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Risk Prediction Model for Long-Term Mortality after Percutaneous Coronary Intervention

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ABSTRACT

Introduction: There are many risk prediction models utilized to see effects of risk factors to dependent variables with final aims to aid clinicians and patients making decisions. This study mainly aimed to develop a risk prediction model for long-term mortality after percutaneous coronary intervention (PCI) for cardiovascular disease patients.

Methodology: Data on 10,511 patients who underwent PCI procedure between 2008 to 2012 were obtained from a source data provider center for National Cardiovascular Disease Database (NCVD)-PCI registry. The data were randomly divided into development and validation datasets. After variable selection process, multiple logistic regression technique was used to develop a predictive model using the development dataset, then the model was validated using the validation samples. The goodness-of-fit and the performance of the models in both samples were evaluated by Hosmer-Lemeshow, and area under the receiver operating characteristic (ROC) curve.

Result: Mortality rate in three years after PCI was 9.6%. Eight predictors were associated with the 3-year mortality of PCI and included in the final model. The area under the ROC curves were 0.7809 and 0.7780 in the development and validation dataset respectively.

Conclusion: An accurate and reliable model was produced to predict three-year mortality after PCI procedure.

Keywords: Risk Prediction Model, Percutaneous Coronary Intervention, Long-term Mortality.

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INTRODUCTION

Percutaneous coronary intervention (PCI) is extensively used for treating coronary artery disease. At the current rate, there are more than 10 thousand such procedures performed annually in Malaysia. PCI is associated with favorable long-term outcomes (Stone et al., 2019). On the other side of the coin, there are potential adverse outcomes as a result of the procedure. Cardiologists may be able to envisage an outcome given 1 or 2 variable predictors but, as the number of predictors grow, the job to predict gets complicated even for human experts. As a result, a mechanism based on combination of predictors relates to the adverse outcomes feasibly helpful to making proper informed decision.

In relation to this, a mathematical-based risk prediction model, is commonly used in medical informatics to relate risk factors and an outcome. Several prediction models are available to predict long-term mortality after PCI, but none are sufficiently accurate for Malaysian population simply because they were not developed and validated on Malaysian natural data which are multi-racial with the onset cardiovascular disease are younger than other countries worldwide (Ahmad, Zambahari, et al., 2011).

Advanced patient information system is utilized in National Cardiovascular Disease Database (NCVD)-PCI registry. It collects structured data on patients' demographics, status before event, clinical examination and baseline investigation, previous interventions, cardiac status at PCI procedure, Cath-lab visit information, procedure details, and outcomes in which readily available in digital (Ahmad, Ali, et al., 2011). This actual information of Malaysian cardiovascular patients provides the baseline data to facilitate the establishment the risk prediction model in this study.

Having stated all above, in relation, the aim of this study was to: determine significant risk factors of three-year mortality after PCI procedure, develop a risk prediction model for three-year mortality, and validate the resulted model. All works were based on available data gathered from NCVD-PCI registry.

METHODOLOGY

This study involved secondary data of 10,511 Malaysian who were above 18 years old and had gone through PCI procedure between January 2008 and December 2012 at the National Heart Institute (NHI) which acted as a source data provider for NCVD-PCI registry. Data on patients' demographics, status before event, clinical examination, baseline investigation, previous interventions, cardiac status at PCI procedure, and Cath lab visit information were used as potential predictors to predict the outcome. The outcome was the death status of each patient within three years after PCI which were obtained from National Registration Department.

In addition to the above predictor variables a few more technical jargons were used in this report for the sake of discussion clarity. For examples: glomerular filtration rate (GFR) was an approximate correspondence to the Modified Diet and Renal Disease equation; overweight and obesity was categorized according to the Asian-Pacific cutoff points; intra-aortic balloon pump (IABP) indicated the technique was applied during the procedure; acute coronary syndrome (ACS) meant the patient suffered either unstable angina pectoris (UAP), Non-ST-elevation myocardial infarction (NSTEMI), or ST-Elevation Myocardial Infarction (STEMI). In order to preserve uniformity of the data, variables with more than 50% missing values were excluded from the analysis. There was no amputation done to the data, instead a complete-case analysis approach was applied in the overall analysis. The data was split randomly into 70% for development and 30% for validation cohorts.

1) Data Analysis

Independent t-test was performed for comparing the means for continuous variables and chi-square test was used for categorical variables. Variable that has p-value less than 0.25 was further included in the logistic stepwise variable selection. The best subset of predictors was determined based on Aikaike information criterion (AIC) value (Akaike, 1974) to be used in the development model.

Multiple logistic regression was used to build the predictive model in the development cohort. Adjusted odds ratio (OR) was computed to show the relationship between each predictor and the outcome while the other predictors in the model are controlled. Higher value of OR indicates a stronger relationship. No multicollinearity between independent variables was ensured and only significant variables were included in the final model. Then the developed final model was further evaluated by measuring its performance by area under the receiver operating characteristic (ROC) curve. Area under the ROC curve is varying between 0 to 1 in which a value of 0.5 is uninformative and a value of > 0.75 is clinically useful (Fan, Upadhye, & Worster, 2006). The goodness-of-fit of the model was assessed by Hosmer-Lameshow test with the significant level was set at 0.05. If the model has good prediction, the observed outcomes are matched with the expected outcomes resulting the P value of the test is more than 0.05.

Finally, the mathematical algorithm produced by the developmental model was applied on the validation cohort. Similar evaluation technique i.e Hosmer-Lameshow test and area under ROC curve were used to measure its goodness-of-fit performance. Performance in both cohorts were compared, and all analysis was done by STATA software.

RESULT

1) Independent and Dependent Variables

Patients' characteristics, co-morbidities status, and coronary risk factors before PCI procedure were the variables in the study. Table 1 presents the information of the variables and some of them were significant to be the independent variables in the study. Majority of the patients were males which was at 81.9% with the average of 57.9 (±10.1) years old. Malay was the highest ethnic group who had undergone PCI procedure in the study which was 57%. With regards to BMI, the most prevalent BMI group was overweight and obese group (84%). Dyslipidaemia and hypertension were the most common co-morbidity in the patients with the percentages were at 80.1% and 75% respectively. History of heart failure, cerebrovascular disease and chronic renal failure were present in a substantial minority.

Table 1: Demographics characteristic and status before PCI procedure of patients

Variable	Data available	Frequency	Percentage
Male	10511	8603	81.9
>50 years old	10511	8173	77.76
Malay	10506	5988	57.0
Nonsmoker	9212	4074	44.2
Overweight & obese	9501	7980	84.0
Dyslipidaemia	10456	8379	80.1
Hypertension	10479	7862	75.0
Diabetes	10487	5335	50.9
Family history of premature cardiovascular disease	9991	2225	22.3
Myocardial infarction history	10473	5179	49.4
Documented CAD	10484	6572	62.9
History of heart failure	10485	384	3.7
Cerebrovascular disease	10483	161	1.5
Peripheral vascular disease	10482	90	0.9
Chronic renal failure	10485	733	7.0

The dependent variable (i.e. death status) in this study is displayed in Figure 1. Out of a total of 10,511 patients involved in PCI at the center between year 2008 and 2012, 1011 (9.6%) died within three years after PCI procedure; of which 446 died within the first year, 298 in the second year and 264 in the third year.

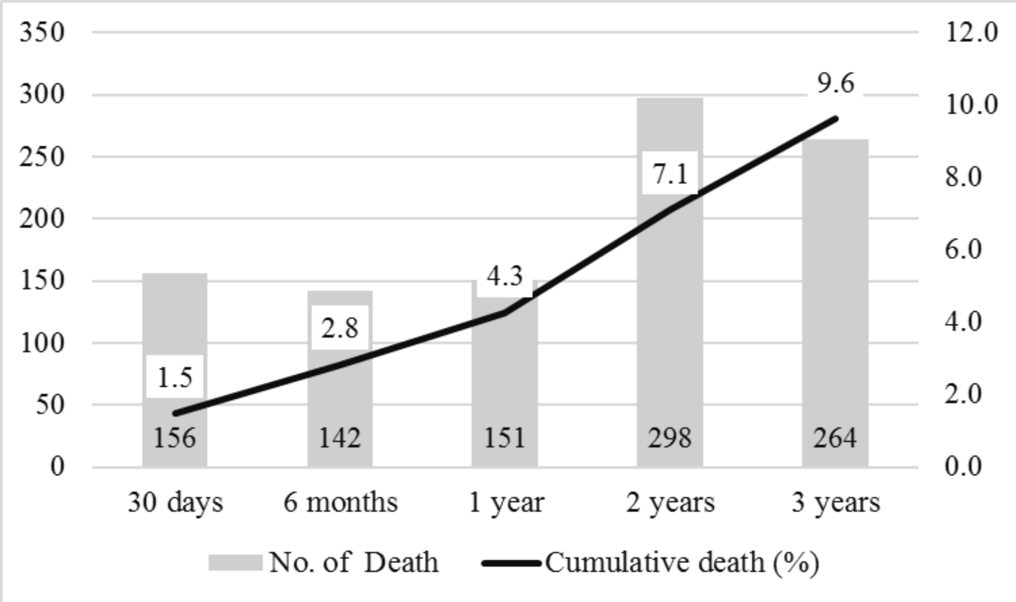

Figure 1: Total and cumulative death by time after PCI

2) Model Development and Validation

The 10511 patients in the study population were randomly divided into a development cohort with 7357 patients (70%) and a validation cohort with 3154 patients (30%).

In a multivariate stepwise logistic regression analysis, significant variables associated with mortality after PCI included age, heart rate, diabetes mellitus, GFR, history of heart failure (HF), ACS, Intra-aortic balloon pump (IABP), and femoral percutaneous entry. The variables are listed in Table 2.

Those who had ≥ 90 beats/minute heart rate at start of PCI were likely to die (OR 1.727, 95% CI 1.333, 2.238, p value <0.001) compared to patients who have lower heart rate. Patients aged more than 60 years also have higher mortality risk compared to patients who were less than 40 years old (OR 2.298, 95% CI 1.140, 4.631, p value <0.020). Meanwhile, patients who had diabetes mellitus were 2.107 (95% CI 1.735, 2.560, p value <0.001) times likely to die than who had no diabetes.

Lower glomerular filtration rate was strongly associated with 3-year mortality outcome. Those who had history of heart failure and suffered from an ACS event were most likely to die. Intra-aortic balloon pump (IABP) user and femoral percutaneous entry patients were also identified as higher risk group with the adjusted OR of 2.843 (95% CI: 1.763, 4.584) and 1.415 (95% CI: 1.169, 1.714) respectively.

Table 2: Multivariate logistic regression in predicting long-term mortality after PCI

Predictor	Adjusted OR	[95% Conf. Interval]		SE	z	P value
Heart rate						
≥ 90 / <90 beats/minutes	1.727	(1.333,	2.238)	0.228	4.13	<0.001
Age						
41-60 / ≤ 40 years old	1.365	(0.678,	2.749)	0.488	0.87	0.384
>60 / ≤ 40 years old	2.298	(1.140,	4.631)	0.822	2.33	0.020
Diabetes (yes/no)	2.107	(1.735,	2.560)	0.209	7.51	<0.001
GFR						
45- <60 / ≥ 60	2.208	(1.738,	2.805)	0.270	6.48	<0.001
30- <45 / ≥ 60	3.642	(2.742,	4.836)	0.527	8.93	<0.001
15- <30 / ≥ 60	5.386	(3.750,	7.736)	0.995	9.11	<0.001
<15 / ≥ 60	12.636	(9.217,	17.323)	2.034	15.76	<0.001
History of HF (yes/no)	2.160	(1.537,	3.036)	0.375	4.44	<0.001
ACS (yes/no)	1.290	(1.076,	1.546)	0.119	2.76	0.006
IABP (yes/no)	2.843	(1.763,	4.584)	0.693	4.29	<0.001
Femoral entry (yes/no)	1.415	(1.169,	1.714)	0.138	3.56	<0.001
Constant	0.014	(0.007,	0.029)	0.005	-11.71	<0.001

The result of predictive mathematical algorithm given by the development work was applied to the validation data set. The comparative results are given in Table 3 and Figure 2. P-value of <0.05 of Hosmer-Lemeshow test on development and validation samples indicated the model predicted similarly as observed data on both datasets (see Table 3).

Table 3: Hosmer-Lameshow tests on the development and validation cohorts

	Development	Validation
Number of observations	6714	2883
Hosmer-Lameshow X^2 (8)	6.78	11.17
P-value	0.5604	0.1922

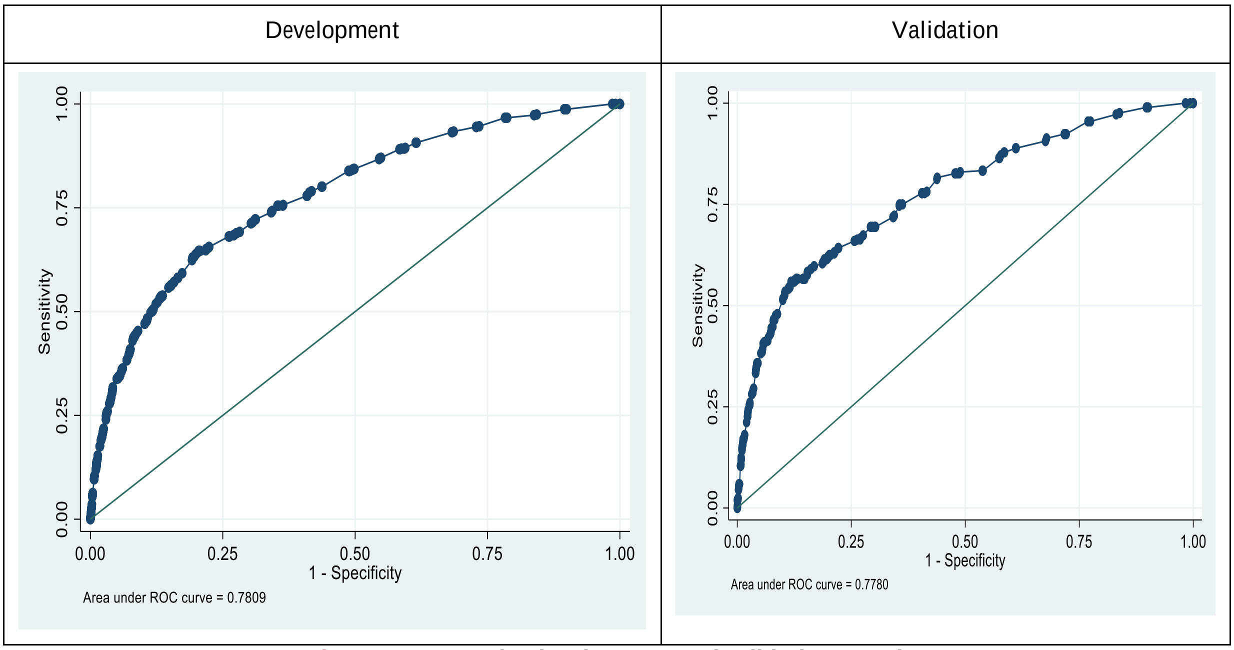

Figure 2: ROC on the development and validation samples

The area under the ROC on the development and validation datasets are 0.7809 and 0.7780 respectively (see Figure 2). They indicate the model is clinically useful in predicting long-term mortality for that samples.

DISCUSSION

The total number (after data cleansing) of patients in this study was 10,511 with the mean age of 57.9 (±10.1) years old, which was similar to other published studies using the same registry (Ahmad et al., 2013; Ahmad, Ali, et al., 2011). Moreover, the patient's characteristic with regards to gender and ethnicity among patients involved in this study were comparatively similar with national NCVD-PCI registry's data in 2015 and 2016 (Ahmad, 2018). Hence, the finding of this study did represent Malaysian population who had gone through PCI procedure.

This work found the three-year mortality rate among the patients after PCI procedure in Malaysia was 9.6%. It was slightly higher than Australian and Japanese's rate reported as 8.2% and 9.3% respectively (Tanaka et al., 2012; Wilson et al., 2011), but lower than New York's 9.8% mortality rate of similar case (Wu et al., 2014). However, the mean age of patients who went through PCI in Malaysia was younger compared to those countries.

This study managed to determine best set of predictors which became the main input to develop a risk prediction model for long term mortality in a Malaysian population. However, there were some established risk factors such as left ventricular function, which was unfortunately left out in the analysis due to its large portion of unavailability in the sample data. Only if the variable had been available, the model's performance should had been superior

Older age, higher heart rate at start of PCI, diagnosed with diabetes mellitus, lower GFR, history of heart failure, presence of acute coronary syndrome, and IABP were identified as significant independent predictors for long-term mortality after PCI in this study. Similar variables were shortlisted by various other risk scores (Tanaka et al., 2012; Wu et al., 2014, Wongpraparut et al., 2014). Interestingly, vascular access site (referred as femoral entry) in Table 2 was not shortlisted as significant independent predictor in earlier studies but it was found to be significant in this study. Vascular access site is the spot where a catheter is inserted to arterial system during PCI procedure be it femoral, brachial, or radial. A systematic review by (Jolly, Amlani, Hamon, Yusuf, & Mehta, 2009) concluded that femoral entry site access in the PCI was associated with higher bleeding complications and therefore, it should be considered in the mortality predictive model after a primary PCI (Ruano-Ravina, et al., 2013). All shortlisted variables identified above were successfully employed by the developmental model and subsequently produced an algorithm of prediction. The algorithm built by the developmental model was proven to be competent when tested in the validation dataset.

Area under the ROC curve is widely used in medicine field to evaluate the discrimination power for logistic regression. In relation to this, this study also used the same approach for comparison purpose. The area under the ROC curve was 0.7809 in the development cohort indicates the model is clinically useful in predicting long-term mortality for that samples (Fan et al., 2006). The model was consistently shown a satisfactory performance in the out-of-sample predictions (validation) cohort with the area value of 0.7780. Nevertheless, more accurate method such as advanced statistics, random forest or machine learning approach possibly used to enhance the model.

CONCLUSION

The three-year after PCI's mortality rate was low in Malaysia. Using actual Malaysian patients' data from the main data provider for national cardiovascular registry, the work has identified significant predictors out of many factors for Malaysian cases. Based on these significant predictors, a reliable predictive model with good discrimination and calibration was successfully developed to predict long-term mortality after percutaneous coronary intervention. With the validation exercise gave convincing evidence of the performance, the model is ready to take further steps i.e. to transform itself into a simple risk score tool in order to be considered as a helpful aid for clinicians and other healthcare professionals.

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CONFLICT OF INTEREST

None

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