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ORIGINAL ARTICLE
Cardiovascular Intervention

Primary Percutaneous Coronary Intervention in Elderly Patients With Acute Myocardial Infarction
— An Analysis From a Japanese Nationwide Claim-Based Database —

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Background: Primary percutaneous coronary intervention (pPCI) is strongly recommended by guidelines for patients presenting with acute myocardial infarction (AMI), but its applications in elderly patients are less clear.

Methods and Results: The JROAD-DPC is a Japanese nationwide registry for patients with cardiovascular diseases combined with an administrative claim-based database. Among 2,369,165 records from 2012 to 2015, data for 115,407 AMI patients were extracted for this study. Elderly patients (≥75 years) comprised 45,645 subjects (39.6%), and received pPCI less frequently (62.2%) than younger patients (79.2%, P<0.001). Clinical variables such as higher age, female sex, higher Killip class, and renal dysfunction, but not functional status on admission, were predictors of non-application of pPCI. Endpoint 30-day mortality increased with aging, and was significantly higher in elderly patients (10.7%) than in younger patients (3.8%, P<0.001). Indeed, pPCI was independently associated with lower 30-day mortality only in subgroups of patients aged ≥60 years. Propensity score-matching analysis confirmed a similar reduction in endpoint 30-day mortality with pPCI in elderly patients. Duration of hospitalization was significantly shorter and functional ability on discharge was significantly better in elderly patients who underwent pPCI.

Conclusions: Elderly patients with AMI underwent pPCI less frequently, but it was consistently associated with better clinical outcome in these patients. Our findings support the proactive application of pPCI for elderly AMI patients when they are eligible for an invasive strategy.

Key Words: Acute myocardial infarction; Elderly; Outcome; Primary percutaneous coronary intervention

Primary percutaneous coronary intervention (pPCI) is an established and standard medical care for acute coronary syndrome, and several international guidelines have strongly recommended the application of this invasive treatment for patients with acute myocardial infarction (AMI).[1–3] In fact, pPCI has significantly improved acute revascularization rates as well as both in-hospital and long-term clinical outcomes.[4,5] However, in real-world clinical practice, pPCI is not applied to all AMI patients because of concurrent factors related to patient and/or medical institutional background. In particular, older patients with AMI often have multiple comorbidities and physical disabilities,[6,7] which might have negative effects on decisions regarding pPCI made by general or interventional cardiologists. The global population is progressively aging, and the rate of aging in Japan has exceeded 25%, ahead of any other country in the world.[8] Although the crude incidence of AMI has been decreasing in Western

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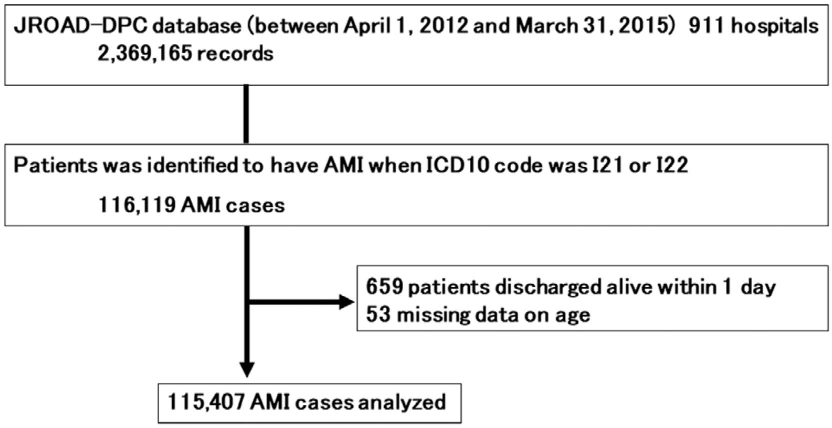

Figure 1. Study flow chart. AMI, acute myocardial infarction; ICD, International Classification of Diseases; JROAD-DPC, Japanese Registry Of All cardiac and vascular Diseases with Japanese administrative case-mix Diagnostic Procedure Combination.

countries,[9,10] several cohort studies have confirmed an ongoing expansion of elderly patients with AMI.[11–13] One study from Denmark even reported that the population of octogenarians with AMI referred for pPCI almost doubled from 2002 to 2009.[13]

The Japanese Registry Of All cardiac and vascular Diseases (JROAD) is a nationwide registry established by the Japanese Circulation Society (JCS),[14–16] and this database has registered more than 700,000 medical records annually since 2004. In addition, diagnoses of cardiovascular disease and indications for medical care in this database are supervised by JCS-certified cardiologists. By analyzing clinically reliable data from the JROAD, we investigated the current status of medical practice for AMI, and tried to examine what concurrent factors might be influencing the choice of invasive treatment strategy, and what effect pPCI is having on clinical outcomes among elderly patients.

Methods

Date Source

Because the original JROAD did not include individual patient data, a new database was developed in 2014 by combining the JROAD database with a nationwide Japanese administrative case-mix Diagnostic Procedure Combination (DPC) system (JROAD-DPC). In brief, the JCS certifies teaching hospitals to provide cardiology training programs for physicians who wish to become JCS board-certified cardiologists. Hospitals are graded into 3 categories: Class A JCS-certified teaching hospitals need more than 2 JCS board-certified cardiologists and 30 cardiovascular beds; Class B need more than 1 JCS board-certified cardiologists and 15 cardiovascular beds; and Class C do not match any of these criteria. All teaching hospitals contribute to the JROAD. Each hospital is requested to annually report hospital activities and DPC discharge data, and 911 hospitals submitted their DPC datasets during the study period.

Study Population

We screened all hospitalization records registered in the JROAD and JROAD-DPC databases between April, 2012 and March, 2015. Based on the International Classification of Diseases, 10th revision (ICD-10) codes registered as the main diagnosis and/or admission-precipitating diagnosis and/or most resource-consuming diagnosis, each patient was identified as having AMI when the relevant ICD10 code was I21 or I22. Patients discharged alive within the first day of admission (n=659) or for whom age data were missing (n=53) were excluded.

The following data were extracted from the database: patient age and sex, body mass index (BMI), admission route, Killip classification, functional status on admission/discharge, comorbidities on admission, type of in-hospital medical care, and hospital characteristics. Admission route was identified using an 'emergency' admission code. Comorbidities were determined primarily from ICD-10 codes, but were also checked against the medications and procedures. Functional ability status on admission and at discharge was assessed using the Barthel index (BI),[17,18] as either a perfect or non-perfect score.

Elderly patients were defined as age ≥75 years, in accordance with the statement from the Japan Geriatrics Society.[19] Younger patients were aged <75 years. We defined pPCI as a PCI procedure performed on the day of or the day following admission. Clinical outcome was assessed as all-cause death at 24 h and 30 days after admission. The primary endpoint of this study (endpoint 30-day mortality) was defined as 30-day all-cause death occurring later than 24 h after admission, as death within 24 h was considered likely to largely be accounted for by patients who were dead on arrival and/or with recovery of spontaneous circulation after resuscitation, whose clinical condition might be beyond interventional treatment.

Ethics Statement

This research plan was approved by the institutional review boards of the National Cerebral and Cardiovascular Center (No. 2016-09-01) and Kawasaki Medical School (No. 2717). Each hospital anonymized patient IDs using the code-change equations made by each hospital in the original DPC data, which were sent to the Ministry of Health, Labour and Welfare. Patients were notified through homepages or posters in each hospital that their information was being collected for this study. Patients could opt-out of collection of their information from the database if they wished to be excluded.

Statistical Analysis

Continuous variables are summarized as mean ± standard

Table 1. Clinical Characteristics of the Study Population Stratified by Age

	Total	≥75 years old	<75 years old	P value
No. of patients	115,407	45,645 (39.6)	69,762 (60.4)	–
Female, n (%)	32,360 (28.0)	20,398 (44.7)	11,962 (17.1)	<0.001
Age, years, mean±SD	69.7±13.3	82.6±5.4	61.3±9.6	<0.001
Female, mean±SD	76.8±11.7	84.0±5.7	64.5±8.7	<0.001
Male, mean±SD	67.0±12.8	81.5±4.9	60.7±9.7	<0.001
BMI (mean±SD)	23.4±4.6	22.0±4.8	24.3±4.3	<0.001
Clinical factors				
Admission route, n (%)				<0.001
Emergency with ambulance	72,631 (63.0)	29,690 (65.1)	42,941 (61.6)	
Emergency without ambulance	33,541 (29.1)	11,991 (26.3)	21,550 (30.9)	
Not emergency	9,174 (8.0)	3,947 (8.7)	5,227 (7.5)	
Killip class, n (%)				<0.001
I	48,777 (44.4)	15,196 (35.5)	33,581 (50.1)	
II	29,399 (26.8)	11,793 (27.6)	17,606 (26.3)	
III	8,915 (8.1)	4,475 (10.5)	4,440 (6.6)	
IV	15,327 (14.0)	7,423 (17.4)	7,904 (11.8)	
Unclassifiable	7,380 (6.7)	3,885 (9.1)	3,495 (5.2)	
Mechanical ventilation	18,914 (16.4)	9,497 (20.8)	9,417 (13.5)	<0.001
Full score Barthel Index at admission, n (%)	29,573 (25.6)	8,856 (19.4)	20,717 (29.7)	<0.001
Previous IHD	16,483 (14.3)	6,090 (13.3)	10,393 (14.9)	<0.001
Hypertension	71,423 (61.9)	25,769 (56.5)	45,654 (65.4)	<0.001
Diabetes mellitus	32,787 (28.4)	10,961 (24.0)	21,826 (31.3)	<0.001
Hyperlipidemia	63,584 (55.1)	19,267 (42.2)	44,317 (63.5)	<0.001
Chronic renal failure	3,347 (2.9)	1,894 (4.1)	1,453 (2.1)	<0.001
Atrial fibrillation	5,875 (5.1)	3,250 (7.1)	2,625 (3.8)	<0.001
Life-threatening arrhythmia	7,225 (6.3)	2,987 (6.5)	4,238 (6.1)	0.001
Circulatory shock	9,333 (8.1)	3,946 (8.6)	5,387 (7.7)	<0.001
Procedure, n (%)				
Overall CAG	100,919 (87.5)	35,476 (77.7)	65,443 (93.8)	<0.001
PCI	89,955 (78.0)	31,243 (68.4)	58,712 (84.2)	<0.001
Primary PCI	83,658 (72.5)	28,410 (62.2)	55,248 (79.2)	<0.001
CABG	1,608 (1.4)	536 (1.2)	1,072 (1.5)	<0.001
Hospital characteristics, n (%)				<0.001
Facility level				
A	107,578 (93.0)	41,958 (91.9)	65,620 (94.1)	
B	6,723 (5.8)	3,138 (6.9)	3,585 (5.1)	
C	1,106 (1.0)	549 (1.2)	557 (0.8)	
Hospital case volume				<0.001
Very low (0–128)	29,044 (25.1)	12,328 (27.0)	16,716 (24.0)	
Low (129–204)	29,078 (25.2)	11,508 (25.2)	17,570 (25.2)	
High (205–318)	28,709 (24.9)	11,045 (24.2)	17,664 (25.3)	
Very High (319–807)	28,576 (24.8)	10,764 (23.6)	17,812 (25.5)	

BMI, body mass index; CABG, coronary artery bypass graft; CAG, coronary angiography; IHD, ischemic heart disease; PCI, percutaneous coronary intervention.

deviation, and categorical variables as frequencies or percentages. For continuous variables, comparisons between groups were made using the unpaired t-test. Categorical variables were compared using the χ^2 test. Uni- and multivariate mixed-effects logistic regression analyses with institution as a random intercept were performed to evaluate whether pPCI was independently associated with endpoint 30-day mortality, and also to investigate independent factors negatively correlated with non-application of pPCI. The variance inflation factor was calculated to check for multicollinearity among variables included in the model. Multicollinearity was not found to be a concern (variance inflation factor >10). Factors showing a value of P<0.001 in the univariate analysis were entered into the multivariate model. The results are summarized as odds ratios (OR) and 95% confidence intervals (CIs). We categorized hospitals into quartiles based on case volume: very low, low, high, and very high. Quartiles were analyzed for trends using the Cochran-Armitage trend test.

We used propensity score-matching to evaluate whether pPCI was independently associated with endpoint death among elderly patients (≥75 years old). Propensity score-matching using the nearest-neighbor matching method was constructed by logistic regression modeling, adjusting for

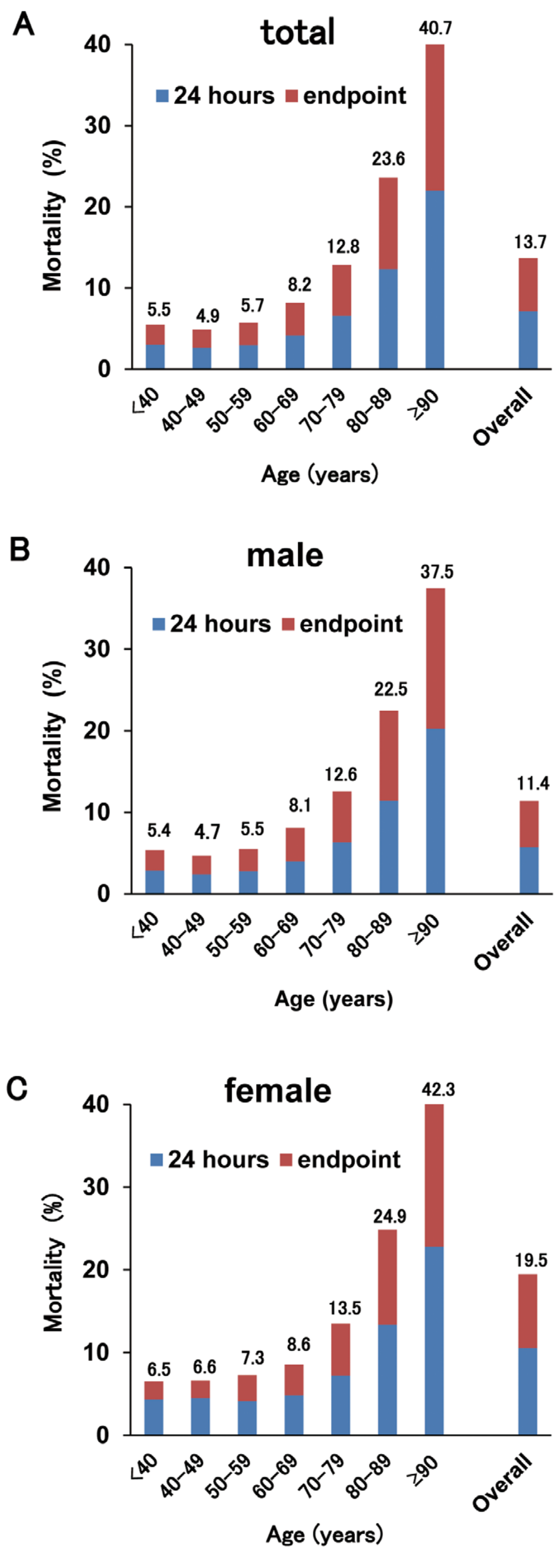

Figure 2. (**A**–**C**) Mortality rates of patients with acute myocardial infarction by age and sex. Blue bars represent death within 24 h, and red bars represent endpoint 30-day death.

the variables listed in **Table 3**. Matching was performed in a 1:1 ratio without replacements with 0.001 as a caliper. Standard mean differences were calculated.

All statistical analyses were conducted using STATA version 15 statistical software (Stata Corp, College Station, TX, USA).

Results

A total of 2,369,165 DPC records were registered in the JROAD-DPC database during the study period. According to the prespecified ICD-10 codes, 116,119 patients were diagnosed with AMI, and 115,407 patients were finally analyzed in this study (**Figure 1**).

Current Clinical Features of AMI

Clinical characteristics of the study population are shown in **Table 1**. The AMI patient group comprised 32,360 women (28.0%) and 83,047 men (72.0%). Mean age was 69.7±13.3 years: 76.8±11.7 years for women, and 67.0±12.8 years for men. Peak age groups were 60–69 years for men and 80–89 years for women (**Supplementary Figure 1**). Elderly patients (≥75 years old) comprised 39.6% of the study population (45,645 individuals), which included 21.3% octogenarians and 4.6% nonagenarians or older (**Supplementary Table 1**). In terms of severity of AMI, Killip 1 classification was the most common, but the proportion with Killip 3 or 4 increased with aging, and 9,333 patients (8.1%) were diagnosed as having circulatory shock at presentation. The proportion of patients with perfect-score BI at admission was significantly lower among elderly patients (19.4%) than among younger patients (29.7%, P<0.001).

The endpoint 30-day mortality rate was 13.7% (n=15,761), and death occurred within 24 h of admission in 7.1% (n=8,205). The 24-h and 30-days mortality increased significantly with aging, reaching 40.7% among nonagenarians (**Figure 2**). The endpoint 30-day mortality rate was significantly higher in elderly patients (10.7%) than in younger patients (3.8%, P<0.001).

Factors Negative Influencing pPCI Application

During hospitalization, a total of 100,919 patients (87.5%) underwent coronary angiography (CAG), and pPCI was performed in 83,658 patients (72.5%). As shown in **Table 1** and **Figure 3**, pPCI was less frequently performed for elderly patients (62.2%) than for younger patients (79.2%, P<0.001), and only 39.7% of nonagenarians underwent pPCI (**Supplementary Table 1**). Female patients received pPCI significantly less frequently than males, irrespective of age (62.2% vs. 76.5%, respectively; P<0.01).

Multivariate analysis showed that factors of higher age, female sex, higher Killip class, and chronic renal failure correlated negatively with application of pPCI (**Table 2**). However, BI on admission was not associated with application of pPCI. By contrast, emergency admission, presence of life-threatening arrhythmias, circulatory shock, and hospital case volume correlated positively with application of pPCI.

Clinical Benefit of pPCI in Elderly Patients With AMI

Clinical background differed significantly between patients who did or did not undergo pPCI (**Supplementary Table 2**), but pPCI was associated with significantly lower 24-h mortality irrespective of sex and age categories (**Figure 4A**). Endpoint 30-day mortality was significantly lower in

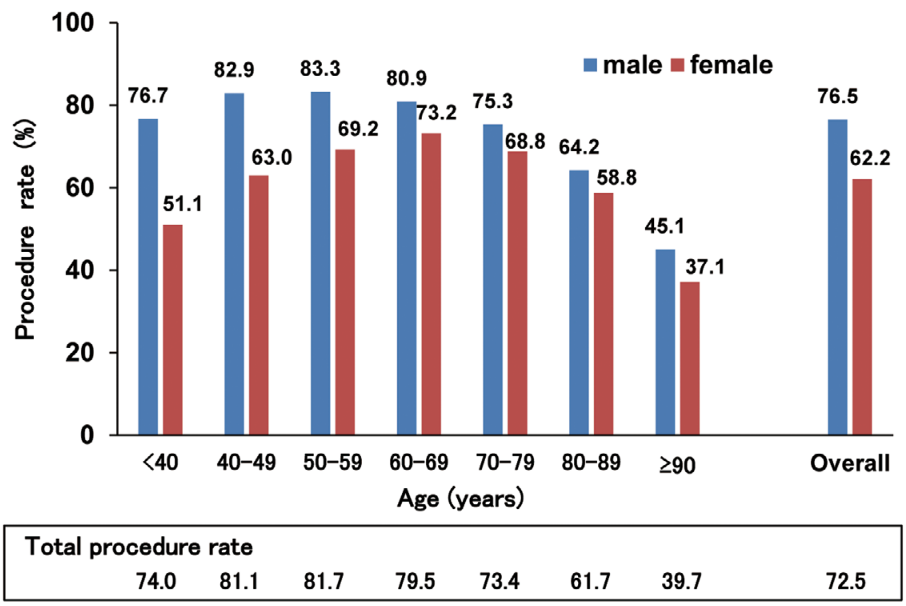

Figure 3. Application rate of primary percutaneous coronary intervention for acute myocardial infarction. Note the progressive decrement in application rate with aging after 70 years.

Table 2. Univariate and Multivariate Logistic Regression Analyses of Performance of Primary PCI

Variables (n=91,823)	Univariate	Multivariate	
		OR (95% CI)	P value
Age (reference, <60 years)			
60–69	<0.001	1.03 (0.97–1.09)	0.288
70–79	<0.001	0.90 (0.85–0.96)	0.001
80–89	<0.001	0.67 (0.63–0.71)	<0.001
≥90	<0.001	0.32 (0.29–0.35)	<0.001
Female	<0.001	0.72 (0.69–0.75)	<0.001
BMI	<0.001	1.03 (1.02–1.03)	<0.001
Admission route (reference, not emergency)	<0.001		
Emergency without ambulance		6.83 (6.39–7.29)	<0.001
Emergency with ambulance		11.48 (10.76–12.24)	<0.001
Killip (reference, I)	<0.001		
II		1.00 (0.96–1.05)	0.897
III		0.72 (0.68–0.77)	<0.001
IV		0.80 (0.75–0.86)	<0.001
Mechanical ventilation	<0.001	0.59 (0.56–0.63)	<0.001
Non-full score Barthel index at admission	0.13	–	–
Ischemic heart disease	0.61	–	–
Hypertension	<0.001	1.44 (1.38–1.50)	<0.001
Diabetes mellitus	<0.001	1.09 (1.05–1.14)	<0.001
Hyperlipidemia	<0.001	2.35 (2.25–2.45)	<0.001
Chronic renal failure	<0.001	0.76 (0.69–0.84)	<0.001
Atrial fibrillation/flutter	<0.001	0.90 (0.83–0.97)	0.009
Life-threatening arrhythmia	<0.001	2.01 (1.83–2.21)	<0.001
Shock	<0.001	2.03 (1.87–2.19)	<0.001
Hospital characteristics (reference, Facility level C)	<0.001		
Facility level A		2.85 (2.12–3.83)	<0.001
Facility level B		2.03 (1.47–2.80)	<0.001
Hospital case volume (reference, very low (0–128))	<0.001		
Low (129–204)		1.16 (1.01–1.33)	0.040
High (205–318)		1.21 (1.03–1.42)	0.020
Very high (319–807)		1.10 (0.90–1.34)	0.348

BMI, body mass index; PCI, percutaneous coronary intervention.

Table 3. Multivariate Logistic Regression Analysis of the Endpoint 30-Day Death by Age Group

Variables	<60 years (n=21,025)		60–69 years (n=24,324)	
	OR (95% CI)	P value	OR (95% CI)	P value
Primary PCI	1.11 (0.80–1.53)	0.543	0.76 (0.62–0.92)	0.006
Female	1.23 (0.85–1.79)	0.271	0.83 (0.66–1.03)	0.091
BMI	1.02 (0.99–1.04)	0.114	0.99 (0.97–1.01)	0.310
Admission route				
Emergency with ambulance	0.41 (0.25–0.68)	0.001	0.62 (0.44–0.88)	0.007
Emergency without ambulance	0.44 (0.25–0.75)	0.003	0.61 (0.42–0.88)	0.008
Killip (reference, I)				
II	1.44 (0.84–2.47)	0.179	1.53 (1.12–2.09)	0.008
III	3.73 (2.15–6.45)	<0.001	3.74 (2.68–5.22)	<0.001
IV	14.27 (9.17–22.22)	<0.001	9.69 (7.30–12.84)	<0.001
Mechanical ventilation	7.02 (5.17–9.54)	<0.001	3.63 (2.99–4.40)	<0.001
Non-full score Barthel index at admission	0.63 (0.44–0.91)	0.014	0.62 (0.48–0.79)	<0.001
Ischemic heart disease	0.55 (0.35–0.87)	0.011	0.69 (0.52–0.91)	0.009
Hypertension	0.56 (0.43–0.74)	<0.001	0.52 (0.43–0.62)	<0.001
Diabetes mellitus	1.18 (0.90–1.54)	0.225	1.00 (0.84–1.19)	0.994
Hyperlipidemia	0.39 (0.29–0.53)	<0.001	0.35 (0.29–0.43)	<0.001
Chronic renal failure	4.48 (2.50–8.02)	<0.001	2.55 (1.84–3.54)	<0.001
Atrial fibrillation/flutter	0.89 (0.43–1.83)	0.749	1.22 (0.86–1.72)	0.257
Life-threatening arrhythmia	1.06 (0.80–1.41)	0.682	1.03 (0.82–1.29)	0.797
Shock	1.78 (1.36–2.33)	<0.001	1.70 (1.40–2.07)	<0.001
Hospital characteristics (reference, Facility level C)				
Facility level A	0.53 (0.17–1.69)	0.285	0.84 (0.30–2.34)	0.742
Facility level B	0.62 (0.17–2.18)	0.454	0.88 (0.30–2.60)	0.817
Hospital case volume (reference, very low (0–128))				
Low (129–204)	0.96 (0.67–1.37)	0.804	1.12 (0.86–1.45)	0.397
High (205–318)	1.20 (0.83–1.74)	0.341	1.16 (0.89–1.52)	0.277
Very high (319–807)	1.05 (0.71–1.55)	0.792	1.29 (0.97–1.71)	0.085

PCI, percutaneous coronary intervention; BMI, body mass index.

(**Table 3** continued the next page.)

patients who underwent pPCI (5.2%) than in those who did not (9.5%, P<0.01). Multivariate analysis showed that pPCI was independently associated with a lower rate of endpoint 30-day mortality in patients aged ≥60 years (**Table 3**). By contrast, this association was not observed in younger patients (**Figure 4B**). The propensity-matched population comprised 8,161 elderly patients per group, with and without pPCI (**Supplementary Table 3**). This analysis also showed that pPCI was independently associated with reduced endpoint 30-day mortality in elderly patients (OR, 0.58; 95% CI, 0.53–0.64; P<0.001) (**Supplementary Figure 2**).

Furthermore, the proportion of patients with a perfect BI at discharge was significantly higher among patients who underwent pPCI, irrespective of age category, and this trend was overt, particularly among patients aged ≥70 years (**Figure 4C**). Propensity score-matching analysis also showed a higher rate of perfect BI at discharge among elderly AMI patients with pPCI than for those without pPCI (OR, 1.61; 95% CI, 1.51–1.71, P<0.001) (**Supplementary Table 4**, **Supplementary Figure 3**). Mean hospitalization period was significantly shorter for patients with pPCI (17.5±13.4 days) than for those without (18.8±19.5 days, P<0.001) among patients discharged alive from hospital.

In addition, among the total population, 10,964 (0.95%) patients underwent diagnostic CAG without subsequent pPCI, and it was consistently observed that endpoint 30-day mortality was significantly lower and BI was significantly better in patients who underwent CAG without pPCI than patients who did not (**Supplementary Figure 4A**,**B**).

Discussion

The salient findings of the present study were as follows: (1) the subject population with AMI in the JROAD-DPC comprised 39.6% elderly patients; (2) 72.5% of AMI patients underwent pPCI in modern clinical practice in Japan, but performance of pPCI was significantly lower among elderly patients than among younger patients; (3) factors on admission, including higher age, female sex, higher Killip class, and chronic renal failure correlated negatively with undergoing pPCI; and (4) pPCI was associated with shorter hospitalization period, better functional ability status at discharge, and lower 30-day mortality in elderly patients.

A large subject population compared with previous studies is the major strength of the present study,[4,5,11,20,21] and this nationwide registry covers various types of cardiovascular hospital in every region of Japan. In addition, diagnosis of AMI and decisions on patient management, including pPCI, were performed by JCS-certified cardiologists. These features of the JROAD-DPC seem likely to reflect the actual situation of current cardiovascular practice in Japan, and it is anticipated that this apparently

70–79 years (n=25,372)		80–89 years (n=17,883)		≥90 years (n=3,219)	
OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
0.65 (0.56–0.75)	<0.001	0.56 (0.50–0.62)	<0.001	0.51 (0.42–0.62)	<0.001
1.06 (0.92–1.21)	0.432	1.10 (0.99–1.22)	0.075	1.05 (0.85–1.28)	0.665
0.99 (0.98–1.01)	0.271	1.00 (0.98–1.01)	0.512	0.99 (0.97–1.01)	0.327
0.47 (0.38–0.59)	<0.001	0.73 (0.60–0.89)	0.002	1.05 (0.74–1.50)	0.779
0.46 (0.36–0.58)	<0.001	0.75 (0.61–0.93)	0.008	1.04 (0.71–1.52)	0.856
1.82 (1.47–2.25)	<0.001	2.11 (1.78–2.51)	<0.001	2.00 (1.49–2.69)	<0.001
3.85 (3.05–4.85)	<0.001	4.57 (3.80–5.49)	<0.001	4.19 (3.06–5.74)	<0.001
9.05 (7.36–11.12)	<0.001	6.87 (5.75–8.20)	<0.001	4.36 (3.20–5.95)	<0.001
2.63 (2.28–3.04)	<0.001	1.74 (1.54–1.97)	<0.001	1.34 (1.05–1.71)	0.017
0.78 (0.66–0.93)	0.005	0.68 (0.58–0.80)	<0.001	0.69 (0.47–1.00)	0.052
0.67 (0.54–0.82)	<0.001	0.78 (0.66–0.93)	0.005	0.80 (0.58–1.09)	0.162
0.60 (0.52–0.69)	<0.001	0.63 (0.56–0.70)	<0.001	0.74 (0.61–0.91)	0.004
1.02 (0.89–1.16)	0.805	1.07 (0.95–1.22)	0.259	1.15 (0.89–1.50)	0.286
0.46 (0.39–0.53)	<0.001	0.47 (0.41–0.54)	<0.001	0.59 (0.46–0.76)	<0.001
1.64 (1.28–2.10)	<0.001	1.61 (1.31–1.99)	<0.001	1.03 (0.69–1.54)	0.882
1.18 (0.93–1.50)	0.171	1.06 (0.88–1.28)	0.539	1.31 (0.96–1.78)	0.086
0.95 (0.78–1.15)	0.583	0.93 (0.76–1.13)	0.454	0.76 (0.49–1.17)	0.209
1.54 (1.31–1.80)	<0.001	1.39 (1.19–1.62)	<0.001	1.21 (0.89–1.65)	0.217
0.58 (0.33–1.03)	0.065	0.99 (0.62–1.58)	0.956	1.14 (0.56–2.30)	0.723
0.59 (0.32–1.12)	0.106	1.07 (0.65–1.77)	0.785	1.17 (0.55–2.47)	0.685
1.05 (0.86–1.28)	0.644	1.09 (0.93–1.27)	0.312	0.90 (0.69–1.14)	0.353
1.14 (0.92–1.40)	0.227	0.90 (0.76–1.07)	0.240	1.03 (0.79–1.34)	0.834
1.13 (0.90–1.41)	0.281	1.03 (0.86–1.23)	0.761	0.81 (0.60–1.10)	0.186

reliable dataset will enable us to elucidate the clinical issues in dealing with elderly AMI patients.

Aging is an established risk factor for the development of cardiovascular disease. Patients aged ≥75 years comprised almost 40% of the study population in the present investigation, and the rate of patients aged ≥80 years was even higher in the present study than the same patient subgroup researched in 2010.[13] In a previous report with a large patient cohort published in 2000, patients aged ≥75 years comprised approximately 30% of all AMI patients.[22] A more recent registry study, published in 2010, showed a steady trend of increasing prevalence for elderly AMI patients over the preceding 3 decades.[13] The elderly population is growing rapidly in developed countries, and the aging rate in Japan is estimated to reach as high as 39.9% by 2060.[8] Although the incidence of ST-elevation MI has started to decrease in Western countries,[9,10] the epidemiologic data predict a continuing increase in the actual number of elderly patients with AMI, and indicate an urgent need to establish appropriate treatment strategies applicable to this patient subgroup.

Performance of pPCI in Elderly Patients With AMI

With the continuous increase in the aging population worldwide, more elderly patients with AMI will be likely referred for pPCI. Although the possible benefits of pPCI on clinical outcomes for elderly patients have been shown in several cohort studies, few investigations have reported the practical application rate of pPCI in this patient subgroup. One national registry for England and Wales has shown incremental reductions in the use of intensive management, including pPCI, with increasing age.[23] The present study showed that 38% of elderly patients did not undergo pPCI. As the incidence of CAG in this study was significantly higher than that of pPCI, physicians objectively deferred pPCI in some patients based on anatomic features of the coronary arteries, presumably including spontaneous recanalization and MI with non-obstructive coronary arteries (MINOCA).[24] Even considering this situation, >20% of elderly patients did not undergo diagnostic CAG. By accounting for the generally observed complex clinical background of elderly patients,[25,26] emergency physicians and interventional cardiologists might be biased towards hesitating in consulting about or undertaking pPCI in very elderly patients, even if the patient is eligible for invasive treatment. In addition, limited evidence is available at this time regarding the efficacy and safety of pPCI among elderly AMI patients, because elderly patients are commonly excluded by the entry criteria of randomized clinical trials. Preconceptions of worse clinical features in elderly patients and the lack of concrete evidence may be among the reasons for under-utilization of pPCI in elderly AMI patients.

The application rate of pPCI in this study was relatively lower than reported in other recent studies, which have described rates of 85–90%.[18,19,27] The application rate of pPCI may depend on various clinical factors, including average patient age, type of participating hospital (i.e.,

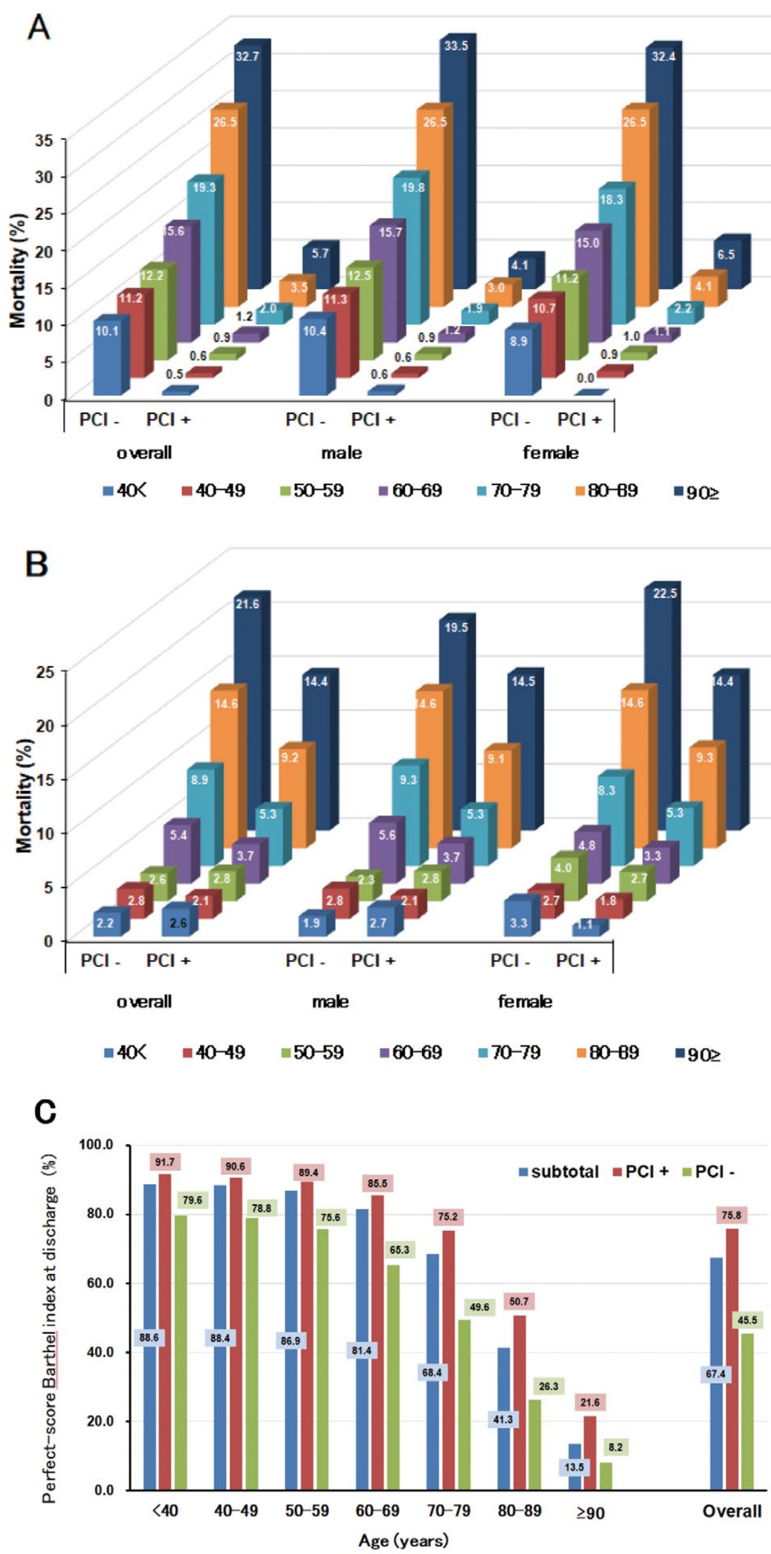

Figure 4. Relationship between primary percutaneous coronary intervention and clinical outcome: (**A**) 24-h death, (**B**) endpoint 30-day death, (**C**) perfect-score Barthel index at discharge.

with or without cardiac catheterization equipment), and so on. Non-nationwide multicenter registries are assumed to often comprise higher-volume and more-active hospitals than ordinary institutes. On the other hand, in the nationwide JROAD, the characteristics of both patients and hospitals are more variable, indicating that our results could be more representative of actual medical practice in Japan.

Factors Negatively Influencing Application of pPCI

As expected, the application rate of pPCI in this study was significantly lower among elderly patients than among younger patients, and higher age was an independent predictor of non-application of pPCI for AMI. The reason is likely to be multifactorial, as a composite situation in which pPCI is judged as non-beneficial for the patient by the physician, and one in which admission after onset of AMI is extensively delayed.[8,28] Our study also showed that, in addition to higher age, female sex, higher Killip class, and renal dysfunction correlated independently with non-performance of pPCI. Both advanced age and female sex are well-known factors for delayed hospital visits,[29,30] increased risk of bleeding and vascular complications with PCI, and higher mortality, and such background factors are undoubtedly considered by emergency physicians. In addition, further efforts to shorten the time interval from symptom onset to hospital visit should be undertaken, especially in the elderly population.

In contrast, functional ability on admission as evaluated by BI was not associated with application of pPCI in this study. Physicians may tend to decide on the application of pPCI mainly based on the chronological age of the patient and objective laboratory data, and not on the actual physical and functional ability of the patient on admission. Current life expectancy in elderly patients is increasing because of comprehensive progress in medical care. As functional ability is not always parallel to chronological age, decision-making based on objective and proper evaluation of physical and mental status is pivotal for the indication of pPCI.

Patients with renal dysfunction underwent pPCI 24% less often than other patients. This was likely attributable to a desire to avoid contrast-induced nephropathy (CIN),[31] which is an established risk for poor prognosis and introduction of hemodialysis. The development of strategies to prevent CIN should be helpful for greater application of pPCI and better clinical outcomes among elderly patients with AMI.

Effect of pPCI on Clinical Outcomes of Elderly Patients With AMI

Introduction of pPCI has significantly reduced in-hospital deaths of AMI patients, but the latest studies have shown that in-hospital mortality rates have plateaued in recent decades.[13] Two possible reasons for this are the increasing age of AMI patients and the under-utilization of pPCI among elderly patients.[32] This study showed that, in elderly patients, pPCI was independently associated with a significantly lower 30-day mortality. Supporting our findings, a recent randomized clinical trial has shown that an invasive strategy including early CAG and PCI was superior to a conservative strategy in elderly patients aged ≥80 years, although their study population was limited in patients with non-ST-elevation MI and unstable angina.[33]

Besides death, our study also showed that pPCI correlated with higher BI at discharge, indicating the benefit of pPCI on activities of daily living after discharge of elderly patients.[17,18] In addition, the hospitalization period in patients with pPCI was significantly shorter than with a conservative strategy.

In addition, patients who underwent diagnostic CAG without subsequent pPCI consistently showed lower endpoint 30-day mortality and better discharge BI than patients who did not undergo CAG. We can speculate that patients who underwent CAG without subsequent pPCI were mainly diagnosed to have MINOCA, recanalized culprit lesions, severe 3-vessel disease, or failure of pPCI because of arterial access problem. However, it is not possible to elucidate the exact reason for non-pPCI selection of each patient because of the limitations of the JROAD database.

We were also surprised to discover that pPCI was not associated with improved endpoint 30-day mortality in the younger patient subgroup aged <60 years. The reasons for this unexpected result are unknown, but it is possible that multiple factors are involved in this observation. We need to perform additional study about this issue in the future.

Appropriate patient selection for pPCI remains difficult, even with progress in cardiovascular medicine. In particular, elderly patients frequently have multiple comorbidities and organ dysfunctions, together with more extensive and complex coronary lesions, and higher rates of late PCI-related complications.[23,24] These factors are also an obstacle to successful pPCI. Further research on optimal treatment strategies, including patient selection and effective pPCI for elderly patient, is warranted.

Even in the modern PCI treatment era, pPCI was under-utilized in elderly patients with AMI. Our findings strongly support proactive application of pPCI for elderly AMI patients when they are judged to be eligible for an invasive treatment.

Study Limitations

Several important limitations must be considered when interpreting the results of this study. First, the DPC system focused on JCS-certified hospitals. Although these institutions account for 29% of all hospital beds in Japan, the applicability of our findings to non-certified or non-specialist hospitals is unclear. Second, the type of ST-elevation or non-ST-elevation MI was not distinguished in this study. Third, the definition of pPCI was not limited to performance in an emergency setting, and whether pPCI was successful with TIMI flow grade 3 was unclear. Onset-to-door time was not assessed in this study. Further studies using well-defined time periods are needed. Data validation with chart review and reevaluation of discrepant cases could improve the precision of the JROAD-DPC. Fourth, the lack of long-term outcome measures represents an important constraint on this study.

Conclusions

Elderly patients with AMI less frequently underwent pPCI, but when applied, this treatment was associated with shorter hospitalization period, higher functional ability, and better clinical outcomes. Our findings indicated the necessity of improving the strategies for applying pPCI in elderly patients with AMI.

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Disclosures

All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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Supplementary Files

Please find supplementary file(s);
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