Predictors of mortality in patients with Acute Coronary Syndrome (ACS) undergoing Percutaneous Coronary Intervention (PCI): Insights from National Cardiovascular Disease Database (NCVD), Malaysia

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SUMMARY

The aim of this study is to determine risks factor of mortality among patient with post percutaneous coronary intervention. Estimation of post operative mortality risk factor is essential for planning prevention modalities. This is retrospective cohort study based on secondary data extracted from the National Cardiovascular Disease Database (NCVD-ACS and NCVD PCI). Both these registries were interlinked and was further matched to JPN (Jabatan Pendaftaran Negara/National registration Department) to assess mortality among the patients who underwent PCI and all death which occurred in between 2007, 2008 and 2009. There were 630 patients in this studied. Age, history of diabetes mellitus, peripheral vascular, renal failure and previous percutaneous coronary intervention were univariately associated with mortality. However based on logistics stepwise method, only age and history of renal failure had showed statistically significant and sizeable odds ratio in predicting the patient died of coronary death. Older age and renal failure are the predicting factors for mortality among patients with post percutaneous coronary intervention.

KEY WORDS:
Cardiac mortality, mortality, post percutaneous coronary intervention

INTRODUCTION

Coronary heart disease is the number one cause of death in the world. According to the World Health Organisation (WHO report, 2008), cardiovascular diseases kills more people every year than any others. In 2008, 7.3 million people died of coronary heart disease which account to 12.7% death worldwide. The consequences of acute coronary syndrome (ACS) are not benign. Among those who survive to reach hospital alive approximately 12% of patient with ST segment elevation myocardial Infarction (MI), 13% of those with non ST-segment elevation ACS and 8% with unstable angina will die in the succeeding six months (GRACE Registry) [1].

Extensive epidemiological research has established cigarette smoking, diabetes, hyperlipidemia, and hypertension as independent risk factors for Coronary Heart disease (CHD) and these factors could be treated and has convincingly shown to reduce the risk of future cardiac events[2].

However at present, mortality prediction after Percutaneous Coronary Intervention (PCI) is based on clinical characteristics. Patient age, renal function and the presence of acute coronary syndrome are the main predictor of procedural risk of death[3]. Once a patient has undergone PCI, restenosis post PCI seem to be a major issue as initial restenosis rate for angioplasty have been estimated to be about 33%. Large follow up studies have documented restenosis as high as 43%[4]. Much effort has been exerted to reduce these risk factors that predispose these patients to restenosis, repeated PCI, increasing the risk factors and complications ultimately leading to death. Multiple large retrospective studies have been performed to assess these risk factors associated with restenosis and only three clinical risk factors have been found to be independent predictors. The factors are Diabetes mellitus, unstable angina and male (sex) however these three factors lack sensitivity and specificity[4]. In addition, the study based on large cohort of patients with PCI reported that the long-term major adverse cardiac event rates were low all-comers for PCI[5]. Measuring and comparing the risk factors while assessing the impact of secondary prevention are crucial because acute coronary syndromes (ACSs) often recur in patients despite appropriate therapy. Favaloro and Ringqvist *et al.* in previous studies for patient with ischemic heart disease post coronary intervention of either CABG or PCI stated that location of lesion both with respect to the vessel in which it is located and the location within the vessel is essential for long term mortality [6]. Any therapy of coronary heart disease should not only relieve symptoms but also ideally should alter the disease process and avert progression.

Measuring the burden of risk factors for PCI and its outcome is critical for several reasons. Estimation of post operative mortality is important for patients seeking health care, physicians making management decisions and controlling the risk factors to prevent relapse of ACS and other complications. Finally, justifying using an expensive intervention (PCI) with not much emphasis on follow up to reduce risk factors and recurrent intervention is at waste of resources. This is a study to determine the association of modifiable risk component in post PCI patient for risk factor management. This is to facilitate public health initiative to enhance efforts to promote important lifestyle changes such as dietary modification and cessation of smoking. However the question arises that once a patient has undergone PCI does he face the same risk factors as an Acute Myocardial

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Table I: Association between profile characteristics of respondents and outcome (N=630)

Risk factors - Profile	Non-suvivor n (%)	Survivor n (%)	P-value
Gender			0.119
Male	71 (74.0)	432 (80.9)	
Female	25 (26.0)	102 (19.1)	
Age (years)	59.8 (11.4)	55.2 (10.6)	<0.001
Age group (years)			0.001
≤ 50	21 (21.9)	186 (34.8)	
51 – 60	27 (28.1)	184 (34.5)	
61 – 70	30 (31.3)	120 (22.5)	
≥ 70	18 (18.8)	44 (8.2)	
Race			0.845
Malay	42 (43.8)	250 (46.8)	
Chinese	24 (25.0)	141 (26.4)	
Indian	26 (27.1)	124 (23.2)	
Others	4 (4.2)	19 (3.6)	
Smoking (n=508)			0.446
Non-smoker	27 (38.0)	146 (33.4)	
Smoker	44 (62.0)	291 (66.6)	

Table II: Association between risk factors of medical conditions and outcome

Risk factors - Medical	Non-survived n (%)	Survived n (%)	P-value
History of dyslipidemia (n=534)			0.704
Yes	54 (71.1)	335 (73.1)	
No	22 (28.9)	123 (26.9)	
History of hypertension (n=600)			0.102
Yes	69 (76.7)	347 (68.0)	
No	21 (23.3)	163 (32.0)	
History of diabetes mellitus (n=595)			0.027
Yes	49 (55.7)	218 (43.0)	
No	39 (44.3)	289 (57.0)	
History of CVD (n=527)			0.568
Yes	16 (22.2)	88 (19.3)	
No	56 (77.8)	367 (80.7)	
History of MI (n=573)			0.252
Yes	31 (39.2)	228 (46.2)	
No	48 (60.8)	266 (53.8)	
History of cerebrovascular (n=612)			0.610
Yes	2 (2.3)	8 (1.5)	
No	86 (97.7)	516 (98.5)	
History of peripheral vascular (n=612)			0.042
Yes	2 (2.3)	2 (0.4)	
No	86 (97.7)	522 (99.6)	
History of Renal failure (n=611)			<0.001
Yes	12 (13.6)	13 (2.5)	
No	76 (86.4)	510 (97.5)	
Previous PCI (n=628)			0.048
Yes	22 (22.9)	79 (14.8)	
No	74 (77.1)	453 (85.2)	
Previous CABG (n=629)			0.174
Yes	7 (2.3)	22 (4.1)	
No	89 (92.7)	511 (95.9)	

Infarction (AMI) patient in relation to death or does he face a different set of risk factor?

MATERIALS AND METHODS

Patient population

This study involves patients registered with the Acute Coronary Syndrome (ACS) Registry and Percutaneous Coronary Intervention (PCI) Registry from January 1st 2007 to 31st December 2007. Five major Ministry of Health (MOH) Heart centres which perform cardiac catheterisation participated in this retrospective cohort study.

A standardized case report form version-1.4 (as attached in appendix A) was used by all participating sites. These data were linked to the National Registration Department (NRD) Malaysia to track death records for the year 2007, 2008 and 2009. The patients registered in NCVD-ACS have to either have the presence of at least two of the following: a clinical presentation, electrocardiography changes or cardiac enzyme elevation to be registered in this registry. This registry only records any patient age 18 and above who is diagnosed with ACS including ST-elevation myocardial infarction (STEMI), non-STEMI and unstable angina (UA). These data can come from the private, public and university sectors.

Table III: Result of logistic regression using selective predictors (p-value < 0.05 from univariate test) to predict non-survived using enter and stepwise backward likelihood method

Risk factors	Unstandardized			Standardized		
	OR	95%CI	P-value	OR	95%CI	P-value
Age group (years)						
≤ 50		ref			ref	
51 – 60	1.435	0.720, 2.859	0.305	1.459	0.733, 2.903	0.282
61 – 70	2.321	1.161, 4.637	0.017	2.425	1.220, 4.819	0.011
≥ 70	3.916	1.746, 8.786	0.001	4.056	1.817, 9.052	0.001
History of diabetes mellitus						
Yes	1.231	0.752, 2.014	0.409		-	
No		ref				
History of peripheral vascular						
Yes	3.236	0.401, 26.131	0.271		-	
No		ref				
History of Renal failure						
Yes	4.274	1.738, 10.513	0.002	4.698	1.968, 11.215	<0.001
No		ref			ref	
Previous PCI						
Yes	1.008	0.527, 1.928	0.981		-	
No		ref				

Patients who died of non-cardiac causes were excluded from this study. Patients underwent PCI in year 2008 will be automatically excluded even thou admitted late 2007. Death during the same admission as the procedure was identified using the registries while death after discharge following the procedure was identified using the data from the NRD. However death certificate lacks accurate or detailed clinical information especially on causes of death and it can have cause of death certified by non medical personnel. Deaths were coded into cardiac death and non- cardiac death based on ICD 10. However if cause of death was unknown or sudden, it was considered as cardiac death. Unspecified multi organ failure (MOF) was also considered under cardiac death. Data were keyed in at individual sites by nurses and in sites where there are no internet facilities or nurse available, case report form were sent to registry office to be keyed in.

It is important to note that in patient who underwent subsequent revascularization the analysis was taken on the first procedure performed regardless on how many or what kind of revascularization was done latter in the same period of study.

Ethical approval

NCVD Governance board permission was obtained before the linkages between the registries were done. Study was registered under NMRR (National Medical Research Registry) in accordance to the guideline and ethical approval was approved by Medical Review & Ethics Committee (MREC). A Patient consent waiver was requested from "The Medical Research and Ethics Committee" (MREC) since the registry has already obtained a consent waiver.

Statistical analysis

Descriptive summary were presented in frequency (n) and percentages (%). Pearson Chi-square test and independent sample t-test were used to determine the association between the risk factors and outcome. Binary logistics was then applied to test the risk factors simultaneously towards the outcome. Odds ratio with its 95% confidence interval and the p-value were reported to determine the strength of association towards the outcome. Analyses were carried out using SPSS (IBM SPSS version 20.0).

RESULTS

Baseline characteristics

There were 630 patients that were confirmed having Acute Coronary Syndrome and underwent PCI with completed data, within the Registry for 2007. The mean (SD) baseline age of the participant was 55.9 (10.8) years. The mean (SD) age among the alive was 55.2 (10.6) and mean (SD) age among the dead was 59.8 (11.4).The percentage of patient who died was 15.2%. The youngest patient in this study was 26 years old and the oldest among them was 83 years old. The ratio between male and female was approximately 4:1. The ethnic composition was 46.3% Malays, 26.2% Chinese, 23.8%Indian and 3.7% were other Malaysian.

Table I shows the distribution between the demographic profile of patients and outcome. Only age group was significant where older age group (61 and above) were at higher risk for mortality within 3 years compared to the younger group. The others were not significant including status of smoking. Table II shows the association between history of disease toward the outcome of mortality within three years. Out of 10 predictors, history of diabetes mellitus, peripheral vascular, renal failure, and previous PCI were associated with the outcome from the univariate analysis.

The multivariate analysis is shown in Table III. Out of four predictors, only age group and history of renal failure were remain significant based on enter and stepwise method. Although peripheral vascular was not significant perhaps due to small sample size, however it showed sizeable effect (OR=3.236, based on enter method). Out of four patients with peripheral vascular, two died.

DISCUSSION

The mean (SD) baseline age of the participants in this study was 55.9 (10.8) years. When compared to other registries (SCAAR (Swedish Coronary Angiography and Angioplasty Registry), Dynamic Registry, Melbourne interventional group (MIG)), this is almost a decade younger than the other populations. (55.9 years old in NCVD vs 62.0 in Dynamic Registry vs 64.7 in MIG). The mean age between males and females were not much different .The mean age of female patients was 57.1 (10.7) years as compared to males with a mean of 55.6 (10.9) years. This studies had a higher proportion of males (4:1) compared to females. According to the Framingham Heart Study, it is known that CHD rates increase linearly for both sexes with the peak incidence for male in the fifth and sixth decades and the peak for females were 10 years after that of males[7]. However this did not apply to our population of patients. Both our male and female patient presented at almost the same age.

In the univariate analysis, we found that age group, history of diabetes mellitus; peripheral vascular, renal failure and previous PCI were associated with outcome. Others predictors were not, although previous studies may have found significance. For example, smoking tobacco or cigarettes doubles the incidence and mortality of cardiovascular disease. According to Neaton, J.D & Wentworth, D (1992), the likelihood of cardiovascular even increases in proportion to the dose of tobacco which magnifies other coronary risk factors[8]. This study did not take the amount of cigarettes into consideration, however we found that status of smoker and non-smoker was not associated with mortality. Differences in the accuracy of measurement of exposure status also may account for some uncertainty in the evaluation of risk of mortality. In the Annual report Of NCVD –PCI Registry for 2007 (the same patient population) it was noted that more that 28% of the patients have quit smoking more than 30days and 16% of the patient have not taken any tobacco within the last 30 days.

PCI did not reduce the risk of death, among ACS patients, when added to optimal medical therapy. This finding was in line with the COURAGE trial. Where the clinical outcome over the 5-year period showed no difference in death or MI between the PCI and medical groups (19% vs. 18.5%, p = NS)[9]. This study also did not find significant association between antecedent hypertension and mortality post PCI. However, in contrast other studies our study did not find that a history of hypertension independently contributes to a higher mortality during the three years of follow-up. The poor outcomes after CHD are probably attributable not to antecedent hypertension but to the concomitant existence of other risk factors such as an old age, and multivessel disease and other co morbidity,

Diabetes mellitus continues to be a strong independent predictor to death among the CAD patients. Based on univariate analysis, the three years mortality in patents with past history of Diabetes contributed significantly to the outcome among those who had ASC and underwent percutaneous coronary intervention. However, the finding was not significant in the multivariate phase. This may due to other co-morbidity that influences the outcome among the diabetes patients. Diabetic patients with AMI showed an improved long-term prognosis when they were treated with statins and beta-blockers. Although we could not confirm such a beneficial effect of statins and beta-blockers for diabetic patients with post PCI in the present study, we believe that these factors should be considered[9].

From previous studies it was known that patients with past history of MI had a relative risk of 5 to7 times than in person without overt Coronary Disease[10] and their risk factors for MI remain high in spite of intervention. However in this study there is no significant difference between the past history of MI and death post PCI. Past history of peripheral vascular disease among the dead and alive in post PCI patients in our study was no significant. This might be due to the small sample size and the design of the study since it was cross sectional study. There was one patient in our study who was dead with this risk factor.

Based on multivariate analysis, age group and renal failure were significant to contribute to mortality within three years post PCI. Those in the age group of 61 to 70 and more than 70 years were 2.4 and 4.7 respectively times more likely to die compared to age group less than 50 years. Renal dysfunction is a common complication for recurrent MI, restenosis and death. The presence of pre-existing chronic kidney disease (CKD) may worsen due to intraprocedural exposure to contrast agents. Our results found that those with renal failure were almost five times more likely to get higher risk of dying compared to those without renal failure.

Therefore we suggest clinicians should emphasise implications of and the importance of careful evaluation for the need of PCI especially for the higher risk older patient and those with renal failure.

Limitations

Not all laboratories can provide prompt, high-quality PCI. Even centers with interventional cardiology facilities may not be able to provide the service efficiently as required by the guidelines. PCI appears to have its greatest mortality benefit in high-risk patients[11]. Then again we have no data on the PCI performance and success rate which is one major determinant to assess the success of PCI intervention. Due to the current system in justification of death, death certificate lacks accurate or detailed clinical information especially on causes of death since it can have cause of death certified by non medical personnel. Besides that, only those limited co morbid illnesses and variable were used in this study. Variables, like stent design, medication and various other complication , infection, inflammatory, and some unknown factors that can influence death was not studied in this study.

CONCLUSION

From our findings, we found that older age and patients with renal failure were at higher risk to die within three years after post PCI. Therefore, preventive action needs to be made for this group before do their post PCI.

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