Author's response to reviews

Title: Atrial fibrillation following cardiac surgery: Risk analysis and long-term survival

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Author's response to reviews: see over
July 3rd, 2012

Re: Review of manuscript "Atrial fibrillation following cardiac surgery: Risk analysis and long-term survival" (MS ID: 6360555737219384)

Dear Dr. Vipin Zamvar,

Thank you for your letter regarding our manuscript. We have revised the manuscript in accordance with the reviewers’ suggestions and hope that the manuscript is now acceptable for publication in The Journal of Cardiothoracic Surgery.

Yours sincerely,

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Letter to reviewer

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July 3rd, 2012

Re: Review of manuscript "Atrial fibrillation following cardiac surgery: Risk analysis and long-term survival" (MS ID: 6360555737219384)

On behalf of the authors I would like to thank the reviewer for good and constructive comments and suggestions. We have read them thoroughly and revised the manuscript accordingly. In the text below are our comments and explanations regarding changes in the manuscript.

Yours sincerely,

Tomas Gudbjartsson, MD, PhD.

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Reviewer 1

Major comments:
In a multivariate analysis, the authors show that AVR (OR 4.4), a preoperative history of cardiac failure (OR 1.8), higher EuroSCORE (OR 1.1), and advanced age (OR 1.1) were independent prognostic (predictive?/risk?) factors for POAF. Without having consulted statistical expertise I am concerned on this part of the analysis. I believe that a finalized logistic regression model must be based on independent risk factors for POAF; however cardiac failure (Ejection fraction), AVR (other surgery than CABG) and age are all components of EuroSCORE, and therefore the proposed risk factors are closely interrelated. To avoid this interference, I will suggest a more straightforward analysis in which the individual (or major) components of Euroscore are included in the regression model (e.g. age, LVEF, AVR, previous surgery, pulmonary, renal cerebrovascular disease) to identify essential risk-factors for POAF. The remaining statistical analysis appears sound and well controlled.

Reply: We would like to thank for this comment. As EuroSCORE is a standard risk measurement done for all patients we felt that its inclusion in the model was justified. As age adds up to the standard EuroSCORE in a stepwise manner (i.e. 1 point for every 5 years of age over 60), we decided to add a linear component of age to account for its importance in AF. Also as shown by others and us in the manuscript, AVR comes with a particularly high risk of POAF; yet AVR only adds 2 points to the standard EuroSCORE. We therefore felt that it was necessary to add AVR independently to account for its importance. A finalized logistic model can indeed include variables in multiple dimensions (such as square root, second power etc), and we have not violated any basic assumption of the logistic model.

Reviewer 2

Major Compulsory Revisions:
Please consider adding applicability data of the risk table, e.g. applying it to another cohort of Icelandic patients (from 2007-2009, for example) and judge the accuracy of the prediction.

Reply: This is a valid comment. There is an ongoing study in our hospital where we use the risk table for evaluating another cohort of CABG and AVR patients. Results are pending and we actually hope to conclude this study in the next year.

Minor Essential Revisions:
In abstract, please consider correcting the phrase "POAF was detected in almost every other patient".

Reply: See revised document

Reviewer 3

Major comments:
1. As the strength of the study is the large patient cohort included from a single institution, this fact also remains the weakness of the study: the heterogeneous demographics of the patients undergoing different surgery, not only CABG, but also off pump CABG, including patients with AVR. Certainly, the operational details such as aortic cross clamp time and perfusion time also affect outcome, as discussed in the manuscript. Why did the authors choose such a heterogeneous study group?
Reply: Finding the balance between a large as well as homogeneous patient cohort can be difficult in a study like this. From the outset we decided to include patients that underwent all the most common procedures; CABG, OPCAP and AVR, which together count over 85% of open-heart surgery in Iceland. As the number of each of these procedures is high, it can be justified to evaluate them together.

2. The Figures are excellent, why was gender and EF deleted from the risk profile/probability? Please explain.

Reply: Gender and EF were not found to be independent risk factors for POAF and therefore not included in the risk profile.

3. Legends of figures do not match

Reply: We would like to thank the reviewer for pointing this out. Corrections have been made and can be seen in the revised document.

4. There is a rather high percentage of patients undergoing off pump CABG, what were the indications for off pump instead of traditional CABG?

Reply: This is true. OPCAB has been more common in Iceland than in many other countries, including the other Nordic countries. A previous Icelandic study has shown comparable outcomes between the OPCAB and CABG procedures and the choice of operation type was usually based on the performing surgeons preference.

5. How was cardioplegia administered, via ante-/ or retrograde? E.g. did you have warm or cold cardioplegia.

Reply: Warm cardioplegia was always administered, via antegrade for CABG and antegrade for AVR +/-CABG.


Reply: We agree that the role of preoperative statins on the incidence of POAF is not straightforward and we are aware of the article by Virani et al and even more recent articles, including the study of Liaikopoulos et al from the Cochrane database (Preoperative statin therapy for patients undergoing cardiac surgery. Liaikopoulos OJ, et al. 2012, Issue 4). During the study period (2002-2006) ablation surgery (Cox-Maze procedure etc.) was not performed in our institution, however, for the last 3 years we have performed it as a concomitant procedure in selected cases with preoperative history of AF (mostly cryo-Maze).

7. Abbreviations could be included on Tables for clarification.

Reply: We added abbreviations in the revised document.

8. While some postoperative complications may be explained due to postoperative atrial fibrillation, the incidence of arrhythmia in itself may also be the consequence of various complications after surgery. Would it be possible to categorize postoperative atrial fibrillation into paroxysmal, persistent
and permanent?

Reply: Theoretically yes, but to our best knowledge this has not been used in other studies on POAF. POAF is most commonly a temporary phenomenon, lasting hours to days, but is rarely present after discharge. Therefore we did not deem it necessary to categorize POAF differently from what we, as well as other studies, have done already.

9. Did the patients have thyroid disease or excess alcohol consumption, factors importantly affecting incidence of atrial fibrillation

Reply: Uncontrolled thyroid disease was not present in any of the patients but information on alcohol consumption was not collected specifically.

Minor comments:

10. Page 7 and 10, what is "sternal insufficiency"?

Reply: We apologize for this mistake, this should have been sternal dehiscence and has been changed in the manuscript.

11. Please clarify 1rst sentence of Discussion.

Reply: The sentence "POAF was common in this cohort of patients who underwent cardiac surgery, or 44%" has been changed to “Following cardiac surgery in Iceland POAF was found to be high, relative to previous retrospective studies, or 44%”.

12. Discussion, 2nd paragraph: "revascularization"?

Reply: This has been corrected to revascularization.

13. Discussion, 4th paragraph: "recieved"?

Reply: Corrected to received

14. Discussion, 6th paragraph: "potenially"?

Reply: Corrected to potentially

15. Discussion, 7th paragraph, the wording "necessarily" of the sentence?

Reply: The sentence “Using the entire population to create the risk model was considered necessarily to obtained sufficient power. ” has been changed to read "Using the entire population to create the risk model was considered necessary to obtain sufficient power. ”

Reviewer 4
Major comments:
1) The major comment to the paper is the extremely high incidence of POAF reported. With similar diagnostic criteria we found about half incidence of POAF

Reply: The high incidence of POAF following cardiac surgery in Iceland has been a topic of extensive research. Ongoing prospective studies show that the rate is comparable to that seen in our retrospective studies. The reasons remain largely unclear, but the incidence of AF seems to be unusually high in the Icelandic population. We discuss these findings further in the Discussion section.

2) The authors do not report the number of patients discharged in AF and if persistence of AF is related to decreased long-term survival in the POAF group

Reply: Almost all patients were discharged in sinus rhythm. However, patients with a pre-operative history of AF (which were excluded from this study) were more often discharged with AF and received warfarin postoperatively.

3) We agree that age is an independent factor related to POAF, no information is given between OP and CBP surgery.

Reply: Age was an independent predictor of POAF, both for CABG and OPCAB procedures.

4) Another point to be discussed is the relative clinical weight of short asymptomatic POAF and symptomatic episodes or episodes requiring treatment, for which may be hypothesized a different clinical impact

Reply: This is valid point, however, as the study was retrospective it was difficult to evaluate the clinical effect of POAF from our database. In the future this could be an elegant prospective study.

5) In the discussion section a more detailed analysis of the higher incidence of POAF in present study, also compared with studies with similar diagnostic criteria should be added

Reply: We have added some text on the high incidence of POAF in our cohort compared to other studies in the Discussion part.