and low-output syndrome, respectively.
These informations were added to the Results section of the manuscript.