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ORIGINAL ARTICLE

Institutional Characteristics and Prognosis of Acute Myocardial Infarction With Cardiogenic Shock in Japan
— Analysis From the JROAD/JROAD-DPC Database —

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Background: The high mortality of acute myocardial infarction (AMI) with cardiogenic shock (i.e., Killip class IV AMI) remains a challenge in emergency cardiovascular care. This study aimed to examine institutional factors, including the number of JCS board-certified members, that are independently associated with the prognosis of Killip class IV AMI patients.

Methods and Results: In the Japanese registry of all cardiac and vascular diseases-diagnosis procedure combination (JROAD-DPC) database (years 2012–2016), the 30-day mortality of Killip class IV AMI patients (n=21,823) was 42.3%. Multivariate analysis identified age, female sex, admission by ambulance, deep coma, and cardiac arrest as patient factors that were independently associated with higher 30-day mortality, and the numbers of JCS board-certified members and of intra-aortic balloon pumping (IABP) cases per year as institutional factors that were independently associated with lower mortality in Killip class IV patients, although IABP was associated with higher mortality in Killip classes I–III patients. Among hospitals with the highest quartile (≥9 JCS board-certified members), the 30-day mortality of Killip class IV patients was 37.4%.

Conclusions: A higher numbers of JCS board-certified members was associated with better survival of Killip class IV AMI patients. This finding may provide a clue to optimizing local emergency medical services for better management of AMI patients in Japan.

Key Words: Board-certified member; Coronary artery bypass graft surgery; Education; Extracorporeal circulation; Percutaneous coronary intervention

The in-hospital mortality rate of acute myocardial infarction (AMI) has been decreased to 4–5% owing to the spread of coronary care units and the generalization of emergency coronary reperfusion therapy.[1,2] However, a recent report from the Japanese Circulation Society (JCS) Cardiovascular Shock Registry (2012–2015), a prospective, observational, multicenter, cohort study that accumulated 979 cardiovascular shock patients among 82 JCS-certified teaching hospitals, revealed that the 30-day mortality of acute coronary syndrome (ACS) with cardiogenic shock was as high as 34%, which remains a challenge in emergency cardiovascular medicine.[3,4]

Because comprehensive management of cardiogenic shock state as well as early reperfusion therapy is vitally important for the treatment of AMI with cardiogenic shock (i.e., Killip class IV), functionally sufficient medical facilities

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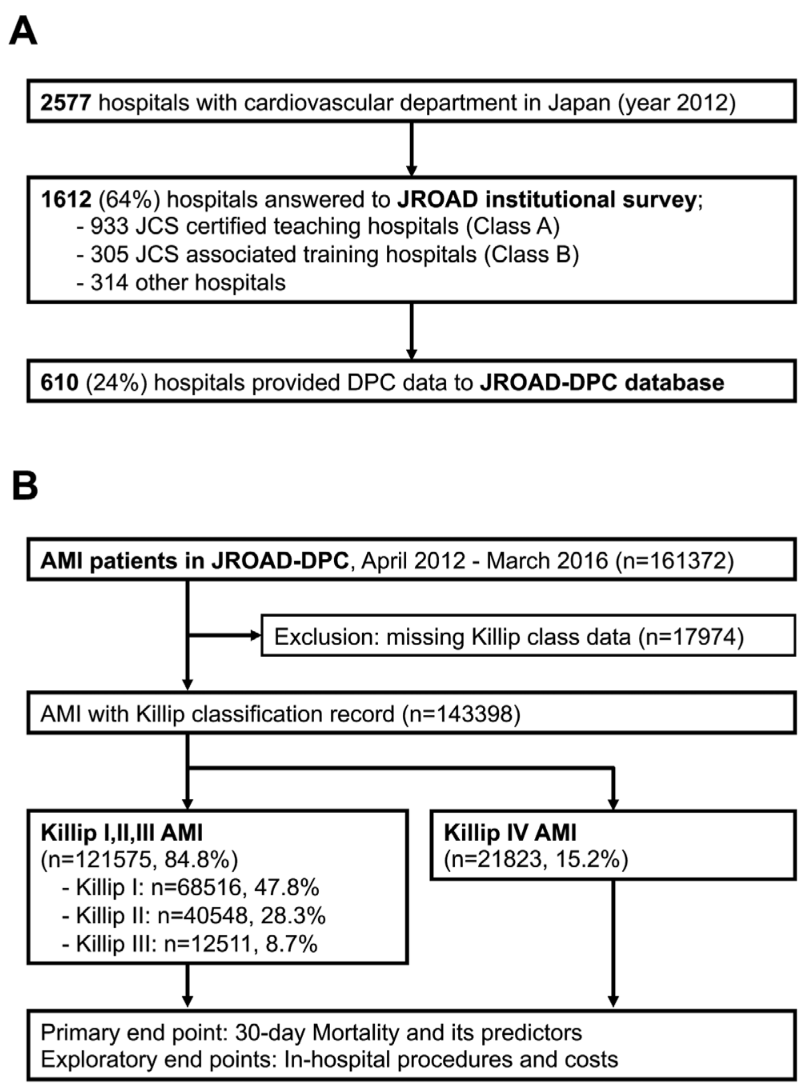

Figure 1. Study flowcharts. (**A**) Structure of JROAD institutional survey and JROAD-DPC database. (**B**) Patient enrollment. AMI, acute myocardial infarction; DPC, diagnosis procedure combination; JROAD, Japanese registry of all cardiac and vascular diseases.

and experienced medical staff are indispensable to increasing the chance of survival of patients with Killip class IV AMI. Current guidelines, including the JCS 2018 guideline on diagnosis and treatment of ACS[5] and US guideline for the management of ST-elevation myocardial infarction (STEMI),[6] state that patients with suspected STEMI should be transported to a primary percutaneous coronary intervention (PCI) capable center, but there is no mention of any other institutional factors based on a cardiogenic shock state. Because PCI capability is available atmore than 1,000 hospitals in Japan,[7] it is important to identify institutional characteristics in addition to PCI capability that are associated with outcomes of patients with Killip class IV AMI, in order to optimize the response of the local community emergency medical service (EMS) system.

The Japanese registry of all cardiac and vascular diseases (JROAD) study is a questionnaire-based survey steered by the JCS among hospitals with cardiovascular medicine and surgery. The JROAD study has been accumulating the diagnosis procedure combination (DPC)-based per-diem payment health insurance claim data in a voluntary manner since 2012. One study based on the JROAD-DPC database during the year 2012–13 showed an association between the number of JCS board-certified members per

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cardiovascular beds and the death of AMI patients;[8] however, no study has clarified whether the effect of the number of JCS board-certified members on the mortality rate was independent of other institutional factors, although Kanaoka et al described in-hospital management and medical cost as consequences of the difference in the number of JCS board-certified members.[8]

This study aimed to examine institutional factors, including the number of JCS board-certified members, together with patient factors, that are independently associated with the prognosis of Killip class IV AMI patients, and to characterize hospitals with different numbers of JCS board-certified members, using the JROAD and JROAD-DPC database (years 2012–2015).

Methods

Database

The annual JROAD questionnaire includes inquiry about institutional characteristics such as the numbers of hospital beds, and JCS board-certified members (cardiologists and surgeons), patient admissions per year, and the numbers of PCI or coronary artery bypass graft (CABG) procedures per year, which are potentially associated with the outcomes of Killip class IV AMI patients. In the year 2012, 1,612 hospitals with cardiovascular beds, including all JCS-certified teaching hospitals, 933 JCS-certified teaching hospitals (Class A) with 2 JCS board-certified members and 30 cardiovascular beds, and 305 JCS-associated training hospitals (class B) with 1 JCS board-certified member and 15 cardiovascular beds in all districts in Japan participated in the JROAD survey.[9] The questionnaire items are listed in the **Supplementary Table 1**. Among these hospitals, 610 provided DPC/PDPS claim data of all patients discharged from their cardiovascular beds between April 1, 2012, and March 31, 2016, which was used to construct the JROAD-DPC database (**Figure 1A**). This dataset extracts records that contain all types of cardiovascular disease in any category of diagnosis from the DPC dataset defined by the Japanese Ministry of Health, Labour and Welfare (MHLW).[10,11] The following data were collectable in the JROAD-DPC database: patient age and sex, international classification of diseases (ICD)-10 diagnosis codes, Killip classification, route of admission, Japan coma scale on admission, treatment procedures, discharge status, and medical costs. The JROAD institutional survey data were merged with the per-patient data in the JROAD-DPC database to assess the association of institutional factors with the prognosis of each patient.

Definitions

The diagnosis of AMI was determined by the physician and identified according to the ICD-10 codes for AMI (I21.0, I21.1, I21.2, I21.3, I21.4, and I21.9) as the main diagnosis, the admission-precipitating diagnosis, or the most resource-consuming diagnosis for the hospitalization, as recorded in the DPC/PDPS claim data. The Killip classification on admission was determined by the attending physician: class I patients are free of rales and a 3rd heart sound (S3); class II patients have rales, but only to a mild to moderate degree (<50% of lung fields); class III patients have rales in more than half of each lung field; class IV patients have cardiogenic shock.[12] Deep coma was determined by the conscious levels of the Japan coma scale 300 (300, 300A, 300I, 300 IA, 300R, 300RA, 300 RI and 300RIA in the DPC data). The Japan coma scale comprises 4 main categories: 0 and 1-, 2-, and 3-digit codes corresponding to alert, awake without stimuli, arousable with some stimuli, and unarousable by a forceful stimulus, respectively. Each code is further divided into 3 subcategories: 1, 2 and 3 in the 1-digit code, 10, 20, and 30 in the 2-digit code, and 100, 200, and 300 in the 3-digit code. The Japan coma scale of 0 is equal to the Glasgow coma scale of 15 (E4V5M6), while a Japan coma scale of 300 corresponds to Glasgow coma scale of 3 (E1V1M1).[13] Cardiac arrest was determined by the ICD-10 diagnosis code I46.0 (Cardiac arrest with successful resuscitation).

Outcomes

We defined death on day 30 from admission as the primary outcome of this study, which was identified from the JROAD-DPC database. Because the DPC database covers in-hospital medical procedures and survival or death, survival at discharge before day 30 was handled as survival on day 30. Given that the number of JCS board-certified members independently predicts the prognosis of AMI, we characterized other institutional factors, patient factors, in-hospital procedures, including coronary revascularization (i.e,. PCI or CABG), or circulatory support with veno-arterial extracorporeal membrane oxygenation (VA-ECMO), and medical costs for patients grouped according to the quartiles of the number of JCS board-certified members in their hospitals to dertermine the consequence of having JCS board-certified members. The medical costs were calculated as the sum of DPC/PDPS bundled payment and fee-for-service, including surgical and medical procedures, but excluding the food fees.[14]

Statistical Analysis

Data are presented as mean±SD for normally distributed data, and as median interquartile range (IQR) for asymmetrically distributed data, or absolute number (proportion) for categorical data. The differences among quartiles were compared using analysis of variance for continuous variables and chi-square test for non-continuous and categorical variables. The main outcome measure was 30-day mortality. The predictors of mortality were assessed by univariate analysis and a multivariate logistic regression model. The tendency for quartile 30-day mortality was analyzed using the Cochran-Armitage trend test. We defined statistical significance as $P<0.05$. Stata version 14.2 for Windows (StataCorp, College Station, TX, USA) was used for statistical analyses.

Ethics Statement

JROAD-DPC study was planned in accordance with the World Medical Association Declaration of Helsinki and approved by the institutional review board of the National Cerebral and Cardiovascular Center (NCVC), Osaka, Japan, which waived the requirement for individual informed consent according to the "opt-out" principle. Each participating hospital anonymized each patient's identity in the DPC/PDPS claim data by a code change equation and submitted the DPC/PDPS claim data to the NCVC. The specific study plan of this study was reviewed and approved by the Ethics Committee of the Kyushu University Hospital, Fukuoka, Japan (institutional study no. 28-358).

Results

Patient Characteristics

In the per-patients JROAD-DPC database, 161,372 patients with AMI were identified according to the ICD-10 codes

Table 1. Baseline Characteristics of the Study

Factors	Overall (n=143,398)	Killip I–III (n=121,575)	Killip IV (n=21,823)	P value Killip I–III vs. IV
Patient factors (JROAD-DPC)				
Age, median [IQR]	70 [61, 79]	70 [60, 79]	74 [64, 82]	<0.001
Female sex, n (%)	38,521 (27%)	31,737 (26%)	6,784 (31%)	<0.001
Admission by ambulance, n (%)	94,256 (66%)	76,784 (63%)	17,472 (80%)	<0.001
Deep coma, n (%)	6,342 (4%)	1,018 (1%)	5,324 (24%)	<0.001
Cardiac arrest	1,509 (1.1%)	352 (0.3%)	1,157 (5.3%)	<0.001
Institutional factors (JROAD survey)				
Hospital beds, n	465 [343, 612]	462 [343, 610]	481 [347, 641]	<0.001
JCS board-certified members, n	5 [3, 8]	5 [3, 8]	5 [3, 8]	<0.001
AMI patients, n/year	84 [54, 127]	85 [55, 129]	81 [51, 121]	<0.001
HF patients, n/year	214 [152, 298]	215 [152, 299]	211 [151, 294]	<0.001
PCI, n/year	281 [182, 414]	286 [184, 420]	258 [170, 395]	<0.001
Emergency PCI, n/year	90 [54, 132]	90 [55, 134]	87 [50, 128]	<0.001
IABP, n/year	23 [11, 42]	23 [11, 42]	23 [11, 40]	<0.001
VA-ECMO, n/year	5 [1, 12]	5 [1, 11]	5 [2, 12]	<0.001
Cardiac surgery, n/year	98 [54, 172]	99 [54, 172]	93 [54, 158]	<0.001

AMI, acute myocardial infarction; DPC, diagnosis procedure combination; HF, heart failure; IABP, intra-aortic balloon pump; IQR, interquartile range; JCS, Japanese Circulation Society; JROAD, Japanese registry of all cardiac and vascular diseases; PCI, percutaneous coronary intervention; VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

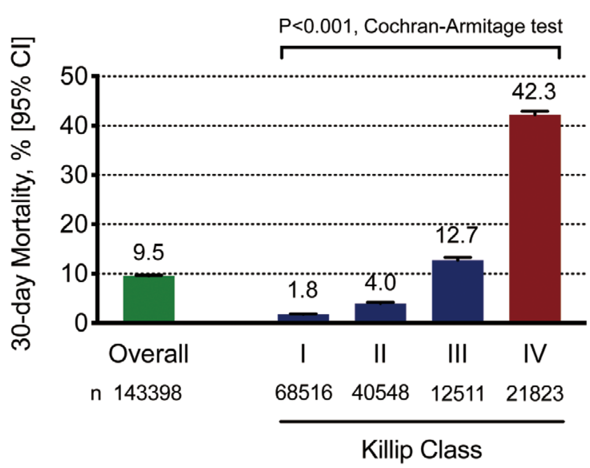

Figure 2. 30-day mortality of AMI patients per Killip classification in Japan (2012–2016). The 30-day mortality of AMI patients with different severity (Killip classes I–IV) was analyzed for trend with the Cochrane-Armitage test. AMI, acute myocardial infarction; CI, confidence interval.

for AMI (I21.0, I21.1, I21.2, I21.3, I21.4, and I21.9) as the main diagnosis, admission-precipitating diagnosis, or most resource-consuming diagnosis for the hospitalization. After exclusion of 17,974 patients who were missing Killip classification records, we analyzed 143,398 patients: 121,575 (84.8%) Killip class I, II or III patients and 21,823 (15.2%) Killip class IV (**Figure 1B**). Baseline characteristics of patients according to the Killip classifications are shown in the **Table 1**. Median age was 70 in the Killip class I–III group and 74 in the Killip class IV group. Female sex, admission by ambulance, deep coma (Japan coma scale 300/Glasgow coma scale E1V1M1), and resuscitated cardiac arrest (ICD-10 I46.0) were more frequently observed in the Killip class IV group (**Table 1**). For the institutional factors collected from the JROAD survey, the numbers of hospital beds and JCS board-certified members were larger in the Killip class IV group. The numbers of patients with AMI or heart failure per year, and all therapeutic procedures except VA-ECMO were larger in the Killip class I–III group (**Table 1**). Because the DPC/PDPS claim data contain only 4 comorbidities besides the primary diagnosis, several comorbidities might not be listed in the JROAD-DPC database. Therefore, we investigated the prescription data on admission in the database, although data were still missing for significant numbers of patients in the Killip class I–III group (40,883, 34%) and especially in the Killip class IV group (11,779, 54%, P<0.001) (**Supplementary Table 2**). Based on available data, medications for hypertension and diabetes, statins, and antithrombotic drugs were more frequently prescribed on admission in the Killip class IV group, suggesting that the prevalence of comorbidities was higher in patients with AMI and cardiogenic shock.

Mortality of Patients With AMI in the JROAD-DPC Database

The primary outcome, 30-day mortality of patients of AMI in this study was 9.5% (95% confidence interval (CI) 9.4–9.7%) during the period 2012–2015 in JCS teaching hospitals in Japan. The mortality of patients in Killip class I (n=68,515), II (n=40,546), and III (n=21,823) AMI was 1.8% (CI 1.7–1.9%), 4.0% (CI 3.8–4.2%), and 12.7% (CI 12.2–13.3%), respectively, and that of Killip class IV AMI (n=21,823) patients was as high as 42.3% (CI 41.6–42.9%), with a significant difference (P<0.001 by Cochran-Armitage test) (**Figure 2**).

Factors Associated With 30-Day Mortality

We examined the factors associated with 30-day mortality in the Killip class I–III and class IV patients separately, with regard to patients' characteristics and the institutional characteristics where each patient was treated. All patient

Table 2. Factors Associated With 30-Day Mortality: Univariate Analysis

Factors	Killip I–III (n=121,575)		Killip IV (n=21,823)	
	OR [95% CI]	P value	OR [95% CI]	P value
Patient factors (JROAD-DPC)				
Age <60 years (n=31,725)	Reference	–	Reference	–
Age 60–69 (n=36,921)	2.44 [2.05, 2.91]	<0.001	1.19 [1.07, 1.31]	0.001
Age 70–79 (n=39,140)	5.05 [4.30, 5.94]	<0.001	1.68 [1.53, 1.85]	<0.001
Age ≥80 (n=35,461)	17.64 [15.13, 20.57]	<0.001	3.40 [3.10, 3.74]	<0.001
Female sex	2.36 [2.22, 2.51]	<0.001	1.70 [1.59, 1.80]	<0.001
Admission by ambulance	1.59 [1.48, 1.70]	<0.001	1.66 [1.54, 1.79]	<0.001
Deep coma	27.43 [24.03, 31.31]	<0.001	8.74 [8.07, 9.47]	<0.001
Cardiac arrest	7.70 [5.93, 10.00]	<0.001	1.66 [1.45, 1.89]	<0.001
Institutional factors (JROAD survey)				
Hospital beds (n), per 100	0.95 [0.93, 0.97]	<0.001	0.96 [0.93, 0.98]	0.001
JCS board-certified members (n)	0.97 [0.97, 0.98]	<0.001	0.97 [0.96, 0.98]	<0.001
AMI patients (n/year), per 100	0.72 [0.66, 0.78]	<0.001	0.80 [0.72, 0.88]	<0.001
HF patients (n/year), per 100	0.97 [0.95, 0.99]	0.003	0.94 [0.92, 0.96]	<0.001
PCI (n/year), per 100	0.93 [0.91, 0.95]	<0.001	0.95 [0.93, 0.98]	0.001
IABP (n/year), per 10	0.97 [0.95, 0.99]	<0.001	0.94 [0.92, 0.96]	<0.001
VA-ECMO (n/year)	0.99 [0.99, 1.00]	<0.001	0.99 [0.99, 1.00]	0.042
Cardiac surgery (n/year), per 100	0.92 [0.88, 0.96]	<0.001	0.90 [0.86, 0.95]	<0.001

CI, confidence interval; OR, odds ratio. Other abbreviations as in Table 1.

Table 3. Factors Associated With 30-Day Mortality: Multivariate Regression Analysis

Factors	Killip I–III (n=121,575)		Killip IV (n=21,823)	
	OR [95% CI]	P value	OR [95% CI]	P value
Patient factors (JROAD-DPC)				
Age <60 years (n=31,725)	Reference	–	Reference	–
Age 60–69 (n=36,921)	2.38 [1.94, 2.93]	<0.001	1.26 [1.10, 1.43]	0.001
Age 70–79 (n=39,140)	4.75 [3.92, 5.75]	<0.001	1.94 [1.71, 2.20]	<0.001
Age ≥80 (n=35,461)	16.60 [13.79, 19.98]	<0.001	3.94 [3.47, 4.47]	<0.001
Female sex	1.35 [1.25, 1.46]	<0.001	1.27 [1.17, 1.39]	<0.001
Admission by ambulance	1.34 [1.23, 1.46]	<0.001	1.17 [1.05, 1.29]	0.003
Deep coma	36.92 [30.75, 44.34]	<0.001	9.57 [8.63, 10.61]	<0.001
Cardiac arrest	1.33 [0.90, 1.94]	0.148	0.65 [0.54, 0.77]	<0.001
Institutional factors (JROAD survey)				
Hospital beds (n), per 100	0.99 [0.97, 1.02]	0.623	1.02 [0.99, 1.05]	0.182
JCS board-certified members (n)	0.98 [0.97, 0.99]	<0.001	0.98 [0.96, 0.99]	0.001
AMI patients (n/year), per 100	0.84 [0.74, 0.95]	0.004	0.99 [0.86, 1.15]	0.944
HF patients (n/year), per 100	1.01 [0.99, 1.03]	0.451	0.98 [0.95, 1.00]	0.069
PCI (n/year), per 100	0.98 [0.96, 1.01]	0.297	1.02 [0.98, 1.06]	0.301
IABP (n/year), per 10	1.03 [1.00, 1.05]	0.024	0.97 [0.94, 0.99]	0.017
VA-ECMO (n/year)	1.00 [0.99, 1.00]	0.600	1.00 [1.00, 1.01]	0.228
Cardiac surgery (n/year), per 100	1.00 [0.95, 1.06]	0.967	0.99 [0.92, 1.06]	0.778

Abbreviations as in Tables 1,2.

factors included in the univariate analysis (i.e., increasing age groups, female sex, admission by ambulance, deep coma and cardiac arrest) were associated with higher 30-day mortality in both Killip class I–III and class IV AMI patients (**Table 2**). In the multivariate analysis, cardiac arrest was associated with lower 30-day mortality in Killip class IV patients, and all of the other patient factors were independently associated with higher mortality (**Table 3**). All of the institutional factors based on the JROAD survey, namely numbers of hospital beds, JCS board-certified members, hospitalizations for AMI or heart failure per year, PCI, IABP or VA-ECMO procedures per year, and cardiac surgeries per year were associated with lower 30-day mortality in the univariate analysis in both Killip class I–III and class IV patients (**Table 2**). In the multivariate analysis of Killip class I–III patients, the number of JCS board-certified members per hospital (odds ratio (OR) 0.98, CI 0.97–0.99), and the number of AMI patients per year (OR 0.84, CI 0.74–0.95 per 100 patients) was independently associated with lower 30-day mortality, whereas the number of IABP procedures per year was associated with higher mortality. By contrast, in Killip class IV patients,

Table 4. Clinical Characteristics According to the Quartiles of JCS Board-Certified Members

Factors	No. of JCS board-certified members				
	0–3 (n=36,802)	4–5 (n=44,015)	6–8 (n=31,442)	≥9 (n=31,120)	P value
Institutional factors					
JCS board-certified members, n [IQR]	3 [2, 3]	4 [4, 5]	7 [6, 8]	12 [10, 16]	<0.001
Hospital beds, n [IQR]	354 [275, 435]	464 [346, 560]	514 [383, 660]	636 [441, 899]	<0.001
AMI patients, n/year [IQR]	54 [35, 84]	78 [55, 115]	100 [75, 132]	130 [82, 186]	<0.001
HF patients, n/year [IQR]	160 [115, 222]	200 [152, 259]	251 [190, 315]	303 [200, 435]	<0.001
PCI, n/year [IQR]	176 [104, 260]	241 [169, 347]	349 [250, 437]	417 [311, 582]	<0.001
IABP, n/year [IQR]	11 [5, 23]	20 [9, 36]	30 [18, 44]	44 [25, 60]	<0.001
VA-ECMO, n/year [IQR]	1 [0, 6]	4 [1, 8]	8 [4, 14]	11 [5, 18]	<0.001
Cardiac surgery, n/year [IQR]	52 [23, 98]	70 [42, 113]	98 [65, 156]	193 [120, 298]	<0.001
Patient factors					
Killip class IV, n (%)	5,931 (16%)	6,823 (16%)	4,611 (15%)	4,453 (14%)	<0.001
Age, median [IQR]	71 [61, 80]	70 [61, 79]	70 [61, 79]	70 [61, 79]	<0.001
Female sex, n (%)	10,461 (28%)	11,884 (27%)	8,276 (26%)	7,896 (25%)	<0.001
Admission by ambulance, n (%)	22,954 (62%)	28,571 (65%)	20,691 (66%)	22,028 (71%)	<0.001
Deep coma, n (%)	1,873 (5%)	1,957 (4%)	1,232 (4%)	1,280 (4%)	<0.001
Cardiac arrest	259 (0.7%)	432 (1.0%)	387 (1.2%)	431 (1.4%)	<0.001
In-hospital procedures and cost for Killip class IV AMI					
Length of hospitalization, days	11 [2, 22]	13 [2, 23]	14 [3, 26]	15 [4, 27]	<0.001
Any revascularization, n (%)	3,896 (66%)	4,993 (73%)	3,624 (79%)	3,593 (81%)	<0.001
PCI, n (%)	3,813 (64%)	4,824 (71%)	3,451 (75%)	3,336 (75%)	<0.001
CABG, n (%)	129 (2%)	250 (4%)	236 (5%)	327 (7%)	<0.001
VA-ECMO, n (%)	450 (8%)	675 (10%)	644 (14%)	695 (16%)	<0.001
30-day Mortality, n (%)	2,840 (48%)	2,899 (42%)	1,818 (39%)	1,666 (37%)	<0.001
Hospitalization cost, USD	17,033 [3,338, 27,843]	19,604 [10,111, 31,831]	24,438 [14,874, 38,139]	26,101 [16,367, 41,702]	<0.001

1 USD=110 JPY. Abbreviations as in Tables 1,2.

the number of JCS board-certified members (OR 0.98, CI 0.96–0.99) and the number of IABP procedures per year (OR 0.97, CI 0.94–0.99 per 10 IABP/year) was independently associated with lower mortality (**Table 3**).

JCS Board-Certified Members

Because a higher number of JCS board-certified members was associated with lower 30-day mortality of Killip class IV AMI patients, we analyzed the background, in-hospital procedures, medical costs and outcomes by stratifying the patients by the quartiles of the number of JCS board-certified members in the hospital where each patient was treated (n=143,379, excluding 19 patients with data deficits). In the 1st quartile (n=36,801), patients were treated in hospitals with 0–3 JCS board-certified members, 2nd quartile (n=44,013) with 4–5, 3rd quartile (n=31,442) with 6–8, and 4th quartile (n=31,120) with ≥9 (**Table 4**). Larger numbers of JCS board-certified members were positively associated with all of the institutional factors assessed, including the numbers of PCI, IABP and VA-ECMO procedures per year. Importantly, fractions of the Killip class IV patients were rather larger in the lower quartiles (**Table 4**). Higher numbers of JCS board-certified members were associated with lower mortality especially in the Killip class IV group. Among hospitals with the highest quartile (≥9 JCS board-certified members, n=4,453), the 30-day mortality of Killip class IV patients was 37.4% (**Figure 3A**). Regarding the in-hospital management, hospitals with larger numbers of JCS board-certified members were more likely to execute coronary revascularization or VA-ECMO (**Figure 3B**,**C**; **Table 4**). Finally, hospitalization costs (shown in USD, at an exchange rate of 1 USD=110 JPY) of treating Killip class IV AMI patients weresignificantly higher in the higher quartiles, in which more invasive strategies (i.e., coronary revascularization and VA-ECMO) were used.

Discussion

In this study, we examined the institutional and patient factors associated with 30-day mortality of AMI patients with cardiogenic shock using the JCS JROAD-DPC health insurance claim database. Major findings were: (1) the mortality rate of Killip class IV AMI was as high as 42.3% in JCS-certified teaching hospitals and associated training hospitals in Japan; and (2) the number of JCS board-certified members was an independent institutional factor that was associated with lower 30-day mortality of Killip class IV AMI patients.

JROAD-DPC Database

The strength of this study stems from the large data set obtained from the Japanese DPC/PDPS claim data. According to the Japanese MHLW, 1,505 hospitals in Japan, including 82 university hospitals and the NCVC, utilized DPC/PDPS in 2012 (https://www.e-stat.go.jp/). The JROAD-DPC collected data from 610 hospitals with cardiovascular beds; therefore, this study may represent mainstream emergency cardiovascular medical practice in Japan. The DPC system

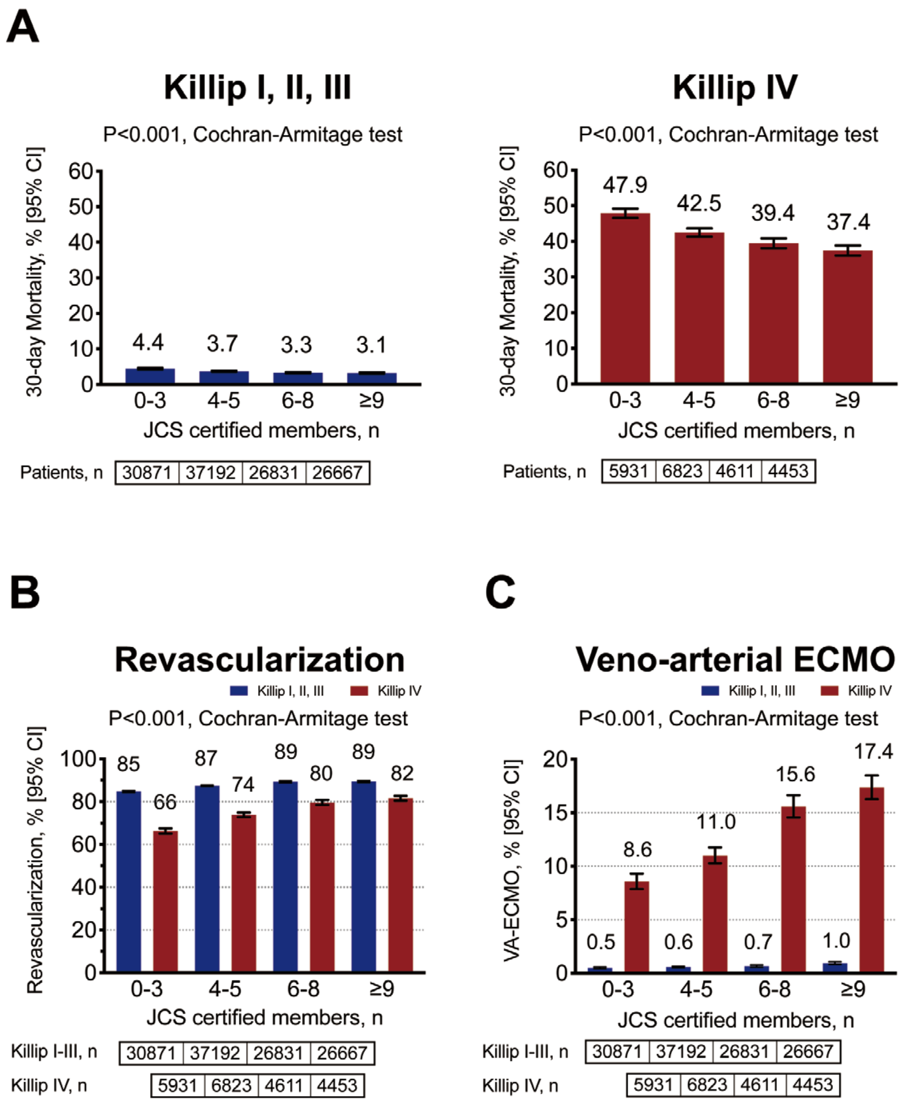

Figure 3. Impact of JCS board-certified members on clinical course of AMI patients. (**A**) 30-day mortality of patients with Killip class I, II, or III AMI (**Left**) or Killip class IV AMI (**Right**). (**B**) Proportion with 95% CI of patients undergoing coronary revascularization (PCI or CABG) among patients with Killip class I, II, or III AMI or Killip class IV AMI. (**C**) Proportion with 95% CI of patients undergoing veno-arterial ECMO among patients with Killip class I, II, or III AMI or Killip class IV AMI. Trends by the numbers of JCS bord-certified members were analyzed with Cochrane-Armitage test. AMI, acute myocardial infarction; CABG, coronary artery bypass grafting; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; PCI, percutaneous coronary intervention.

is similar to the Nationwide Inpatient Sample in the USA,[15] but has some distinct advantages. First, physicians provide the diagnostic codes until the time of patient discharge, which ensures diagnostic accuracy. Second, the DPC system distinguishes post-admission events from comorbidities that were already present at admission.[10] In this study, we stratified AMI patients by Killip classification described on admission for DPC claim, excluding 17,974 (11%) patients without Killip classification data (**Figure 1B**). Recently, the J-PCI registry of the Japanese Association of Cardiovascular Intervention and Therapeutics (CVIT) that covers approximately 85% of PCI procedures in Japan[7] indicated that in-hospital mortality of ACS patients with cardiogenic shock who underwent PCI was 13.2% during 2014–2016.[16] The present study included patients who did not undergo PCI (15% of Killip class IV patients) and 30-day mortality was 42.3% (**Figure 2**), which was also higher than the 30.6% in-hospital mortality rate in the CathPCI registry in the USA during 2011–2013.[17] Patient selection bias (i.e., inclusion of patients without coronary revascularization) as well as bias of DPC/PDPS qualified teaching hospitals and life-saving emergency centers that care for severely ill patients with cardiovascular disease might affect the high mortality in this population. Even still, the difference in short-term mortality rates among registries should be analyzed in the future.

Patient Factors Associated With 30-Day Mortality

In this study, age ≥80 years and deep coma on admission presented high OR for 30-day mortality in both Killip classification groups (**Table 3**), which is consistent with our prospective cohort study in a Japanese population in the JCS Shock Registry.[3,18] Female sex was associated with higher mortality, a difference that is unexplained by this study, but is in accordance with previous Japanese and international cohort studies.[19–21] In this study, cardiac arrest, observed in 5.3% of Killip class IV patients, was independently associated with lower mortality (adjusted OR 0.65, CI 0.54–0.77), which is unexplainable from this study. Our prospective JCS Shock Registry revealed that out-of-hospital cardiac arrest is associated with higher 30-day mortality (adjusted OR 1.62, CI 1.05–2.51) in overall cardiovascular shock patients, whereas this association was inverse in the subgroup of ACS (adjusted OR 0.73, CI 0.32–1.67),[3,4] suggesting an interaction between cause of cardiac arrest and effect on mortality.

Institutional Factors Associated With 30-Day Mortality

The present study established a database by combining per-patient DPC and JROAD institutional survey data to examine the effect of institutional characteristics on survival of Killip class IV AMI patients. Although coronary revascularization as well as mechanical circulatory support whenever necessary are important in-hospital procedures to attain better survival of patients with AMI,[5,22,23] the number of JCS board-certified members or IABP procedures per year, but not the numbers of PCI, cardiac surgery or VA-ECMO procedures per year, were independently associated with lower 30-day mortality of Killip class IV AMI patients (**Table 3**), suggesting that these factors indicate better quality of care for cardiogenic shock, although the routine use of IABP in patient with cardiogenic shock is not recommended.[5,24] In Killip class I–III AMI patients, however, the number of IABP procedures per year was associated with higher mortality, while the number of JCS board-certified members or AMI cases per year was associated with better outcomes. It is speculated that the number of IABP procedures per year may be associated with the number of potentially severe patients who are initially Killip class I–III, but unexpectedly worsen and require IABP.

JCS Board-Certified Members

The JCS established board-certified membership in 1989 for the purpose of educating and training cardiovascular specialists in Japan. The requisite for the certification includes (1) success in a written examination conducted by the JCS, (2) board-certified membership of the Japanese Society of Internal Medicine, (3) membership of the JCS for ≥6 years or on-the-job training in a JCS-certified teaching hospital for ≥3 years, and (4) advanced cardiovascular life support provider certification by the American Heart Association. In the year 2012, there were 12,441 board-certified members of the JCS, which increased to 12,777 in 2013, 13,142 in 2014, and 13,424 in 2015.[11] In this study, higher numbers of JCS board-certified members were associated with lower mortality, especially in the Killip class IV group (**Figure 3A**). JCS board-certified members might play multiple roles in the management of coronary revascularization, circulatory support, and the prevention of multiple organ failure and death. In this respect, the presence of JCS board-certified members is a good indicator of quality of care for patients with AMI. The effect of implementing coronary revascularization or VA-ECMO on the prognosis of each patient needs to be examined in a prospective study in the future.

Emergency Medical Service in Japan

The EMS is provided from the fire defense headquarters of local governments in Japan. There are 3 categories of emergency facilities; in 2012, there were 1,186 primary emergency facilities, 3,259 secondary emergency hospitals, and 249 tertiary emergency hospitals, the latter being called "life-saving emergency centers". Ambulance crews in the EMS are responsible for selecting the appropriate hospital for a patient under indirect medical control.[25] The JCS 2018 guideline on diagnosis and treatment of acute coronary syndrome[5] addresses one of the important roles of EMS as shortening the time from onset to reperfusion. The American College of Cardiology/AHA guideline for the management of STEMI[6] also recommends EMS transport directly to a PCI-capable hospital, without mentioning institutional characteristics other than PCI capability. In the present study, Killip class IV AMI patients were not transferred to a hospital on the basis of the number of board members (**Table 4**), which consequently had an effect on the patients' chances of survival (**Figure 3**). As a perspective from this study, it may be considered desirable for the EMS system to transfer Killip class I–III AMI patients to hospitals with higher numbers of AMI patients per year, and Killip class IV patients selectively to hospitals with higher number of JCS board-certified members, balancing the workload among hospitals in the local community. To further obtain better survival of Killip class IV patients, it may be effective to establish cardiac shock centers in local communities, in which JCS board-certified members would manage critically ill patients in cooperation with interventional cardiologists, emergency physicians, and intensive care physicians.[26]

Medical Cost of Treating Killip Class IV AMI Patients

In the present study, direct hospitalization costs, and procedure-based costs added to the DPC-based flat-fee, were collected from the DPC/PDPS claim data. The hospitalization cost was larger for patients treated in hospitals with larger numbers of JCS board-certified members: USD 17,033 (IQR 3,338–27,843) in the 1st quartile, and USD 26,101 (IQR 16,367–41,702) in the 4th quartile (**Table 4**). A recent report from the Nationwide Inpatient Sample regarding outcomes and costs of STEMI complicated with cardiogenic shock in the USA[15] showed that the in-hospital mortality of STEMI with cardiogenic shock was 36.6% and the hospitalization cost was USD 40,175 (IQR 22,431–72,379) in safety-net hospitals (SNH), and those in non-SNH were 32.7% and USD 38,012 (IQR 23,112–67,271). Although several differences exist between the health insurance systems Japan and the USA, the hospitalization costs in Japan and the increase according to the number of JCS board-certified members was modest, especially considering the improvement in 30-day mortality.

Study Limitations

There were several to note. First, the JROAD-DPC database has a bias in the selection of the hospital, JCS affiliation and DPC/PDPS integration; therefore, this analysis may not reflect the full picture of care for AMI in Japan. Second, we could not assess STEMI or non-STEMI separately, because the ICD-10 system does not always include the diagnosis of ST-segment elevation or non-ST-segment elevation for AMI. The inclusion of non-STEMI patients might affect the frequencies of revascularization and other procedures, and the outcomes. Third, the JROAD survey did not include the numbers of PCI for patients with shock vital signs, which is potentially associated with the prognosis of patients with AMI with cardiogenic shock; therefore, we were unable to assess this number in this study.

Conclusions

Our study evaluated the prognosis of patients with AMI with shock in Japan during 2012–2015, and found the number of JCS board-certified members in a hospital is an independent institutional factor for survival of patients of AMI with cardiogenic shock. Higher numbers of JCS board-certified members were associated with better survival with modest increases in hospitalization costs. These findings suggest optimizing the EMS in the local communities for better management of AMI patients with cardiogenic shock in Japan.

Disclosures

The authors have no conflicts of interest to disclose related to this study.

Supplementary Materials

Supplementary materials associated with this article can be found in the online version of the manuscript.

Disclosures

Co-authors Drs. Takanori Ikeda and Hiroyuki Tsutsui are members of *Circulation Journal*'s Editorial Team. Other members declared no conflict of interest regarding this study.

IRB Information

The institutional ethics committee of the Kyushu University Hospital; reference no. 28-358.

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Supplementary Files

Please find supplementary file(s);
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