

Five-Year Outcomes after Acute Myocardial Infarction in Patients with and without Diabetes Mellitus in Taiwan, 1996-2005

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Background: Diabetes mellitus (DM) is a strong risk factor of cardiovascular disease. To date, the impact of DM on outcomes after acute myocardial infarction (AMI) in Taiwan is undetermined. The aim of this study was to compare five-year outcomes after AMI in patients with and without diabetes in Taiwan.

Methods: A nationwide cohort of 25,028 diabetic and 56,028 non-diabetic patients who were first hospitalized with AMI between 1996 and 2005 was enrolled through linkage with the Taiwan National Health Insurance research database. Patient mortality rates within 30 days after AMI, and 1, 3, and 5 years thereafter were compared.

Result: Length of hospital stay (8.9 ± 8.7 vs. 8.2 ± 8.0 days, $p < 0.01$) and medical cost during admission (in Taiwan dollars: $\$129,123 \pm \$158,073$ vs. $\$121,631 \pm \$157,018$, $p < 0.01$) were significantly higher in diabetic patients. The difference in mortality rate within 30 days was insignificant between diabetic and non-diabetic patients (18.1% vs. 17.6%, $p = 0.06$). Mortalities within 1 year (31.0% vs. 26.8%, $p < 0.01$), 3 years (42.4% vs. 34.7%, $p < 0.01$), and 5 years (50.6% vs. 41.1%, $p < 0.01$) were significantly higher in diabetic patients. In patients with AMI who underwent percutaneous coronary intervention (PCI) during index admission, the mortality rate within 30 days was insignificant (6.3% vs. 6.4%, $p = 0.70$) but mortalities within 1 year (15.2% vs. 11.6%, $p < 0.01$), 3 years (24.1% vs. 17.2%, $p < 0.01$), and 5 years (32.2% vs. 22.6%, $p < 0.01$) were significantly higher in diabetic patients.

Conclusions: The average patient length of hospital stay and medical cost during admission were significantly higher in diabetic patients. Additionally, the difference in mortality rate within 30 days after AMI was insignificant between diabetic and non-diabetic patients. Also, long-term mortality after AMI was significantly higher in diabetic patients.

Key Words: Acute myocardial infarction • Diabetes mellitus • Length of hospital stay • Medical cost • Mortality • National health insurance

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INTRODUCTION

Cardiovascular disease (CVD) has become the second-most prevalent cause of death in Taiwan since 2004, just behind cancer. In 2011, CVD was responsible for 16,513 deaths (10.9% of total mortality) in Taiwan.¹ Coronary artery disease (CAD), which often is the consequence of atherosclerosis, is the leading cause of CVD. Acute myocardial infarction (AMI), the most urgent and serious status of CAD, frequently requires immediate revascularization to prevent further potentially

lethal arrhythmia, hemodynamic instability, or death.²

Diabetes mellitus (DM) is well-known as a coronary artery equivalent disease and a strong risk factor associated with CVD.³ Some studies have demonstrated that in-hospital or short-term mortality after AMI was similar between diabetic and non-diabetic patients.^{4,5} But conflicting results were found in other studies, which revealed that in-hospital or short-term mortality was significant higher in diabetic patients.⁶⁻¹⁰

Diabetic patients with AMI may experience more severe CAD and a greater number of complications (left ventricular dysfunction, heart failure, or significant ventricular arrhythmia) than non-diabetic patients.¹⁰ As a result, long-term mortality after AMI may be different in patients with and without diabetes. In fact, some studies have revealed that diabetic patients have a higher long-term mortality rate.^{5,7,11}

Some studies revealed that the length of hospital stay and the medical cost of CVD were significantly higher in diabetic patients, which were related to the older age and added complications in patients with diabetes.^{12,13}

As we know, previous studies focusing on both short-term and long-term impact of DM on the outcomes after AMI in a Taiwanese population have been limited. Therefore, the aim of this study was to compare the length of hospital stay, the medical cost, the mortality rate within 30 days and the long-term mortality after patients were first hospitalized with AMI with and without diabetes, through data linkage from the National Health Insurance Research Database (NHIRD) of Taiwan.

MATERIALS AND METHODS

Data sources

This study used the data from Taiwan's NHIRD. The applicable data set included all claims data from the National Health Insurance (NHI) program in Taiwan, which finances the healthcare of all residents in Taiwan and offers unrestricted access to any healthcare provider that patients may choose. The single-payer NHI program was launched in Taiwan on March 1, 1995, and now approximately 99% of the country's entire population is enrolled.¹⁴ The NHIRD is one of the largest database sets in the world, and it was encrypted in order to protect

the privacy of all patients enrolled. Because the database consists of de-identified secondary data released to the public for research purposes, this study was exempt from full review by the Institutional Review Board.

Study population

This retrospective cohort study included all patients who were admitted to hospitals with the main diagnosis of AMI (ICD-9-CM code from 410 to 410.92) between January 1996 and December 2005. We excluded the patients who had been previously admitted due to AMI, whose gender was undetermined, and whose age was younger than 18 years. After selection, 76,556 patients were selected. The diagnosis of DM is defined whenever any of the ICD-9-CM codes of the index admission was recorded as 250 to 250.90. Mortality within 30 days after AMI is defined when the ending date of coverage from NHI minus the date of hospital admission is less than or equal to 30 days. The mortality within 1 year, 3 years or 5 years is defined when the ending date of coverage from NHI minus the date of admission is less than or equal to 1 year, 3 years, or 5 years, respectively. Because NHI is compulsory, there are very few occasions that a patient, especially an ill patient, can be dropped from insurance coverage for any cause other than death. Moreover, given that the NHI premium is paid on a monthly basis, coverage can easily be dropped immediately after death. Thus, the ending date of coverage from NHI is a good proxy for the mortality date.¹⁵ The age of patients was divided into four groups: below 45 years, over or equal to 45 years but below 60 years, over or equal to 60 years but below 75 years, and over or equal to 75 years. Patients who underwent percutaneous coronary intervention (PCI) was defined when any of the ICD-9-CM procedure codes during index admission was recorded as 36.0, 36.01, 36.02, 36.05, 36.06, or 36.09. The length of hospital stay was defined as the number of days a patient remained in the acute inpatient ward. The medical cost during admission was defined as the financial cost incurred by the medical institution noted on their application to NHI. The unit of medical cost was Taiwan Dollars (TWD).

Statistical analyses

Extraction and computation of the data were performed by Microsoft SQL Server 2005 (Microsoft Corp.,

Redmond, WA, USA). Statistical analysis was performed by SPSS software (version 18.0, SPSS Inc., Chicago, Illinois, USA). All data were expressed as the frequency (percentage) for categorical data or as mean and standard deviation (SD) for continuous data. Logistic regressions were used to determine the difference of gender, age groups, and mortality between diabetic and non-diabetic patients. Simple linear regression was used to determine the difference of age, length of hospital stay, and medical cost between diabetic and non-diabetic patients. Odds ratio (OR) with 95% confidence interval (95% CI) was presented for categorical data and two-sided values of $p < 0.05$ were considered statistically significant.

RESULTS

Basic characteristics

The characteristics of diabetic and non-diabetic patients when first hospitalized for AMI were presented in Table 1. During January 1996 and December 2005, 76,556 patients were enrolled, including 25,028 diabetic patients and 56,028 non-diabetic patients. The majority (72.1%) of the patients were men, either with diabetes (62.7%) or without diabetes (75.5%). The average age was significantly older in diabetic patients than in non-diabetic patients (66.4 ± 11.5 vs. 66.1 ± 13.8 years, $p = 0.01$). The ratio of PCI during index admission was similar in diabetic and non-diabetic patients (32.7% vs. 33.2%, $p = 0.17$). The age distribution of diabetic patients tended to be younger or older than non-diabetic patients (age below 45 years: 8.3% vs. 4.0%, $p < 0.01$; age over or equal to 75 years: 29.2% vs. 23.1%, $p < 0.01$).

Length of hospital stay and medical cost during admission

The length of hospital stay after AMI (Figure 1) was significantly longer in patients with diabetes (8.9 ± 8.7 vs. 8.2 ± 8.0 days, $p < 0.01$), including those who underwent PCI during index admission (8.7 ± 7.2 vs. 8.2 ± 6.6 days, $p < 0.01$). The medical cost during admission (Figure 2) was significantly higher in AMI patients with diabetes [Taiwan Dollars (TWD) $\$129,123 \pm \$158,073$ vs. $\$121,631 \pm \$157,018$, $p < 0.01$], including those who underwent PCI during index admission (TWD $\$188,556 \pm \$120,717$ vs. $\$187,005 \pm \$129,728$, $p < 0.01$).

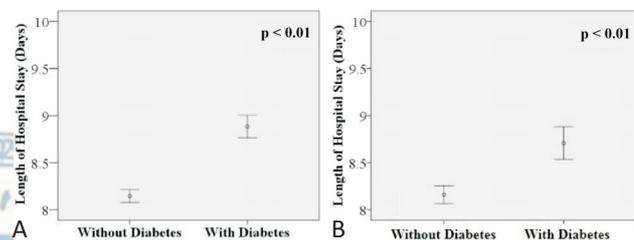


Figure 1. Mean and 95% confidence interval of the length of hospital stay of first acute myocardial infarction hospitalized patients with and without diabetes mellitus: (A) length of hospital stay of all patients; (B) length of hospital stay of patients who underwent PCI.

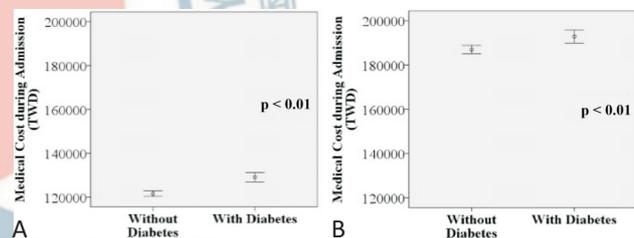


Figure 2. Mean and 95% confidence interval of the medical cost during admission of first acute myocardial infarction hospitalized patients with and without diabetes mellitus: (A) medical cost during admission of all patients; (B) medical cost during admission of patients who underwent PCI. TWD, Taiwan Dollars.

Table 1. Characteristics of first hospitalized diabetic and non-diabetic patients with acute myocardial infarction in Taiwan

	With diabetes	Without diabetes	p value
Number of patients	20,528 (26.8)	56,028 (73.2%)	
Gender (Male)	12,880 (62.7%)	42,329 (75.5%)	< 0.01
Age at admission (years \pm SD)	66.4 \pm 11.5	66.1 \pm 13.8	0.01
PCI	6,706 (32.7%)	18,600 (33.2%)	0.17
Age			
< 45years	821 (4.0%)	4,644 (8.3%)	< 0.01
45-60 years	4,988 (24.3%)	13,017 (23.2%)	< 0.01
60-75 years	9,768 (47.6%)	22,003 (39.3%)	< 0.01
\geq 75 years	4,951 (23.1%)	16,364 (29.2%)	< 0.01

Values are mean \pm standard deviation or number (%). SD, Standard deviation; PCI, percutaneous coronary intervention.

Mortality within 30 days after AMI

Mortality within 30 days after AMI was shown in Table 2. The overall mortality within 30 days after AMI was insignificant between diabetic and non-diabetic patients (18.1% vs. 17.6%, respectively, where $p = 0.06$).

Long-term mortality after AMI

Long-term mortality after AMI was showed in Table 2. The overall mortalities within 1 year, 3 years and 5 years after AMI were significantly higher in diabetic patients (within 1 year: 31.0% vs. 26.8%, $p < 0.01$; within 3 years: 42.4% vs. 34.7%, $p < 0.001$; within 5 years: 50.6% vs. 41.1%, $p < 0.01$).

Mortality after AMI with different age

Mortality after AMI in patients differing in age was shown in Table 2. The mortalities within 30 days after AMI were insignificant between diabetic and non-dia-

betic patients when the age was below 45 years (6.3% vs. 5.7%, $p = 0.46$) and over or equal to 75 years (29.4% vs. 30.9%, $p = 0.05$). In the age groups between 45 and 60 years and between 60 and 75 years, the mortalities within 30 days after AMI were significant higher in diabetic patients (45-60 years: 8.7% vs. 7.1%, $p < 0.01$; 60-75 years: 18.2% vs. 16.3%, $p < 0.01$). The mortalities within 1 year, 3 years, and 5 years after AMI were significant higher in diabetic patients of all ages, except patients over or equal to 75 years within 1 year (49.4% vs. 48.0%, $p = 0.06$).

Mortality after AMI of patients who underwent PCI during index admission

Mortality after AMI of patients who underwent PCI during index admission was showed in Table 3. The mortalities after AMI of patients who underwent PCI during index admission were significantly lower than those of

Table 2. Mortality within 30 days and long-term mortality of first hospitalized diabetic and non-diabetic patients with acute myocardial infarction

	With diabetes		Without diabetes		Odds ratio (95% confidence interval)	p value
	Death (N)	Death (%)	Death (N)	Death (%)		
Patients with all age						
Within 30 days	3,724	18.1%	9,834	17.6%	1.04 (1.00-1.09)	0.06
Within 1 year	6,363	31.0%	14,996	26.8%	1.23 (1.19-1.27)	< 0.01
Within 3 years	8,706	42.4%	19,417	34.7%	1.39 (1.34-1.44)	< 0.01
Within 5 years	10,396	50.6%	23,031	41.1%	1.47 (1.42-1.52)	< 0.01
Patients with age < 45 years						
Within 30 days	52	6.3%	264	5.7%	1.12 (0.83-1.53)	0.46
Within 1 year	89	10.8%	348	7.5%	1.50 (1.17-1.92)	< 0.01
Within 3 years	119	14.5%	454	9.8%	1.56 (1.26-1.94)	< 0.01
Within 5 years	143	17.4%	590	12.7%	1.45 (1.19-1.77)	< 0.01
Patients with age between 45 and 60 years						
Within 30 days	436	8.7%	929	7.1%	1.25 (1.11-1.40)	< 0.01
Within 1 year	767	15.4%	1,289	9.9%	1.65 (1.50-1.82)	< 0.01
Within 3 years	1,122	22.5%	1,717	13.2%	1.91 (1.76-2.08)	< 0.01
Within 5 years	1,393	27.9%	2,143	16.5%	1.97 (1.82-2.12)	< 0.01
Patients with age between 60 and 75 years						
Within 30 days	1,782	18.2%	3,590	16.3%	1.14 (1.08-1.22)	< 0.01
Within 1 year	3,063	31.4%	5,498	25.0%	1.37 (1.30-1.45)	< 0.01
Within 3 years	4,247	43.5%	7,183	32.6%	1.59 (1.51-1.67)	< 0.01
Within 5 years	5,132	52.5%	8,680	39.4%	1.70 (1.62-1.78)	< 0.01
Patients with age \geq 75 years						
Within 30 days	1,454	29.4%	5,051	30.9%	0.93 (0.87-1.00)	0.05
Within 1 year	2,444	49.4%	7,861	48.0%	1.06 (1.00-1.13)	0.06
Within 3 years	3,218	65.0%	10,063	61.5%	1.17 (1.09-1.25)	< 0.01
Within 5 years	3,728	75.3%	11,618	71.0%	1.25 (1.16-1.34)	< 0.01

Table 3. Mortality within 30 days and long-term mortality of first hospitalized diabetic and non-diabetic patients with acute myocardial infarction underwent percutaneous coronary intervention (PCI) during index admission

	With diabetes		Without diabetes		Odds ratio (95% Confidence interval)	p value
	Death (N)	Death (%)	Death (N)	Death (%)		
Patients with all age underwent PCI						
Within 30 days	420	6.3%	1190	6.4%	0.98 (0.87-1.10)	0.70
Within 1 year	1020	15.2%	2157	11.6%	1.37 (1.26-1.48)	< 0.01
Within 3 years	1615	24.1%	3190	17.2%	1.53 (1.43-1.64)	< 0.01
Within 5 years	2162	32.2%	4212	22.6%	1.63 (1.53-1.73)	< 0.01
Patients with age < 45 years underwent PCI						
Within 30 days	10	2.6%	36	1.9%	1.39 (0.68-2.82)	0.37
Within 1 year	22	5.7%	61	3.2%	1.83 (1.11-3.02)	0.02
Within 3 years	31	8.1%	87	4.6%	1.83 (1.20-2.80)	0.01
Within 5 years	42	11.0%	138	7.3%	1.57 (1.09-2.26)	0.02
Patients with age between 45 and 60 years underwent PCI						
Within 30 days	59	2.8%	153	2.6%	1.07 (0.79-1.45)	0.66
Within 1 year	144	6.8%	246	4.2%	1.67 (1.35-2.05)	< 0.01
Within 3 years	248	11.7%	378	6.4%	1.93 (1.63-2.28)	< 0.01
Within 5 years	347	16.4%	530	9.0%	1.98 (1.71-2.29)	< 0.01
Patients with age between 60 and 75 years underwent PCI						
Within 30 days	192	6.2%	472	6.4%	0.96 (0.81-1.14)	0.65
Within 1 year	523	16.8%	889	12.1%	1.47 (1.31-1.66)	< 0.01
Within 3 years	835	26.8%	1313	17.8%	1.69 (1.53-1.87)	< 0.01
Within 5 years	1127	36.2%	1753	23.8%	1.82 (1.66-1.99)	< 0.01
Patients with age \geq 75 years underwent PCI						
Within 30 days	159	14.6%	529	15.3%	0.94 (0.78-1.14)	0.55
Within 1 year	331	30.4%	961	27.8%	1.13 (0.97-1.31)	0.11
Within 3 years	501	46.0%	1412	40.9%	1.23 (1.07-1.41)	< 0.01
Within 5 years	646	59.3%	1791	51.9%	1.35 (1.18-1.55)	< 0.01

patients without PCI treatment (within 30 days: 6.4% vs. 23.3%, $p < 0.01$; within 1 year: 12.6% vs. 35.5%, $p < 0.01$; with 3 years: 19.0% vs. 45.5%, $p < 0.01$; and within 5 years: 25.2% vs. 52.8%, $p < 0.01$). Regarding diabetic status, mortality within 30 days after AMI of patients who underwent PCI during index admission was insignificant between diabetic and non-diabetic patients (6.3% vs. 6.4%, $p = 0.70$), which included all age groups. Mortalities within 1 year, 3 years and 5 years after AMI were significantly higher in diabetic patients (within 1 year: 15.2% vs. 11.6%, $p < 0.01$; within 3 years: 24.1% vs. 17.2%, $p < 0.01$; within 5 years: 32.2% vs. 22.6%, $p < 0.01$), including all age groups, excepting patients over or equal to 75 years within 1 year (30.4% vs. 27.8%, $p = 0.11$).

DISCUSSION

This study provides a nationwide estimate in Taiwan

about the outcomes after 5-year follow-up among first hospitalized AMI patients with and without diabetes. The number of patients who participated was quite large, and nearly all the residents in Taiwan were enrolled. The duration of follow-up was also quite long. The length of hospital stay and the medical cost during admission were significantly higher in diabetic patients. The overall mortality within 30 days after AMI was insignificant, but the long-term mortality after AMI was significantly higher in diabetic patients than in non-diabetic patients. In patients with AMI who underwent PCI during index admission, the mortality rate within 30 days was insignificant, but the long-term mortality was significantly higher in diabetic patients than in non-diabetic patients. The mortalities within 30 days after AMI were insignificant when patients were under 45 years of age, or over or equal to 75 years, but they became significantly higher in diabetic patients between 45 and 60 years of age, or between 60 and 75 years. The

long-term mortality after AMI was significantly higher in diabetic patients of all ages, except for those patients over or equal to 75 years of age within 1 year.

Krumholz et al. found that the 30-day mortality rates of AMI patients in the United States were 18.9% in 1995 and 17.6% in 2006.¹⁶ In our study, the 30-day mortality rates of AMI patients were 18.1% in diabetic and 17.6% in non-diabetic patients during the study period. The mortality rates of AMI patients between the United States and Taiwan were similar.

Lopez-de-Andres et al. found that in patients admitted to hospital due to AMI from 2001 to 2006 in Spain, the mean hospital stay was significantly higher in diabetic patients than in non-diabetic patients (10.1 ± 8.7 vs. 9.2 ± 9.2 days, $p < 0.05$), but the medical cost did not differ significantly.¹⁷ However, Carral et al. found that diabetic patients hospitalized for CVD had longer hospital stays and were more costly than non-diabetic patients.¹³ In our study, both the length of hospital stay and the medical cost during admission were significantly higher in diabetic patients. Older age and additional comorbid conditions could explain the increased medical cost in diabetic patients.¹⁸ Local healthcare policy, such as diagnosis-related group (DRG), may also have an influence on the medical cost in different countries.¹⁹

Some studies have shown that short-term mortality after AMI was insignificant between diabetic and non-diabetic patients.^{4,5,20} However, the results of some other studies reached opposite results, which revealed that diabetic patients had a higher rate of short-term mortality after AMI than non-diabetic patients.^{6-10,17,21} Regarding those patients with AMI who underwent revascularization during index admission, some studies found that short-term mortality was insignificant between diabetic and non-diabetic patients.^{9,22} Nevertheless, other studies had a conflicting result, which discovered that diabetic patients have a higher short-term mortality.²³⁻²⁵ The influence of diabetes on short-term mortality after AMI seemed inconsistent, including in overall patients and in patients underwent revascularization, according to the finding of above studies. In our study, the mortality within 30 days after AMI was insignificant between diabetic and non-diabetic patients, including in overall patients and in patients underwent PCI during index admission. The differences of race, duration of follow-up, and predictors of mortality enrolled

should influence the impact of diabetes on short-term mortality. The strength of our study in part relied on the large sample size, the lack of selection of the cohort, and the long duration of follow-up.

Previous studies found that the long-term mortality after AMI was significantly higher in diabetic patients,^{7,9,21} which was consistent with our study. Besides, the difference in mortality after AMI between diabetic and non-diabetic patients increased with time in our study [OR ranging from 1.23 (95% CI 1.19-1.27) within 1 year to 1.39 (95% CI 1.34-1.44) within 3 years and 1.47 (95% CI 1.42-1.52) within 5 years], which was identical with another study.²⁶ In patients with AMI who underwent PCI, the long-term mortality was significant higher in diabetic patients and the difference also increased with time, compatible with previous studies.²³⁻²⁵ However, when patient age exceeded or was equal to 75 years, the mortality after AMI within 1 year became insignificant between diabetes and non-diabetes, including in overall patients and in patients underwent PCI. Nicolau et al. found that in patients with AMI, hyperglycemia was a better predictor for mortality in younger patients than in an elderly population, and advanced age itself was a strong independent risk factor for mortality in patients with AMI.²⁷ Therefore, diabetes had a weaker impact in elderly population, which was consistent with our study.

The mortality after AMI was significantly lower in patients who underwent PCI during index admission than in patients with conservative treatment. Gasior et al. found that the intervention group of AMI had significantly lower short-term and long-term mortalities than the conservative group,⁹ which was consistent with our study. As a result, the strategy of intervention should be a priority for consideration in patients with AMI to decrease the mortality, if the clinical conditions meet the suggestion of current guidelines for interventional treatment.^{28,29}

Study limitation

There are several limitations of our study. First, the date of mortality was defined as the ending date of coverage from NHI. However, Lien et al. found that the ending date of coverage from NHI is a good proxy for the mortality date.¹⁵ Second, some predictors of mortality after AMI, such as Killip classifications, ST or

non-ST elevation myocardial infarction, left ventricular ejection fraction, the medication used and renal function could not be jointly evaluated with diabetes, due to the limitation of NHIRD. The impacts of these predictors on diabetic and non-diabetics patients with AMI might need further investigation.

CONCLUSIONS

The length of hospital stay and the medical cost of admission were higher in diabetic patients. Mortality within 30 days after AMI was insignificant, including in the overall enrolled patient population, and in patients who underwent PCI. Long-term mortality after AMI was significantly higher in diabetic patients and the difference increased with time. Diabetes has a stronger influence on long-term mortality. Therefore, diabetic patients with AMI should be reinforced with the importance of vigorous preventive measures by lifestyle modification and medication adherence, to decrease long-term mortality.

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