Analytical Plan for Study design for the association between peak troponin levels and post-surgery mortality in an Australian hospital

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Document version

Version	Alterations
01	Initial version

1 ABBREVIATIONS

- CI: confidence interval
- HR: hazards ratio
- ICU: Intensive care unit
- SD: standard deviation

2 CONTEXT

2.1 Objectives

Study design for the association between peak troponin measurements and in hospital mortality adjusting for scores on EURO scores and APACHE.

2.2 Hypotheses

2.3 Study design

Prospective cohort.

3 DATA

3.1 Raw data

Upon study start the raw data will be collected in a raw table, that will be processed before analysis. The raw dataset to be collected will have 10 variables collected on 200 observations.

This dataset will include the dates of entry and exit of the cohort, or the date of hospital admission and the date where the endpoint was reached (either an event, or hospital discharge). Table 1 shows the structure of the raw dataset.

Table 1 *Raw dataset structure.*

id	date_admission	date_outcome	outcome	troponin	euroscore	apache	surg_type	surg_length	icu_length
1									
2									
3									
…									
200									

Each row represents all information collected from each study participant, and each participant included will require a unique study ID. The outcome should be recorded as a binary variable: either the study participant reached the endpoint (death) or survived and was discharged. This information can be recorded in either text form, or an indicator (death = 1, discharge = 0).

Surgery length should be recorded in minutes, and ICU length in days.

Surgery type will be recorded as a categorical variable. It is recommended that the number of classes (types of surgery) be as small as possible, to avoid loss of precision in the analysis estimates, without the need to increase the sample size. Broader categories of surgeries should be preferred, whenever possible.

3.2 Analytical dataset

The analytical dataset will be created by cleaning the raw data and applying the study's inclusion and exclusion criteria. Time under observation will be calculated in days from the dates of entry and exit of the cohort.

The total number of observations excluded due to incompleteness (missing data) and due to exclusion criteria will be reported in the analysis.

All variables in the analytical set will be labeled according to the raw data provided and values will be labeled according to the data dictionary for the preparation of production-quality results tables and figures.

4 STUDY PARAMETERS

4.1 Inclusion and exclusion criteria

Inclusion and exclusion criteria will be defined in the study protocol.

4.2 Exposures

Peak troponin levels, measured as a continuous scale.

4.3 Outcomes

Specification of outcome measures (Zarin, 2011):

1. (Domain) Mortality
2. (Specific measurement) In hospital death counts
3. (Specific metric) Time to event
4. (Method of aggregation) Hazards ratio

Primary outcome

In hospital mortality rates after 30 days.

4.4 Covariates

Hazard ratios will be adjusted for Euro score, APACHE score, type of surgery, length of surgery and length of ICU stay.

5 STATISTICAL METHODS

5.1 Statistical analyses

5.1.1 Descriptive analyses

The epidemiological profile of the study participants will be described. Demographic (sex, age and BMI) and clinical variables (EURO score, APACHE score, type of surgery, length of surgery and length of ICU stay) will be described as mean (SD) or as counts and proportions (%), as appropriate. The distributions of participants' characteristics will be summarized in tables and visualized in exploratory plots.

5.1.2 Inferential analyses

All inferential analyses will be performed in the statistical models (described in the next section). Survival rates and time to event will be reported, with their respective CI.

5.1.3 Statistical modeling

Hospital mortality will be evaluated with a Cox regression model.

Two models are planned to be created to evaluate the impact of the troponin levels in mortality. A simpler univariate model including only the exposure will be created to serve as a base of comparison for the main model. The main model will adjust the HR between mortality and troponin levels by controlling for the type of surgery, surgery length, ICU length of stay and the risk scores APACHE and EURO.

No variable selection is planned for this analysis. It is assumed that the variables included in the main model to control for confounding and bias were selected based on literature sources and clinical relevance. If the analysis suffers from lack of statistical power due to poor sample variability, then this analysis plan will be revised.

5.1.4 Missing data

No missing data imputation will be performed. All evaluations will be performed as complete case analyses.

5.2 Significance and Confidence Intervals

All analyses will be performed using the significance level of 5%. All significance hypothesis tests and confidence intervals computed will be two-tailed.

5.3 Study size and Power

The study protocol defines an intended sample size of 200 patients.

5.4 Statistical packages

This analysis will be performed using statistical software R version 4.1.3.

6 OBSERVATIONS AND LIMITATIONS

N/A

7 REFERENCES

- **SAR-2022-019-v01** – Study design for the association between peak troponin levels and post-surgery mortality in an Australian hospital
- Zarin DA, et al. The ClinicalTrials.gov results database – update and key issues. N Engl J Med 2011;364:852-60 (https://doi.org/10.1056/NEJMsa1012065).
- Gamble C, et al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. JAMA. 2017;318(23):2337–2343 (https://doi.org/10.1001/jama.2017.18556).

8 APPENDIX

This document was elaborated following recommendations on the structure for Statistical Analysis Plans (Gamble, 2017) for better transparency and clarity.

8.1 Availability

All documents from this consultation were included in the consultant's Portfolio.

The portfolio is available at:

https://philsf-biostat.github.io/SAR-2022-019/