

Comparison of Outcomes After Percutaneous Coronary Intervention in Elderly Patients, Including 10 628 Nonagenarians: Insights From a Japanese Nationwide Registry (J-PCI Registry)

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Background—Scarce data exist about the outcomes after percutaneous coronary intervention (PCI) in old patients. This study sought to provide an overview of PCI in elderly patients, especially nonagenarians, in a Japanese large prospective nationwide registry.

Methods and Results—We analyzed 562 640 patients undergoing PCI (≥ 60 years of age) from 1018 Japanese hospitals between 2014 and 2016 in the J-PCI (Japanese percutaneous coronary intervention) registry. Among them, 10 628 patients (1.9%), including 6780 (1.2%) with acute coronary syndrome (ACS) and 3848 (0.7%) with stable coronary artery disease, were ≥ 90 years of age. We investigated differences in characteristics and in-hospital outcomes among sexagenarians, septuagenarians, octogenarians, and nonagenarians. Older patients were more frequently women and had a greater frequency of heart failure and chronic kidney disease than younger patients. In addition, older patients had a higher rate of in-hospital mortality, cardiac tamponade, cardiogenic shock after PCI, and bleeding complications requiring blood transfusion. Nonagenarians had the highest risk of in-hospital mortality (odds ratio, 3.60; 95% CI, 3.10–4.18 in ACS; odds ratio, 6.24; 95% CI, 3.82–10.20 in non-ACS) and bleeding complications (odds ratio, 1.79; 95% CI, 1.35–2.36 in ACS; odds ratio, 2.70; 95% CI, 1.68–4.35 in non-ACS) when referenced to sexagenarians. More important, transradial intervention was an inverse independent predictor of both in-hospital mortality and bleeding complications.

Conclusions—Older patients, especially nonagenarians, carried a greater risk of in-hospital death and bleeding compared with younger patients after PCI. Transradial intervention might contribute to risk reduction for periprocedural complications in elderly patients undergoing PCI. (*J Am Heart Assoc.* 2019;8:e011017. DOI: 10.1161/JAHA.118.011017.)

Key Words: nonagenarians • octogenarians • percutaneous coronary intervention • transradial intervention

Because populations in advanced nations, including Japan, are aging thanks to the progress made in medical science, the number of elderly patients with coronary artery disease (CAD) undergoing percutaneous coronary intervention (PCI) has been increasing.^{1–4} Previous studies have reported that older patients have an increased risk for adverse outcomes during and after PCI compared with younger patients.^{5,6} However, details on the characteristics and outcomes after

PCI in old patients, especially nonagenarians, remain uncertain, as such patients are often excluded from major clinical trials of cardiovascular interventions because of concerns about the increased risk of adverse events and limited life expectancy.⁷ In addition, older patients with CAD are less likely than younger patients to receive invasive revascularization strategies, even in current clinical practice.^{2,8–10} Consequently, the sample size of this group of patients who underwent PCI was limited, and only

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Clinical Perspective

What Is New?

- Although populations in advanced nations are aging because of advancements in medical science, details on the characteristics and outcomes after percutaneous coronary intervention in old patients, especially nonagenarians, remain uncertain, because such patients are often excluded from major clinical trials of cardiovascular interventions.
- This study provided an overview of percutaneous coronary intervention in elderly patients (≥ 60 years of age), including 10 628 nonagenarians, in a Japanese large prospective nationwide registry.

What Are the Clinical Implications?

- Older patients, especially nonagenarians, had a greater risk of in-hospital death and bleeding than younger patients after percutaneous coronary intervention.
- Transradial intervention might contribute to the reduction of risk for periprocedural complications after percutaneous coronary intervention in elderly patients.

dozens or hundreds of nonagenarians were included in previous studies.^{11–22} Therefore, available data about outcomes after PCI in nonagenarians have differed widely.²³ In addition, although some previous studies have investigated clinical outcomes after PCI in nonagenarians with acute coronary syndrome (ACS),^{2,3,12–17} few have specifically examined this issue in patients with stable CAD.^{11,20}

The purpose of the current study, which included one of the largest cohorts of nonagenarians who underwent PCI for both acute and elective indications, was to compare the in-hospital outcomes among elderly patients, including septuagenarians, octogenarians, and nonagenarians, in a contemporary Japanese nationwide coronary intervention registry.

Methods

The data, methods used in the analysis, and materials used to conduct the research will not be made available to any researchers for purposes of reproducing the results or replicating the procedure.

The J-PCI (Japanese percutaneous coronary intervention) registry is an ongoing, prospective, multicenter registry of the Japanese Association of Cardiovascular Intervention and Therapeutics, which was designed to record clinical characteristics and outcomes of patients who undergo PCI.^{24–27} Since 2013, it has been incorporated into the National Clinical Data system, which is a nationwide prospective online registration system. Each hospital has a data manager who is responsible for

collecting PCI data and entering them into a computer database. The Japanese Association of Cardiovascular Intervention and Therapeutics holds an annual meeting of data managers to secure appropriate data collection and performs random audits to check the quality of registered data. The study protocol of the J-PCI registry was approved by the Institutional Review Board Committee at the Network for Promotion of Clinical Studies (a specified nonprofit organization affiliated with Osaka University Graduate School of Medicine [Osaka, Japan]) and complied with the principles contained within the Declaration of Helsinki. Written informed consent was waived because of the retrospective and observational study design.

The current study included patients who underwent PCI and were recorded in the J-PCI registry between January 2014 and December 2016. Overall, the J-PCI registry contained 680 579 patients who underwent PCI in this study period. We excluded 117 939 patients who were < 60 years of age or had missing data for age, diagnosis, and in-hospital complications. As a result, a total of 562 640 patients ≥ 60 years of age who underwent PCI for ACS and stable CAD from 1018 Japanese hospitals were finally included in this study (Figure 1). Sexagenarians, septuagenarians, octogenarians, and nonagenarians were defined as patients between the age ranges of 60 to 69, 70 to 79, 80 to 89, and 90 to 99 years, respectively. A small number of centenarians (≥ 100 years of age, $n=102$) were included in the cohort of nonagenarians.

According to the J-PCI protocol, patients with ACS included those with ST-segment-elevation myocardial infarction (STEMI), non-STEMI, and unstable angina; and patients with stable CAD included those with non-ACS CAD, such as stable angina, old myocardial infarction, and silent ischemia. Cardiogenic shock was defined as a sustained episode of systolic blood pressure < 80 mm Hg, a cardiac index of < 1.8 L/min per m^2 determined to be secondary to cardiac dysfunction, and/or the requirement for parenteral inotropic or vasopressor agents or mechanical support, including an intra-aortic balloon pump, to maintain blood pressure and a cardiac index above the specified levels within 24 hours before the PCI procedures. Acute heart failure was defined as symptoms of heart failure within 24 hours before the PCI procedures, including dyspnea on mild activity, orthopnea, body fluid retention, moist rales, neck vein distention, and pulmonary edema, which were equivalent to congestive heart failure of New York Heart Association functional classification class IV. Chronic kidney disease (CKD) in this registry was defined as the presence of proteinuria, serum creatinine ≥ 1.3 mg/dL, or estimated glomerular filtration rate ≤ 60 mL/min per $1.73 m^2$, according to guidelines from the Japanese Society of Nephrology (<https://cdn.jsn.or.jp/guideline/pdf/CKDguide2012.pdf>). Successful PCI was defined as achievement of TIMI (Thrombolysis in Myocardial Infarction) flow grade III with a residual stenosis $\leq 25\%$ in the target lesion.

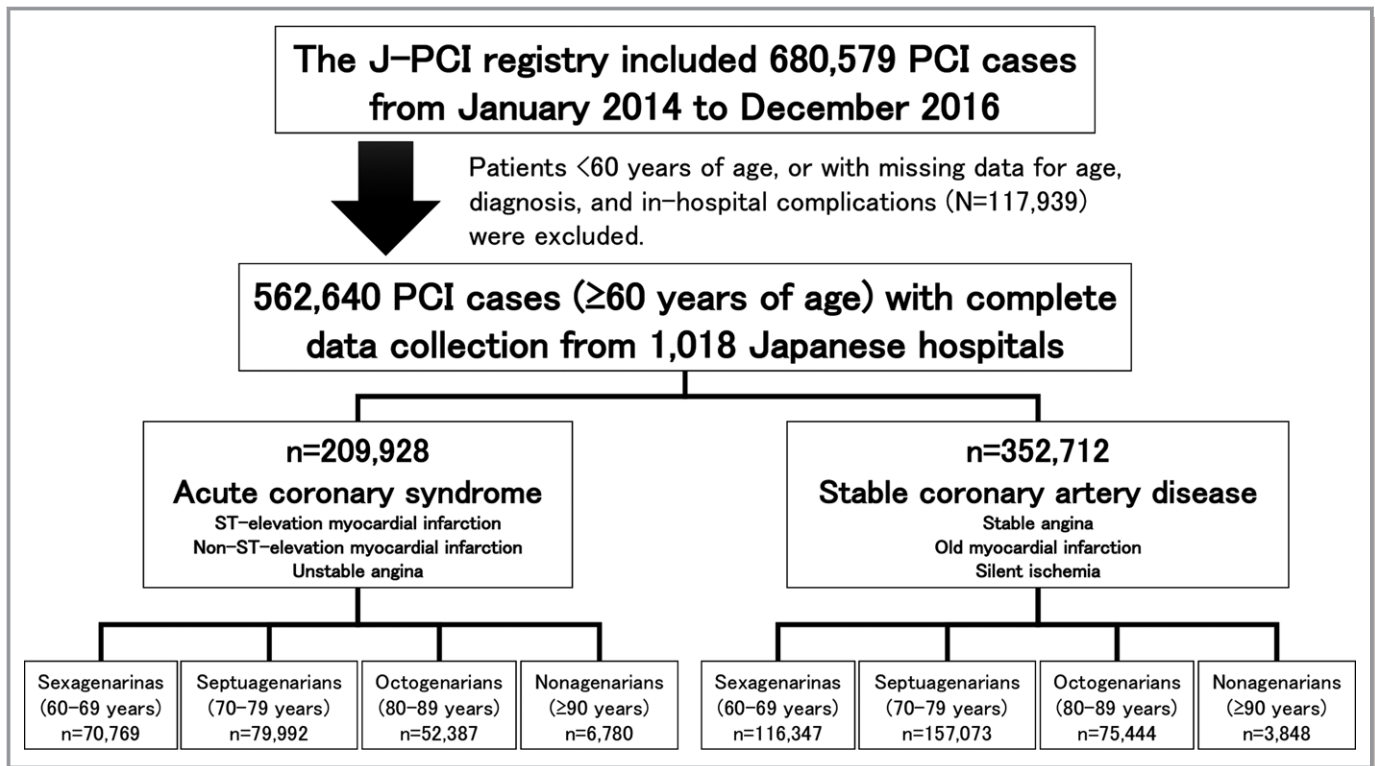


Figure 1. Flow chart of study enrollment. J-PCI registry indicates Japanese percutaneous coronary intervention registry; PCI, percutaneous coronary intervention.

In-hospital complications included in-hospital death within 30 days after PCI, cardiac tamponade, cardiogenic shock during and after PCI, emergency operations, bleeding complications, and other complications. A bleeding complication was defined as a bleeding event during or after PCI requiring blood transfusion, including access- and non-access-site bleeding. The full definitions of these J-PCI variables are available online (http://www.cvit.jp/registry/jpci_definition.pdf).

For statistical analysis, continuous variables are expressed as mean±SD, and categorical variables are expressed as frequency and percentage. For the comparison of baseline clinical characteristics, angiographic data, procedural data, and in-hospital complications among sexagenarians, septuagenarians, octogenarians, and nonagenarians, continuous variables were compared using ANOVA, and differences between categorical variables were examined using Pearson's χ^2 test. Logistic random-effects regression models were used to determine independent predictors of in-hospital mortality and bleeding complications. In the ACS cohort, we included the following variables: age (using sexagenarians as reference), female sex, history of heart failure, acute heart failure, presentation or diagnosis (using unstable angina as reference), cardiogenic shock, diabetes mellitus, CKD, 3-vessel disease, left main trunk (LMT) lesion, and access site (using transfemoral intervention as reference). In the stable CAD cohort, we included the following variables: age (using

sexagenarians as reference), female sex, history of heart failure, diabetes mellitus, CKD, 3-vessel disease, LMT lesion, and access site (using transfemoral intervention as reference). In addition, the precise relationships between age (continuous variable) and in-hospital adverse outcomes were summarized using cubic splines. We included institutes as a random intercept in all multivariable models.

All variables had <3% missingness. To account for missing data, single imputation was used for each variable: “male” for sex, “STEMI” for type of myocardial infarction, “transradial intervention” (TRI) for access site, and “no” for others. All statistical calculations and analyses were performed using R statistical software, version 3.3.3 (Free Software Foundation, Boston, MA). $P<0.05$ was considered statistically significant.

Results

Baseline characteristics of the 562 640 study patients who underwent PCI for ACS or stable CAD, stratified by age, are shown in Tables 1 and 2. A total of 209 928 patients (37.3%) underwent PCI for ACS and 352 712 patients (62.7%) underwent PCI for stable CAD. Among them, 6780 patients (1.2%) in the ACS cohort and 3848 patients (0.7%) in the stable CAD cohort were nonagenarians.

Overall, older patients were more frequently women and had a greater frequency of comorbidities, such as heart failure

Table 1. Baseline Clinical Characteristics in Patients With ACS

Characteristics	Sexagenarians (60–69 y)	Septuagenarians (70–79 y)	Octogenarians (80–89 y)	Nonagenarians (≥90 y)	P Value
	(n=70 769)	(n=79 992)	(n=52 387)	(n=6780)	
Age, y	65.0±2.7	74.5±2.8	83.7±2.7	92.2±2.3	<0.001
Female sex	12 301 (17.5)	22 304 (28.0)	21 640 (41.5)	4078 (60.4)	<0.001
Hypertension	48 506 (68.5)	58 410 (73.0)	40 053 (76.5)	5093 (75.1)	<0.001
Hyperlipidemia	43 731 (61.8)	46 412 (58.0)	26 774 (51.1)	2530 (37.3)	<0.001
Diabetes mellitus	28 451 (40.2)	32 306 (40.4)	18 344 (35.0)	1551 (22.9)	<0.001
Current smoker	29 561 (41.8)	21 990 (27.5)	9027 (17.2)	643 (9.5)	<0.001
History of percutaneous coronary intervention	19 864 (28.3)	25 506 (32.1)	16 374 (31.5)	1597 (23.8)	<0.001
History of coronary artery bypass grafting	1727 (2.5)	2920 (3.7)	1891 (3.6)	107 (1.6)	<0.001
History of heart failure	5256 (7.6)	8091 (10.4)	7802 (15.2)	1311 (19.8)	<0.001
History of myocardial infarction	11 707 (16.8)	13 930 (17.7)	9289 (18.0)	1085 (16.4)	<0.001
Peripheral artery disease	2500 (3.5)	4415 (5.5)	3411 (6.5)	357 (5.3)	<0.001
Chronic obstructive pulmonary disease	917 (1.3)	1932 (2.4)	1629 (3.1)	156 (2.3)	<0.001
Cardiogenic shock	4782 (6.9)	5434 (6.9)	4274 (8.3)	729 (10.9)	<0.001
Acute heart failure	5294 (7.6)	6866 (8.7)	6185 (12.0)	1121 (16.8)	<0.001
Chronic kidney disease	8650 (12.2)	12 933 (16.2)	10 943 (20.9)	1599 (23.6)	<0.001
Dialysis	3651 (5.2)	3961 (5.0)	1926 (3.7)	132 (1.9)	<0.001
Cardiopulmonary arrest on arrival	2904 (4.2)	2701 (3.4)	1582 (3.1)	184 (2.7)	<0.001
Presentation or diagnosis					
ST-segment–elevation myocardial infarction	33 072 (46.7)	33 484 (41.9)	22 129 (42.2)	3653 (53.9)	<0.001
Non–ST-segment–elevation myocardial infarction	7916 (11.2)	9098 (11.4)	6720 (12.8)	769 (11.3)	<0.001
Unstable angina	28 255 (39.9)	35 756 (44.7)	22 416 (42.8)	2196 (32.4)	<0.001
Access site					
Transfemoral intervention	26 432 (37.4)	30 176 (37.7)	20 527 (39.2)	2779 (41.0)	<0.001
Transradial intervention	41 597 (58.8)	46 167 (57.7)	29 175 (55.7)	3616 (53.3)	
Others	2739 (3.9)	3648 (4.6)	2685 (5.1)	385 (5.7)	
No. of diseased vessels					
1-Vessel disease	41 569 (58.7)	44 610 (55.8)	27 853 (53.2)	3500 (51.6)	<0.001
2-Vessel disease	18 790 (26.6)	22 375 (28.0)	15 041 (28.7)	1975 (29.1)	<0.001
3-Vessel disease	10 058 (14.2)	12 633 (15.8)	9222 (17.6)	1290 (19.0)	<0.001
Left main trunk lesion	2868 (4.1)	4077 (5.1)	3112 (5.9)	398 (5.9)	<0.001
Target coronary artery					
Right coronary artery	25 291 (35.7)	29 170 (36.5)	19 340 (36.9)	2668 (39.4)	<0.001
Left main trunk–left anterior descending artery	37 021 (52.3)	41 611 (52.0)	27 987 (53.4)	3782 (55.8)	<0.001
Left circumflex artery	16 554 (23.4)	18 987 (23.7)	12 375 (23.6)	1399 (20.6)	<0.001
Bypass graft	323 (0.5)	605 (0.8)	382 (0.7)	19 (0.3)	<0.001
Devices					
Stent use (drug-eluting stent and/or bare-metal stent)	63 085 (89.1)	70 537 (88.2)	46 088 (88.0)	6006 (88.6)	<0.001
Drug-eluting stent (at least one drug-eluting stent)	58 584 (82.8)	66 005 (82.5)	42 949 (82.0)	5423 (80.0)	<0.001
Bare-metal stent (at least one bare-metal stent)	4784 (6.8)	4804 (6.0)	3331 (6.4)	612 (9.0)	<0.001

Continued

Table 1. Continued

Characteristics	Sexagenarians (60–69 y)	Septuagenarians (70–79 y)	Octogenarians (80–89 y)	Nonagenarians (≥90 y)	P Value
	(n=70 769)	(n=79 992)	(n=52 387)	(n=6780)	
Drug-coated balloon	3260 (4.6)	4124 (5.2)	2472 (4.7)	241 (3.6)	<0.001
Rotational atherectomy	1072 (1.5)	1918 (2.4)	1549 (3.0)	171 (2.5)	<0.001

Continuous variables are reported as mean±SD. Categorical variables are reported as number (percentage). For the comparison of characteristics among sexagenarians, septuagenarians, octogenarians, and nonagenarians, continuous variables were compared using ANOVA, and differences between categorical variables were examined using Pearson’s χ^2 test. ACS indicates acute coronary syndrome.

and CKD, than younger patients. Conversely, younger patients had a higher prevalence of traditional coronary risk factors, such as hyperlipidemia, diabetes mellitus, and smoking habit. In the ACS cohort, more than half of the nonagenarians (4078 patients [60.4%]) were women, and older patients were more likely than younger patients to present with cardiogenic shock and acute heart failure. More than half of the nonagenarians (3653 patients [53.9%]) underwent PCI with a diagnosis of

STEMI in the ACS cohort. For angiographic data, older patients had more complex lesions than younger patients, including multivessel disease and LMT lesions, in both ACS and stable CAD cohorts.

In-hospital outcomes in the ACS and stable CAD cohorts are shown in Tables 3 and 4. Procedural success rate was lower in older patients than in younger patients in the ACS cohort. In addition, older patients had a higher rate of in-hospital

Table 2. Baseline Clinical Characteristics in Patients With Stable CAD

Characteristics	Sexagenarians (60–69 y)	Septuagenarians (70–79 y)	Octogenarians (80–89 y)	Nonagenarians (≥90 y)	P Value
	(n=116 347)	(n=157 073)	(n=75 444)	(n=3848)	
Age, y	65.2±2.7	74.5±2.8	83.1±2.6	91.8±2.2	<0.001
Female sex	19 779 (17.1)	40 323 (25.8)	27 379 (36.4)	2000 (52.2)	<0.001
Hypertension	88 089 (75.7)	122 890 (78.2)	60 587 (80.3)	3054 (79.4)	<0.001
Hyperlipidemia	79 644 (68.5)	101 722 (64.8)	43 337 (57.4)	1773 (46.1)	<0.001
Diabetes mellitus	58 934 (50.7)	73 835 (47.0)	30 255 (40.1)	1058 (27.5)	<0.001
Current smoker	39 728 (34.1)	38 187 (24.3)	12 695 (16.8)	404 (10.5)	<0.001
History of percutaneous coronary intervention	67 727 (59.1)	89 262 (57.8)	41 436 (55.7)	1926 (50.6)	<0.001
History of coronary artery bypass grafting	5362 (4.7)	8420 (5.5)	3597 (4.8)	93 (2.4)	<0.001
History of heart failure	14 798 (13.1)	21 305 (14.0)	15 612 (21.3)	1312 (35.1)	<0.001
History of myocardial infarction	32 853 (28.8)	38 428 (25.0)	17 841 (24.2)	967 (25.8)	<0.001
Peripheral artery disease	9002 (7.7)	15 224 (9.7)	8017 (10.6)	425 (11.0)	<0.001
Chronic obstructive pulmonary disease	1666 (1.4)	3557 (2.3)	2221 (2.9)	104 (2.7)	<0.001
Chronic kidney disease	18 583 (16.0)	27 739 (17.7)	16 065 (21.3)	923 (24.0)	<0.001
Dialysis	10 712 (9.2)	10 648 (6.8)	3990 (5.3)	143 (3.7)	<0.001
Presentation or diagnosis					
Stable angina	71 882 (61.8)	100 274 (63.8)	48 217 (63.9)	2328 (60.5)	<0.001
Old myocardial infarction	12 170 (10.5)	13 516 (8.6)	6364 (8.4)	354 (9.2)	<0.001
Silent ischemia	32 295 (27.8)	43 283 (27.6)	20 863 (27.7)	1166 (30.3)	0.002
Access site					
Transfemoral intervention	31 274 (26.9)	40 335 (25.7)	19 609 (26.0)	954 (24.8)	<0.001
Transradial intervention	78 479 (67.5)	107 218 (68.3)	50 739 (67.3)	2553 (66.3)	
Others	6594 (5.7)	9516 (6.1)	5094 (6.8)	341 (8.9)	

Continued

Table 2. Continued

Characteristics	Sexagenarians (60–69 y)	Septuagenarians (70–79 y)	Octogenarians (80–89 y)	Nonagenarians (≥90 y)	P Value
	(n=116 347)	(n=157 073)	(n=75 444)	(n=3848)	
No. of diseased vessels					
1-Vessel disease	74 429 (64.0)	99 845 (63.6)	46 376 (61.5)	2346 (61.0)	<0.001
2-Vessel disease	29 041 (25.0)	39 745 (25.3)	19 849 (26.3)	1030 (26.8)	<0.001
3-Vessel disease	12 541 (10.8)	16 986 (10.8)	9012 (11.9)	466 (12.1)	<0.001
Left main trunk lesion	4126 (3.5)	6284 (4.0)	3403 (4.5)	180 (4.7)	<0.001
Target coronary artery					
Right coronary artery	38 998 (33.5)	51 969 (33.1)	24 994 (33.1)	1306 (33.9)	0.072
Left main trunk–left anterior descending artery	56 878 (48.9)	78 508 (50.0)	38 697 (51.3)	2113 (54.9)	<0.001
Left circumflex artery	32 165 (27.6)	42 203 (26.9)	20 024 (26.5)	971 (25.2)	<0.001
Bypass graft	854 (0.7)	1382 (0.9)	557 (0.7)	16 (0.4)	<0.001
Devices					
Stent use (drug-eluting stent and/or bare-metal stent)	100 022 (86.0)	134 740 (85.8)	65 873 (87.3)	3417 (88.8)	<0.001
Drug-eluting stent (at least one drug-eluting stent)	97 853 (84.1)	131 504 (83.7)	64 080 (84.9)	3275 (85.1)	<0.001
Bare-metal stent (at least one bare-metal stent)	2477 (2.1)	3670 (2.3)	2037 (2.7)	159 (4.1)	<0.001
Drug-coated balloon	11 478 (9.9)	15 838 (10.1)	6712 (8.9)	266 (6.9)	<0.001
Rotational atherectomy	4758 (4.1)	8051 (5.1)	4262 (5.6)	182 (4.7)	<0.001

Continuous variables are reported as mean±SD. Categorical variables are reported as number (percentage). For the comparison of characteristics among sexagenarians, septuagenarians, octogenarians, and nonagenarians, continuous variables were compared using ANOVA, and differences between categorical variables were examined using Pearson’s χ^2 test. CAD indicates coronary artery disease.

mortality, cardiac tamponade, cardiogenic shock after PCI, and bleeding complications in both ACS and stable CAD cohorts.

The results of multivariable logistic regression analyses on in-hospital mortality and bleeding complications in the ACS and stable CAD cohorts are shown in Tables 5 and 6, respectively. When the reference group comprised sexagenarians, multivariable analyses showed that septuagenarians, octogenarians, and nonagenarians were at greater risk of in-hospital mortality and bleeding complications in both ACS and

stable CAD cohorts (Figure 2). Adjusted odds ratios (ORs) increased gradually in the higher age groups, and nonagenarians had the highest risk of in-hospital mortality (OR, 3.60; 95% CI, 3.10–4.18; $P<0.001$ in ACS; OR, 6.24; 95% CI, 3.82–10.20; $P<0.001$ in non-ACS) and bleeding complications (OR, 1.79; 95% CI, 1.35–2.36; $P<0.001$ in ACS; OR, 2.70; 95% CI, 1.68–4.35; $P<0.001$ in non-ACS). In addition to the age groups, female sex, acute heart failure, acute myocardial infarction, cardiogenic shock, CKD, 3-vessel disease, and LMT

Table 3. In-Hospital Outcomes in Patients With ACS

Outcomes	Sexagenarians (60–69 y)	Septuagenarians (70–79 y)	Octogenarians (80–89 y)	Nonagenarians (≥90 y)	P Value
	(n=70 769)	(n=79 992)	(n=52 387)	(n=6780)	
Procedural success (final TIMI III flow)	69 510 (98.2)	78 426 (98.0)	51 156 (97.7)	6600 (97.3)	<0.001
In-hospital mortality	864 (1.22)	1248 (1.56)	1383 (2.64)	351 (5.18)	<0.001
Cardiac tamponade	78 (0.11)	160 (0.2)	175 (0.33)	20 (0.29)	<0.001
Cardiogenic shock	1105 (1.56)	1404 (1.76)	1225 (2.34)	198 (2.92)	0.001
Emergency operation	111 (0.16)	140 (0.18)	94 (0.18)	4 (0.06)	<0.001
Bleeding complications	242 (0.34)	400 (0.5)	404 (0.77)	76 (1.12)	<0.001
Access-site bleeding	125 (0.18)	216 (0.27)	227 (0.43)	46 (0.68)	0.001
Non-access-site bleeding	124 (0.18)	199 (0.25)	190 (0.36)	30 (0.44)	0.172

Values are reported as number (percentage). For the comparison of in-hospital outcomes among sexagenarians, septuagenarians, octogenarians, and nonagenarians, Pearson’s χ^2 test was used. ACS indicates acute coronary syndrome; TIMI, Thrombolysis in Myocardial Infarction.

Table 4. In-Hospital Outcomes in Patients With Stable CAD

Outcomes	Sexagenarians (60–69 y)	Septuagenarians (70–79 y)	Octogenarians (80–89 y)	Nonagenarians (≥90 y)	P Value
	(n=116 347)	(n=157 073)	(n=75 444)	(n=3848)	
Procedural success (final TIMI III flow)	113 905 (97.9)	154 105 (98.1)	74 048 (98.1)	3777 (98.2)	<0.001
In-hospital mortality	76 (0.07)	144 (0.09)	156 (0.21)	24 (0.62)	<0.001
Cardiac tamponade	85 (0.07)	217 (0.14)	164 (0.22)	15 (0.39)	<0.001
Cardiogenic shock	291 (0.25)	510 (0.32)	365 (0.48)	32 (0.83)	<0.001
Emergency operation	48 (0.04)	83 (0.05)	55 (0.07)	4 (0.1)	0.83
Bleeding complications	154 (0.13)	276 (0.18)	259 (0.34)	21 (0.55)	<0.001
Access-site bleeding	107 (0.09)	191 (0.12)	176 (0.23)	8 (0.21)	<0.001
Non-access-site bleeding	48 (0.04)	92 (0.06)	85 (0.11)	13 (0.34)	<0.001

Values are reported as number (percentage). For the comparison of in-hospital outcomes among sexagenarians, septuagenarians, octogenarians, and nonagenarians, Pearson's χ^2 test was used. CAD indicates coronary artery disease; TIMI, Thrombolysis in Myocardial Infarction.

lesions were the independent predictors of in-hospital mortality and bleeding complications in the ACS cohort, whereas female sex, history of heart failure, CKD, and LMT lesions were independently associated with these adverse outcomes in the stable CAD cohort. More important, TRI was inversely

associated with in-hospital mortality (OR, 0.41; 95% CI, 0.37–0.45; $P<0.001$ in ACS; OR, 0.27; 95% CI, 0.22–0.35; $P<0.001$ in non-ACS) and bleeding complications (OR, 0.38; 95% CI, 0.33–0.45; $P<0.001$ in ACS; OR, 0.13; 95% CI, 0.11–0.16; $P<0.001$ in non-ACS).

Table 5. Multivariable Logistic Regression Analyses in Patients With ACS

Variable	In-Hospital Mortality			Bleeding Complications		
	OR	95% CI	P Value	OR	95% CI	P Value
Age						
Sexagenarians (reference)
Septuagenarians	1.29	1.17–1.42	<0.001	1.30	1.11–1.53	0.002
Octogenarians	1.99	1.80–2.19	<0.001	1.62	1.37–1.92	<0.001
Nonagenarians	3.60	3.10–4.18	<0.001	1.79	1.35–2.36	<0.001
Female sex	1.13	1.04–1.22	0.002	2.00	1.76–2.26	<0.001
History of heart failure	1.37	1.24–1.51	<0.001	1.18	1.00–1.39	0.056
Acute heart failure	2.52	2.30–2.75	<0.001	1.50	1.26–1.78	<0.001
Presentation						
Unstable angina (reference)
Non-ST-segment-elevation myocardial infarction	2.20	1.92–2.53	<0.001	1.50	1.23–1.83	<0.001
ST-segment-elevation myocardial infarction	3.35	3.00–3.75	<0.001	1.39	1.19–1.63	<0.001
Cardiogenic shock	7.08	6.47–7.75	<0.001	2.90	2.45–3.44	<0.001
Diabetes mellitus	1.02	0.95–1.10	0.587	0.84	0.74–0.95	0.007
Chronic kidney disease	1.50	1.38–1.63	<0.001	1.60	1.39–1.84	<0.001
3-Vessel disease	1.33	1.23–1.45	<0.001	1.30	1.13–1.50	<0.001
Left main trunk lesion	2.09	1.89–2.32	<0.001	2.28	1.93–2.70	<0.001
Access site						
Transfemoral intervention (reference)
Transradial intervention	0.41	0.37–0.45	<0.001	0.38	0.33–0.45	<0.001
Other	1.10	0.94–1.29	0.25	0.95	0.73–1.27	0.713

ACS indicates acute coronary syndrome; OR, odds ratio.

Table 6. Multivariable Logistic Regression Analyses in Patients With Stable CAD

Variable	In-Hospital Mortality			Bleeding Complications		
	OR	95% CI	P Value	OR	95% CI	P Value
Age						
Sexagenarians (reference)
Septuagenarians	1.37	1.03–1.81	0.028	1.24	1.02–1.51	0.034
Octogenarians	2.58	1.95–3.43	<0.001	2.05	1.67–2.52	<0.001
Nonagenarians	6.24	3.82–10.20	<0.001	2.70	1.68–4.35	<0.001
Female sex	1.27	1.02–1.57	0.029	2.52	2.16–2.93	<0.001
History of heart failure	2.47	1.99–3.06	<0.001	1.25	1.05–1.49	0.013
Diabetes mellitus	0.87	0.71–1.07	0.184	0.84	0.72–0.98	0.024
Chronic kidney disease	1.94	1.56–2.41	<0.001	1.53	1.29–1.81	<0.001
3-Vessel disease	1.81	1.42–2.31	<0.001	1.19	0.97–1.47	0.097
Left main trunk lesion	1.80	1.30–2.51	<0.001	1.52	1.17–1.99	0.002
Access site						
Transfemoral intervention (reference)
Transradial intervention	0.27	0.22–0.35	<0.001	0.13	0.11–0.16	<0.001
Other	0.72	0.50–1.05	0.088	0.33	0.24–0.46	<0.001

CAD indicates coronary artery disease; OR, odds ratio.

Spline curves (Figure 3) demonstrated the nonlinear relationship between age and in-hospital adverse outcomes (in-hospital death or bleeding). The risks of in-hospital adverse outcomes rapidly increased at ≥ 80 years of age and further escalated in nonagenarians (≥ 90 years of age) in both ACS and stable CAD cohorts.

Discussion

This is the largest study to date reporting in-hospital outcomes after PCI in old patients, such as octogenarians and nonagenarians, compared with younger patients in both ACS and stable CAD cohorts. The most important advantage of this study was inclusion of the largest number of nonagenarians who underwent PCI in a single contemporary registry.

Of the advanced nations, Japan harbors the largest number of older patients with CAD in a seriously aging society. Previous studies reported that most nonagenarians underwent PCI for ACS, especially with a diagnosis of STEMI.^{4,8,11} By contrast, our study results showed that PCI was performed even in selected nonagenarians with either ACS or stable CAD. The current Japanese situation may be related to the increased life expectancy associated with advancements in medical science. The Japanese national statistical survey from the Ministry of Health, Labor, and Welfare reported that the mean life expectancy of individuals who were 90 years old in 2015 was 4.38 years for men and 5.70 years for women

(<https://www.mhlw.go.jp/english/database/db-hh/>; Chapter 2, Table 1-43). Taking these relatively long life expectancies into account, it may be reasonable to perform PCI for selected nonagenarians with either ACS or stable CAD.

Although advanced age itself is not a contraindication of PCI, there are a paucity of data about the outcomes after PCI in these patients. This is because old patients, such as nonagenarians, are often excluded from major clinical trials of cardiovascular interventions largely because of concerns about the increased risk of adverse events and limited life expectancy.⁷ In addition, PCI remains underused in elderly patients, even in current clinical practice.^{2,8–10} Because none of the randomized clinical trials on coronary intervention have included sufficient numbers of nonagenarians, outcome data of this high-risk patient group should be collected from large-scale multicenter registries, as described in this study.¹ Some previous small registry-based studies reported the outcomes after PCI in dozens or hundreds of nonagenarians.^{11–22} However, study results, particularly about outcomes in nonagenarians after PCI, have differed widely mainly because of limited sample sizes.²³ The in-hospital mortality of nonagenarians who underwent PCI has been reported to vary from 4.1% to 34.2%,^{2–4,12,13,15–21} and major bleeding complications in these patients range from 0% to 25.0%.^{2,12,16–19} Accordingly, the available data on the outcomes after PCI in nonagenarians have significant limitations and should be generalized to real-world practice only with utmost caution.

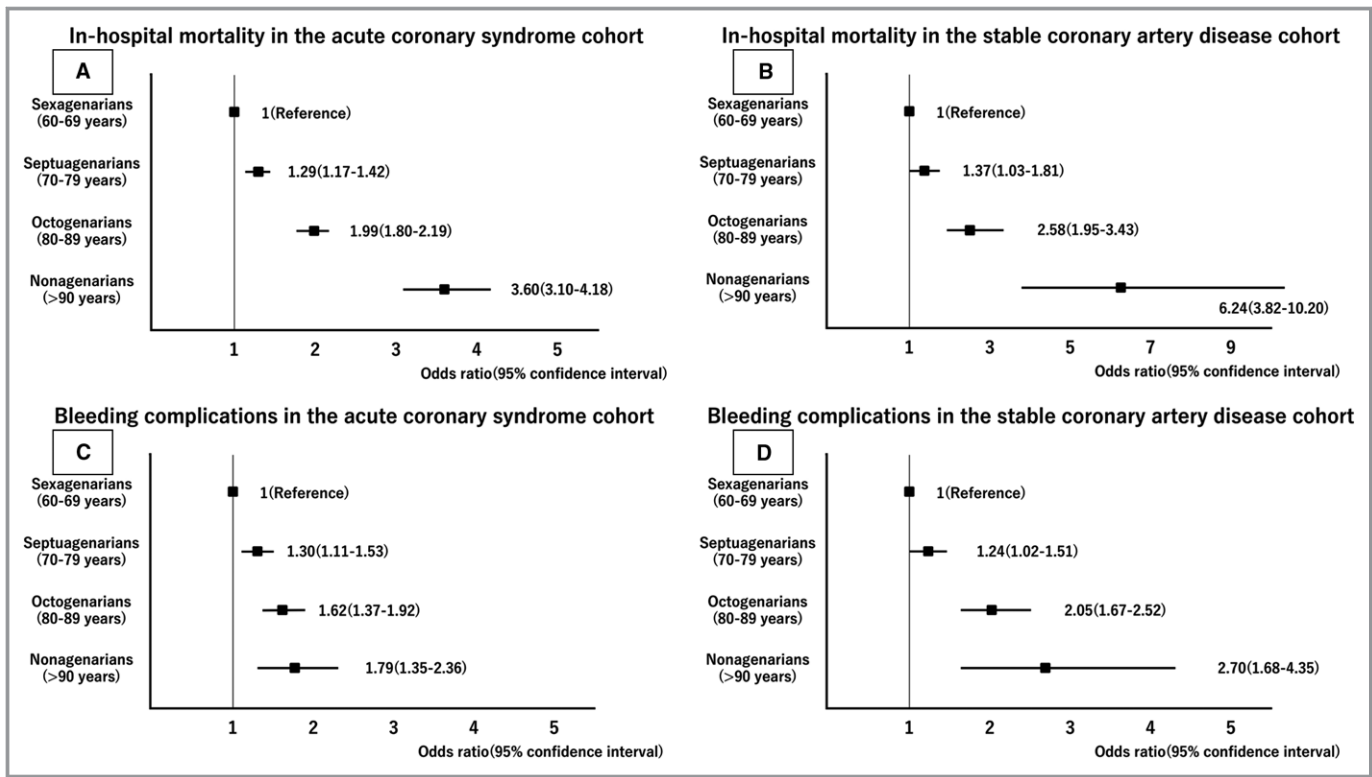


Figure 2. Adjusted odds ratios for in-hospital mortality and bleeding complications in each age group. Separate multivariable logistic regression analysis was performed for in-hospital mortality and bleeding complications in each cohort. Adjusted models include age, female sex, history of heart failure, acute heart failure, presentation or diagnosis, cardiogenic shock, diabetes mellitus, chronic kidney disease, 3-vessel disease, left main trunk lesion, and access site in the acute coronary syndrome cohort (A and C); and age, female sex, history of heart failure, diabetes mellitus, chronic kidney disease, 3-vessel disease, left main trunk lesion, and access site in the stable coronary artery disease cohort (B and D).

In the contemporary nationwide registry used herein, the in-hospital mortality in nonagenarians who underwent PCI was 5.2% in the ACS cohort and 0.6% in the stable CAD cohort. In this group of patients, bleeding complications requiring blood transfusion occurred in 1.1% in the ACS cohort and 0.6% in the stable CAD cohort. Although mortality and bleeding events were observed more frequently in older than in younger patients, these results might be acceptable in comparison with previous studies.^{2-4,12,13,15-21} Recent developments in devices and techniques, including TRI, new-generation drug-eluting stents, and smaller sheaths and catheters, may be associated with the improvement in procedural outcomes after PCI in elderly patients.^{4,11,12} In fact, more than half of the patients in the ACS cohort and approximately two thirds of those in the stable CAD cohort underwent transradial PCI, with a high procedural success rate in this registry. More important, on multivariate analyses, TRI was an inverse-independent predictor for both in-hospital mortality and bleeding complications in both ACS and stable CAD cohorts. The relatively low incidence of bleeding complications in this registry may also be related to the frequent use of radial access in Japan.²⁵ Taking these study results into account, TRI plays a pivotal role in current PCI

practice and should be especially considered for elderly patients with a high risk of bleeding.^{11,12,15}

Although advancement in technologies may enable elderly patients with multiple comorbidities to undergo invasive treatment with acceptable outcomes, it must be recognized that age is one of the strongest predictors of adverse outcomes after PCI.⁵ Batchelor et al⁶ reported that there was a curvilinear relationship between age and mortality rate, ranging from 0.5% for patients <55 years old to nearly 5% for patients >85 years old. Largely consistent with previous studies, adjusted ORs for in-hospital mortality and bleeding complications after PCI increased gradually in the higher age groups in this study. The OR for in-hospital mortality was >3-fold higher in nonagenarians compared with sexagenarians in the ACS cohort, and >6-fold higher in the stable CAD cohort. Because patients with ACS are at high risk regardless of age and PCI is associated with better outcomes, even in elderly patients,^{3,8,9,28} undergoing PCI in patients with presentation of ACS may be reasonable, even in selected nonagenarians. By contrast, taking the higher ORs for adverse outcomes in nonagenarians into account, indications of PCI for stable CAD in old patients should be considered carefully. In addition, in old patients with stable CAD, it remains unclear whether PCI

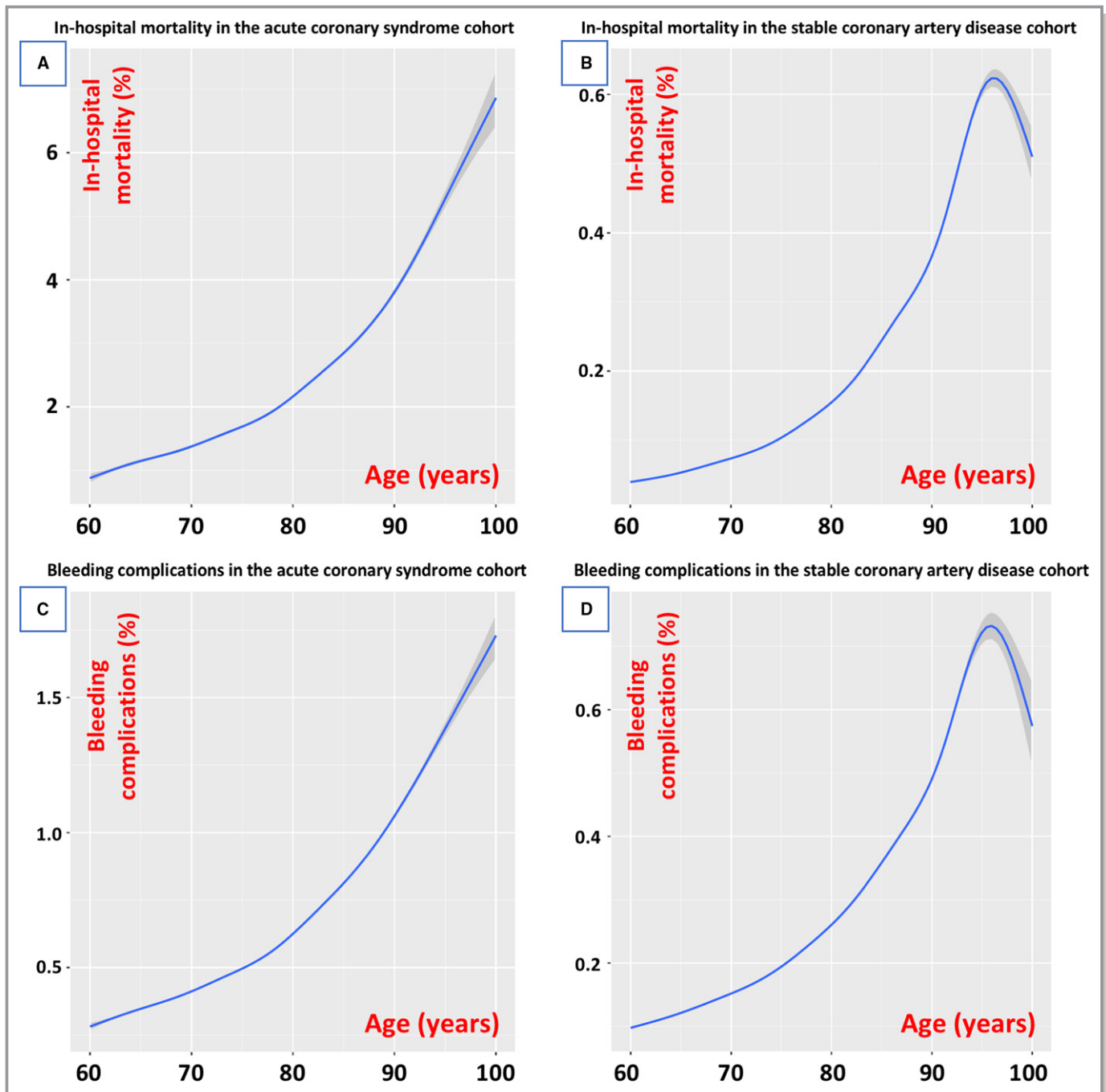


Figure 3. Cubic spline models for in-hospital mortality and bleeding complications. Separate cubic spline modeling was performed for in-hospital mortality and bleeding complications in each cohort. The smoothed spline plots are shown as a blue line, and the gray area represents the 95% CIs. Adjusted models include age, female sex, history of heart failure, acute heart failure, presentation or diagnosis, cardiogenic shock, diabetes mellitus, chronic kidney disease, 3-vessel disease, left main trunk lesion, and access site in the acute coronary syndrome cohort (A and C); and age, female sex, history of heart failure, diabetes mellitus, chronic kidney disease, 3-vessel disease, left main trunk lesion, and access site in the stable coronary artery disease cohort (B and D).

is associated with better prognosis in comparison with conservative treatment, such as optimal medical therapy. Cubic spline curves also demonstrated that higher age (particularly ≥ 80 years of age) was significantly associated with a higher rate of in-hospital adverse outcomes, and this

rate further escalated in nonagenarians (≥ 90 years of age). The decreased complication rates in patients with an extremely high age (≥ 95 years of age) in the stable CAD cohort were observed mainly because of the limited sample size and selection bias in this group of patients.

The causes of poor outcomes after PCI in elderly patients are considered to be multifactorial. First, older patients tend to have a higher prevalence of comorbidities than younger patients, especially CKD and heart failure, and these are known predictors of adverse outcomes after PCI.^{1,9,11} Other unmeasured confounders, including frailty, malnutrition, diseased immunity, and cognitive impairment, may also affect adverse outcomes. Second, older patients are more likely to have complex CAD, including tortuous and calcified lesions, multivessel disease, and significant LMT lesions.^{2,4,13,15,17,20} More important, in the ACS cohort of this study, older patients were more likely than younger patients to present with cardiogenic shock. These results are consistent with previous studies that reported a strong association between shock status and in-hospital mortality, even in nonagenarians.^{1,4,18,19} Older patients with ACS tend to have atypical or no symptoms more frequently than younger patients, which may result in treatment delay and a higher prevalence of cardiogenic shock on admission.^{15,22,28} Last, older patients tend to receive fewer guideline-recommended medications, including statins, renin-angiotensin system inhibitors, and β blockers, than younger patients, largely because of concerns for the increased risk of adverse effects.^{9,28,29}

The management of old patients with CAD is still challenging, even in current clinical practice, and patient selection for an invasive revascularization strategy is the most important issue. The high-risk profiles of periprocedural complications, including mortality and bleeding, along with clinical, functional, and cognitive status of the patients should be considered appropriately when performing PCI for elderly patients.

Study Limitations

This study had several important limitations. First, it was not a randomized controlled trial but an observational clinical study. Although this study included one of the largest numbers of nonagenarians who underwent PCI in a single contemporary registry, results should be cautiously interpreted to real-world practice because of its observational nature. Second, we analyzed data from patients who underwent PCI, but the J-PCI registry did not include patients with CAD undergoing coronary artery bypass grafting or receiving only conservative medical therapy. In addition, we did not record data about activities of daily living, cognitive function, financial status, and overall frailty of the elderly patients.²⁹ These factors might have been associated with the selection of the patients for an invasive revascularization strategy. Although we performed multivariable logistic regression analyses to adjust for covariate imbalances, residual confounding factors might not have been completely adjusted for in our statistical models. Third, lack of long-term follow-up results and lack of data about quality of life

after PCI were also important limitations. Fourth, the definition of bleeding complications in this study was different from standardized definitions, such as the definition from the Bleeding Academic Research Consortium criteria,³⁰ which may have resulted in an underestimation of the actual incidence of bleeding complications after PCI. Last, precise data about medical therapies, including antithrombotic agents and the size of sheaths and catheters, were lacking in this study. These factors might be associated with the rate of complications after PCI, particularly bleeding events.

Conclusions

In current Japanese clinical practice, PCI is performed in old patients, including selected nonagenarians, either with or without ACS. Older patients, especially nonagenarians, carry a greater risk of in-hospital death and bleeding after PCI than younger patients. TRI might contribute to risk reduction for periprocedural complications after PCI in elderly patients.

Appendix

J-PCI (Japanese Percutaneous Coronary Intervention) Registry Investigators

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References

1. Sawant AC, Josey K, Plomondon ME, Maddox TM, Bhardwaj A, Singh V, Rajagopalan B, Said Z, Bhatt DL, Corbelli J. Temporal trends, complications, and predictors of outcomes among nonagenarians undergoing percutaneous coronary intervention: insights from the Veterans Affairs Clinical Assessment, Reporting, and Tracking Program. *JACC Cardiovasc Interv.* 2017;10:1295–1303.
2. Kim JY, Jeong MH, Choi YW, Ahn YK, Chae SC, Hur SH, Hong TJ, Kim YJ, Seong IW, Chae IH, Cho MC, Yoon JH, Seung KB; Korea Acute Myocardial Infarction Registry Investigators. Temporal trends and in-hospital outcomes of primary percutaneous coronary intervention in nonagenarians with ST-segment elevation myocardial infarction. *Korean J Intern Med.* 2015;30:821–828.
3. Mandawat A, Mandawat A, Mandawat MK. Percutaneous coronary intervention after ST-segment elevation myocardial infarction in nonagenarians: use rates and in-hospital mortality. *J Am Coll Cardiol.* 2013;61:1207–1208.
4. From AM, Rihal CS, Lennon RJ, Holmes DR Jr, Prasad A. Temporal trends and improved outcomes of percutaneous coronary revascularization in nonagenarians. *JACC Cardiovasc Interv.* 2008;1:692–698.
5. Brennan JM, Curtis JP, Dai D, Fitzgerald S, Khandelwal AK, Spertus JA, Rao SV, Singh M, Shaw RE, Ho KK, Krone RJ, Weintraub WS, Weaver WD, Peterson ED. Enhanced mortality risk prediction with a focus on high-risk percutaneous coronary intervention: results from 1,208,137 procedures in the NCDR (National Cardiovascular Data Registry). *JACC Cardiovasc Interv.* 2013;6:790–799.
6. Batchelor WB, Anstrom KJ, Muhlbaier LH, Grosswald R, Weintraub WS, O'Neill WW, Peterson ED; for the National Cardiovascular Network Collaboration. Contemporary outcome trends in the elderly undergoing percutaneous coronary interventions: results in 7,472 octogenarians. *J Am Coll Cardiol.* 2000;36:723–730.
7. Gurwitz JH, Goldberg RJ. Age-based exclusions from cardiovascular clinical trials: implications for elderly individuals (and for all of us): comment on "the persistent exclusion of older patients from ongoing clinical trials regarding heart failure." *Arch Intern Med.* 2011;171:557–558.
8. Schoenenberger AW, Radovanovic D, Windecker S, Iglesias JF, Pedrazzini G, Stuck AE, Erne P; AMIS Plus Investigators. Temporal trends in the treatment

and outcomes of elderly patients with acute coronary syndrome. *Eur Heart J.* 2016;37:1304–1311.

9. Zaman MJ, Stirling S, Shepstone L, Ryding A, Flather M, Bachmann M, Myint PK. The association between older age and receipt of care and outcomes in patients with acute coronary syndromes: a cohort study of the Myocardial Ischaemia National Audit Project (MINAP). *Eur Heart J.* 2014;35:1551–1558.
10. Skolnick AH, Alexander KP, Chen AY, Roe MT, Pollack CV Jr, Ohman EM, Rumsfeld JS, Gibler WB, Peterson ED, Cohen DJ. Characteristics, management, and outcomes of 5,557 patients age \geq 90 years with acute coronary syndromes: results from the CRUSADE Initiative. *J Am Coll Cardiol.* 2007;49:1790–1797.
11. Gayed M, Yadak N, Qamhia W, Daralammouri Y, Ohlow MA. Comorbidities and complications in nonagenarians undergoing coronary angiography and intervention. *Int Heart J.* 2017;58:180–184.
12. Petroni T, Zaman A, Georges JL, Hammoudi N, Berman E, Segev A, Juliard JM, Barthelemy O, Silvain J, Choussat R, Le Feuvre C, Helft G. Primary percutaneous coronary intervention for ST elevation myocardial infarction in nonagenarians. *Heart.* 2016;102:1648–1654.
13. Mizuguchi Y, Hashimoto S, Yamada T, Taniguchi N, Nakajima S, Hata T, Takahashi A. Percutaneous coronary intervention for nonagenarian patients with ST-segment elevation myocardial infarction: experience of a single Japanese center. *J Cardiol.* 2016;67:331–334.
14. Petroni T, Zaman A, Georges JL, Hammoudi N, Berman E, Segev A, Juliard JM, Barthelemy O, Silvain J, Choussat R, Le Feuvre C, Helft G. Primary percutaneous coronary intervention for ST elevation myocardial infarction in nonagenarians: a multicenter study. *J Am Geriatr Soc.* 2015;63:384–386.
15. Helft G, Georges JL, Mouranche X, Loyeau A, Spaulding C, Caussin C, Benamer H, Garot P, Livarek B, Teiger E, Varenne O, Monsegu J, Mapouata M, Petroni T, Hammoudi N, Lambert Y, Dupas F, Laborne F, Lapostolle F, Lefort H, Juliard JM, Letarnec JY, Lamhaut L, Lebaill G, Boche T, Jouven X, Bataille S; e-MUST and CARDIO-ARSIF Registries. Outcomes of primary percutaneous coronary interventions in nonagenarians with acute myocardial infarction. *Int J Cardiol.* 2015;192:24–29.
16. Rigattieri S, Cera M, Sciahbasi A, Di Russo C, Fedele S, Ferraiuolo G, Altamura G, Pugliese FR, Loschiavo P. Primary percutaneous coronary intervention in nonagenarians: six-month outcomes from a single-center registry. *J Invasive Cardiol.* 2013;25:242–245.
17. Salinas P, Galeote G, Martin-Reyes R, Perez-Vizcayno MJ, Hernandez-Antolin R, Mainar V, Moreu J, de la Torre JM, Zueco J, Tello A, Jimenez-Valero S, Sanchez-Recalde A, Calvo L, Plaza I, Alfonso F, Mariscal F, Lopez de Sa E, Macaya C, Lopez-Sendon JL, Moreno R. Primary percutaneous coronary intervention for ST-segment elevation acute myocardial infarction in nonagenarian patients: results from a Spanish multicentre registry. *EuroIntervention.* 2011;6:1080–1084.
18. Hendler A, Katz M, Gurevich Y, Reicher M, Blatt A, Gabara Z, Zyssman I, Vered Z, Krakover R. 30-Day outcome after percutaneous coronary angioplasty in nonagenarians: feasibility and specific considerations in different clinical settings. *J Invasive Cardiol.* 2011;23:521–524.
19. Lemesle G, Bonello L, De Labriolle A, Steinberg DH, Roy P, Slotow TL, Torguson R, Kaneshige K, Xue Z, Suddath WO, Satler LF, Kent KM, Lindsay J, Pichard AD, Waksman R. Impact of bivalirudin use on outcomes in nonagenarians undergoing percutaneous coronary intervention. *J Interv Cardiol.* 2009;22:61–67.
20. Teplitsky I, Assali A, Lev E, Brosh D, Vaknin-Assa H, Kornowski R. Results of percutaneous coronary interventions in patients \geq 90 years of age. *Catheter Cardiovasc Interv.* 2007;70:937–943.
21. Presutti DG, D'Ascenzo F, Omede P, Biondi-Zoccai G, Moretti C, Bollati M, Sciuto F, Lee MS, Moreno R, Bikkina M, Di Cuia M, Resmini C, Gaita F, Sheiban I. Percutaneous coronary intervention in nonagenarian: a meta-analysis of observational studies. *J Cardiovasc Med (Hagerstown).* 2013;14:773–779.
22. Antonsen L, Jensen LO, Terkelsen CJ, Tilsted HH, Junker A, Maeng M, Hansen KN, Lassen JF, Thuesen L, Thayssen P. Outcomes after primary percutaneous coronary intervention in octogenarians and nonagenarians with ST-segment elevation myocardial infarction: from the Western Denmark heart registry. *Catheter Cardiovasc Interv.* 2013;81:912–919.
23. Biondi Zoccai G, Abbate A, D'Ascenzo F, Presutti D, Peruzzi M, Cavarretta E, Marullo AG, Lotrionte M, Frati G. Percutaneous coronary intervention in nonagenarians: pros and cons. *J Geriatr Cardiol.* 2013;10:82–90.
24. Yamaji K, Kohsaka S, Morimoto T, Fujii K, Amano T, Uemura S, Akasaka T, Kadota K, Nakamura M, Kimura T; J-PCI Registry Investigators. Relation of ST-segment elevation myocardial infarction to daily ambient temperature and air pollutant levels in a Japanese Nationwide Percutaneous Coronary Intervention Registry. *Am J Cardiol.* 2017;119:872–880.

25. Numasawa Y, Inohara T, Ishii H, Kuno T, Kodaira M, Kohsaka S, Fujii K, Uemura S, Amano T, Kadota K, Nakamura M. Comparison of outcomes of women versus men with non-ST-elevation acute coronary syndromes undergoing percutaneous coronary intervention (from the Japanese Nationwide Registry). *Am J Cardiol*. 2017;119:826–831.
26. Inohara T, Kohsaka S, Yamaji K, Amano T, Fujii K, Oda H, Uemura S, Kadota K, Miyata H, Nakamura M ; J-PCI Registry Investigators. Impact of institutional and operator volume on short-term outcomes of percutaneous coronary intervention: a report from the Japanese Nationwide Registry. *JACC Cardiovasc Interv*. 2017;10:918–927.
27. Sakakura K, Inohara T, Kohsaka S, Amano T, Uemura S, Ishii H, Kadota K, Nakamura M, Funayama H, Fujita H, Momomura SI. Incidence and determinants of complications in rotational atherectomy: insights from the National Clinical Data (J-PCI Registry). *Circ Cardiovasc Interv*. 2016;9:e004278.
28. Fach A, Bunger S, Zabrocki R, Schmucker J, Conradi P, Garstka D, Fiehn E, Hambrecht R, Wienbergen H. Comparison of outcomes of patients with ST-segment elevation myocardial infarction treated by primary percutaneous coronary intervention analyzed by age groups (<75, 75 to 85, and >85 years): (results from the Bremen STEMI Registry). *Am J Cardiol*. 2015;116:1802–1809.
29. Afilalo J, Alexander KP, Mack MJ, Maurer MS, Green P, Allen LA, Popma JJ, Ferrucci L, Forman DE. Frailty assessment in the cardiovascular care of older adults. *J Am Coll Cardiol*. 2014;63:747–762.
30. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, Kaul S, Wiviott SD, Menon V, Nikolsky E, Serebruany V, Valgimigli M, Vranckx P, Taggart D, Sabik JF, Cutlip DE, Krucoff MW, Ohman EM, Steg PG, White H. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the bleeding academic research consortium. *Circulation*. 2011;123:2736–2747.