Prediction of early and long-term mortality after transcatheter aortic valve implantation in Australia: A machine learning based risk prediction model (PREDICT-TAVI)

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**STATEMENT OF COMPLIANCE**

This document is a protocol for a clinical research study. The study will be conducted in compliance with all stipulations of this protocol, the conditions of ethics committee approval, the NHMRC National Statement on Ethical Conduct in Human Research (2007) and the Note for Guidance on Good Clinical Practice (CPMP/ICH--‐135/95).

**1. INVESTIGATORS AND FACILITIES**

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This study will be undertaken at Royal North Shore Hospital.

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**2. INTRODUCTION AND BACKGROUND**

**2.1 Background Information, rationale for current study and aim**

Transcatheter aortic valve implantation (TAVI) has transformed the management of patients with severe, symptomatic aortic stenosis (AS) with favourable outcomes demonstrated in patients at all levels of risk.(1, 2, 3) A high burden of comorbidities is often encountered in patients under evaluation for TAVI that presents unique challenges in predicting outcomes following successful implantation.(4) TAVI is generally recommended in patients with an expected survival beyond 12 months; with a view to optimising therapeutic benefit and broadly managing financial/resource allocation. Therefore, risk assessment remains key in the pre-procedural evaluation of patients for TAVI. Several prediction models are available; however, most models focus on short-term outcomes (i.e., in-hospital or 30-day) and the available models that quantify long-term outcomes (i.e., 1 year) largely have limited generalisability, with patients recruited from a single centre or a few centres or have limited technical performance.(5, 6, 7, 8, 9, 10, 11) The extensive evaluation required for TAVI provides a wealth of pre-procedural and procedural data that lends favourably for an artificial intelligence-based machine learning approach for risk prediction.

The Australasian Cardiac Outcomes Transcatheter Aortic Valve Implantation (ACOR-TAVI) Registry is a clinical quality registry developed as part of quality control and monitoring of procedural and clinical outcomes of patients undergoing aortic valve replacement via a transcatheter approach in Australia (https://acor.net.au/aims/). All patients undergoing TAVI in Australia are included in the ACOR-TAVI Registry. The ACOR-TAVI Registry provides an accurate, large dataset with longitudinal outcomes that can be leveraged to effectively develop such a risk prediction model. The aim of this study is to leverage the ACOR-TAVI Registry to develop a machine learning based risk prediction model for early and long-term mortality.

**3. STUDY OBJECTIVES**

**3.1 Primary Objective(s)**

1. To develop machine-learning based risk prediction models to estimate in-hospital, 30-day and 1-year mortality respectively following transcatheter aortic valve implantation in Australia.

**4. STUDY DESIGN**

**4.1 Type of Study**

This will be an observational study that leverages data from the ACOR-TAVI Registry to develop a machine-learning based risk prediction model for all-cause mortality.

**4.2 Patient Population**

This study will include all patients included in the ACOR-TAVI Registry by May 2023. There are no exclusion criteria.

**4.3 Recruitment**

All patients undergoing TAVI in Australia are included in the ACOR-TAVI Registry. This study will include all patients included in the ACOR-TAVI Registry by May 2023. An application has been made to the ACOR TAVI Research and Publications Committee – who require an ethics application to be submitted to the local HREC at the time of application.

**4.4 Patient Consent**

The consent process for patients recruited to the ACOR-TAVI registry is handled and coordinated by the ACOR organisation. Their data is available for research applications, with review by the ACOR TAVI Research and Publications Committee.

**4.5 Study Protocol**

National Australian data from the Australasian Cardiac Outcomes Transcatheter Aortic Valve

Implantation (ACOR TAVI) Registry will be analysed. Pertinent clinical, biochemical, imaging,

angiographic and procedural parameters will be extracted. Outcomes variables include in-hospital mortality, 30-day mortality and 1-year mortality. The data analysis plan is detailed in Section 8.

**5. PRIMARY AND SECONDARY OUTCOME MEASURES**

**Primary**

* 1-year mortality

**Secondary**

* In-hospital mortality
* 30-day mortality

**6. ADVERSE EVENTS**

This is an observational study; the investigators do not expect any adverse events related to the collection of routinely obtained clinical data.

**7. FUNDING AND TRIAL MANAGAMENT**

Investigators will conduct this study as part of their existing clinical roles. Any additional funding required will be covered by the existing educational grants. The trial management team is detailed in Section 1.

**8. DATA ANALYSIS**

Data Preprocessing

Categorical variables will be transformed into dummy variables. Variables with missing values will be imputed with kMeans, or using the mode or will have a dummy variable to represent the missing-ness. Continuous variables may be normalized and may be transformed using log or Box-Cox transformations.

Feature Selection

The most important predictors will be selected based on their variances and/or performance of univariate statistical tests such as chi-squared and/or L1-based feature selection and/or selected via forward or backward sequential feature selection.

Model Training

The data will be divided into training and test datasets for building the model and evaluation the performance of the model respectively. The models that will be evaluated would include linear methods such as logistic regression and non-linear methods such as XGboost, random forest and neural networks.

Assessment of Performance

The models will be evaluated on accuracy, AUC-ROC, precision, recall and F1 score.

**9. DATA MANAGEMENT**

The principal and associate investigators will be responsible for data management. Patients will be recruited from the existing ACOR-TAVI Registry. The dataset is stored with two layers of security, where the data is stored in NSLHD’s internal servers in a MS SQL database. Only those with a StaffLink ID with permissions granted by eHealth is able to access this internal server and must either be on the hospital network or have a VPN to connect to this server. Furthermore, only the admin of the SQL database (Harrison Nguyen - Investigator on Study) is able to grant the required permissions to view the data.

After analysis of this data and the end of patient follow-up, all data shall be stored in accordance with research guidelines and destroyed after 5 years in accordance with the Australian Code for the responsible conduct of Research, TGA ICH – GCP and the National Statement on Ethical conduct in Human Research.

**10. USE OF DATA AND PUBLICATIONS POLICY**

The results of this study shall, and not limited to, be disseminated in the scientific media (i.e. publications in scientific journals, conference presentations and inter-hospital presentations in the first instance).

**11. REFERENCES**

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