Author's response to reviews

Title: Ethnic differences in the occurrence of acute coronary syndrome: results of the Malaysian National Cardiovascular Disease (NCVD) Database Registry (March 2006- February 2010)

Authors:

Hou Tee Lu (lu.hou.tee@monash.edu)
Rusli Bin Nordin (rusli.nordin@monash.edu)

Version: 2 Date: 2 September 2013

Author's response to reviews: see over
**REPLY TO REVIEWER 1**

**MS Review**

Re: 'Ethnic differences in the occurrence of acute coronary syndrome: results of the Malaysian National Cardiovascular Disease (NCVD) Database Registry (March 2006- February 2010)'

Hou Tee Lu and Rusli Bin Nordin

**General Comments:** The manuscript is interesting and addresses an important and a not well-understood topic, and therefore, deserves consideration for publication. However, the paper is purely descriptive and has a number of shortcomings including methodological deficiencies, and spelling and grammatical mistakes. The results section is cluttered with numbers, which makes it difficult to read and follow through. Furthermore, the authors failed to adequately elaborate in the discussion section on possible explanations for important observations (e.g. lower rates of reperfusion therapy among Chinese population and lower use of enoxaparin in Malay people. Late presentation or presence of contraindications in the first instance could have been the reason for lower rates of reperfusion therapy, and religious beliefs can be one of the reasons for lower use of enoxaparin among Malay population).

**REPLY:** Thank you for your comments. We will do the necessary corrections as commented in the various sections of the manuscript. Spelling and grammatical errors will be corrected using the Microsoft Word's proofing section for spelling and grammar. In the “RESULTS” section, we will improve the presentation of the tables for clarity and readability and minimize the amount of numerical presentations in the text. We will also revise the “DISCUSSION” section with plausible explanations of the research findings including those highlighted above pertaining to the lower rates of reperfusion therapy among Chinese population and lower use of enoxaparin in Malay people.

**Specific comments**

**A- Abstract**

1-Major: The abstract is very long and therefore, the following has to be considered:
-Background should be shortened.
-Results section is also long and contains too many numbers, making it very difficult to read and follow through. Authors should cite only the most important positive observations and reorganize this section to make it easy to read and follow through.
-The conclusion has to be short and to the point.

**REPLY:** Done (see Revised Abstract below).

2-Results section, paragraph # 3, line #1, NVCD should be changed to NCVD (Minor issue).

**REPLY:** Done (see Revised Abstract below).

3-Results section, paragraph # 3, the percentage for others, (line #10) should be 5.83% and not 58.3% (Minor issue).

**REPLY:** The sentence has been deleted (see Revised Abstract below).
Revised Abstract

Background

The National Cardiovascular Disease (NCVD) Database Registry represents one of the first prospective, multi-center registries to treat and prevent coronary artery disease (CAD) in Malaysia. Since ethnicity is an important consideration in the occurrence of acute coronary syndrome (ACS) globally, therefore, we aimed to identify the role of ethnicity in the occurrence of ACS among high-risk groups in the Malaysian population.

Methods

The NCVD involves more than 15 Ministry of Health (MOH) hospitals nationwide, universities and the National Heart Center and enrolls patients presenting with ACS [ST-elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI) and unstable angina (UA)]. We analyzed ethnic differences across socio-demographic characteristics, hospital medications and invasive therapeutic procedures, treatment of STEMI and in-hospital clinical outcomes.

Results

We enrolled 13,591 patients. The distribution of the NCVD population is as follows: 49.0% Malays, 22.5% Chinese, 23.1% Indians and 5.3% Others (representing other indigenous groups and non-Malaysian nationals). The mean age (SD) of ACS patients at presentation was 59.1 (12.0) years. More than 70% were males. A higher proportion of patients within each ethnic group had more than two coronary risk factors. Malays had higher body mass index (BMI). Chinese had highest rate of hypertension and hyperlipidemia. Indians had higher rate of diabetes mellitus (DM) and family history of premature CAD. Overall, more patients had STEMI than NSTEMI or UA among all ethnic groups. The use of aspirin was more than 94% among all ethnic groups. Utilization rates for elective and emergency percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) were low among all ethnic groups. In STEMI, fibrinolysis (streptokinase) appeared to be the dominant treatment options (>70%) for all ethnic groups. In-hospital mortality rates for STEMI across ethnicity ranged from 8.1% to 10.1% (p=0.35). Among NSTEMI/UA patients, the rate of in-hospital mortality ranged from 3.7% to 6.5% and Malays recorded the highest in-hospital mortality rate compared to other ethnic groups (p=0.000). In binary multiple logistic regression analysis, differences across ethnicity in the age and sex-adjusted ORs for in-hospital mortality among STEMI patients was not significant; for NSTEMI/UA patients, Chinese [OR 0.71 (95%CI 0.55, 0.91)] and Indians [OR 0.57 (95%CI 0.43, 0.76)] showed significantly lower risk of in-hospital mortality compared to Malays (reference group).

Conclusions

Risk factor profiles and ACS stratum were significantly different across ethnicity. Despite disparities in risk factors, clinical presentation, medical treatment and invasive management, ethnic differences in the risk of in-hospital mortality was not significant among STEMI patients. However, Chinese and Indians showed significantly lower risk of in-hospital mortality compared to Malays among NSTEMI and UA patients.
B-Background
1- Paragraph #3, line #1 (Race.............. preventive cardiology). This sentence is ambiguous.
REPLY: Done (see corrected Background).

C-Results
1-The results section is very long and has multiple comparisons and appears very cluttered. Many of the difference are statistically significant but the absolute differences between comparators were very small and clinically irrelevant (e.g. differences in total cholesterol and LDL levels between the groups). The authors should focus in this section only on the most important findings. They should reduce the amount of numbers in the text and just refer the reader to the tables and figures. Salient findings can be highlighted in a figure format, which is a very powerful way of displaying differences among multiple comparators (e.g. mortality differences between different ethnic groups).
REPLY: Done (see corrected Results).

2-Most of the negative findings should not to be mentioned.
REPLY: Done (see corrected Results).

3-NVCD in Paragraph #1 should be changed to NCVD (minor issue).
REPLY: Done (see corrected Results).

4- “Treatment of STEMI section”. Lines # 1, 3 and 8, the word “revascularization” should be changed to “reperfusion”. Similar change should be considered for table # 6 (Minor issue).
REPLY: Done (see corrected Results).

5-The authors should report door to balloon times for primary PCI.
REPLY: Done (see corrected Results).

6-The authors reported unadjusted mortalities and did not attempt to adjust for baseline differences. Reporting adjusted mortalities is essential for the current study, contrary to what they mentioned in the discussion section that this would be considered for a future study.
REPLY: Done (see corrected Results).

7-The authors should report symptom to presentation time, as this could be the reason why Chinese patients received less thrombolytic therapy and more primary PCI.
REPLY: This data was not captured in the NCVD Registry.

8-The authors presented their descriptive statistics and baseline variables as percentages or means with standard deviations, including the door to needle time. This is appropriate only if their data is normally distributed which is unlikely in the case of door to needle time. In such case reporting the median with IQR is the accepted standard.
REPLY: Done (see corrected Results).

9-The door to needle time is very long and it is worthwhile to report, which components of this time were beyond the recommended limits.
REPLY: Done (see corrected Results).

Furthermore, the authors should specify where and who gives thrombolytic therapy; in emergency department by emergency physicians or in CCU by cardiologists.
REPLY: This data was not captured in the NCVD Registry. Furthermore, they should also report the proportion of patients who received thrombolytic therapy within 30 minutes from presentation to emergency department, as this is more meaningful.
REPLY: Done (see corrected Results).

D- Discussion
1-Socio-demographics and Coronary Risk Factors section, paragraph #2, line # 7, the sentence (.... Compared to........ and EHS-ACS-II) is ambiguous.
2-Treatment of STEMI section, Paragraph #2, line 1-4, (Similar to other developing countries..... obtain the large benefit) should either be removed or supported by references.
3-In-hospital Clinical Outcomes section, line #13 “both gender” should be changed to “both genders” (Minor issue).
4-In-hospital Clinical Outcomes section, line # 16 “different gender” should be changed to “different genders” (Minor issue).
REPLY: Done (see corrected Discussion).
REPLY TO REVIEWER 2
Reviewer's report
Title: Ethnic differences in the occurrence of acute coronary syndrome: results of the Malaysian National Cardiovascular Disease (NCVD) Database Registry (March 2006- February 2010)
Version: 1 Date: 9 July 2013
Reviewer: Davor Horvat
Reviewer's report:
1. Is the question posed by the authors well defined?
The question is well defined.
2. Are the methods appropriate and well described?
It is necessary to further clarify including criteria for STEMI, NSTEMI, UA (clinical, ECG and biochemical parameters).
Reply: Done (see Methods section).
Entry criteria of ACS include risk stratum of patients presenting with clinical features consistent with an ACS (chest pain or overwhelming shortness of breath) and defined by accompanying clinical, electrocardiographic and biochemical features. The final diagnosis of ACS was made by the attending physician using the following criteria: STEMI was diagnosed on the basis of the presence of acute chest pain with new or presumably new ST segment elevations more than 1 mm in two consecutive leads or the presence of a new left bundle branch block on the index or subsequent ECG with positive cardiac markers of necrosis [72]. NSTEMI is defined by ECG ST-segment depression or prominent T-wave inversion and/or positive biomarkers of necrosis in the absence of ST-segment elevation and in an appropriate clinical setting (chest discomfort or angina equivalent). UA was defined as angina pectoris (or equivalent type of ischemic discomfort) with any one of the three following features: a) angina occurring at rest and prolonged, usually more than 20 min; b) new-onset angina of at least Canadian Cardiovascular Society (CCS) classification III severity; c) recent acceleration of angina reflected by an increase in severity of at least one CCS class to at least CCS class III. The patient must also have normal cardiac biomarkers [69].
Reply: Done (see Methods section): Risk factors were quantified using adjusted ORs (95% CI) in the multivariate binary logistic regression analysis (outcome was in-hospital mortality). Ways of treatment were reported in earlier publications.
3. Are the data sound?
Yes, but insufficient for the extended method.
4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes.
5. Are the discussion and conclusions well balanced and adequately supported by the data?
Yes.
6. Are limitations of the work clearly stated?
Yes.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
Yes.

8. Do the title and abstract accurately convey what has been found?
Yes.

9. Is the writing acceptable?
**Minor revisions and acceptable.**
Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests.