Acta Cardiol Sin 2020;36:416–427

Original Article doi: 10.6515/ACS.202009_36(5).20200421A

Coronary Artery Disease

Effects of National Hospital Accreditation in Acute Coronary Syndrome on In-Hospital Mortality and Clinical Outcomes

Ta Ko,[1] Chia-Hung Yang,[2]* Chun-Tai Mao,[1] Li-Tang Kuo,[1] Ming-Jer Hsieh,[2] Dong-Yi Chen,[2] Chao-Yung Wang,[2] Yu-Sheng Lin,[3] I-Chang Hsieh,[2] Shao-Wei Chen,[4] Ming-Jui Hung,[1] Wen-Jin Cherng[2] and Tien-Hsing Chen[1]*

Background: Acute coronary syndrome (ACS) is a life-threatening medical condition that accounts for an annual expenditure of more than $300 billion in the United States. Hospital accreditation has been shown to improve patient and hospital outcomes for various conditions.

Objectives: This study aimed to determine the benefits of hospital accreditation in patients with ACS.

Methods: This nationwide population-based cohort study used Taiwan's National Health Insurance Research Database from 1997 to 2011 (n = 249,354). Multivariable logistic regression was used to analyze the risk of in-hospital events among those treated in accredited and non-accredited hospitals, and to compare outcomes in hospitals before and after accreditation. The effect of accreditation on these events was also stratified by accreditation grade.

Results: A total of 823 hospitals were included, of which 2.4% were medical centers, 13.7% were regional hospitals, and 83.8% were district hospitals. The in-hospital mortality [odds ratio (OR), 0.82; 95% confidence interval (CI), 0.79-0.85; p < 0.001] and recurrent acute myocardial infarction (AMI) admission (OR, 0.81; 95% CI, 0.71-0.93; p = 0.003) rates were significantly lower in the after-accreditation group than in the before-accreditation group. There was a substantial and marked decrease in the in-hospital mortality rate after accreditation in 2008.

Conclusions: This cohort study demonstrated that ACS accreditation was associated with better in-hospital mortality and recurrent AMI admission rates in ACS patients.

Key Words: Acute coronary syndrome • Hospital accreditation • In-hospital mortality

INTRODUCTION

Cardiovascular disease is the leading cause of death in the United States, Europe, and Taiwan,[1-4] accounting for almost 1.8 million deaths or 20% of all deaths in Europe annually, even after optimal medical treatment.[2] Moreover, the estimated annual cost is more than $300 billion in the United States and €196 billion in Europe[2,5] and the associated recurrence rate is high,[6,7] especially for acute coronary syndrome (ACS). Due to this high mortality rate and heavy economic burden, health care systems seek to optimize the management of ACS.

Guideline-based hospital accreditation may improve ACS outcomes. Peterson et al. demonstrated that hospi-

Received: May 31, 2019 Accepted: April 21, 2020

[1]Division of Cardiology, Department of Internal Medicine, Community Medicine Research Center, Chang Gung Memorial Hospital, Keelung; Chang Gung University College of Medicine, Taoyuan; [2]Division of Cardiology, Department of Internal Medicine, Percutaneous Coronary Intervention Center, Chang Gung Memorial Hospital, Linkou; Chang Gung University College of Medicine, Taoyuan; [3]Division of Cardiology, Department of Internal Medicine, Chang Gung Memorial Hospital, Chiayi; Chang Gung University College of Medicine, Taoyuan; [4]Department of Cardiac Surgery, Chang Gung Memorial Hospital, Linkou; Chang Gung University College of Medicine, Taoyuan, Taiwan.

Corresponding author: Dr. Tien-Hsing Chen, Division of Cardiology, Department of Internal Medicine, Community Medicine Research Center, Chang Gung Memorial Hospital, No. 222, Maijin Road, Keelung, Taiwan. Tel: 886-2-2432-9292 ext. 3181; E-mail: skyheart0826@gmail.com

* Ta Ko and Chia-Hung Yang contributed equally to this study.

tals with guideline-recommended treatment had lower in-hospital mortality rates than those that did not follow guideline-recommended treatment. Furthermore, every 10% increase in composite adherence at a hospital has been associated with a 10% decrease in the likelihood of in-hospital mortality, after risk adjustment.[8] Eagle et al. reported that using the Guidelines Applied in Practice program for acute myocardial infarction (AMI) care improved the 30-day and 1-year mortality rates.[9] Velasco et al. likewise found that adequate hospital process performance could reduce the length of stay, costs, and inappropriate application of procedures.[10] Ross et al. further showed that hospital accreditation could improve hospital compliance with guideline-based treatment.[11] Accordingly, a guideline-based hospital process performance guaranteed by hospital accreditation may be a way to improve the outcomes of ACS. In Taiwan, the Ministry of Health and Welfare (MOHW) and the Joint Commission of Taiwan (JCT) established hospital accreditation rules based on the American College of Cardiology/American Heart Association (ACC/AHA) and European Society of Cardiology (ESC) guidelines, and they have conducted hospital accreditation for ACS care every 3 years since 2009. However, the effects of this hospital accreditation program have not been proven. Therefore, this study aimed to determine the benefits of the MOHW and the JCT hospital accreditation program on ACS care.

METHODS

Data collection

We collected patient data from Taiwan's National Health Insurance Research Database (NHIRD), which covers approximately 23 million Taiwanese residents and included 99.0% and 99.5% of the Taiwanese population in 2004 and 2010, respectively.[12] The NHIRD includes data on personal characteristics, family relationships, clinical information, prescription details, examinations, and operations. Diagnoses in the NHIRD are coded according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. The accuracy of this coding has been validated.[13] All patient data and records were deidentified before analysis. This study was approved by the Ethics Institutional Review Board of Chang Gung Memorial Hospital.

Study cohorts and definitions

This nationwide population-based cohort study compared the effects of hospital accreditation on in-hospital mortality and recurrent AMI admission rates within 14 days in patients with AMI. We enrolled all patients aged ≥ 18 years with AMI admitted to hospitals between January 1, 1997, and December 31, 2011. The occurrence of AMI was detected using the discharge diagnoses during hospitalization (any myocardial infarction ICD-9-CM codes in one principal diagnosis and four secondary diagnoses). We divided the hospitals into two groups: control (unaccredited) and accredited (before and after accreditation) groups, to compare the effects of guideline-based accreditation. In addition, the hospitals in the accredited group were subdivided into high- and moderate-grade primary percutaneous coronary intervention (pPCI)-eligible groups according to the rules established by the MOHW and the JCT.

Accreditation program

The hospital accreditation program evaluated in this study was for certification for emergent and critical care according to the MOHW and JCT. The hospitals certified by this program are listed on the website of MOHW (https://dep.mohw.gov.tw/DOMA/np-980-106.html).[14] This program standardizes the management of acute stroke, ACS, acute trauma, emergent medical care, intensive medical care, and pediatric and obstetric emergencies.[14]

For the management of ACS, and especially ST-elevation myocardial infarction (STEMI), this accreditation program divides hospitals into high- and moderate-grade groups according to the time of the first electrocardiogram at arrival, the time of the first cardiac enzyme examination at arrival, dual-antiplatelet therapy in the emergency department, percutaneous coronary intervention (PCI) within 90 minutes, and fibrinolytic therapy within 30 minutes after arrival. In high-grade pPCI-eligible hospitals, > 80% of the patients receive the first electrocardiography (ECG) < 10 minutes after arrival, dual-antiplatelet therapy in the emergency department and fibrinolytics < 30 minutes after arrival; and > 75% of the patients receive PCI < 90 minutes after arrival. Hospitals with > 60% but < 75% of a door to balloon time < 90 minutes in pPCI are defined as moderate-grade hospitals.[14]

Study group

Figure 1 illustrates the study design and grouping. We analyzed the hospitals that were accredited from 2009 to 2011. In the hospitals which were accredited during 2009, the years 2008 to 2011 were defined as the after-accreditation period and the years before 2007 were defined as the before-accreditation period. In the hospitals which were accredited during 2010, the years 2009 to 2011 were defined as the after-accreditation period and the years before 2008 were defined as the before-accreditation period. In the hospitals which were accredited during 2011, the years 2010 to 2011 were defined as the after-accreditation period and the years before 2009 were defined as the before-accreditation period. As the NHIRD contained data until 2011, the hospitals that were accredited after 2012 were not analyzed. In the hospitals that did not join the accreditation program, we compared the years 1997-2007 with 2008-2011 (Supplemental Figure 1).

Outcomes and covariate measurements

We used ICD-9-CM codes to identify all outcomes for the index hospitalization. The primary outcomes consisted of in-hospital mortality and recurrent AMI admissions within 14 days. We also analyzed other consequences including heart failure within 14 days of admission, length of hospital stay, length of intensive care unit (ICU) stay, intra-aortic balloon pump (IABP) support, extracorporeal membrane oxygenation (ECMO) support, de novo dialysis, and cardiac rehabilitation. The definitions of cardiovascular death or death from other causes met the criteria of the Standardized Definitions for End Point Events in Cardiovascular Trials drafted by the Food and Drug Administration.[15]

Statistical analysis

Patient characteristics among the study groups (control, before-accreditation, after-accreditation) were compared using the chi-squared test for categorical variables and one-way analysis of variance for continuous variables with Bonferroni multiple comparisons (post hoc). We compared the control group in the early and late stages to analyze the time effects of accreditation on ACS outcomes. Furthermore, we compared the risk of in-hospital events among the study groups by using multivariable logistic regression after adjustments for hospital and patient characteristics. The total medical expenditure, length of hospital stay, and length of ICU stay during the index hospitalization were compared among study groups using multivariable linear regression. Moreover, we evaluated the effects of accreditation on in-hospital events stratified by accreditation grade (moderate versus high grade). The sensitivity analysis (comparing after accreditation with before accreditation) was restricted to the patients who were admitted with a principal discharge diagnosis of AMI and received a PCI during the same hospitalization. Statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS Version 22.0.; IBM Corp., Armonk, NY, USA).

RESULTS

Hospital characteristics

A total of 823 hospitals were included in this cohort study, of which 2.4% were tertiary hospitals, 13.7% were secondary hospitals, and 83.8% were district hospitals. Of all hospitals, 767 were unaccredited (control), 29 were moderate-grade pPCI-eligible, and 27 were high-grade pPCI-eligible hospitals. In total, 6.8% of the hospitals were accredited for ACS by the MOHW and the JCT, of which more than 50% were proprietary hospitals (72.3%). The median number of beds in these hospitals was 89 (Table 1).

Patient characteristics of the control group

Of the 249,354 patients admitted for AMI between

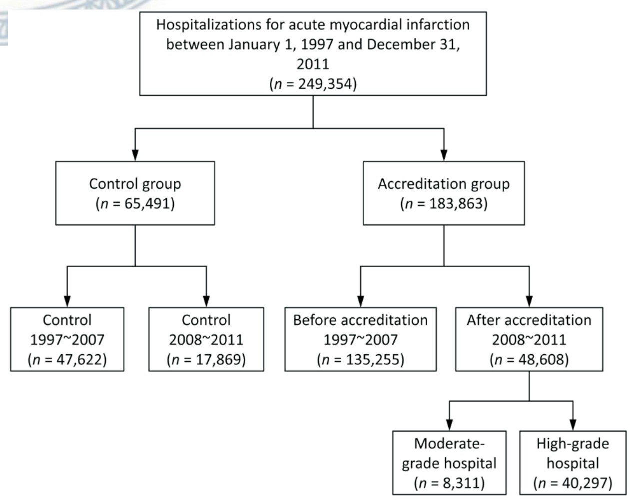


***Figure 1.** Flowchart of inclusion.*

Table 1. Hospital characteristics (N = 823)

Variables	Total	Control	Moderate-grade	High-grade
Number of hospital	823	767	29	27
Hospital level				
Medical center	20 (2.4)	0 (0.0)	0 (0.0)	19 (70.4)
Region hospital	113 (13.7)	78 (10.2)	28 (96.6)	8 (29.6)
District hospital	690 (83.8)	689 (89.8)	1 (3.4)	0 (0.0)
Owner type				
Government	71 (8.6)	62 (8.1)	6 (20.7)	3 (11.1)
Non-profit	119 (14.5)	87 (11.3)	16 (55.2)	14 (51.9)
Proprietary	595 (72.3)	585 (76.3)	7 (24.1)	5 (18.5)
Military	38 (4.6)	33 (4.3)	0 (0.0)	5 (18.5)
Hospital location				
North	237 (28.8)	216 (28.2)	11 (37.9)	10 (37.0)
Middle	217 (26.4)	206 (26.9)	6 (20.7)	5 (18.5)
South	325 (39.5)	306 (39.9)	9 (31.0)	10 (37.0)
East/offshore islands	44 (5.3)	39 (5.1)	3 (10.3)	2 (7.4)
Number of beds	89 [47, 894]	80 [44, 582]	707 [532, 1301]	1330 [1026, 3199]
Number of ICU beds	0 [0, 70]	0 [0, 38]	50 [28, 102]	98 [74, 287]
Number of cardiologist	0 [0, 4]	0 [0, 2]	4 [3, 10]	7 [4, 21]
Number of cardiac surgeon	0 [0, 2]	0 [0, 1]	1 [0, 3]	3 [2, 9]
Number of AMI admissions*	18 [4, 1689]	14 [4, 439]	1882 [1402, 3529]	4133 [2155, 9567]

* Total number from 1997 to 2011.
Data source: https://dep.mohw.gov.tw/DOMA/np-980-106.html. Department of Medical Affairs, Ministry of Health and Welfare. The announcement from 2010 to 2012.
AMI, acute myocardial infarction; ICU, intensive care unit.

1997 and 2011, 65,491 (26.3%) were included in the control group. Patients in the late-stage control group (2008-2011) were older, had higher prevalence rates of previous myocardial infarction and stroke, peripheral arterial disease, hypertension, dyslipidemia, diabetes mellitus, coronary artery disease, heart failure, chronic kidney disease, dialysis, atrial fibrillation, gout, and malignancy, and received more PCIs and coronary artery bypass grafting (CABG) than those in the early-stage control group (1997-2007). Noticeably, no significant difference was observed in in-hospital mortality between the early- and late-stage control groups (Table 2).

Patient characteristics of the accreditation group

A total of 183,863 patients were included in the accreditation group. Patients in the after-accreditation group were older, had higher prevalence rates of previous myocardial infarction and stroke, peripheral arterial disease, hypertension, dyslipidemia, diabetes mellitus, coronary artery disease, heart failure, chronic kidney disease, dialysis, atrial fibrillation, gout, chronic obstructive pulmonary disease, and malignancy, and received more CABG and PCIs than those in the before-accreditation group. The rate of in-hospital mortality was significantly lower in the after-accreditation group than in the before-accreditation group (Table 3).

In-hospital outcomes

After adjusting for comorbidities and age, the rate of in-hospital mortality was significantly lower in the after-accreditation group [odds ratio (OR), 0.82; 95% confidence interval (CI), 0.79-0.85; $p < 0.001$] than in the before-accreditation group. After further adjusting for IABP, ECMO, dopamine use, epinephrine use, norepinephrine use, ICU duration, and presence of heart failure during the AMI admission, the in-hospital mortality rate was still lower in the after-accreditation group than in the before-accreditation group (OR, 0.74; 95% CI, 0.71-0.77; $p < 0.001$) (Supplemental Table 1). The incidence of recurrent AMI admissions within 14 days was lower in the after-accreditation group. In contrast, accreditation was not significantly associated with the rate of heart failure admission within 14 days. In the after-accreditation group, IABP support (OR, 1.06; 95% CI, 1.02-1.10)

Table 2. Characteristics and in-hospital outcomes of patients who were hospitalized in the non-accreditation hospitals (N = 65,491)

Variables	Control 1997~2007	Control 2008~2011	p value
Number of admissions	47,622	17,869	–
Characteristics			
Age (year)	71.8 [61.5, 79.0]	73.9 [61.1, 82.2]	< 0.001
Male gender	31,032 (65.3)	11,525 (64.5)	0.071
Prior myocardial infarction	6,933 (14.6)	3,599 (20.1)	< 0.001
Prior stroke	7,861 (16.5)	4,653 (26.0)	< 0.001
Peripheral arterial disease	2,483 (5.2)	1,565 (8.8)	< 0.001
Prior PCI	2,282 (4.8)	2,269 (12.7)	< 0.001
Prior CABG	494 (1.0)	353 (2.0)	< 0.001
Prior carotid stenting	3 (0.0)	22 (0.1)	< 0.001
Prior other comorbidities			
Hypertension	24,795 (52.1)	12,218 (68.4)	< 0.001
Dyslipidemia	7,186 (15.1)	5,043 (28.2)	< 0.001
Diabetes mellitus	16,680 (35.0)	8,188 (45.8)	< 0.001
Coronary artery disease	9,094 (19.1)	5,284 (29.6)	< 0.001
Heart failure	7,270 (15.3)	3,936 (22.0)	< 0.001
Chronic kidney disease	3,330 (7.0)	1,815 (10.2)	< 0.001
Dialysis	1,114 (2.3)	990 (5.5)	< 0.001
Atrial fibrillation	3,915 (8.2)	2,061 (11.5)	< 0.001
Gout	3,683 (7.7)	1,795 (10.0)	< 0.001
COPD	12,680 (26.6)	4,631 (25.9)	0.066
Malignancy	2,566 (5.4)	1,612 (9.0)	< 0.001
In-hospital outcomes			
Categorical outcome			
In-hospital mortality	10,292 (21.6)	3,903 (21.8)	0.524
Re-AMI admission within 14 days	472 (1.0)	126 (0.7)	0.001
HF admission within 14 days	223 (0.5)	107 (0.6)	0.036
IABP replacement	755 (1.6)	638 (3.6)	< 0.001
ECMO replacement	428 (0.9)	167 (0.9)	0.667
de novo dialysis	776 (1.6)	575 (3.2)	< 0.001
Cardiac rehabilitation	552 (1.2)	567 (3.2)	< 0.001
Continuous outcome			
Length of stay (day)	5 [2, 10]	5 [3, 11]	< 0.001
Length of ICU stay (day)	1 [0, 3]	2 [0, 4]	< 0.001
Total medical expense ($\times 10^3$ NTD)	32.9 [13.7, 83.9]	76.9 [28.7, 157.9]	< 0.001

CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation; HF, heart failure; IABP, intra-aortic balloon pump; ICU, intensive care unit; PCI, percutaneous coronary intervention.

was more frequently used, but ECMO support (OR, 0.52; 95% CI, 0.50-0.56) was less frequently used. After accreditation, the rate of de novo kidney dialysis and cardiac rehabilitation significantly increased. The total medical expenditure of the index hospitalization increased in the after-accreditation group (Table 4). In addition, we performed sensitivity analysis including the patients who were admitted with a principal discharge diagnosis of AMI and received a PCI. The results showed that the in-hospital mortality rate was significantly lower in the after-accreditation group than in the before-accreditation group (OR, 0.91; 95% CI, 0.85-0.98; p = 0.011) (Supplemental Table 2).

Subgroup analysis by pPCI eligibility

Both moderate- and high-grade pPCI-eligible hospitals had a decreased mortality rate after accreditation, and this effect was the same for both groups (p for interaction = 0.137). The effect of accreditation on increasing IABP use was similar in both hospital types (p for interaction = 0.534); however, the effect of accreditation on decreasing the use of ECMO support was more

Table 3. Patient characteristics of the accreditation group (N = 183,863)

Variables	Before accreditation 1997~2007	After accreditation 2008~2011	p value
Number of admissions	135,255	48,608	–
Age (year)	68.7 [57.3, 77.1]	69.3 [57.3, 79.2]	< 0.001
Male gender	95,497 (70.7)	34,289 (70.5)	0.630
Prior myocardial infarction	27,979 (20.7)	11,346 (23.3)	< 0.001
Prior stroke	18,138 (13.4)	8,636 (17.8)	< 0.001
Peripheral arterial disease	7,817 (5.8)	3,742 (7.7)	< 0.001
Prior PCI	14,805 (10.9)	8,786 (18.1)	< 0.001
Prior CABG	2,371 (1.8)	1,601 (3.3)	< 0.001
Prior carotid stenting	49 (0.0)	123 (0.3)	< 0.001
Prior other comorbidities			
Hypertension	74,222 (54.9)	32,079 (66.0)	< 0.001
Dyslipidemia	35,854 (26.5)	17,897 (36.8)	< 0.001
Diabetes mellitus	51,057 (37.7)	21,287 (43.8)	< 0.001
Coronary artery disease	30,365 (22.5)	14,792 (30.4)	< 0.001
Heart failure	18,067 (13.4)	8,561 (17.6)	< 0.001
Chronic kidney disease	9,834 (7.3)	4,030 (8.3)	< 0.001
Dialysis	4,861 (3.6)	3,289 (6.8)	< 0.001
Atrial fibrillation	11,385 (8.4)	4,786 (9.8)	< 0.001
Gout	10,764 (8.0)	4,420 (9.1)	< 0.001
COPD	19,459 (14.4)	6,815 (14.0)	0.048
Malignancy	8,233 (6.1)	4,349 (8.9)	< 0.001
In-hospital mortality	21,580 (16.0)	6,761 (13.9)	< 0.001

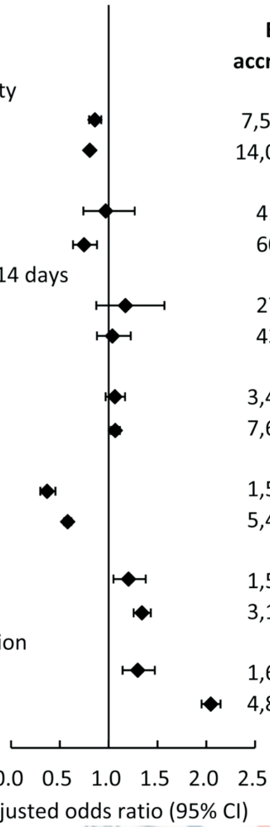
CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention.

Table 4. In-hospital outcomes of patients who were hospitalized in the accreditation hospitals

Variable	Number of event (%)		Adjusted odds ratio or *B* and 95% CI for after accreditation*	
	Before accreditation (n = 135,255)	After accreditation (n = 48,608)	OR/*B* (95% CI)	p
Categorical outcome				
In-hospital mortality	21,580 (16.0)	6,761 (13.9)	0.82 (0.79-0.85)	< 0.001
Re-AMI admission within 14 days	1,018 (0.8)	284 (0.6)	0.81 (0.71-0.93)	0.003
HF admission within 14 days	712 (0.5)	304 (0.6)	1.07 (0.92-1.23)	0.389
IABP replacement	11,155 (8.2)	4,363 (9.0)	1.06 (1.02-1.10)	0.006
ECMO replacement	6,976 (5.2)	1,557 (3.2)	0.52 (0.50-0.56)	< 0.001
de novo dialysis	4,688 (3.5)	2,174 (4.5)	1.31 (1.23-1.38)	< 0.001
Cardiac rehabilitation	6,440 (4.8)	4,756 (9.8)	1.85 (1.77-1.93)	< 0.001
Continuous outcome				
Length of stay (day)#	7 [4, 13]	7 [4, 13]	-0.40 (-0.55, -0.24)	< 0.001
Length of ICU stay (day)#	3 [1, 5]	3 [1, 5]	-0.07 (-0.14, 0.01)	0.092
Total medical expense ($\times 10^3$ NTD)#	129 [57, 198]	149 [88, 223]	12.78 (9.98, 15.58)	< 0.001

* Adjusted for the variables listed in Table 1 and Table 2. # Regression coefficient and its 95% confidence interval (CI).

apparent in moderate-grade hospitals (p for interaction = 0.004). The rate of cardiac rehabilitation after accreditation was significantly higher in high-grade hospitals than in moderate-grade hospitals (p for interaction < 0.001; Figure 2). Figure 3 demonstrates the trend of decreasing in-hospital mortality rates across the study period (before and after accreditation) in both the moderate-grade and high-grade hospitals. As mentioned earlier, the observed effect of accreditation between the moderate-grade and high-grade hospitals was not signifi-



	Event (%) Before accreditation	Event (%) After accreditation	Adjusted odds ratio (95% CI)	*P* value	*P* value for interaction
In-hospital mortality					0.137
Moderate-grade	7,552 (15.4)	1,172 (14.1)	0.86 (0.80, 0.92)	<0.001	
High-grade	14,028 (16.3)	5,589 (13.9)	0.81 (0.78, 0.84)	<0.001	
AMI with 14 days					0.190
Moderate-grade	417 (0.8)	66 (0.8)	0.97 (0.74, 1.27)	0.817	
High-grade	601 (0.7)	218 (0.5)	0.75 (0.64, 0.88)	0.001	
Heart failure with 14 days					0.766
Moderate-grade	279 (0.6)	58 (0.7)	1.17 (0.87, 1.57)	0.292	
High-grade	433 (0.5)	246 (0.6)	1.04 (0.88, 1.23)	0.657	
IABP support					0.534
Moderate-grade	3,460 (7.0)	602 (7.2)	1.06 (0.97, 1.17)	0.196	
High-grade	7,695 (8.9)	3,761 (9.3)	1.07 (1.02, 1.12)	0.003	
ECMO support					0.004
Moderate-grade	1,506 (3.1)	104 (1.3)	0.37 (0.30, 0.45)	<0.001	
High-grade	5,470 (6.4)	1,453 (3.6)	0.58 (0.55, 0.62)	<0.001	
de novo dialysis					0.118
Moderate-grade	1,557 (3.2)	303 (3.6)	1.20 (1.05, 1.38)	0.008	
High-grade	3,131 (3.6)	1,871 (4.6)	1.34 (1.26, 1.43)	<0.001	
Cardiac rehabilitation					<0.001
Moderate-grade	1,637 (3.3)	347 (4.2)	1.30 (1.14, 1.47)	<0.001	
High-grade	4,803 (5.6)	4,409 (10.9)	2.05 (1.95, 2.15)	<0.001	

Figure 2. *Subgroup analysis of pPCI-eligible hospitals showed no significant difference in the rate of in-hospital mortality (p for interaction = .137) and significant difference in the rate of ECMO use (p for interaction = .004) and cardiac rehabilitation (p for interaction < .001) between the two groups. Adjusted for the variables listed in Table 1 and Table 2.*

cantly different (p for interaction = 0.137; Figure 2).

DISCUSSION

This nationwide population-based cohort study of patients with AMI demonstrated that the national accreditation program was significantly associated with a better prognosis in the ACS patients. This finding was proven by comparing unaccredited and accredited hospitals. Furthermore, consistent results were also found by comparing the same hospital before and after accreditation. The ACS accreditation program was independently associated with lower rates of in-hospital mortality and recurrent AMI admissions within 14 days. Among the hospitals with different accreditation grades, no significant differences were observed in in-hospital mortality and recurrent AMI admissions within 14 days.

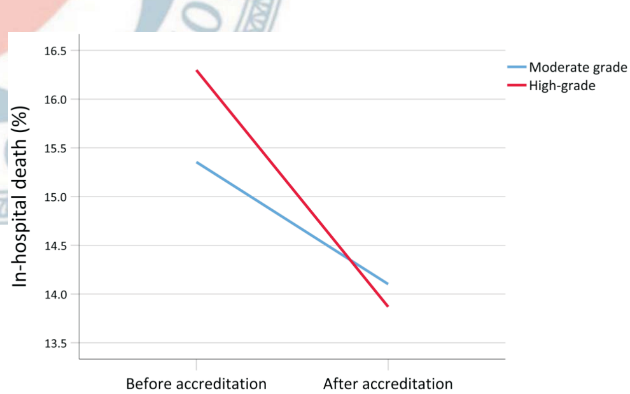


Figure 3. *The trend of decreasing in-hospital mortality rates before and after accreditation in both the moderate-grade or high-grade hospitals.*

Accreditation programs to improve a patient's life span and quality of life have been implemented for many diseases, surgical procedures, and in many types of hospitals.[11,16-18] Shaw et al. reported that accreditation was positively associated with a standardized medical care pathway according to guidelines, especially for AMI and stroke.[15] In addition, Eagle et al. reported that guideline-based standardized care was correlated with a 21% to 26% reduction in mortality, particularly at 30 days and one year.[9] Our study also revealed decreased in-hospital mortality in an accredited hospital, which is consistent with previous studies.

Our study period included the eras of bare-metal stents and first-generation and second-generation drug-eluting stents (DES), and the evolution of stent technology may have improved the prognosis of patients with coronary artery disease.[19-22] However, an in-depth systemic review by Feinberg et al. found that patients receiving DESs had a lower incidence of target vessel revascularization than those receiving BMSs, and that the all-cause mortality rate was similar between them.[22] The SPIRIT III, SPIRIT IV, and COMPARE trials also revealed a similar risk of mortality between first-generation and second-generation DESs.[21,23] Therefore, advances in stent technology may not have affected our primary outcome (in-hospital mortality). Furthermore, our study demonstrated that hospital accreditation was still a strong independent factor associated with improved in-hospital mortality after full adjustments.

Unlike accreditation programs in other countries, the rules for ACS accreditation in Taiwan are specified by the MOHW and the JCT according to the health insurance policies of the Taiwanese government. By using these policies, accredited hospitals can receive more reimbursements for treating the same diseases. Hence, health policies change not only patient safety systems and clinical review but also clinical practice. This cohort study demonstrated that, when cardiologists started actively following pPCI, the rates of in-hospital mortality and recurrent AMI admissions within 14 days decreased. Significant improvements in outcomes were noted in the patients and hospitals, and were considered to be highly associated with the accreditation program.

The ACS accreditation program involves guideline-based performance metrics and includes dual-antiplatelet therapy in the emergency department, the first ECG < 10 minutes after arrival, and PCI < 90 minutes or fibrinolytic therapy < 30 minutes after arrival.[14,24] Because this guideline-based accreditation system and its effects have been previously reported, the medical staff can reliably follow the accreditation program to improve clinical outcomes.[25] However, this accreditation program does not involve the administration of beta-blockers and renin-angiotensin system inhibitors. Most randomized trials on beta-blockers and renin-angiotensin system inhibitors in ACS patients were performed in the era where reperfusion or fibrinolytic therapy was not available, and these medications can provide long-term survival in heart failure patients. A modern observational study evaluating the effects of early versus delayed oral beta-blockers in ACS showed similar in-hospital mortality in both groups after full adjustments.[26] Another recent cohort study demonstrated that ACS patients with or without beta-blockers had a similar survival rate at 30 days, 6 months and 1 year if they did not have heart failure or left ventricular dysfunction.[27] A recent systematic review in the Cochrane library revealed that angiotensin-converting enzyme inhibitors may reduce mortality after 10 days,[28] whereas the medium ACS hospital course was 7 days in our study cohort. Therefore, in-hospital mortality, our major outcome, may not be influenced by these medications.

The in-hospital mortality rate in this study was 13.9% from 2008 to 2011, whereas an important ACS study in Taiwan, the Taiwan ACS Full Spectrum Registry, published in 2011 reported an in-hospital mortality rate of 1.8% from 2008 to 2010, which is much lower than ours.[29] This registry included 3183 patients at 39 hospitals focusing on unstable angina and type 1 AMI composed of STEMI and non-ST elevation myocardial infarction (NSTEMI) with a mean age of 63 years. In addition, 52.3% of their patients were diagnosed with STEMI, and 87.7% of the analyzed population received coronary revascularization procedures such as PCI and CABG.[29] On the other hand, we enrolled patients with traditional AMI defined as a rise and/or fall in cardiac enzymes combined with symptoms of acute myocardial ischemia (e.g., chest pain and dyspnea) or new ECG changes.[30] Therefore, both type 1 and type 2 AMI patients were included in our study.[30] In addition, The mean age of our study cohort was 69 years, which is older than the patients in the Taiwan registry, and only 41% of our study population received PCI. These factors may have led to the higher in-hospital mortality. After further analyzing the results of AMI patients undergoing PCI in our study population (Supplemental Table 2), the in-hospital mortality rate was 5.9%, which is compatible with the results of the Global Registry of Acute Coronary Events which reported in-hospital mortality rates of 7% and 6% in patients with STEMI and NSTEMI, respectively.[31] However, our results are still worse than those in the Taiwan ACS registry even after subgroup analysis. Patient selection bias and medication adherence may have caused this difference.

Some intriguing changes occurred following ACS hospital accreditation. First, the use of ECMO support significantly decreased but that of IABP support significantly increased, which implies that early activated PCI can avoid severe cardiogenic shock and reduce the complications of AMI.[32,33] Second, the incidence of de novo kidney dialysis significantly increased. According to the mandate of ACS accreditation, patients with STEMI are eligible to receive pPCI irrespective of their age or renal function, after informed consent has been received for the procedure. Therefore, the patients in the after-accreditation group were older and had a higher prevalence of diabetes mellitus and chronic kidney disease than those in the before-accreditation group, which may have resulted in de novo kidney dialysis. Third, the rate of cardiac rehabilitation in the after-accreditation group significantly increased and represented improved health care after AMI. Finally, among the pPCI-eligible hospitals with different grades, no significant difference was observed in in-hospital mortality. This result provides evidence that emergency medical systems can transfer ACS patients to moderate-grade pPCI-eligible hospitals when emergent PCI is available, and then reduce the burden on high-grade pPCI-eligible hospitals.

Our study has some limitations. First, we could not identify the severity of AMI, SYNTAX score of coronary artery disease or post-AMI left ventricular systolic function, all of which may affect the outcomes of ACS patients. However, we identified and adjusted for some possible proxy variables of AMI severity, including IABP, ECMO, dopamine use, epinephrine use, norepinephrine use, ICU duration, and presence of post-AMI heart failure. Second, we lacked laboratory data such as liver function, renal function, lactate level and N-terminal-proB-type natriuretic peptide level, which may have provided more detailed information. However, we included a history of chronic kidney disease, dialysis, heart failure, and other important comorbidities. Third, we did not clarify some factors that can influence long-term outcomes such as smoking, obesity, and the administration of beta-blockers and renin-angiotensin inhibitors, even though previous studies have reported no strong associations between these and short-term outcomes.[28,34,35] Finally, we did not categorize the ACS patients into STEMI or NSTEMI groups, as we found that the ICD-9-CM codes of STEMI were largely under-diagnosed in the NHIRD. This indicates that our cohort included both STEMI and NSTEMI patients, however, the accreditation program may not be able to affect the short-term outcomes of NSTEMI patients. Therefore, the benefits of the accreditation program observed in this study may be under-estimated.

CONCLUSIONS

This cohort study clearly demonstrated that ACS accreditation was independently and significantly associated with lower rates of in-hospital mortality and recurrent AMI admissions in ACS patients.

ACKNOWLEDGMENT

This work was supported by grants from the Chang Gung Memorial Hospital, Taiwan (CGRPG2F0011, CLRPG 2C0021, CLRPG2C0022, CLRPG2C0023, CLRPG2C0024, CLRPG2G0081, CLRPG2G0082, and CLRPG2H0041).

We also thank Hsing-Fen Lin for statistical assistance during the completion of this manuscript.

CONFLICT OF INTEREST

All the authors declare no conflict of interest.

FINANCIAL DISCLOSURE

None.

REFERENCES

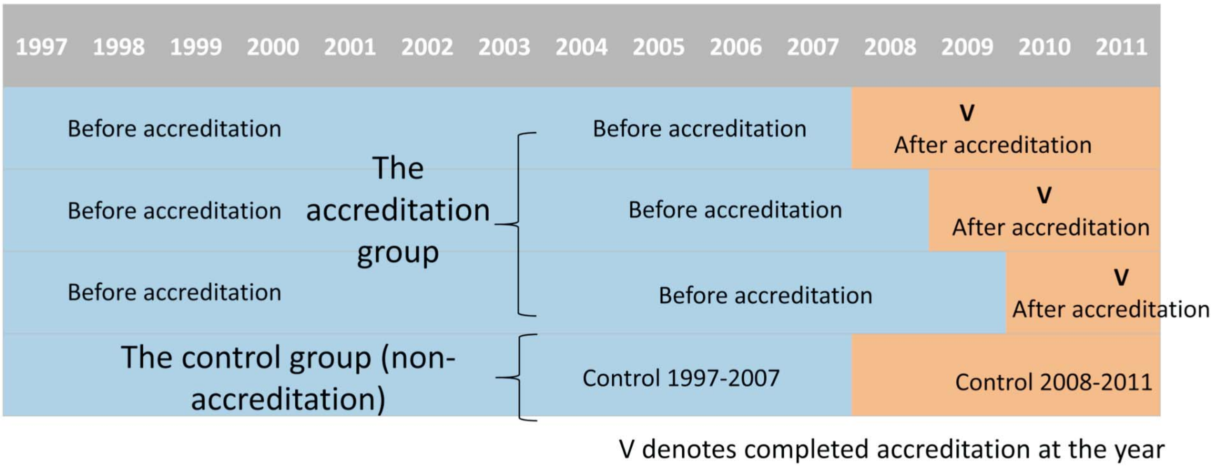
1. Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics-2019 update: a report from the American Heart Association. *Circulation* 2019;139:e56-528.

2. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe 2014: epidemiological update. *Eur Heart J* 2014;35:2929.
3. Peters SAE, Wang X, Lam TH, et al. Clustering of risk factors and the risk of incident cardiovascular disease in Asian and Caucasian populations: results from the Asia Pacific Cohort Studies Collaboration. *BMJ Open* 2018;8:e019335.
4. Ministry of Health and Welfare (Taiwan). Taiwan's leading causes of death in 2016. Available from: https://www.mohw.gov.tw/cp-115-33347-2.html. Accessed March 16, 2019.
5. Korsnes JS, Davis KL, Ariely R, et al. Health care resource utilization and costs associated with nonfatal major adverse cardiovascular events. *J Manag Care Spec Pharm* 2015;21:443-50.
6. Roshandel G, Khoshnia M, Poustchi H, et al. Effectiveness of polypill for primary and secondary prevention of cardiovascular diseases (PolyIran): a pragmatic, cluster-randomised trial. *Lancet* 2019;394:672-83.
7. Qamar A, Giugliano RP, Bohula EA, et al. Biomarkers and clinical cardiovascular outcomes with ezetimibe in the IMPROVE-IT Trial. *J Am Coll Cardiol* 2019;74:1057-68.
8. Peterson ED, Roe MT, Mulgund J, et al. Association between hospital process performance and outcomes among patients with acute coronary syndromes. *JAMA* 2006;295:1912-20.
9. Eagle KA, Montoye CK, Riba AL, et al. Guideline-based standardized care is associated with substantially lower mortality in medicare patients with acute myocardial infarction: the American College of Cardiology's Guidelines Applied in Practice (GAP) Projects in Michigan. *J Am Coll Cardiol* 2005;46:1242-8.
10. Velasco FT, Ko W, Rosengart T, et al. Cost containment in cardiac surgery: results with a critical pathway for coronary bypass surgery at the New York Hospital-Cornell Medical Center. *Best Pract Benchmarking Healthc* 1996;1:21-8.
11. Ross MA, Amsterdam E, Peacock WF, et al. Chest pain center accreditation is associated with better performance of centers for Medicare and Medicaid services core measures for acute myocardial infarction. *Am J Cardiol* 2008;102:120-4.
12. Cheng SH, Chiang TL. The effect of universal health insurance on health care utilization in Taiwan. Results from a natural experiment. *JAMA* 1997;278:89-93.
13. Cheng CL, Lee CH, Chen PS, et al. Validation of acute myocardial infarction cases in the national health insurance research database in Taiwan. *J Epidemiol* 2014;24:500-7.
14. Department of Medical Affairs, the Ministry of Health and Welfare, Taiwan. Emergent and Critical Care Accreditation. 2019. Available from: https://dep.mohw.gov.tw/DOMA/np-980-106.html. Accessed March 16, 2019.
15. Hicks KA, Mahaffey KW, Mehran R, et al. 2017 cardiovascular and stroke endpoint definitions for clinical trials. *Circulation* 2018;137:961-72.
16. Shaw CD, Groene O, Botje D, et al. The effect of certification and accreditation on quality management in 4 clinical services in 73 European hospitals. *Int J Qual Health Care* 2014;26 Suppl 1:100-7.
17. Telem DA, Talamini M, Altieri M, et al. The effect of national hospital accreditation in bariatric surgery on perioperative outcomes and long-term mortality. *Surg Obes Relat Dis* 2015;11:749-57.
18. Demetriades D, Martin M, Salim A, et al. Relationship between American College of Surgeons trauma center designation and mortality in patients with severe trauma (injury severity score > 15). *J Am Coll Surg* 2006;202:212-5; quiz A45.
19. Stettler C, Wandel S, Allemann S, et al. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. *Lancet* 2007;370:937-48.
20. Schomig A, Dibra A, Windecker S, et al. A meta-analysis of 16 randomized trials of sirolimus-eluting stents versus paclitaxel-eluting stents in patients with coronary artery disease. *J Am Coll Cardiol* 2007;50:1373-80.
21. Kereiakes DJ, Sudhir K, Hermiller JB, et al. Comparison of everolimus-eluting and paclitaxel-eluting coronary stents in patients undergoing multilesion and multivessel intervention: the SPIRIT III (A Clinical Evaluation of the Investigational Device XIENCE V Everolimus Eluting Coronary Stent System [EECSS] in the Treatment of Subjects With De Novo Native Coronary Artery Lesions) and SPIRIT IV (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Subjects With De Novo Native Coronary Artery Lesions) randomized trials. *JACC Cardiovasc Interv* 2010;3:1229-39.
22. Feinberg J, Nielsen EE, Greenhalgh J, et al. Drug-eluting stents versus bare-metal stents for acute coronary syndrome. *Cochrane Database Syst Rev* 2017;8:Cd012481.
23. Kedhi E, Joesoef KS, McFadden E, et al. Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice (COMPARE): a randomised trial. *Lancet* 2010;375:201-9.
24. Puymirat E, Caudron J, Steg PG, et al. Prognostic impact of non-compliance with guidelines-recommended times to reperfusion therapy in ST-elevation myocardial infarction. The FAST-MI 2010 registry. *Eur Heart J Acute Cardiovasc Care* 2017;6:26-33.
25. Cannon CP, Hand MH, Bahr R, et al. Critical pathways for management of patients with acute coronary syndromes: an assessment by the National Heart Attack Alert Program. *Am Heart J* 2002;143:777-89.
26. Bugiardini R, Cenko E, Ricci B, et al. Comparison of early versus delayed oral beta blockers in acute coronary syndromes and effect on outcomes. *Am J Cardiol* 2016;117:760-7.
27. Dondo TB, Hall M, West RM, et al. Beta-blockers and mortality after acute myocardial infarction in patients without heart failure or ventricular dysfunction. *J Am Coll Cardiol* 2017;69:2710-20.
28. Perez MI, Musini VM, Wright JM. Effect of early treatment with anti-hypertensive drugs on short and long-term mortality in patients with an acute cardiovascular event. *Cochrane Database Syst Rev* 2009:Cd006743.
29. Shyu KG, Wu CJ, Mar GY, et al. Clinical characteristics, management and in-hospital outcomes of patients with acute coronary syndrome-observation from the Taiwan ACS full spectrum regis-

try. *Acta Cardio Sin* 2011;27:135-44.

30. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). *Circulation* 2018;138:e618-51.
31. Steg PG, Goldberg RJ, Gore JM, et al. Baseline characteristics, management practices, and in-hospital outcomes of patients hospitalized with acute coronary syndromes in the Global Registry of Acute Coronary Events (GRACE). *Am J Cardiol* 2002;90:358-63.
32. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003;361:13-20.
33. Babaev A, Frederick PD, Pasta DJ, et al. Trends in management and outcomes of patients with acute myocardial infarction complicated by cardiogenic shock. *JAMA* 2005;294:448-54.
34. Yadav M, Mintz GS, Genereux P, et al. The smoker's paradox revisited: a patient-level pooled analysis of 18 randomized controlled trials. *JACC Cardiovasc Interv* 2019;12:1941-50.
35. Global BMI Mortality Collaboration, Di Angelantonio E, Bhupathiraju Sh N, et al. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet* 2016;388:776-86.

SUPPLEMENT



Supplemental Figure 1. *The illustration of comparing the 'after-accreditation', the 'before-accreditation' and the control groups (non-accreditation hospitals).*

Supplemental Table 1. In-hospital outcomes among the study groups

Variable	Number of event (%)			Adjusted odds ratio and 95% CI*			
				After accreditation vs. control 2008~2011		After accreditation vs. Before accreditation	
	Control between 2008~2011 (n = 17,869)	Before accreditation 1997~2007 (n = 135,255)	After accreditation 2008~2011 (n = 48,608)	OR/*B* (95% CI)	p	OR/*B* (95% CI)	p
In-hospital mortality	3,903 (21.8)	21,580 (16.0)	6,761 (13.9)	0.61 (0.56-0.66)	< 0.001	0.74 (0.71-0.77)	< 0.001

* Adjusted for the variables listed in Table 1 and Table 2 and further adjusted for IABP, ECMO, dopamine use, epinephrine use, norepinephrine use, ICU duration, and heart failure during the AMI admission. # Regression coefficient and its 95% CI.

Supplemental Table 2. In-hospital outcomes of patients who were hospitalized in the accreditation hospitals and who were admitted with a principal discharge diagnosis of AMI and received percutaneous coronary intervention during the same hospitalization

Variable	Number of event (%)		Adjusted odds ratio or *B* and 95% CI for after accreditation*	
	Before accreditation (n = 48,953)	After accreditation (n = 22,718)	OR/*B* (95% CI)	p
Categorical outcome				
In-hospital mortality	3,008 (6.1)	1,331 (5.9)	0.91 (0.85-0.98)	0.011
Re-AMI admission within 14 days	275 (0.6)	98 (0.4)	0.78 (0.61-1.0003)	0.0503
HF admission within 14 days	234 (0.5)	129 (0.6)	1.07 (0.85-1.35)	0.557
IABP replacement	5,705 (11.7)	2,525 (11.1)	0.98 (0.93-1.04)	0.552
ECMO replacement	882 (1.8)	421 (1.9)	1.03 (0.91-1.16)	0.696
de novo dialysis	986 (2.0)	610 (2.7)	1.22 (1.09-1.37)	0.001
Cardiac rehabilitation	1,030 (2.1)	1,891 (8.3)	3.67 (3.37-3.99)	< 0.001
Continuous outcome				
Length of stay (day)#	6 (4, 9)	5 (4, 8)	-0.62 (-0.78, -0.47)	< 0.001
Length of ICU stay (day)#	3 (2, 4)	2 (2, 4)	-0.29 (-0.38, -0.21)	< 0.001
Total medical expense ($\times 10^3$ NTD)#	161.9 (133.3, 207.5)	163.3 (136.9, 212.5)	3.36 (0.46, 6.26)	0.023

* Adjusted for the variables listed in Table 1 and Table 2. # Regression coefficient and its 95% CI.