One-Year Outcome After Percutaneous Coronary Intervention for Acute Coronary Syndrome

— An Analysis of 20,042 Patients From a Japanese Nationwide Registry —

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Background: Acute coronary syndrome (ACS) hospital survivors experience a wide array of late adverse cardiac events, despite considerable advances in the quality of care. We investigated 30-day and 1-year outcomes of ACS hospital survivors using a Japanese nationwide cohort.

Methods and Results: We studied 20,042 ACS patients who underwent percutaneous coronary intervention (PCI) in 2017: 10,242 (51%) with ST-elevation myocardial infarction (STEMI), 3,027 (15%) with non-ST-elevation myocardial infarction (NSTEMI), and 6,773 (34%) with unstable angina (UA). The mean ($\pm$ SD) age was 69.6 ± 12.4 years, 77% of the patients were men, and 20% had a previous history of PCI. The overall 30-day all-cause, cardiac, and non-cardiac mortality rates were 3.0%, 2.4%, and 0.6%, respectively. The overall 1-year incidence of all-cause, cardiac, and non-cardiac death was 7.1%, 4.2%, and 2.8%, respectively. Compared with UA patients, STEMI patients had a higher risk of all fatal events, non-fatal ischemic stroke, and acute heart failure, and NSTEMI patients had a higher risk of heart failure.

Conclusions: The results from our ACS hospital survivor PCI database suggest the need to improve care for the acute myocardial infarction population to lessen the burden of 30-day mortality due to ACS, heart failure, and sudden cardiac death, as well as 1-year ischemic stroke and heart failure events.

Key Words: Acute coronary syndrome; Acute myocardial infarction; Mortality; Outcome; Percutaneous coronary intervention

Revascularization via percutaneous coronary intervention (PCI) remains the cornerstone of care for patients presenting with acute coronary syndrome (ACS).¹ The procedural technique has improved over time due to advances in pharmacotherapy, the application of coronary stents, and the establishment of patient care flows targeted at fulfilling performance and quality measures;^{2,3} however, patients presenting with ACS remain susceptible to a wide array of late adverse cardiac events, such as sudden cardiac death, stent thrombosis, recurrent ACS, stroke, and heart failure.^{4,5} Large-scale observational studies have been performed to investigate the real-world outcomes of revascularized patients.^{6–8} However, the lack

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of comprehensively collected data extending beyond cross-sectional studies, administrative databases, or clinical trials has hindered the process of identifying and delivering appropriate care for ACS patients in the contemporary era.

In Japan, approximately 260,000 PCIs are performed annually, mainly for the purposes of operator and institutional certification by the Cardiovascular Intervention and Therapeutics (CVIT), the leading academic organization for cardiovascular and endovascular interventions.⁹ The J-PCI OUTCOME project was developed in collaboration

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with the Japanese Circulation Society (JCS) and funded by the Japan Agency for Medical Research and Development to collect 1-year follow-up information for patients in the J-PCI Registry. This registry was the first of its kind to capture incident fatal and non-fatal events after initial PCI, including repeat revascularization at a nationwide scale, without linking to administrative databases for purpose of acquiring outcome data. The overall objective of establishing the registry was to reveal the diverse post-discharge status of care provided by PCI hospitals in Japan.

For this initial analysis, we used the J-PCI OUTCOME registry established in 2017, which extended the cross-sectional procedure-based J-PCI Registry to a nationwide longitudinal cohort that covered all 47 prefectures from 8 regions of Japan (Hokkaido, Tohoku, Kanto, Chubu, Kinki, Chugoku, Shikoku, and Kyushu/Okinawa) to report the 1-year outcomes of ACS hospital survivors and identify any potential problems and possible solutions to the current status of care as a foundation for quality improvement.

Methods

The J-PCI and J-PCI OUTCOME Registries

The J-PCI Registry is an ongoing prospective multicenter nationwide PCI registry led by the CVIT.¹⁰ The J-PCI Registry aims to provide national, regional, and institutional information on general aspects of patients, including background, clinical presentation, angiographic and procedural details, and in-hospital outcomes, as a foundation for further quality improvement.^{11–13} In addition, the J-PCI Registry has been incorporated into the National Clinical Data system, a nationwide prospective web-based registry linked to medical and surgical board certification, since 2013.¹⁴ Cardiac catheterization procedures are performed in both publicly and privately funded hospitals in Japan, and because registration in the J-PCI database is mandatory for both systems, data completeness is high. Based on annual reports from the insurance claims data, it is estimated that approximately 85% of all PCI procedures are registered in the J-PCI Registry.

Over 1,000 representative PCI centers from the 47 prefectures in Japan that fulfilled the selection criteria of exceeding an annual PCI case volume of 200 procedures¹⁵ performed at each standardized performance site and were invited to participate in the J-PCI OUTCOME study in

December 2017. In all, 599 hospitals responded and 179 hospitals volunteered to participate and proceeded with the study protocol (**Supplementary Appendix**). The 172 institutions that registered over 10 patients during the study period were included in the final analysis to ensure data quality (**Supplementary Figure**).

Each center provided data on PCI patient outcomes. One-year mortality including all-cause death, cardiac death with information as to the mode of death, non-fatal events necessitating hospitalization for ACS, stroke, bleeding, acute heart failure, and repeat revascularization were registered for patients in the cohort. All 1-year outcome data were registered from August 2018 to March 2019 via a secure web-based electronic data capture system managed by the National Clinical Database with linkage to the J-PCI 2017 registry. Data were collected by data entry personnel either by reviewing health record charts or by contacting individual patients by telephone, and were reviewed by data managers responsible for each site. The final data were fixed in September 2019, and the analysis for the present study was performed from November 2019 to January 2020.

The study protocol was approved by a third-party central ethics committee at the Clinical Research Promotion Network Japan and local institutional review boards of each site. Patient consent was obtained through an opt-out format notification on websites and posters, and the procedures were conducted in accordance with the principles of the Declaration of Helsinki.

Patient Information

The participating hospitals included in the J-PCI OUTCOME cohort covered all 8 regions of Japan (Hokkaido, Tohoku, Kanto, Chubu, Kinki, Chugoku, Shikoku, and Kyushu/Okinawa). For the present analysis, patients who underwent PCI from January 1, 2017 to December 31, 2017 were selected to form a patient-based cohort from a consecutively collected case-based 2017 J-PCI Registry. The date of the follow-up started from the date when the PCI preformed. All ACS patients that survived and were discharged after hospitalization were included in this study. Patient and PCI characteristics comparing the study population in the J-PCI OUTCOME cohort and 2017 J-PCI Registry are provided in **Supplementary Table 1**. The proportion of ACS and chronic kidney disease (CKD) patients and patients treated for proximal coronary lesions was

	STEMI (n=10,242)	NSTEMI (n=3,027)	UA (n=6,773)	P value
Age (years)	68.3±13.0	70.0±12.5	70.7±11.4	<0.001
Age group				
<65 years	3,539 (35)	896 (30)	1,744 (26)	
65 years≤age<75 years	3,109 (30)	922 (30)	2,256 (33)	<0.001
75 years≤age<80 years	3,594 (35)	1,209 (40)	2,773 (41)	
≥80 years	2,265 (22)	781 (26)	1,620 (24)	<0.001
Male sex	7,862 (77)	2,303 (76)	5,080 (75)	<0.001
Previous PCI	1,137 (11)	589 (19)	2,260 (33)	<0.001
Previous CABG	104 (1)	104 (3)	316 (5)	<0.001
Previous MI	875 (9)	479 (16)	1,198 (18)	<0.001
Previous HF	461 (5)	348 (11)	789 (12)	<0.001
Diabetes	3,478 (34)	1,161 (38)	2,856 (42)	<0.001
Hypertension	6,817 (67)	2,203 (73)	5,154 (76)	<0.001
Dyslipidemia	5,637 (55)	1,820 (60)	4,469 (66)	<0.001
Smoking	4,237 (41)	1,139 (38)	2,307 (34)	<0.001
CKD	1,562 (15)	632 (21)	1,302 (19)	<0.001
Hemodialysis	230 (2)	150 (5)	468 (7)	<0.001
COPD	245 (2)	79 (3)	163 (2)	<0.001
AAA/PAD	301 (3)	177 (6)	454 (7)	<0.001
Cardiogenic shock	1,300 (13)	256 (8)	116 (2)	<0.001
Cardiac arrest	726 (7)	152 (5)	59 (1)	<0.001
Any antiplatelet use prior to PCI	8,298 (81)	2,612 (86)	6,091 (90)	<0.001
Aspirin	8,154 (80)	2,564 (85)	5,907 (87)	<0.001
Clopidogrel	1,129 (11)	601 (20)	1,958 (29)	<0.001
Prasugrel	6,410 (63)	1,747 (58)	3,458 (51)	<0.001
Ticagrelor	8 (0)	1 (0)	4 (0)	<0.001
Other	74 (1)	40 (1)	153 (2)	<0.001
Any oral anticoagulant use	377 (4)	170 (6)	397 (6)	<0.001
Warfarin	181 (2)	76 (3)	182 (3)	<0.001
Dabigatran	15 (0)	11 (0)	20 (0)	<0.001
Rivaroxaban	50 (0)	31 (1)	74 (1)	<0.001
Apixaban	53 (1)	32 (1)	64 (1)	<0.001
Edoxaban	36 (0)	19 (1)	46 (1)	<0.001
Other	62 (1)	12 (0)	18 (0)	<0.001
Preprocedural Hb (g/dL)	13.8±2.2	13.3±2.2	13.2±2.1	<0.001
Preprocedural Cr (mg/dL)	0.9 [0.7–1.1]	0.9 [0.7–1.1]	0.9 [0.7–1.1]	<0.001
Median (Q1–Q3) if STEMI	70 [53–90]	NA	NA	
Door-to-balloon time ≤90 min	6,806	NA	NA	

Unless indicated otherwise, data are presented as the mean±SD, median [interquartile range], or n (%). AAA, abdominal aortic aneurysm; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; Cr, creatinine; Hb, hemoglobin; HF, heart failure; MI, myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; UA, unstable angina.

higher in the OUTCOME cohort, whereas the proportion of patients with a previous history of PCI or myocardial infarction was lower than in the 2017 J-PCI Registry.

Data completeness of all collected variables was >95%, with the exception of door-to-balloon time, total fluoroscopy time, total procedure time, total anesthesia time, preprocedural hemoglobin level, and preprocedural creatinine level, which were newly added from January 2017 as optional entry variables.

Definition of Key Variables

ACS patients were selected as the main study population after excluding patients receiving PCI for elective indica-

tions (**Figure 1**). Further, the ACS population was subdivided according to the clinical presentation of ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina (UA). All ACS categories were diagnosed based on clinical presentation, electrocardiographic findings, and elevation of serum cardiac troponin or creatinine kinase concentrations.

Cardiogenic shock was defined as a sustained episode of systolic blood pressure <80 mmHg and/or a cardiac index of <1.8 L·min⁻¹·m⁻² (regardless of the measurement methods), despite the maximum treatment and determined to be secondary to cardiac dysfunction, and/or the need for parenteral inotropic or vasopressor agents or mechanical

	STEMI (n=10,242)	NSTEMI (n=3,027)	UA (n=6,773)	P value
Access site				
Transfemoral	3,798 (37)	847 (27)	1,554 (23)	<0.001
Transradial	6,086 (59)	2,074 (28)	4,864 (72)	
Other	358 (3)	106 (69)	355 (5)	
No. vessels treated during PCI				
One	6,301 (62)	1,600 (53)	3,983 (59)	<0.001
Two	2,544 (25)	845 (28)	1,783 (26)	0.002
Three	1,387 (14)	572 (19)	997 (15)	<0.001
LMT lesion	385 (4)	180 (6)	317 (5)	<0.001
Treated coronary lesion location				
Proximal lesion	5,309 (52)	1,528 (50)	3,535 (52)	0.28
PCI to RCA	4,148 (40)	865 (29)	2,190 (32)	<0.001
PCI to LCX	5,504 (54)	1,486 (49)	3,762 (56)	<0.001
PCI to LAD	1,481 (14)	1,101 (36)	1,544 (23)	<0.001
PCI to graft lesion	16 (0.20)	21 (1)	47 (1)	<0.001
PCI to other lesion	11 (0.10)	6 (0.20)	9 (0.10)	<0.001
PCI to LMT	441 (4)	242 (8)	440 (6)	<0.001
Devices used during PCI				
Drug-eluting stent	8,835 (86)	2,532 (84)	5,797 (86)	<0.001
Bare-metal stent	139 (1.40)	30 (1.00)	63 (0.90)	0.03
POBA	8,456 (83)	2,580 (85)	5,761 (85)	<0.001
Drug-eluting balloon	532 (5)	291 (10)	960 (14)	<0.001
Thrombus aspiration	5,809 (57)	771 (25)	500 (7)	<0.001
Rotational atherectomy	60 (1)	86 (3)	330 (5)	<0.001
Direct cutting atherectomy	2 (0.02)	0 (0)	13 (0.19)	<0.001
Distal protection device	1,014 (10)	124 (4)	308 (5)	<0.001
Other devices	309 (3)	68 (2)	117 (2)	<0.001
Unknown device	4 (0.04)	2 (0.07)	2 (0.03)	0.7
PCI success				
Guidewire lesion penetration	10,113 (99)	2,936 (97)	6,664 (98)	<0.001
Fluoroscopy time (min)	14 [17–36]	27 [18–40]	24 [16–36]	<0.001
Procedure time (min)	91 [69–123]	95 [70–130]	90 [66–120]	<0.001
Periprocedural complication				
Cardiac tamponade	22 (0.20)	1 (0.00)	5 (0.10)	0.01
Acute heart failure	248 (2)	53 (2)	36 (1)	<0.001
Acute stent thrombosis	45 (0.40)	5 (0.20)	6 (0.10)	<0.001
Access site bleeding	24 (0.20)	9 (0.30)	8 (0.10)	0.12
Non-access site bleeding	34 (0.30)	8 (0.30)	8 (0.10)	0.02
Emergency heart surgery	12 (0.10)	4 (0.10)	7 (0.10)	0.9

Unless indicated otherwise, data are given as the median [interquartile range] or n (%). LAD, left anterior descending; LCX, left circumflex; LMT, left main trunk; POBA, plain old balloon angioplasty; RCA, right coronary artery. Other abbreviations as in Table 1.

support, including an intra-aortic balloon pump and percutaneous mechanical circulatory device (e.g., venoarterial extracorporeal membrane oxygenation device) to maintain blood pressure and the cardiac index above the specified levels within the 24h prior to PCI. Other definitions of variables included in the J-PCI Registry are available online (http://www.cvit.jp/registry/jpci_definition.pdf).

Definitions of Clinical Outcomes

Clinical endpoints were defined according to the 2017 Cardiovascular and Stroke Endpoint Definitions for Clinical Trials definitions.¹⁶ Definite stent thrombosis was registered for cardiovascular deaths and non-fatal ACS events

according to the Academic Research Consortium-2 Consensus Document.¹⁷ A maximum of 3 events for non-fatal ACS, stroke, bleeding, and acute heart failure and 5 events for planned revascularization were registered in the database. Mode of death was divided into non-cardiac death, death due to unknown cause, cardiac death with subcategories of death due to ACS, sudden cardiac death, death due to heart failure, death due to stroke, death due to procedural complication, and death due to bleeding events. ACS patients were subdivided into those presenting with STEMI, NSTEMI, and UA with or without revascularization. Bleeding events were subdivided into access site bleeding, upper gastrointestinal bleeding, lower gastroin-

Table 3. Post-PCI 30-Day and 1-Year Outcomes

	STEMI (n=10,242)	NSTEMI (n=3,027)	UA (n=6,773)	P value
All-cause death (30 days)	431 (4)	102 (3)	73 (1)	<0.001
Cardiac death	356 (3)	83 (3)	49 (1)	0.008
Cardiac death due to ACS	270 (3)	60 (2)	19 (0.3)	
Cardiac death due to sudden cardiac arrest	18 (0.2)	3 (0.1)	7 (0.1)	
Cardiac death due to AHF	63 (0.6)	20 (0.7)	21 (0.3)	<0.001
Cardiac death due to stroke	2 (0.02)	0 (0)	0 (0)	
Cardiac death due to procedural complications	1 (0.01)	0 (0)	1 (0.01)	
Cardiac death due to bleeding	6 (0.06)	2 (0.07)	2 (0.03)	
Non-cardiac death	75 (1)	19 (1)	24 (0.4)	0.008
Death for unknown reason	6 (0.06)	2 (0.07)	6 (0.09)	
All-cause death (1 year)	752 (7)	214 (7)	243 (4)	<0.001
Cardiac death	523 (5)	128 (4)	115 (2)	<0.001
Cardiac death due to ACS	309 (3)	74 (2.4)	28 (0.4)	
Cardiac death due to sudden cardiac arrest	35 (0.3)	9 (0.3)	20 (0.3)	
Cardiac death due to AHF	134 (1.3)	40 (1.3)	49 (0.7)	<0.001
Cardiac death due to stroke	2 (0.02)	1 (0.03)	1 (0.01)	
Cardiac death due to procedural complications	3 (0.03)	0 (0)	3 (0.04)	
Cardiac death due to bleeding	8 (0.1)	2 (0.1)	3 (0.04)	
Non-cardiac death	263 (2.6)	85 (2.8)	133 (2.0)	<0.001
Death for unknown reason	46 (0.4)	19 (0.6)	35 (0.5)	<0.001
Definite or probable stent thrombosis	31 (0.3)	4 (0.1)	13 (0.2)	0.15
Non-fatal ACS	133 (1)	53 (2)	131 (2)	<0.001
STEMI	76 (1)	16 (1)	13 (0.2)	
NSTEMI	33 (0.3)	23 (1)	28 (0.4)	<0.001
UA	41 (0.4)	21 (1)	101 (1)	
Non-fatal ischemic stroke	93 (1)	23 (1)	46 (1)	0.25
Non-fatal bleeding	171 (2)	43 (1)	122 (2)	0.40
Access site bleeding	19 (0.2)	6 (0.2)	12 (0.2)	
Upper GI	25 (0.2)	8 (0.3)	20 (0.3)	
Lower GI	48 (0.5)	15 (0.5)	41 (0.6)	
Intracranial	22 (0.2)	3 (0.1)	14 (0.2)	0.83
Urogenital	22 (0.2)	3 (0.1)	18 (0.3)	
Other	47 (0.5)	10 (0.3)	30 (0.4)	
Non-fatal AHF	238 (2)	78 (3)	119 (2)	0.01
Planned revascularization	1,774 (17)	563 (19)	1,269 (19)	0.04
Staged PCI	193 (2)	81 (3)	268 (4)	
PCI due to chest discomfort symptoms	419 (4)	124 (4)	241 (4)	
PCI due to proven myocardial ischemia	132 (1)	40 (1)	104 (2)	<0.001
PCI without symptoms/ischemia	1,044 (1)	315 (1)	666 (1)	
CABG	87 (1)	36 (1)	58 (1)	
3-point MACE	608 (6)	164 (5)	168 (2)	<0.001

Unless indicated otherwise, data are given as n (%). ACS, acute coronary syndrome; AHF, acute heart failure; GI, gastrointestinal; MACE, major adverse cardiac events. Other abbreviations as in Table 1.

testinal bleeding, cerebrovascular or spinal bleeding, urogenital bleeding, and bleeding of unknown origin.

Statistical Analysis

Descriptive analysis was performed to compare baseline patient and coronary lesion characteristics, details on specific procedures used, and 1-year outcomes among the STEMI, NSTEMI, and UA groups. Variables are expressed as the mean±SD, median and interquartile range (IQR), or counts and percentages, as appropriate. For comparisons among groups, the χ^2 test was used for categorical variables and 1-way analysis of variance was used for continu-

ous variables.

One-year rates of all-cause death, individual modes of death, ACS, stroke, bleeding, acute heart failure, and repeat revascularization were calculated using the Kaplan-Meier method. Unadjusted and adjusted Cox proportional hazard ratios (HRs) and Fine-Gray competing risks regression models were used to calculate effect estimates as cause-specific HR for Cox models or subdistribution HR for Fine-Gray models,¹⁸ with 95% confidence intervals (CI). To account for the multisite design, all models included the registration hospital site as a random intercept. Univariable and multivariable HRs were calculated,

Table 4. HRs for 1-Year Outcomes

	UA (n=6,773)	NSTEMI (n=3,027)		STEMI (n=10,242)	
		HR (95% CI)	P value	HR (95% CI)	P value
All-cause death					
Univariable Cox regression analysis	Reference	1.97 (1.63–2.39)	<0.001	2.10 (1.81–2.43)	<0.001
Multivariable Cox regression analysis	Reference	1.57 (1.29–1.92)	<0.001	1.91 (1.62–2.26)	<0.001
Cardiac death					
Unadjusted Cox regression analysis	Reference	2.75 (2.09–3.63)	<0.001	3.27 (2.62–4.09)	<0.001
Multivariable Cox regression analysis	Reference	1.94 (1.45–2.61)	<0.001	2.62 (2.04–3.36)	<0.001
Non-cardiac death					
Unadjusted Cox regression analysis	Reference	1.48 (1.14–1.93)	<0.001	1.31 (1.07–1.61)	<0.001
Multivariable Cox regression analysis	Reference	1.40 (1.06–1.84)	<0.001	1.43 (1.14–1.80)	<0.001
3-point MACE: Cardiac death, non-fatal MI, stroke					
Unadjusted Cox regression analysis	Reference	2.17 (1.73–2.71)	<0.001	2.37 (1.99–2.83)	<0.001
Multivariable Cox regression analysis	Reference	1.68 (1.33–2.13)	<0.001	2.12 (1.74–2.59)	<0.001
Non-fatal ACS					
Unadjusted analysis	Reference	0.99 (0.71–1.39)	0.97	0.64 (0.49–0.84)	0.001
Multivariable Cox regression analysis	Reference	1.03 (0.74–1.42)	0.79	0.89 (0.67–1.19)	0.44
Non-fatal ischemic stroke					
Unadjusted Cox regression analysis	Reference	1.16 (0.69–1.97)	0.57	1.45 (1.04–2.01)	0.03
Multivariable Cox regression analysis	Reference	1.11 (0.65–1.89)	0.71	1.70 (1.24–2.33)	0.001
Non-fatal AHF					
Unadjusted Cox regression analysis	Reference	1.42 (1.04–1.92)	0.03	1.38 (1.10–1.73)	0.005
Multivariable Cox regression analysis	Reference	1.48 (1.12–1.97)	0.007	1.78 (1.38–2.29)	<0.001
Non-fatal bleeding					
Unadjusted Cox regression analysis	Reference	0.80 (0.53–1.20)	0.29	0.99 (0.76–1.29)	0.94
Multivariable Cox regression analysis	Reference	0.80 (0.53–1.23)	0.32	1.08 (0.82–1.42)	0.59
Repeat revascularization					
Unadjusted Cox regression analysis	Reference	1.05 (0.92–1.20)	0.49	0.98 (0.89–1.08)	0.66
Multivariable Cox regression analysis	Reference	0.96 (0.84–1.09)	0.55	0.98 (0.89–1.08)	0.74

CI, confidence interval; HR, hazard ratio. Other abbreviations as in Tables 1,3.

with the latter adjusting for covariates associated with in-hospital mortality previously published from the J-PCI Registry,¹⁹ which included age, sex, previous PCI, coronary artery bypass graft surgery, hypertension, dyslipidemia, smoking, CKD, hemodialysis, peripheral vascular disease, previous heart failure, cardiogenic shock, 3-vessel disease, left main trunk (LMT) lesion, performance of PCI to the LMT, and PCI for a proximal left anterior descending (LAD) artery lesion.

All data were managed by the National Clinical Database and by data analysts belonging to the J-PCI Registry statistical analysis team. All analyses were performed using Stata/IC Version 15.1 for Macintosh (StataCorp, College Station, TX, USA). P values are 2-sided and P<0.05 was considered statistically significant.

Results

Baseline Patient Characteristics

In the J-PCI OUTCOME cohort, 49,014 patients were followed up, comprising 16,129 thousand-person days (follow-up rate 79.3%; **Figure 1**). Within the 20,042 ACS patients (51% [n=10,242] STEMI, 15% [n=3,027] NSTEMI, and 34% [n=6,773] UA), the mean age was 69.6±12.4 years, 23% were aged >80 years, 76% were male, 20% had a previous history of PCI, 39% had diabetes, 18% had CKD, and 4% were on hemodialysis. Cardiogenic shock and cardiac arrest occurred in 8% and 5% of study patients,

respectively. Antiplatelet medications were administered within 24 h of PCI for 81% of STEMI patients, 86% of NSTEMI-ACS patients, and 90% of UA patients (**Table 1**). Aspirin and prasugrel were the most preferred antiplatelet agents over clopidogrel and ticagrelor for all 3 indications. The transradial approach and drug-eluting stents (DES) were used in 65% and 86% of all cases, respectively (**Table 2**).

STEMI patients were younger, predominantly male, with a smaller proportion of previous coronary artery disease and comorbidities, and reported a higher proportion of cardiogenic shock and cardiac arrest events than patients in the other 2 groups. The proportion of PCI procedures performed via the transfemoral approach and the use of thrombus aspiration and distal protection devices was highest among STEMI patients, although the implantation rate of DES did not differ significantly among the groups. NSTEMI patients were older (mean age 70.0±12.5 years), with 26% aged above 80 years, and received the greatest proportion of multivessel PCI. Finally, the UA patient group had the highest proportion of cases with previous PCI, diabetes, hemodialysis, and the presence of extracardiac vascular lesions, as well as highest rate of administration of antiplatelet therapy prior to PCI.

Post-PCI 30-Day and 1-Year Mortality Rates

The overall 30-day all-cause, cardiac, and non-cardiac mortality rates were 3.0%, 2.4%, and 0.6%, respectively. Fatal ACS, fatal acute heart failure, and sudden cardiac

A All-cause death

B. Cardiac death

C. Non-cardiac death

Figure 2. Kaplan-Meier curves for (A) all-cause, (B) cardiac, and (C) non-cardiac deaths according to indication. NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; UA, unstable angina.

events were the leading modes of cardiac death. Cardiac deaths predominated over non-cardiac deaths (81% vs. 19%) among all deaths within the first month after PCI. STEMI patients had the highest 30-day all-cause, cardiac, and non-cardiac mortality rates (4.2%, 3.5%, and 0.7%, respectively). NSTEMI patients had the second highest rates, and UA patients had the lowest mortality rates (Table 3). The overall 1-year incidence of all-cause, cardiac, and non-cardiac mortality rates was 7.1%, 4.2%, and 2.8%, respectively (Table 3). An acute increase in the incidence of cardiac deaths was observed within the first 30 days, followed by a plateau with a minimal increase for all indications. In contrast with cardiac deaths, the incidence of non-cardiac deaths exhibited a gradual and constant increase across all indications. The risk-adjusted HRs for 1-year all-cause death, cardiac death, and non-cardiac

death were all significantly higher in STEMI and NSTEMI patients than in UA patients (Table 4; Figure 2). The adjusted HRs for cardiac death were particularly higher for STEMI (HR 2.62; 95% CI 2.04–3.36) and NSTEMI (HR 1.94; 95% CI 1.45–2.61) patients than for UA patients.

Clinical Events at 1 Year

Kaplan-Meier and cumulative incidence curves of non-fatal adverse events, including ACS, ischemic stroke, acute heart failure, major bleeding, and repeat revascularization, are shown in Figures 3,4. The unadjusted and adjusted HRs for subsequent 1-year adverse events accounting for confounders and registered hospitals as random intercepts are presented in Table 4. Of note, compared with UA patients, STEMI patients had higher risks for all fatal events, non-fatal ischemic stroke, and acute heart failure,

A Acute coronary syndrome

B Stroke

C Acute heart failure

D Bleeding

E Repeat revascularization

Figure 3. Kaplan-Meier curves of non-fatal events: (A) acute coronary syndrome, (B) stroke, (C) acute heart failure, (D) bleeding, and (E) repeat vascularization. NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; UA, unstable angina.

and NSTEMI patients had a higher risk for heart failure. Notably, a history of previous heart failure, CKD, and cardiogenic shock at hospital presentation were associated with a higher risk of 1-year major adverse cardiac events (MACE) in all 3 subcategories of ACS (**Supplementary Table 2**). Specifically, for STEMI patients, older age, the presence of 3-vessel disease, and performing PCI for either the LMT or LAD #6 lesion were associated with higher risks of 1-year MACE. For NSTEMI patients, PCI for an LAD #6 lesion was associated with higher risks. Finally,

for UA patients, older age, female sex, and a history of previous PCI were associated with higher risks of 1-year MACE.

Definite and probable stent thrombosis occurred in 0.3%, 0.1%, and 0.2% of STEMI, NSTEMI, and UA patients, respectively, within the 1-year of follow-up. Most cases of stent thrombosis occurred in the first 30 days, although there were a number of cases in the later months seen as late stent thrombosis. With regard to repeat revascularization, 18% of all ACS patients underwent repeat

A Acute coronary syndrome

B Stroke

C Acute heart failure

D Bleeding

E Repeat revascularization

Figure 4. Cumulative incidence of non-fatal events: (A) acute coronary syndrome, (B) stroke, (C) acute heart failure, (D) bleeding, and (E) repeat revascularization. NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; UA, unstable angina.

revascularization within 1 year of the index PCI. Staged PCI was performed in approximately 10% of patients within 30 days, followed by a proportional increase in repeat PCI due to chest discomfort and proven myocardial ischemia in the past 6 months.

Discussion

The improvement in early in-hospital outcomes of ACS patients has been largely attributed to the widespread distribution of PCI-capable hospitals and their expertise in performing prompt revascularization. Nonetheless, data on late outcomes in the real-world setting have remained

scarce in the modern era. This study is the first to evaluate a nationwide cohort extending beyond the limitations of previous representative regional registries, such as the Coronary Revascularization Demonstrating Outcome Study-Kyoto Registry Cohort (CREDO-KYOTO)-1, -2, and -3 and the Japan Cardiovascular Database Keio interhospital Cardiology Study (JCD-KiCS), and collected 1-year outcomes from consecutive PCI patients during 2017 covering all 47 prefectures from 8 regions of Japan. We report that for ACS hospital survivors, cardiac deaths were the main cause of 30-day mortality with ACS, whereas heart failure and sudden cardiac death were the leading modes of cardiac death, particularly among STEMI and NSTEMI

patients. The risk of 1-year subsequent adverse events was generally higher in STEMI and NSTEMI patients than in UA patients.

The crude 30-day and 1-year all-cause mortality and thrombotic event rates, including incident ACS, in the present study were comparable to or lower than those in previous reports from representative real-world registries. The 30-day mortality rate among acute myocardial infarction (AMI) patients was reported to be 7.1% in the Osaka Acute Coronary Insufficiency Study²⁰ (patients registered from January 2002 to December 2010 from 25 hospitals) and 9.4% in the HIJAMI Study²¹ (patients registered from January 1999 to June 2001 from 17 hospitals). Although direct comparison of long-term outcomes between databases is challenging due to differences in patient registration methods, race, ethnicity, timing of registration, approved medications or treatment device, and level of access to care, these numbers are approximately half or one-third the rates reported in studies conducted over a decade ago, with the exception of the Prevention of Atherothrombotic Incidents Following Ischemic Coronary attack registry (2008–2009 from 98 hospitals).²² The results of the present study are also comparable to those of a report from the SWEDEHEART registry (2008), which registered all AMI patients aged 60–69 years,²³ and the NCDR CathPCI Registry Medicare beneficiaries (2009–2014).²⁴

Cardiac deaths occurred frequently during the first 30 days and plateaued thereafter. In contrast, non-cardiac deaths showed an unchanged constant upward trend that overlapped the incidence of cardiac deaths at 1 year after the index PCI. A similar observation has been reported in a single-center study at the Mayo Clinic,²⁵ as well as in a pooled randomized trial database analysis from the Cardiovascular Research Foundation, which demonstrated that the predominant cause of death switched 3 years after PCI.²⁶ The results of the present study re-emphasize the importance of the periodic assessment of long-term causes of specific causes of death and adverse events, because the proportion of these events changes over time. It also underscores the need for the adjustment of treatment thresholds for specific interventions to obtain maximal effect at a given time period.

The leading attributable causes of cardiac deaths were death due to recurrent ACS, heart failure, and sudden cardiac death. In line with the TIMI Study Group NSTEMI-ACS merged patient database, recurrent ACS was the leading cause of 30-day cardiac mortality in the present study. At 30 days after the index procedure, the proportion of leading modes of cardiac death shifted towards heart failure and sudden cardiac deaths. Sudden cardiac deaths occur in the early stage after myocardial infarction, and were observed in our database. Nonetheless, intracardiac defibrillator implantation for primary prevention purposes <40 days after myocardial infarction or <90 days after PCI is prohibited in the US²⁷ based on the results of the 2004 Defibrillator in Acute Myocardial Infarction Trial (DINAMIT)²⁸ trial and the 2009 Immediate Risk-Stratification Improves Survival (IRIS) trial.²⁹ This unmet need may be mitigated through several of the JCS guidelines,³⁰ which propose secondary prevention strategies such as: (1) adherence and uptitration of optimal medical therapies (OMTs) including aspirin, P2Y₁₂ inhibitors, statins, and renin-angiotensin-aldosterone system inhibitors (RAASi);³¹ (2) participation in cardiac rehabilitation programs;³² and

(3) application of wearable cardioverter-defibrillators, if tolerable, in select patients. The 2018 Vest Prevention of Early Sudden Death Trial (VEST) did not show any significant beneficial effects of wearable cardioverter-defibrillators in post-myocardial infarction patients, with an approximate 90% prescription rate of statins, β -blockers, and RAASi.³³ That study suggested that medical therapy is indeed a key component for reducing sudden cardiac deaths and for those who can tolerate the devices.

The timing and incidence of stent thrombosis were similar to those observed in the case-control Retrospective Multicenter Registry of ST After First- and Second-Generation DES Implantation (REAL-ST) study, including 313 definite stent thromboses during a mix of the first- and second-generation DES eras.³⁴ Thoughtful consideration of balancing individual bleeding and thrombotic risks is needed when considering the continuation or discontinuation of dual antiplatelet agents after PCI³⁰ by using locally validated risk scores, such as the PRECISE-DAPT score,³⁵ to minimize overall long-term treatment-related complications. Despite treatment improvement with P2Y₁₂ inhibitors³⁶ and newer generation drug-eluting coronary stents,³⁷ the identification of high-risk patients predisposed to ACS recurrence, including stent thrombosis, remains a challenge.

Study Limitations

The findings of this study should be interpreted in the context of several limitations. First, although study patients and hospitals were chosen from diverse backgrounds, there may have been selection bias. The hospitals included in the J-PCI OUTCOME registry were generally moderate- to high-volume centers that chose to take part in this unique nationwide registry. The nature of such site selection may have introduced bias towards better outcomes compared with other hospitals not included in the study. Nonetheless, differences in patient characteristics observed between this cohort and the 2017 cross-sectional registry were all within expectation, with the former have a higher proportion of ACS and the latter have a higher proportion of elective cases.

Second, outcome events were not extensively adjudicated by a central adjudicating committee; however, randomly selected site visits are performed every year to a total of approximately 20 hospitals to ensure data completeness and integrity. Validation of data reliability remains a future issue; nonetheless, this is the most recent and the largest nationwide cohort study conducted to evaluate extensive 1-year outcomes in patients at moderate- to high-volume PCI hospitals.

Third, the performance of complete revascularization for ACS patients that received Class IIa recommendation from the CVIT expert consensus document is unknown. Furthermore, the effect of repeat revascularization, including staged PCI for residual lesions or de novo coronary stenosis lesions, was not evaluated. Fourth, details on left ventricle ejection fraction, cardiac enzymes, discharge medications, and uptitration of OMT likely to affect long-term prognosis are unknown. This may be one of the most actionable issues to improve the quality of care, because previous reports have demonstrated undertreatment, particularly in individuals who are older and present renal dysfunction.³⁸

Fifth, the duration of dual antiplatelet therapy is unknown within our database and is likely affected by long-term thromboembolic and major bleeding events.

Sixth, bleeding events were not defined according to the standardized bleeding criteria, such as the Bleeding Academic Research Consortium, Global Use of Strategies to Open Occluded Arteries, or Thrombolysis in Myocardial Infarction, due to a lack of feasibility in a nationwide cohort. Finally, our ACS population and 1-year outcomes should be interpreted in the context of patients in whom PCI was deemed feasible at the time of presentation, with patients who underwent emergency coronary artery bypass grafting surgery or conservative medical therapy only not included.

Conclusions

In this nationwide cohort, cardiac deaths were the main cause of 30-day mortality, with ACS, heart failure, and sudden cardiac death as the leading causes of cardiac deaths among ACS hospital survivors. The risk of 1-year subsequent adverse events was generally higher in STEMI and NSTEMI patients than in UA patients. Future research is warranted to improve the quality of secondary prevention for the AMI population in the modern era.

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IRB Information

The study protocol was approved by a third-party central ethics committee at the Clinical Research Promotion Network Japan (Reference no. CVIT-2017) and local institutional review boards of each participating site. The names of the individual sites are provided in the **Supplementary Appendix**. Patient consent was obtained through an opt-out format notification on websites and posters, and procedures were conducted according to the principle of the Declaration of Helsinki.

Data Availability

The deidentified participant data will not be shared.

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Supplementary Files

Please find supplementary file(s);
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