

Reduced Inhospital Mortality in Patients with Acute Myocardial Infarction after Practice of Percutaneous Coronary Intervention at a Remote Hospital in Taiwan

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Background: As of July 2004, our hospital in Taitung, a remote area of Taiwan, has offered a 24-hour primary percutaneous coronary intervention (PCI) service.

Methods: We performed a retrospective analysis of data from 310 patients who suffered an acute myocardial infarction (AMI) from the period 2003 and 2007 according to patient age and survival status.

Results: The mean age for the non-survivors was significantly higher compared to the survivors. Non-survivors were significantly lower in BMI, higher uric acid levels and were considered to be hyperuricemic. The mortality rate among the 148 older patients (≥ 70 years of age) was significantly higher than that among the 162 younger patients (< 70 years of age) group (18.37% vs. 3.09%, $p < 0.0001$). The older patients exhibited higher levels of serum creatine and lower levels of cholesterol, triglycerides, and LDL ($p < 0.05$ for all). A greater fraction of the older patients were in Killip class III-IV compared to the younger patients ($p < 0.0001$) and were more likely to be in shock status on arrival ($p = .0085$). Multivariate logistic regression analysis revealed that age ≥ 70 years (OR 8.49, 95% CI 1.04-68.84, $p = 0.04$) and Killip classes III-IV (OR 7.41, 95% CI 1.54-35.55, $p = 0.01$) independently predicted in-hospital mortality. The primary PCI service significantly reduced the mortality of younger AMI patients ($p = 0.002$). The mortality before and after primary PCI in the older age group, by contrast, was not significantly different.

Conclusion: Our data suggest that greater age (along with Killip class III-IV) appears to predict in-hospital mortality for patients with AMI. Younger patients can benefit from the availability of a primary PCI service.

Key Words: Acute myocardial infarction • Elderly • In-hospital mortality • Primary PCI

INTRODUCTION

In spite of the favorable prognosis conferred by percutaneous coronary intervention (PCI),¹ the in-hospital morbidity and mortality after PCI for acute myocardial infarction (AMI) are known to be affected by independent risk factors such as old age, failed reperfusion, and higher Killip status.^{2,3} The pathophysiology of AMI is dynamic and complex, and in-hospital morbidity is often complicated by the frequent coexistence of multivessel disease and cardiogenic shock.^{4,5}

So far, limited reports are available regarding the in-

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dependent predictors of mortality for the aging population who have undergone PCI post AMI. The in-hospital mortality rates in the elderly population post AMI who underwent PCI and implantation of drug-eluting stents can reach 15%.⁶ For the specific subset of very elderly patients who undergo primary PCI, age ≥ 90 years, Killip class $\geq III$ on admission, and time from symptoms to PCI > 12 h were identified as independent predictors of mortality at long-term follow-up.^{7,8} A multicenter study compared the clinical characteristics and in-hospital outcomes of 7,472 octogenarians (mean age, 83 years) with those of 102,236 younger patients (mean age, 62 years) who underwent PCI at 22 National Cardiovascular Network (NCN) hospitals in Canada. In that study, the independent predictors of mortality in octogenarians were shock, AMI, left ventricular ejection fraction (LVEF) $< 35\%$, renal insufficiency, first PCI, age > 85 years, and diabetes mellitus.⁹

As of 2003, our institution has offered a PCI service. In July 2004, we initiated a 24-hour service for primary PCI. Although on-site cardiac surgery is still not provided, the availability of the primary PCI service has benefited our patients by reducing the time delay between symptoms and revascularization.^{10,11}

The objective of this study was to determine the rates and predictors of in-hospital mortality among the elderly patients with AMI at our institution who had undergone PCI. We also sought to investigate the role and potential impact of primary PCI in all patients with AMI.

METHODS

Patients

This study was approved by the Institutional Review Board of Mackay Memorial Hospital. We performed a retrospective analysis of the mortality rates among 310 patients with AMI after PCI became available between May 2003 and April 2007 at Mackay Memorial Hospital, Taitung Branch. This hospital is situated in a remote area of Taiwan. From May 2003 to July 2004, our hospital began to offer PCI services, although on-site cardiac surgery was not yet provided. Full 24-hour primary PCI service was not initiated until July 2004.

AMI was diagnosed if a patient exhibited 2 of the following 3 criteria: 1) chest pain or classic symptoms of

MI > 30 minutes; 2) ST-segment elevation of at least one millivolt in 2 contiguous leads, new left bundle branch block (LBBB), non-ST elevation acute coronary syndrome (ACS), ST-segment depression, or T-wave inversion persisting for 24 hrs on ECG; and 3) increasing levels of cardiac enzymes, including CPK, CK-MB, and troponin-I.¹² The primary outcome of our study was all-cause in-hospital mortality after AMI.

Definitions and study variables

Patients being treated with antihypertensive drugs or those with a baseline blood pressure of $\geq 140/90$ mmHg were considered to have hypertension (HTN). Diabetes mellitus (DM) was defined by a fasting blood glucose level > 140 mg/dL, a random blood glucose level > 200 mg/dL, or the use of oral hypoglycemic agents or insulin. Hyperlipidemia was defined by a triglyceride level > 200 mg/dL, cholesterol > 230 mg/dL, and low-density lipoprotein (LDL) level > 130 mg/dL. The cut-off points for hyperlipidemia were cited in one of our previous articles.¹¹ In our hospital, we currently use this definition for hyperlipidemia. Other definitions of hyperlipidemia differ slightly from ours. One such definition, i.e., serum total cholesterol ≥ 6.21 mmol/L (240 mg/dL) or current use of hypolipidemic drugs (high total cholesterol) is used by the National Cholesterol Education Program in the United States.¹³ Another definition, i.e., serum total cholesterol ≥ 5.69 mmol/L (220 mg/dL) or current use of hypolipidemic drug was used by the Japanese Atherosclerosis Society (The Fukuoka Heart Study Group).¹⁴

Hyperuricemia was defined by a uric acid level > 7 mg/dL for men and > 6 mg/dL for women.¹⁵ Body-mass index (BMI) was calculated from height and weight and expressed as kg/m^2 . BMI values were used to classify patients according to the Taiwanese Department of Health standard as follows: overweight, BMI = 24-27 kg/m^2 ; obese, BMI ≥ 27 kg/m^2 . Age, sex, race (aborigine or non-aborigine), smoking status (defined as active smoking or duration of smoking cessation ≥ 3 years), Killip class, previous medical history, and clinical variables, such as, ejection fraction (EF) and levels of uric acid (UA) were also included in the analyses.

Statistical analysis

Continuous data were expressed as mean \pm standard deviation (SD) or median (range), and categorical data

were expressed as frequencies and percentages. Demographic features and clinical characteristics were compared using *t* tests, Wilcoxon's ranked-sum test, chi-square test or Fisher's exact test as appropriate. Multivariate stepwise logistic regression models were used to determine odds ratios (ORs) of risk factors for in-hospital mortality. Data were analyzed using SAS 9.0 (SAS Institute Inc., Cary, NC, USA), and a *p* value < 0.05 was considered statistically significant.

RESULTS

Three hundred and ten patients (70.65% males) were included for retrospective analysis, of which 278 (89.7%) were survivors and 32 (10.3%) were non-survivors (Table 1). The mean age for the non-survivors was significantly higher (78.32 ± 8.44 vs. 66.19 ± 12.56) compared to that of the survivors, and among the 32 non-survivors, 84.38% were 70 years of age or older. We, therefore, used the cut-off value of 70 years of age instead of the usually defined elderly cutoff age of 65 years (Table 1).

The percentage of elderly was significantly higher in the non-survivor group (84.38%) compared to that of the survivor group (43.17%; *p* < 0.01). Survivors were overweight (BMI: 25.01 ± 4.49), whereas non-survivors were significantly lower in BMI (BMI: 22.44 ± 3.62). Non-survivors had higher uric acid levels and were considered to be hyperuricemic (8.47 ± 3.38). More than 78% of non-survivors fulfilled the criteria of Killip class III-IV but fewer patients in the non-survival group accepted percutaneous transluminal coronary angioplasty.

Since the mean age for the non-survivors was significantly higher compared to that of the survivors, we further stratified the participants by age (Table 2). There were 162 patients in the younger age group (< 70 years of age), and 148 in the older age group (≥ 70 years of age). The younger patients had a significantly greater BMI than the older patients (*p* < 0.0001) and were more likely to have hyperlipidemia (*p* < 0.0001). The older patients were more likely to be in shock status on arrival (*p* = 0.0085) as compared with the younger patients, and a greater fraction of the older patients were in Killip class III-IV when compared to the younger patients (*p* <

Table 1. Baseline clinical characteristics of patients with acute myocardial infarction (n = 310)

	Total n = 310	Survivors n = 278	Non-survivors n = 32	p-value
Age, years†	67.49 ± 12.74	66.19 ± 12.56	78.32 ± 8.44	< 0.01*
Age ≥ 70‡	147 (47.42)	120 (43.17)	27 (84.38)	< 0.01*
Aborigine‡	94 (30.32)	85 (30.57)	9 (28.13)	0.75
Male‡	219 (70.65)	200 (71.94)	18 (56.25)	0.06
BMI†	24.75 ± 4.47	25.01 ± 4.49	22.44 ± 3.62	< 0.01*
Smoking‡	201 (64.84)	182 (65.47)	19 (59.38)	0.47
Hypertension‡	216 (69.68)	191 (68.70)	24 (75)	0.48
Diabetes‡	127 (40.97)	112 (40.29)	14 (43.75)	0.72
Cholesterol, mg/dl#	174.5 (67-404)	176.5(67,404)	151 (85,296)	0.55
Triglycerides, mg/dl#	105 (25-908)	109 (25,908)	99 (31,301)	0.11
Uric acid, mg/dl†	7.06 ± 2.33	6.94 ± 2.19	8.47 ± 3.38	0.04*
EF, %#	57 (20-78)	58 (20,78)	49 (20,68)	0.12
Length of stay, days#	8.81 ± 9.90, 6 (0-112)	9.06 ± 10.25, 6(1-112)	6.25 ± 5.53, 5(0-23)	0.03*
Prior MI‡	15 (4.84)	15 (5.40)	0 (0.00)	0.38
tPA\$	23 (7.42)	20 (7.19)	3 (9.38)	0.71
Killip classes III-IV‡	112 (36.01)	86 (30.93)	25 (78.13)	< 0.01*
ST-elevation‡	136 (43.87)	125 (44.96)	11 (34.38)	0.24
PTCA‡	255 (82.26)	237 (85.25)	18 (56.25)	< 0.01*
CABG‡	31 (10.00)	31 (11.15)	0 (0.00)	0.23

BMI, body-mass index; EF, ejection fraction; MI, myocardial infarction; tPA, tissue plasminogen activator; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass grafting; Data presented as number (%), mean ± standard deviation or median (range); * Statistical significance, *p* < 0.05; † *t*-test; ‡ Chi-square test; # Wilcoxon's rank sum test; \$ Fisher's exact test.

Table 2. Comparison between older acute myocardial infarction patients (older than 70 years old) and younger patients regarding demographic data and clinical characteristics (n = 310)

Characteristics	Total (n = 310)	Age < 70 yr (n = 162)	Age ≥ 70 yr (n = 148)	p-value
Age, years [†]	67.49 ± 12.74	57.38 ± 8.31	78.56 ± 5.43	< 0.0001*
Male [‡]	219 (70.65)	133 (82.1)	86 (58.11)	< 0.0001
ST-elevation [‡]	136 (43.87)	77 (47.53)	59 (39.86)	0.1743
Aboriginal [‡]	94 (30.32)	54 (33.33)	40 (27.03)	0.2276
Diabetes mellitus [‡]	127 (40.97)	65 (40.12)	62 (41.89)	0.7518
Hypertension [‡]	216 (69.68)	111 (68.52)	105 (70.95)	0.6243
Hyperlipidemia [‡]	145 (46.77)	96 (59.26)	49 (33.11)	< 0.0001*
Smoking [‡]	201 (64.84)	113 (69.75)	88 (59.46)	< 0.058
Shock on arrival [‡]	28 (9.03)	8 (4.94)	20 (13.51)	0.0085*
Arrhythmia [‡]	112 (36.13)	48 (29.63)	64 (43.24)	0.0127
Standstill [§]	5 (1.61)	1 (0.62)	4 (2.7)	0.1964
VT [‡]	32 (10.32)	15 (9.26)	17 (11.49)	0.5775
VF [§]	12 (3.88)	4 (2.47)	8 (5.44)	0.2405
High degree AVB [‡]	42 (13.55)	19 (11.73)	23 (15.54)	0.4065
Killip classes III-IV [‡]	112 (36.13)	40 (24.69)	72 (48.65)	< 0.0001*
CAG [‡]	274 (88.39)	145 (89.51)	129 (87.16)	0.5199
PCI [‡]	255 (82.26)	133 (82.1)	122 (82.43)	0.9388
Death [§]	32 (10.36)	5 (3.09)	27 (18.37)	< 0.0001*
Discharge [‡]	277 (89.35)	156 (96.3)	121 (81.76)	0.0002*
FEE [#]	7323 (468, 63893)	7172 (525, 26267)	7634 (468, 63893)	0.2675
BMI (kg/m ²) [†]	24.75 ± 4.47	26.04 ± 4.26	23.33 ± 4.27	< 0.0001*
Blood pressure (initial) [†]	142.28 ± 38.39	144.32 ± 37.48	140.05 ± 39.37	0.3291
Serum creatine (mg/dL) [#]	1.25 (0.6, 12.5)	1.2 (0.7, 11.9)	1.3 (0.6, 12.5)	0.0334*
Cholesterol (mg/dL) [#]	174.5 (67, 404)	186 (85, 404)	162.5 (67, 351)	0.0005*
Triglycerides (mg/dL) [#]	105 (25, 908)	125.5 (25, 908)	95 (29, 516)	0.0002*
LDL (mg/dL) [#]	114 (24, 336)	121 (24, 336)	105.5 (32, 222)	0.0008*
Uric acid (mg/dL) [#]	6.85 (2.3, 17.2)	6.55 (3, 16.2)	7 (2.3, 17.2)	0.0545
EF (%) [#]	57 (20, 78)	58 (20, 78)	56 (20, 75)	0.2099

Abbreviation: AMI, acute myocardial infarction; VT, ventricular tachycardia; VF, ventricular fibrillation; AVB, heart block; CAG, coronary angiography; PCI, percutaneous coronary intervention; FEE, total cost during hospitalization; Discharge, discharge alive; BMI, body mass index; LDL, low-density lipoprotein; EF, ejection fraction.

Data presented as [†] mean ± standard deviation, [#] median (range), and ^{‡, §} number (%) of deaths between May, 2003 to April, 2007.

*Statistical significance, p < 0.05; [†] t test; [‡] Chi-square test; [#] Wilcoxon's ranked-sum test; [§] Fisher's exact test.

0.0001). Furthermore, the older patients were observed to have higher levels of serum creatine and lower levels of cholesterol, triglycerides, and LDL (p < 0.05 for all). Compared with the younger patients, the older patients were less likely to be discharged from the hospital (81.76% versus 96.3%, p = 0.0002) and more likely to die (p < .0001). There was no significant difference in the number of patients who underwent PCI between these two age groups.

The overall all-cause mortality rate was 10.36% (32 cases out of 310 patients). The mortality rate among the

patients older than 70 years of age was significantly higher than that in the younger group (18.37% vs. 3.09%, p < 0.0001). The patients who died were significantly older (78.32 ± 8.44 vs. 66.19 ± 12.56 years) and in higher Killip class (III-IV, 78.13%; Table 1). As shown in Table 3, the two predictors of in-hospital mortality determined by multivariate logistic regression analysis were older age (≥ 70 years) and higher Killip class (III-IV).

The availability of primary PCI was observed to have a significant impact on patients survival in both age

Table 3. Predictors of in-hospital mortality determined by multivariate logistic regression analysis (n = 310)

Variables	OR	95% CI	p value
Age ≥ 70 years vs. < 70 years	8.49	1.04-68.84	0.0452*
Killip classes III-IV vs. I-II	7.41	1.54-35.55	0.0123*

OR, odds ratio; CI, confidence interval. Variables age, gender, ST-elevation, BMI, triglycerides, uric acid, EF (%), PCI, and Killip class were included in the initial model.

*Statistical significance, $p < 0.05$.

groups, though the younger group gained a greater benefit from primary PCI therapy. As illustrated in Figure 1A, before May, 2003, when no PCI service was available for patients with AMI (pre-PCI), overall mortality in patients with AMI was 26.4%.¹¹ After PCI was made available (May 2003 to July 2004), overall mortality was approximately 21.20% which was significantly different from pre-PCI stage ($p = 0.033$, Figure 1A). In July 2004, the primary PCI 24-hour service was initiated. After July 2004, overall mortality was significantly reduced to 8.9% ($p = 0.002$, Figure 1A), suggesting that the reduction of mortality in patients suffering from AMI correlated with the availability of primary PCI.

In addition, as shown in Figure 1B, the primary PCI service reduced the mortality of elderly AMI patients (≥ 70 years) from 19.5% (before July 2004) to 15.5% (after July, 2004) but this result was not significantly different.

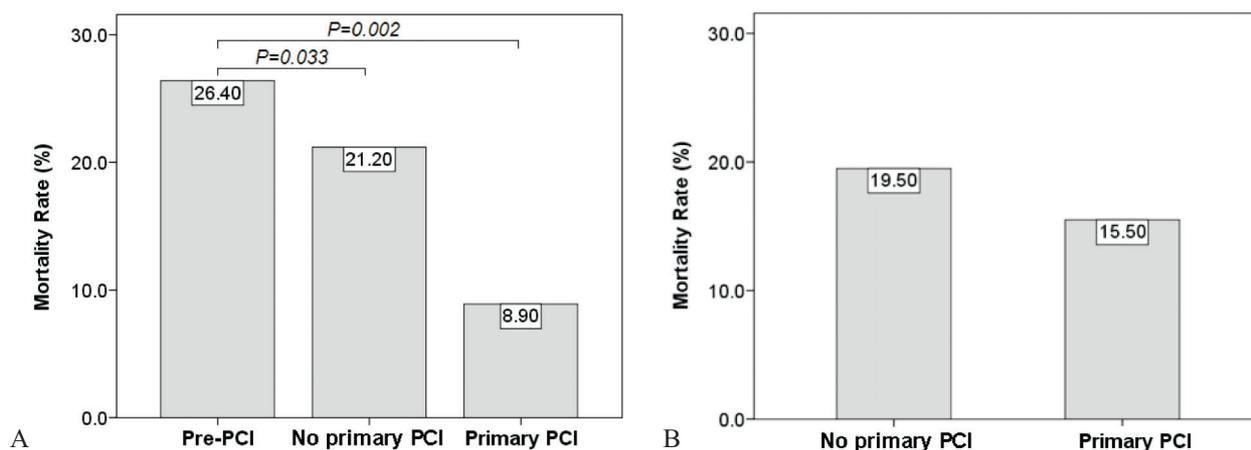


Figure 1. (A) In-hospital rates of mortality for patients in the younger age group (< 70 years of age) before and after primary PCI was initiated. Before May 2003, when there was no PCI service for AMI (pre-PCI), overall mortality for patients with AMI was 26.4%. After PCI was performed, overall mortality was about 21.20% (May, 2003 to July, 2004). But overall mortality declined to 8.9% after the 24-hour service of primary PCI was provided (July, 2004 to April, 2007). (B) In-hospital rates of mortality for patients in the older age group (≥ 70 years of age) before and after primary PCI was provided. The primary PCI service reduced the mortality of elderly AMI patients from 19.5% (before July, 2004) to 15.5% (after July, 2004).

DISCUSSION

We performed a retrospective review of data from 310 patients who suffered from AMI at our hospital after we began to offer both angioplasty and 24-hour primary PCI services on site. The mean age for the non-survivors was significantly higher compared to that of the survivors, and among the 32 non-survivors, 84.38% were 70 years of age or older. Non-survivors were significantly lower in BMI and were considered hyperuricemic. The criteria of hyperuricemia is UA level > 7 mg/dl for males and > 6 mg/dl for females.¹⁰ The two predictors of in-hospital mortality determined by multivariate logistic regression analysis were older age (≥ 70 years) and higher Killip class (III-IV).

Our previous study of AMI risk factors at the same hospital from similar population had similar observation that significant risk factors as a whole included the age, total cholesterol, uric acid, and the Killip Class of AMI. Multiple regression analysis showed that diabetes, age ≥ 70 years, uric acid ≥ 9.0 mg/dL, and Killip class 3 or 4 had relative risk of 1.81, 2.08, 2.89, and 1.63, respectively.¹²

Further investigation into the differences between the younger age group (< 70 years of age) and older age group (≥ 70 years of age) found that the younger patients were more likely to have hyperlipidemia and greater BMI, whereas older patients were in shock status on ar-

rival or were in Killip class III-IV as compared with the younger patients. The older patients also had higher levels of serum creatine and lower levels of cholesterol, triglycerides, and LDL. However, based on the outcome of our analysis, as shown in Table 3, the most crucial difference that closely correlated with mortality was the fraction of the older patients in Killip classes III-IV when compared to the younger patients.

There was no significant difference in the number of patients who underwent PCI between these two age groups, and the availability of primary PCI was observed to have a significant impact on patient survival in both age groups. When the mortality was compared between pre-PCI era¹¹ and post-PCI era, overall mortality of younger age group was significantly reduced after PCI was performed, and even further reduced after the 24-hour service of primary PCI was initiated. Our observation was supported by other reports that young-adult patients with AMI undergoing PCI showed favourable outcome and was proved to be safe and effective.^{16,17}

The primary PCI service reduced the mortality of elderly AMI patients from 19.5% to 15.5%, but this was not significantly different, suggesting that the younger group gained a greater benefit from primary PCI therapy. Our data were distinct from those of some previous reports in the literature.¹⁸⁻²⁰ Tespili et al.¹⁸ found that in elderly patients with acute STEMI, primary PCI yielded positive results, and that successful reperfusion could be achieved in a high proportion of elderly patients with lower mortality rates compared to those reported in non-PCI registries. In a separate study, after adjustment for baseline differences and propensity score, Mehta et al.¹⁹ showed that patients with STEMI receiving primary PCI had a lower rate of re-infarction and greater reduction in mortality compared with thrombolytic therapy. In addition, Wenaweser et al.²⁰ found that clinical outcome after primary PCI for elderly patients (≥ 75 years) with acute STEMI was comparable with that for the middle-aged population and showed favourable outcomes.

The reason why primary PCI therapy showed less benefit in our older patient group might be the relatively high percentage of older patients in Killip classes III-IV. It can be supported by previously published studies showing that advanced age and Killip class were prognostic indicators of mortality in post-AMI patients who underwent PCI.^{1-3,21} One recent study investigating pri-

mary PCI in patients ≥ 75 years of age revealed that age and Killip class were the only independent predictors of cardiac mortality at 6 months after AMI.³ These findings, and the results of the present study, are not unexpected because older patients typically have more comorbidities and a coronary anatomy that is unfavourable for PCI. The overall rate of in-hospital mortality among the elderly patients who underwent primary PCI in our study (15.5%) is higher than the 3.16% reported by Singh et al.²¹ for patients ≥ 80 years of age who underwent PCI, but it is lower than the 30-day mortality of 21% reported by Claessen et al.²² among octogenarians who underwent PCI for ST-elevation myocardial infarction.

In the Japanese Acute Coronary Syndrome Study,²³ Kojima et al. found that serum uric acid (UA) concentrations were modulated by the severity of Killip classification and previous myocardial infarction. Our previous study did observe that patients with higher levels of UA were more likely to suffer an AMI.¹² Nevertheless, the current analysis of the rates of mortality after AMI found no such relationship.

Similarly, although we had previously shown that total cholesterol was associated with an increased risk for AMI,¹² hyperlipidemia was not associated with the risk for mortality in patients with AMI in the current study. This is consistent with the results reported for the Cooperative Cardiovascular Pilot Project,²⁴ in which the long-term prognostic importance of in-hospital total serum cholesterol was evaluated in elderly survivors of AMI. That study found that elevated levels of cholesterol were not associated with higher all-cause mortality. The authors suggested that this inconsistency was the result in part of “the inherent heterogeneity of the lipid profile and the poor specificity of total cholesterol,” as well as the competing risks of death in the elderly and the ambiguities in the timing of measurements of total cholesterol level. It is known that levels of total cholesterol may be reduced by half during the 4 or 5 days after an AMI, as acute clinical events such as AMI can affect cholesterol levels.²⁵ Similar factors may have been responsible for the absence of a relationship between hyperlipidemia and mortality in our study.

Our study had certain inherent limitations due to its retrospective nature. In addition, our study did not evaluate relationships between prognostic determinants,

differential results of serum measurements taken at different intervals, or the waist-to-hip ratio, which has been increasingly considered superior to BMI for predicting cardiovascular risk. It should also be noted that the primary outcome of our study was all-cause in-hospital mortality after AMI, and several other competing risks for death could not be controlled. In particular, lifestyle habits unique to the Taiwanese aborigines, such as use betel (*Areca catechu*) and smoking,¹² which are known to have deleterious effects on the heart, were not fully investigated. The effects of these factors on mortality after AMI in patients of aboriginal descent are interesting topics for future research.

CONCLUSION

This study confirmed that age and Killip class were prognostic determinants of in-hospital mortality for patients with AMI. In addition, BMI was significantly higher in the younger survivors. Multivariate logistic regression analysis revealed that age ≥ 70 years and Killip classes III-IV independently predicted in-hospital mortality. The primary PCI service significantly reduced the mortality of younger AMI patients. The mortality before and after primary PCI in the older age group, by contrast, was not significantly different.

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