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Incremental age-related one-year MACCE after acute myocardial infarction in the drug-eluting stent era (from KAMIR-NIH registry)

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Abstract

Objectives To evaluate the age-related one-year major adverse cardiocerebrovascular events (MACCE) after percutaneous coronary intervention (PCI) in acute myocardial infarction (AMI). We analyzed the association between age and one-year MACCE after AMI. **Methods** A total of 13,104 AMI patients from Korea Acute Myocardial Infarction Registry-National Institue of Health (KAMIR-NIH) between November 2011 and December 2015 were classified into four groups according to age (Group I, < 60 years, n = 4199; Group II, 60–70 years, n = 2577; Group III; 70–80 years, n = 2774; Group IV, ≥ 80 years, n = 1018). Patients were analyzed for one-year composite of MACCE (cardiac death, myocardial infarction, target vessel revascularization, cerebrovascular events) after AMI. **Results** The one-year MACCE in AMI were 3.5% (Group I), 6.3% (Group II), 9.6% (Group III) and 17.6% (Group IV). After adjustment for confounding parameters, the analysis results showed that patients with AMI had incremental risk of one-year MACCE [Group II, adjusted hazard ratios (aHR) = 1.224, 95% CI: 0.965–1.525, P = 0.096; Group III, aHR = 1.316, 95% CI: 1.037–1.671, P = 0.024; Group IV, aHR = 1.975, 95% CI: 1.500–62.601, P < 0.001) compared to Group I. Especially, cardiac death in the composite of primary end point played a major role in this effect (Group II, aHR = 1.335, 95% CI: 0.941–1.895, P = 0.106; Group III, aHR = 1.575, 95% CI: 1.122–2.210, P = 0.009; Group IV, aHR = 2.803, 95% CI: 1.937–4.054, P < 0.001). **Conclusions** Despite advanced techniques and medications for PCI in AMI, age still exerts a powerful influence in clinical outcomes. Careful approaches, even in the modern era of developed cardiology are needed for aged-population in AMI intervention.

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Keywords: Acute myocardial infarction; Aged-population; Major adverse cardiocerebrovascular events

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1 Introduction

Advanced devices, techniques and medical therapies improved clinical outcomes in patients with acute myocardial infarction (AMI) undergoing percutaneous coronary intervention (PCI). In addition, PCI with drug-eluting stents (DES) has demonstrated a decrease in stent restenosis and target lesion revascularization (TLR).[1–3] Nevertheless, coronary intervention in aged population has been challenging due to complex clinical situations such as comorbidities, functional and socioeconomic status, side effects associated with multiple drug administration and greatly reduced cardiac function with severe coronary disease.[4–6] Under this circumstance, it remains unclear whether age could still be an independent powerful factor affecting clinical adverse results in patients with AMI undergoing PCI in the DES era. Thus, the aim of this multicenter, prospective, observational study is to evaluate the major adverse events stratified by age groups after PCI using a large cohort with AMI patients.

2 Methods

2.1 Participants

A total of 13,104 patients with either ST segment elevation myocardial infarction (STEMI) or non-ST segment elevation myocardial infarction (NSTEMI) who had admitted at 20 major cardiovascular centers came under the Korea Acute Myocardial Infarction Registry-National Institutes of Health (KAMIR-NIH) between November 2011 and December 2015. The KAMIR-NIH is a prospective, multicenter, web-based observational cohort study to develop the prognostic and surveillance index of Korean patients with AMI and has been performed to support by a grant of Korea Centers for Disease Control and Prevention since November 2011.

This large observational registry was designed to evaluate clinical outcomes of patients with acute MI including both STEMI and NSTEMI, and included demographic, clinical and angiographic data with 1-year clinical outcome data. Of 13,104 patients, 2193 patients not undergoing primary PCI were excluded and 343 patients with missing data were also excluded. The remaining 10,568 patients were included in the analyses (Figure 1). Among 10,568 patients, 5505 and 5063 patients were diagnosed with STEMI and NSTEMI, respectively and underwent successful PCI. STEMI was diagnosed by the presence of chest pain lasting for more than 20 min in association with electrocardiographic changes (ST-segment elevation of ≥ 1 mm in at least two extremity electrocardiographic leads or ≥ 2 mm in at least contiguous precordial leads, or new-onset left-bundle branch block). NSTEMI was defined as increased cardiac markers with symptoms compatible with myocardial ischemia in the absence of ST-elevation on the index ECG.[7] Meanwhile, in baseline characteristics, chronic kidney disease (CKD) was defined as diagnosed chronic renal failure, renal function less than 60% assessed by the estimated creatinine clearance, using the Cockcroft-Gault equation.

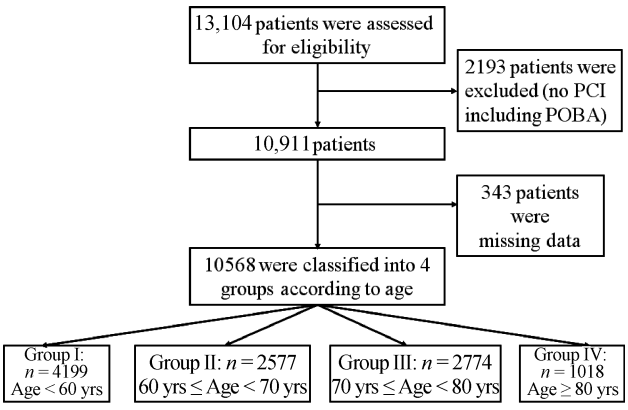

Figure 1. Study population. PCI: percutaneous coronary intervention; POBA: plain old balloon angioplasty.

2.2 PCI procedure and medical treatment

Coronary angiography and PCI were performed according to current standard guidelines. Antiplatelet therapy and administration of periprocedural anticoagulation were carried out in accordance with standard regimens. Aspirin (loading dose, 200 mg) plus clopidogrel (loading dose, 300 mg or 600 mg) or ticagrelor (loading dose 180 mg) or prasugrel (loading dose 60 mg) were prescribed for all patient before or during PCI. After the procedure, aspirin (100–200 mg/day) was maintained indefinitely. Patients with drug-eluting stents were prescribed clopidogrel (75 mg/day), ticagrelor (90mg twice/day), prasugrel (10 mg/day) for at least 12 months. Other cardiac medications were administered at the discretion of treating physicians.

2.3 Study end-points

The primary end-point was major adverse cardiocerebrovascular events (MACCE), defined as the composite of cardiac death (CD), myocardial infarction (MI), target vessel revascularization (TVR) and cerebrovascular events. CD was defined as any death due to a proximate cardiac cause such as MI, low-output failure, arrhythmia and unwitnessed death. MI was defined as newly developed Q wave, raised CK-MB, Tn-I or T above the normal ranges, typical ischemic symptom with accompanied ST elevation. TVR was defined as percutaneous or surgical revascularization of the stented lesion including 5 mm margin segments and more proximal or distal, newly developed lesion. Also, cere-

brovascular events were defined as a stroke or cerebrovascular accident with loss of neurological function caused by an ischemic or hemorrhagic event with residual symptoms at least 24 h after onset or leading to death.

Immediate postprocedural and in-hospital events were recorded. After the discharge, the patients were followed up in the out-patient clinics or by telephone 3, 6, 9 and 12 months after the procedure. Information on censored survival data and death was obtained from hospital records or through telephone calls to relatives of the patients. All clinical outcomes of interest were confirmed by source documents and were centrally adjudicated by a local events committee at the Cardiovascular Center of Chonnam National University Hospital by an independent group of clinicians unaware of patient status. Information about death was validated by records from the National Population Registry of the Korea National Statistical Office using a unique personal identification number for each patient. The study protocol was approved by the institutional review board of each participating institution, and was conducted according to the Declaration of Helsinki. Each patient was provided with written informed consent.

2.4 Statistical analyses

Continuous variables were expressed as the mean ± SD and categorical variables were expressed as *n* (%). ANOVA test with Bonferroni post-hoc analysis and χ^2 test (or the Fisher exact test) were used to compare the means and proportion of baseline demographic, clinical and angiographic characteristics between the four groups. Cox proportional hazard model was used to estimate the hazard ratio (HR) and 95% confidence interval (CI) to assess for the prognostic significance after PCI on the clinical events. Univariate variables with $P < 0.10$ were included in the model to obtain adjusted hazard ratios (aHR) and 95% CI. The variables used were age category, sex, BMI, Killip, diabetes, hypertension, hyperlipidemia, smoking, CKD, prior MI, previous congestive heart failure (CHF), prior PCI, cerebrovascular disease, hemoglobin A1c (HbA1c), pro-brain natriuretic peptide (proBNP), hemoglobin (Hb), triglyceride, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL), clopidogrel, ticagrelor or prasugrel, calcium channel blocker, oral anticoagulant, Gp IIb/IIIa inhibitor, target vessel, lesion classification. The incidence of each adverse event was estimated at 12 months, displayed with Kaplan-Meier curves and compared with the log-rank test.

Meanwhile, multivariable logistic regression analyses were carried out to identify independent predictors associated with MACCE in patients with AMI undergoing PCI. All of the variables (Tables 1 and 2) were included and analyzed to perform univariable logistic regression analysis. On the basis of the variables that were significant ($P < 0.05$) according to univariable logistic regression analysis, a multivariable logistic regression model was constructed.

A *P*-value of < 0.05 was considered statistically significant. All statistical analyses were performed using a Statistical Analysis Software (SAS, version 9.4, SAS Institute, Cary, NC, USA).

3 Results

3.1 Baseline characteristics of the overall study population

Baseline demographic, clinical and laboratory characteristics are presented according to the age (Table 1). A total of 10,568 patients among 11,391 were finally enrolled, including 5505 patients with STEMI and 5063 patients with NSTEMI. Patients were classified into four groups: Group I (*n* = 4199, 39.7% of total population, < 60 years), Group II (*n* = 2577, 24.4%, 60–70 years), Group III (*n* = 2774, 26.2%, 70–80 years), and Group IV (*n* = 1018, 9.6%, ≥ 80 years).

The population distributions for age, sex, BMI, Killip classification, risk factors, history of cardiovascular diseases, laboratory findings, the use of other medications except aspirin and left ventricular ejection fraction (LVEF) differed significantly among the four groups. Their mean ages of the groups were 50.6, 64.4, 74.2, and 83.5 years, respectively. And the proportion of male was the highest in Group I and became lower as the age increased. The incidence of Killip III, IV tended to be relatively higher in the aged groups (Groups III and IV) than in the youthful groups (Groups I and II). Also, incidences of hypertension, CKD, prior CHF, atrial fibrillation/flutter, cerebrovascular disease, proBNP and LVEF < 40% became decremented as the age became younger. Interestingly, lipid profile of the groups were well controlled in the older group compared to the younger one. In addition, while the use of clopoidogrel was higher in the Group IV than Group I, ticagrelor or prasugrel and GpIIb/IIIa inhibitor were used less in the Group IV than Group I. Also, the use of B-blocker, angiotensin converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB) and statin was used relatively less in the aged groups and evidence-based medical therapy is less likely given for this groups.

Meanwhile, in angiographic findings (Table 2), all of target vessels including left anterior descending (LAD), left circumflex (LCX), right coronary artery (RCA) and left main coronary artery (LMCA) occurred more frequently in the aged group than younger groups. There were no signifi-

Table 1. Baseline demographic, clinical and laboratory characteristics.

Variable	Group I (*n* = 4199)	Group II (*n* = 2577)	Group III (*n* = 2774)	Group IV (*n* = 1018)	*P*-value
Demographics					
Age, yrs	50.67 ± 6.30[a]	64.35 ± 2.84[b]	74.22 ± 2.82[c]	83.53 ± 3.16[d]	< 0.001
Male sex	3886 (92.5%)	2036 (79.0%)	1663 (59.9%)	436 (42.8%)	< 0.001
BMI, kg/m^2	25.12 ± 3.21[d]	24.02 ± 2.89[c]	23.18 ± 3.15[b]	22.20 ± 3.44[a]	< 0.001
Killip					< 0.001
Class I	8632 (86.5%)	2088 (81.0%)	2062 (74.3%)	661 (64.9%)	
Class II	230 (5.5%)	200 (8.8%)	286 (10.3%)	139 (13.7%)	
Class III	147 (3.5%)	154 (6.0%)	249 (9.0%)	154 (15.1%)	
Class IV	190 (4.5%)	135 (5.2%)	177 (6.4%)	64 (6.3%)	
Disease classification					
Myocardial infarction					< 0.001
NSTEMI	1794 (42.7%)	1267 (49.2%)	1483 (53.5%)	519 (51.0%)	
STEMI	2405 (57.3%)	1310 (50.8%)	1291 (46.5%)	499 (49.0%)	
Risk factors					
Family history of CAD	424 (10.1%)	156 (6.1%)	93 (3.4%)	25 (2.5%)	< 0.001
Diabetes	889 (21.2%)	805 (31.2%)	962 (34.7%)	263 (25.8%)	< 0.001
Hypertension	1476 (35.2%)	1324 (51.4%)	1753 (63.2%)	701 (68.9%)	< 0.001
Hyperlipidemia	563 (13.4%)	300 (11.6%)	275 (9.9%)	62 (6.1%)	< 0.001
Current/recent smoker	3304 (78.7%)	1505 (58.4%)	1175 (42.4%)	319 (31.3%)	< 0.001
CKD	277 (6.6%)	428 (16.6%)	789 (28.4%)	385 (37.8%)	< 0.001
History of cardiovascular disease					
Prior myocardial infarction	177 (4.2%)	174 (6.8%)	199 (7.2%)	64 (6.3%)	< 0.001
Prior CHF	102 (2.4%)	80 (3.1%)	145 (5.2%)	100 (9.8%)	< 0.001
Prior PCI	227 (5.4%)	223 (8.7%)	306 (11.0%)	96 (9.4%)	< 0.001
Atrial fibrillation/flutter	116 (2.8%)	91 (3.5%)	189 (6.8%)	86 (8.4%)	< 0.001
Cerebrovascular disease	121 (2.9%)	145 (5.6%)	241 (8.7%)	133 (13.1%)	< 0.001
Laboratory finding					
HbA1c	6.55% ± 1.62%[d]	6.52% ± 1.50%[b]	6.42% ± 1.35%[b]	6.28% ± 1.30%[a]	< 0.001
ProBNP, pg/mL	804.61 ± 3923.43[a]	1750.17 ± 4961.35[b]	3052.94 ± 5982.50[c]	5094.78 ± 7315.70[d]	< 0.001
Hb, g/dL	14.97 ± 1.67[d]	14.01 ±1.85[c]	12.94 ± 1.94[b]	12.18 ±1.88[a]	< 0.001
Total cholesterol, mg/dL	192.67 ± 44.97[d]	177.52 ± 43.49[c]	169.66 ± 43.17[a]	168.28 ± 43.75[a]	< 0.001
Triglyceride, mg/dL	168.73 ± 148.34[d]	126.45 ± 101.23[c]	108.87 ±81.79[a]	99.70 ± 74.92[a]	< 0.001
LDL cholesterol, mg/dL	123.16 ± 39.44[d]	112.40 ± 38.14[c]	106.23 ± 39.23[a]	105.23 ± 38.78[a]	< 0.001
HDL cholesterol, mg/dL	41.99 ± 11.15[a]	42.57 ± 11.56[a]	43.39 ±12.81[d]	43.51 ± 12.33[d]	< 0.001
In-hospital medications					
Aspirin	4193 (99.9%)	2574 (99.9%)	2772 (99.9%)	1018 (100.0%)	0.577
Clopidogrel	2992 (71.3%)	1958 (76.0%)	2307 (83.2%)	902 (88.6%)	< 0.001
Ticagrelor or prasugrel	1830 (43.6%)	975 (37.8%)	770 (27.8%)	210 (20.6%)	< 0.001
B-blocker	3712 (88.4%)	2227 (86.4%)	2253 (81.2%)	765 (75.1%)	< 0.001
ACE inhibitor or ARB	3475 (82.8%)	2095 (81.3%)	2169 (78.2%)	747 (73.4%)	< 0.001
Statin	4014 (95.6%)	2398 (93.1%)	2544 (91.7%)	892 (87.6%)	< 0.001
Calcium channel blocker	241 (5.7%)	116 (4.5%)	178 (6.4%)	52 (5.1%)	0.018
Oral anticoagulant	81 (1.9%)	56 (2.2%)	99 (3.6%)	28 (2.8%)	< 0.001
Gp IIb/IIIa inhibitor	756 (18.0%)	377 (14.6%)	355 (12.8%)	113 (11.1%)	< 0.001
LVEF < 40%	470 (11.2%)	354 (13.7%)	518 (18.7%)	244 (24.0%)	< 0.001
LVEF	53.15% ± 10.14%[d]	52.29% ±10.50%[c]	50.92% ± 11.30%[b]	49.56% ± 11.67%[a]	< 0.001

Data are presented as mean ± SD or *n* (%) where appropriate. Group was stratified according to age (Group I < 60 years, Group II 60–70 years, Group III 70–80 years, Group IV ≥ 80 years). Lesion based on American College of Cardiology/American Heart Association lesion classification. In ANOVA analysis, values labeled with the different superscripts in a row indicate significant differences between groups based on Scheffe's multiple comparison tests. ACE inhibitor: angiotensin converting enzyme inhibitor; ARB: angiotensin II receptor blocker; BMI: body mass index; CAD: coronary artery disease; CHF: congestive heart failure; CKD: chronic kidney disease; Hb: haemoglobin; HDL: high-density lipoprotein; LDL: low-density lipoprotein; LVEF: left ventricular ejection fraction; NSTEMI: non-ST segment elevation myocardial infarction; PCI: percutaneous coronary intervention; proBNP: pro-brain natriuretic peptide; STEMI: ST segment elevation myocardial infarction; TC: total cholesterol; TG: triglyceride.

Table 2. Baseline angiographic characteristics.

Variable	Group I (*n* = 4497)	Group II (*n* = 2780)	Group III (*n* = 2993)	Group IV (*n* = 1121)	*P*-value
Target vessel					
LAD	2832 (67.4%)	1821(70.7%)	2006 (72.3%)	770 (75.6%)	< 0.001
LCX	1635 (38.9%)	1178 (45.7%)	1324 (47.7%)	494 (48.5%)	< 0.001
RCA	2057 (49.0%)	1361 (52.8%)	1612 (58.1%)	618 (60.7%)	< 0.001
LMCA	146 (3.5%)	119 (4.6%)	168 (6.1%)	64 (6.3%)	< 0.001
Lesion classification					
A	51 (1.2%)	38 (1.5%)	35 (1.3%)	10 (1.0%)	0.651
B1	502 (12.0%)	319 (12.4%)	315 (11.4%)	113 (11.1%)	0.588
B2	1557 (37.1%)	957 (37.1%)	1025 (37.0%)	421 (41.4%)	0.064
C	2088 (49.7%)	1263 (49.0%)	1399 (50.4%)	474 (46.6%)	0.188
Pre-PCI TIMI 0 or 1	2568 (61.2%)	1421 (55.1%)	1491 (53.7%)	540 (53.0%)	< 0.001
Post-PCI TIMI 0 or 1	12 (0.3%)	3 (0.1%)	12 (0.4%)	4 (0.4%)	0.176
Post-PCI TIMI 3	4117 (98.0%)	2511 (97.4%)	2684 (96.8%)	963 (94.6%)	< 0.001
Number of diseased vessel					< 0.001
One-vessel disease	2388 (56.9%)	1230 (47.7%)	1192 (43.0%)	395 (38.8%)	
Two-vessel disease	1187 (28.3%)	836 (32.4%)	884 (31.9%)	346 (34.0%)	
Three-vessel disease	587 (14.0%)	466 (18.1%)	640 (23.1%)	249 (24.5%)	
Three-vessel disease with LM	37 (0.9%)	45 (1.7%)	58 (2.1%)	28 (2.8%)	
Total number of stent	1.16 ± 0.39[a]	1.18 ± 0.42	1.21 ± 0.44[b]	1.21 ± 0.46[b]	< 0.001
Stent size					
Long, mm	28.68 ± 13.62 [a]	29.56 ± 13.93	30.43 ± 14.87[b]	30.05 ± 14.94[b]	< 0.001
Diameter, mm	3.13 ± 0.56[d]	3.04 ± 0.53[c]	2.97 ± 0.53[a]	2.94 ± 0.50[a]	< 0.001

Data are presented as mean ± SD or *n* (%) where appropriate. In ANOVA analysis, values labeled with the different superscripts in a row indicate significant differences between groups based on Scheffe's multiple comparison tests. TIMI: thrombolysis in myocardial Infarction. LAD: left anterior descending artery; LCX: left circumflex artery; LMCA: left main coronary artery; PCI: percutaneous coronary intervention; RCA: right coronary artery; TIMI : thrombolysis in myocardial infarction.

cant differences in the lesion classification between the four groups. The aged group exhibited significantly more multivessel disease and lower rates of post-PCI TIMI flow grade 3. In addition, the final stent size and total numbers of stent indicated more complex coronary lesion in the aged group.

3.2 Clinical outcomes of the overall population:

The median follow-up duration was one year. Among the patients with AMI, the cumulative rates of primary end-point including CD, MI, TVR and cerebrovascular events were significantly higher in the oldest age group (Group IV) than the youngest age group (Group I) at one year [172 (17.6%) *vs.* 145 (3.5%), $P < 0.001$, Table 3]. And the incidence of CD among all individuals at one year was significantly higher in the oldest age group (Group IV) than the youngest age group (Group I) at one year [138 (13.6%) *vs.* 62 (1.5%), $P < 0.001$, Table 3]. Multivariate Cox regression analysis revealed that age is a potent independent predictor for these events [primary end-points, aHR 1.975 (1.500–2.601), $P < 0.001$ at 12 months, Table 3]. Especially, these primary cardiac events would be mainly driven by cardiac death in MACCE components [cardiac death, aHR 2.803 (1.937–4.054), $P < 0.001$ at 12 months, Table 3] as well as cerebrovascular events [aHR 2.846 (1.252–6.473), $P = 0.013$ at 12 months, Table 3]. Moreover, we revealed that the primary cardiac events in AMI could be independently affected in proportion to an increase in age (Group II, aHR = 1.224, 95% CI: 0.965–1.525, $P = 0.096$; Group III, aHR = 1.316, 95% CI: 1.037–1.671, $P = 0.024$; Group IV, aHR = 1.975, 95% CI: 1.500–2.601, $P < 0.001$) compared to Group I. In addition, only all cause death in secondary outcomes (Table 4) showed a significantly higher prevanlence in proportion to an increase in age (Group II, aHR = 1.595, 95% CI: 1.177–2.162, $P = 0.003$; Group III, aHR = 2.143, 95% CI: 1.601–2.869, $P < 0.001$; Group IV, aHR = 3.283, 95% CI: 2.377–4.535, $P < 0.001$) compared to Group I. Meanwhile, the one-year MACCE in STEMI were 3.1% (Group I, $n = 2405$), 6.4% (Group II, $n = 1310$), 9.1% (Group III, $n = 1291$) and 18.8% (Group IV, $n = 499$) (Table 1S) *vs.* 4.0% (Group I, $n = 1794$), 5.7% (Group II, $n = 1267$), 8.6% (Group III, $n = 1483$) and 15.0% (Group IV, $n = 519$) in

Table 3. One-year primary clinical outcomes in MI patients stratified by age.

	Group		*P*-value	Log-rank *P*-value	HR	95.0% CI		*P*-value	Adjusted HR	95.0% CI		*P*-value
						Lower	Upper			Lower	Upper	
One-year primary end-point			< 0.001	< 0.001								
	Group I	145 (3.5%)			1.000				1.000			
	Group II	156 (6.3%)		< 0.001	1.780	1.420	2.232	< 0.001	1.224	0.965	1.525	0.096
	Group III	245 (9.6%)		< 0.001	2.665	2.170	3.273	< 0.001	1.316	1.037	1.671	0.024
	Group IV	172 (17.6%)		< 0.001	5.499	4.408	6.859	< 0.001	1.975	1.500	2.601	< 0.001
Cardiac death			< 0.001	< 0.001								
	Group I	62 (1.5%)			1.000				1.000			
	Group II	78 (3.0%)		< 0.001	2.068	1.481	2.886	< 0.001	1.335	0.941	1.895	0.106
	Group III	148 (5.3%)		< 0.001	3.698	2.749	4.975	< 0.001	1.575	1.122	2.210	0.009
	Group IV	138 (13.6%)		< 0.001	9.883	7.323	13.338	< 0.001	2.803	1.937	4.054	< 0.001
MI			0.003	< 0.001								
	Group I	44 (1.0%)			1.000				1.000			
	Group II	41 (1.6%)		0.020	1.546	1.010	2.366	0.045	0.996	0.635	1.563	0.985
	Group III	55 (2.0%)		< 0.001	1.985	1.335	2.951	< 0.001	0.956	0.598	1.529	0.852
	Group IV	23 (2.3%)		< 0.001	2.469	1.491	4.089	< 0.001	0.969	0.530	1.771	0.918
Target vessel revascularization			0.076	0.108								
	Group I	25 (0.6%)			1.000				1.000			
	Group II	25 (1.0%)		0.093	1.659	0.953	2.889	0.073	1.403	0.771	2.554	0.268
	Group III	13 (0.5%)		0.787	0.828	0.424	1.618	0.581	0.602	0.274	1.320	0.205
	Group IV	4 (0.4%)		0.877	0.773	0.269	2.220	0.632	0.536	0.163	1.762	0.304
Cerebrovascular events			< 0.001	< 0.001								
	Group I	16 (0.4%)			1.000				1.000			
	Group II	25 (1.0%)		0.001	2.593	1.384	4.856	0.003	2.032	1.056	3.907	0.034
	Group III	44 (1.6%)		< 0.001	4.374	2.468	7.751	< 0.001	2.804	1.453	5.412	0.002
	Group IV	16 (1.6%)		< 0.001	4.753	2.377	9.506	< 0.001	2.846	1.252	6.473	0.013

Data are presented as *n* (%). HR: hazard ratio. Group was stratified according to age (Group I < 60 years, Group II 60–70 years, Group III 70–80 years, Group IV ≥ 80 years). MI: myocardial infarction.

Table 4. One-year secondary clinical outcomes in MI patients stratified by age.

	Group		*P*-value	Log-rank *P*-value	HR	95.0% CI		*P*-value	Adjusted HR	95.0% CI		*P*-value
						Lower	Upper			Lower	Upper	
One-year all cause death			< 0.001	< 0.001								
	Group I	76 (1.8%)			1.000				1.000			
	Group II	112 (4.3%)		< 0.001	2.426	1.813	3.246	< 0.001	1.595	1.177	2.162	0.003
	Group III	232 (8.4%)		< 0.001	4.758	3.672	6.165	< 0.001	2.143	1.601	2.869	< 0.001
	Group IV	180 (17.7%)		< 0.001	10.685	8.171	13.972	< 0.001	3.283	2.377	4.535	< 0.001
Heart failure			< 0.001	< 0.001								
	Group I	102 (2.4%)			1.000				1.000			
	Group II	80 (3.1%)		0.006	1.278	0.954	1.712	0.101	1.011	0.735	1.389	0.948
	Group III	145 (5.2%)		< 0.001	2.152	1.670	2.772	< 0.001	1.010	0.742	1.375	0.950
	Group IV	100 (9.8%)		< 0.001	4.047	3.072	5.332	< 0.001	1.006	0.699	1.445	0.976
Stent thrombosis			0.745	0.686								
	Group I	14 (0.3%)			1.000				1.000			
	Group II	6 (0.2%)		0.611	0.708	0.272	1.843	0.480	0.654	0.236	1.810	0.413
	Group III	11 (0.4%)		0.647	1.234	0.560	2.719	0.602	0.962	0.357	2.591	0.939
	Group IV	4 (0.4%)		0.757	1.318	0.434	4.005	0.626	0.758	0.190	3.027	0.695
TIMI major			0.812	0.812								
	Group I	4 (0.1%)			1.000				1.000			
	Group II	4 (0.2%)		0.517	1.629	0.408	6.515	0.490	1.451	0.305	6.893	0.640
	Group III	2 (0.1%)		0.846	0.757	0.139	4.132	0.748	0.592	0.076	4.614	0.617
	Group IV	1 (0.1%)		0.883	1.031	0.115	9.226	0.978	0.786	0.053	11.599	0.861
TIMI minor			< 0.001	< 0.001								
	Group I	108 (2.6%)			1.000				1.000			
	Group II	69 (2.7%)		0.390	1.041	0.770	1.408	0.794	0.829	0.604	1.137	0.245
	Group III	110 (4.0%)		0.001	1.543	1.183	2.012	0.001	1.025	0.745	1.410	0.882
	Group IV	46 (4.5%)		< 0.001	1.760	1.246	2.485	0.001	0.836	0.545	1.282	0.412

Data are presented as *n* (%). Group was stratified according to age (Group I < 60 years, Group II 60–70 years, Group III 70–80 years, Group IV ≥ 80 years). MI: myocardial infarction; TIMI: thrombolysis in myocardial infarction.

NSTEMI, respectively (Table 2S). After adjustment for confounding parameters, patients with STEMI had the incremental risk of one-year MACCE (Group II, aHR = 1.451, 95% CI: 1.043–2.018, P = 0.027; Group III, aHR = 1.441, 95% CI: 1.0192–0.036, P = 0.039; Group IV, aHR = 2.174, 95% CI: 1.469–3.216, P < 0.001) compared to Group I (Table 1S). Cardiac death had a major role in this effect in patients with STEMI (Group II, aHR = 1.567, 95% CI: 0.985–2.493, P = 0.058; Group III, aHR = 1.808, 95% CI: 1.140–2.869, P = 0.012; Group IV, aHR = 2.707, 95% CI: 1.636–4.480, P < 0.001) compared to Group I (Table 1S). However, there was only significant difference between the Group I and 4 in patients with NSTEMI (Group II, aHR = 1.034, 95% CI: 0.734–1.457, P = 0.846; Group III, aHR = 1.197, 95% CI: 0.859–1.667, P = 0.288; Group IV, aHR = 1.749, 95% CI: 1.184–2.584, P = 0.005, Table 2S).

3.3 Kaplan-Meier and landmark analysis in the overall population

The Kaplan-Meier curve indicated a significantly higher incremental risk for primary end-point in the AMI patients undergoing primary PCI during one year (event-free survival rate: 82% *vs.* 91% *vs.* 94% *vs.* 96%, P < 0.001, Table 3 and Figure 2). Also, Figure 2 showed Kaplan-Meier curves for the incidence of MACCE in both STEMI and NSTEMI patients during one year. They showed comparable results with a significantly higher incremental risk for primary outcomes (event-free survival rate: 80% *vs.* 91% *vs.* 93% *vs.* 97% in STEMI, P < 0.001 and 83% *vs.* 91% *vs.* 94% *vs.* 96% in NSTEMI, P < 0.001, Table 2S and Figure 2).

3.4 Predictors of the major adverse outcomes in AMI

Univariable and multivariable logistic regression analyses were performed to identify independent predictors of MACCE in patients with AMI after PCI. In the multivariable logistic regression model, killip classification 4, hypertension, CKD, atrial fibrillation, ACC/AHA type B2 were independent predictors of the MACCE (Table 5).

Expectantly, age was an independent predictor for the higher prevalence of the primary outcomes (adjusted OR = 1.018, P < 0.001). Meanwhile, not only LVEF and the mean stent diameter but also B-blocker, calcium channel blocker (CCB), ACE inhibitor/ARB and statin among medical therapies showed benign effects for the prevalence of MACCE. Interestingly, BMI also revealed counter-correlation with the occurrence of MACCE in AMI patients.

4 Discussion

This large, multicenter cohort analysis evaluated the outcomes of STEMI and NSTEMI patients during one year according to an increase in age. This study included a relatively large number of patients with STEMI and NSTEMI who had undergone primary PCI. As life expectancy continues to increase, interventional cardiologists can expect to encounter a significant increase in the number of patients with AMI who are ≥ 70 years old. In the era before reperfusion, elderly patients had one-month and one-year mortality rates of 30% and 75%, respectively.[8,9] Our study may help the clinician identify a high-risk subset of elderly patients with AMI, because most of clinical trials were based on a large proportion of relatively younger patients and the population of very elderly AMI patients constitute a very small portion. To our knowledge, this database reveals the largest published series of patients ≥ 70 years old undergoing primary percutaneous intervention for AMI.

Although thrombolytic therapy has been shown to improve survival in elderly patients when compared with placebo,[10,11] multiple studies have shown lower mortality rates when elderly patients are treated with primary percutaneous transluminal coronary angioplasty.[12–14] Mortality for patients > 65 years was 5.7% in the angioplasty group versus 15.0% in the thrombolytic group. In our study, one-year mortality rate for AMI was 1.8% (< 60 years), 4.3% (60–70 years), 8.4% (70–80 years), 17.7% (≥ 80 years) (Table 4). And the one-year rates of overall MACCE recorded in the present study were 3.5% (< 60 years), 6.3% (60–70 years), 9.6% (70–80 years), 17.6% (≥ 80 years). Although aged patients were more likely to have complex culprit lesions and multivessel disease, TIMI III flow was achieved in 96.8% (70–80 years), 94.6% (≥ 80 years) (Table 2). Nevertheless, the results found that mortality and MACCE rates even in the DES era were still higher in the older group. This higher mortality and rates of adverse cardiac events in the elderly patients would be relevant to several comorbidities or cardiovascular risk factors (higher prevalence of hypertension, CKD, prior CHF, atrial fibrillation/flutter, cerebrovascular disease, etc, Table 1) prevalent in the elderly. Older AMI patients may often not receive the optimal medical treatment recommended by current guidelines because of their conditions and comorbidities.[15] The record in the present study was roughly consistent with this result. The use of B-blocker, ACE inhibitor or ARB and statin was relatively lower in the older patients after AMI (Table 1), which might be a possible reason for the higher incidence of adverse effects or suspected contraindications of medical therapy. Also, the present study indicates that this outcome were mainly driven by cardiac death (Table 3), surely although heart failure, cerebrovascular events and myocardial infarction as well as other comorbidities such as diabetes,

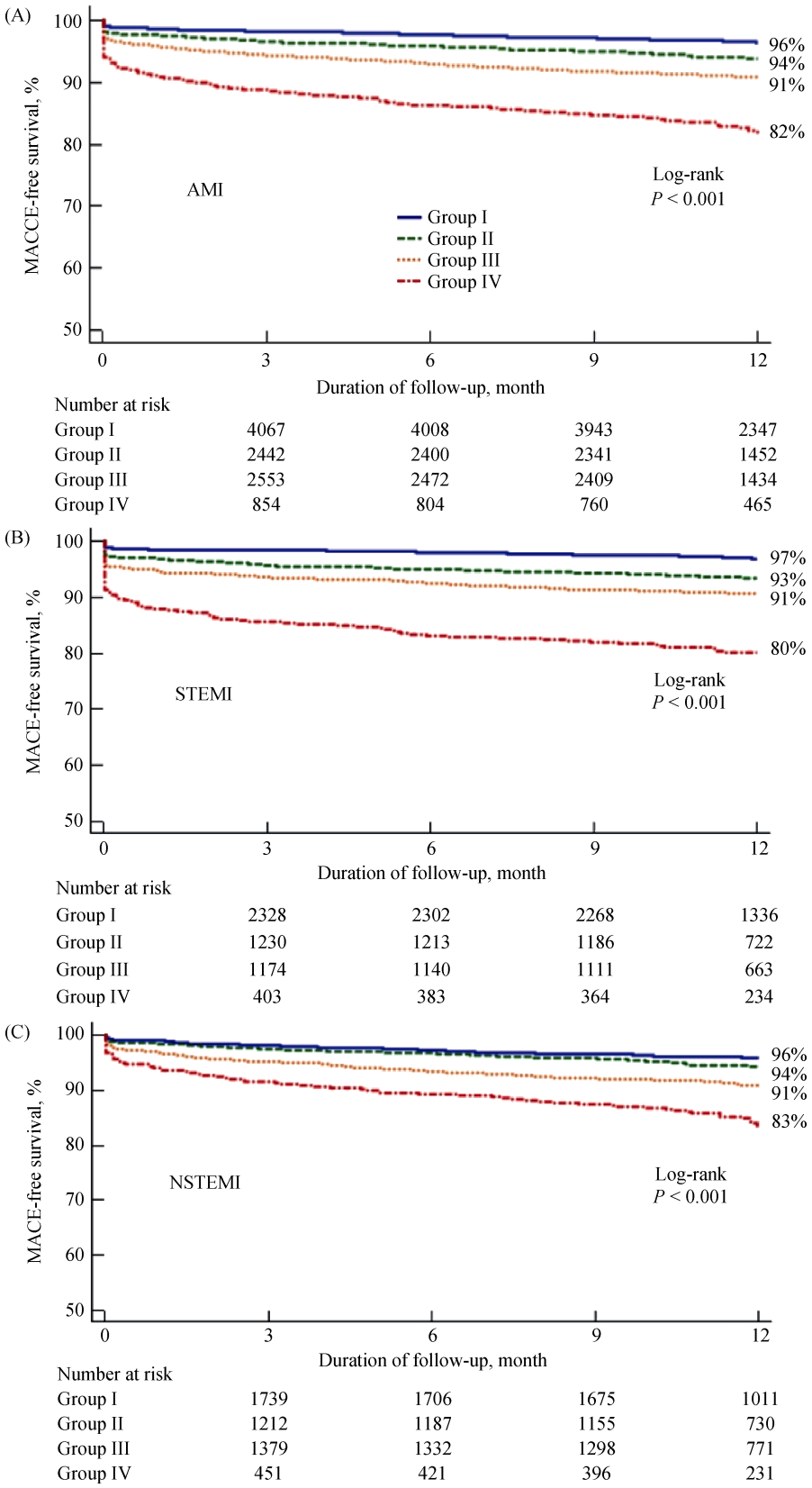

Figure 2. Kaplan-Meier curve for the 12-month probability of MACCE-free survival in patients with AMI (A), STEMI (B) and NSTEMI (C) undergoing primary PCI stratified by age. AMI: acute myocardial infarction; MACCE: major adverse cardiocerebrovascular events; NSTEMI: non-ST segment elevation myocardial infarction; STEMI: ST segment elevation myocardial infarction.

Table 5. Multivariate analysis of MACCE at one-year follow-up.

AMI	Adjusted OR	95% CI		*P*-value		Adjusted OR	95% CI		*P*-value
		Lower	Upper				Lower	Upper	
Killip 4	1.745	1.314	2.319	0.009	ACE inhibitor/ARB	0.563	0.462	0.685	0.002
Hypertension	1.403	1.164	1.690	< 0.001	Use of statin	0.242	0.193	0.303	< 0.001
CKD	1.325	1.073	1.636	0.009	ACC/AHA type B2	1.389	1.159	1.666	< 0.001
Atrial fibrillation	1.439	1.043	1.984	0.027	Age	1.018	1.009	1.028	< 0.001
B-blocker	0.532	0.432	0.654	< 0.001	BMI	0.964	0.938	0.991	0.010
CCB	0.533	0.351	0.809	0.003	LVEF	0.991	0.983	0.999	0.023
					Mean stent diameter	0.784	0.666	0.921	0.003

ACE inhibitor: angiotensin converting enzyme inhibitor; ARB: angiotensin II receptor blocker; ACC/AHA: American College of Cardiology/American Heart Association; BMI: body mass index; CCB: calcium channel blocker; CKD: chronic kidney disease; LVEF: left ventricular ejection fraction.

renal failure, etc. might, in part, affect the mortality rates in older AMI patients. Our study suggests that elderly patients continue to have a higher risk of stroke and death after AMI. However, with primary percutaneous intervention in DES era, the mortality rate of these high risk patients is lower than those observed in thrombotic trials.

Advanced age remains an independent predictor of major cardiac adverse events after acute AMI in our study (aOR = 1.018, 95% CI: 1.009–1.028, $P < 0.001$, Table 5). There are overall obvious differences in cardiac risk factors between younger and older patients with AMI (Tables 1 & 2). Older patients have a higher incidence of hypertension, CKD, prior CHF, atrial fibrillation/flutter and cerebrovascular disease. This is not surprising when considering the fact that these illnesses are closely correlated with advanced age. Conversely, a proportion of male sex, obesity, family history of CAD, hyperlipidemia, current/recent smoker seem to be strongly associated with the development of AMI in younger patients (Table 1). In the study analysis, older patients have more advanced disease and more LV dysfunction. Older patients tend to have a higher incidence of aggravated killip classification and LVEF (Table 1).

Besides age, this study identified the following independent predictors for adverse primary outcomes during 1 year. Killip classification 4, hypertension, CKD, atrial fibrillation, ACC/AHA type B2 were the independent predictors for the prevalence of MACCE. The use of B-blocker, CCB, ACE inhibitor/ARB and statin as well as LVEF and the mean stent diameter were found to be relatively benign predictors for MACCE. Interestingly, an increase of BMI might be also favorably associated with the prevalence of MACCE. Post-procedural coronary flow was not associated with one-year MACCE in this study. The overall high post-TIMI flow rate (96.7%) might have affected these results.

It is well known that elderly MI patients have a higher risk of all-cause death and major cardiac adverse events. DES has been reported to reduce the rate of restenosis and target lesion revascularization compared with bare-metal stents (BMS).[16,17] Meanwhile, PCI with DES might be associated with the prevalence of stent thrombosis due to hypersensitivity reaction with extensive vasculitis,[18,19] delayed healing process with endothelial dysfunction[20,21] and neo-atherosclerosis.[22] Most stent thrombosis in BMS era was early stent thrombosis, while stent thrombosis in 1st generation DES era was reported to happen regardless of stages even though late or very late stent thrombosis was more problematic than early stent thrombosis. As the rate of late or very late stent thrombosis improved in 2nd generation DES era, concerns over the fatal matter in 1st generation DES was belittled.[23,24] In meta-analysis, early stent thrombosis in BMS was about 0.6%, while the rate of stent thrombosis in sirolimus-eluting stent and paclitaxel-eluting stent were reported as 0.5% and 0.5%, respectively.[25,26] In other studies, early or late stent thrombosis using 2nd generation DES was at least comparable, not higher than BMS or 1st generation DES.[27,28] The present study revealed that the rate of early or late stent thrombosis was very low (0.1% *vs.* 0.2% *vs.* 0.1% *vs.* 0.1%, $P = 0.745$ according to an increase in age, Table 4) compared to previous studies, surprisingly even comparable regardless of age difference (Table 4). In addition, the present report also indicated that there was no significant difference in the rate of TVR according to the age. (0.6% *vs.* 1.0% *vs.* 0.5% *vs.* 0.4%, $P = 0.076$, Table 3).

The concerning matter is very late stent thrombosis happening in aged population after 1 year. In our study, the duration was limited to one-year, accordingly we couldn't evaluate the prevalence of very late stent thrombosis according to ARC definition. Elderly patients prescribed with dual anti-platelet agents presented with a high risk for bleeding.[29] However, the finding from this study did not show any significant difference in the occurrence of in-hospital major or minor bleeding between the four groups (Table 4). The unexpected bleeding could be originated from the relatively lower use of ticagrelor or prasugrel (novel antiplatelet)

and the short term duration of follow-up. Large and prospective trials will be necessary to settle this issue more definitely and to assess long-term major or minor bleeding events and the optimal duration of anti-platelet treatment for aged population. According to our study, age over 70 years old is a potential risk factor to generate adverse cardiac outcomes. Especially, the advanced age population over 80 years has the most powerful influence on the outcomes even after the adjustment for several confounders (Table 3). This effect persists not only in STEMI but also in NSTEMI patients (Tables 1S & 2S). Interestingly, the prevalence of MACCE and cardiac death in STEMI patients was significant in the patients over 70 years, while they became significant over 80 years old in NSTEMI patients. Age between 70-80 years is found to be a potential factor affecting the prognosis of STEMI patients.

There are few studies which investigated the adverse outcomes after the DES implantation in aged patients with AMI. The results from the present study propose that occurrence of TVR, stent thrombosis and TIMI major/minor bleeding are not affected by age. In particular, the oldest population over 80 years also showed consistent results.

4.1 Study limitations

There are some limitations in our study. First, it was a nonrandomized study and results might have been influenced by selection bias and confounding factors. However, this study was a prospective, large multicenter cohort study involving most confounders resulting in controlling the baseline differences to the greatest extent in a multivariable Cox regression model. Second, these trials were conducted in a wide variety of hospital settings and the interventions were performed by operators with various degrees of skill and experience. Third, our study only assessed one-year follow-up periods and the mortality and ischemic event rates were relatively low. Also, the proportion of the oldest aged population in this study was relatively low compared to other aged population. Fourth, our study was underpowered to evaluate the ischemic events of the older groups compared to the younger groups, even though we adjusted with statistical method. Lastly, this trial has an intrinsic limitation itself due to several heterogenic components in the groups in terms of angiographic, procedural aspects and different routine laboratory tests performed separately by the different hospitals involved in this study.

4.2 Conclusions

The present study reveals that the elderly undergoing PCI in AMI patients still presents higher mortality and MACCE in the DES era. Several comorbidities and risk factors were more prominent in the elderly and probably related with a higher prevalence of adverse cardiac events. Nevertheless, there were no significant differences in the occurrence of TVR, stent thrombosis and bleeding between the aged groups, which may be owing to the development of device, procedure technique and optimal medical treatments. We expect that the challenging coronary intervention in the elder patients with AMI would be promising and overcome in the near future.

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References

1 Morice MC, Serruys PW, Sousa JE, *et al*. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N Engl J Med* 2002; 346: 1773–1780.
2 Moses JW, Leon MB, Popma JJ, *et al*. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003; 349: 1315–1323.
3 Schofer J, Schluter M, Gershlick AH, *et al*. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-SIRIUS). *Lancet* 2003; 362: 1093–1099.
4 De Gregorio J, Kobayashi Y, Albiero R, *et al*. Coronary artery stenting in the elderly: short-term outcome and long-term angiographic and clinical follow-up. *J Am Coll Cardiol* 1998; 32: 577–583.
5 DeGeare VS, Stone GW, Grines L, *et al*. Angiographic and clinical characteristics associated with increased in-hospital mortality in elderly patients with acute myocardial infarction undergoing percutaneous intervention (a pooled analysis of the primary angioplasty in myocardial infarction trials). *Am J Cardiol* 2000; 86: 30–34.
6 Lindsay J, Jr., Reddy VM, Pinnow EE, *et al*. Morbidity and mortality rates in elderly patients undergoing percutaneous coronary transluminal angioplasty. *Am Heart J* 1994; 128: 697–702.
7 Thygesen K, Alpert JS, Jaffe AS, *et al*. Third universal definition of myocardial infarction. *Eur Heart J* 2012; 33: 2551–2567.
8 Yang XS, Willems JL, Pardaens J, *et al*. Acute myocardial infarction in the very elderly. A comparison with younger age groups. *Acta Cardiol* 1987; 42: 59–68.
9 Goldberg RJ, McCormick D, Gurwitz JH, *et al*. Age-related trends in short- and long-term survival after acute myocardial infarction: a 20-year population-based perspective (1975-1995). *Am J Cardiol* 1998; 82: 1311–1317.

10 Gurwitz JH, Goldberg RJ, Gore JM. Coronary thrombolysis for the elderly? *Jama* 1991; 265: 1720–1723.
11 Topol EJ, Califf RM. Thrombolytic therapy for elderly patients. *N Engl J Med* 1992; 327: 45–47.
12 Grines CL, Browne KF, Marco J, *et al*. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. *N Engl J Med* 1993; 328: 673–679.
13 Stone GW, Grines CL, Browne KF, *et al*. Predictors of in-hospital and 6-month outcome after acute myocardial infarction in the reperfusion era: the primary angioplasty in, myocardial infarction (PAMI) trail. *J Am Coll Cardiol* 1995; 25: 370–377.
14 Holmes DR, Jr., White HD, Pieper KS, *et al*. Effect of age on outcome with primary angioplasty versus thrombolysis. *J Am Coll Cardiol* 1999; 33: 412–419.
15 Wijns W, Kolh P, Danchin N, *et al*. Guidelines on myocardial revascularization. *Eur Heart J* 2010; 31: 2501–2555.
16 Stettler C, Wandel S, Allemann S, *et al*. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. *Lancet* 2007; 370: 937–948.
17 Marroquin OC, Selzer F, Mulukutla SR, *et al*. A comparison of bare-metal and drug-eluting stents for off-label indications. *N Engl J Med* 2008; 358: 342–352.
18 Virmani R, Guagliumi G, Farb A, *et al*. Localized hypersensitivity and late coronary thrombosis secondary to a sirolimus-eluting stent: should we be cautious? *Circulation* 2004; 109: 701–705.
19 Nebeker JR, Virmani R, Bennett CL, *et al*. Hypersensitivity cases associated with drug-eluting coronary stents: a review of available cases from the Research on Adverse Drug Events and Reports (RADAR) project. *J Am Coll Cardiol* 2006; 47: 175–181.
20 Joner M, Finn AV, Farb A, *et al*. Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. *J Am Coll Cardiol* 2006; 48: 193–202.
21 Kotani J, Awata M, Nanto S, *et al*. Incomplete neointimal coverage of sirolimus-eluting stents: angioscopic findings. *J Am Coll Cardiol* 2006; 47: 2108–2111.
22 Park SJ, Kang SJ, Virmani R, *et al*. In-stent neoatherosclerosis: a final common pathway of late stent failure. *J Am Coll Cardiol* 2012; 59: 2051–2057.
23 Silber S, Windecker S, Vranckx P, *et al*. Unrestricted randomised use of two new generation drug-eluting coronary stents: 2-year patient-related versus stent-related outcomes from the RESOLUTE All Comers trial. *Lancet* 2011; 377: 1241–1247.
24 Smits PC, Kedhi E, Royaards KJ, *et al*. 2-year follow-up of a randomized controlled trial of everolimus- and paclitaxel-eluting stents for coronary revascularization in daily practice. COMPARE (Comparison of the everolimus eluting XIENCE-V stent with the paclitaxel eluting TAXUS LIBERTE stent in all-comers: a randomized open label trial). *J Am Coll Cardiol* 2011; 58: 11–18.
25 Bavry AA, Kumbhani DJ, Helton TJ, *et al*. Risk of thrombosis with the use of sirolimus-eluting stents for percutaneous coronary intervention (from registry and clinical trial data). *Am J Cardiol* 2005; 95: 1469–1472.
26 Bavry AA, Kumbhani DJ, Helton TJ, *et al*. What is the risk of stent thrombosis associated with the use of paclitaxel-eluting stents for percutaneous coronary intervention?: a meta-analysis. *J Am Coll Cardiol* 2005; 45: 941–946.
27 Kedhi E, Joesoef KS, McFadden E, *et al*. Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice (COMPARE): a randomised trial. *Lancet* 2010; 375: 201–209.
28 Serruys PW, Silber S, Garg S, *et al*. Comparison of zotarolimus-eluting and everolimus-eluting coronary stents. *N Engl J Med* 2010; 363: 136–146.
29 Bhatt DL, Fox KA, Hacke W, *et al*. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. *N Engl J Med* 2006; 354: 1706–1717.

Table 1S. One year primary clinical outcomes in STEMI patients stratified by age.

	Group		*P*-value	Log-rank *P*-value	HR	95.0% CI		*P*-value	Adjusted HR	95.0% CI		*P*-value
						Lower	Upper			Lower	Upper	
1-year primary end-point			< 0.001	< 0.001								
	Group 1	74 (3.1%)			1.000				1.000			
	Group 2	84 (6.4%)		< 0.001	2.120	1.551	2.898	< 0.001	1.451	1.043	2.018	0.027
	Group 3	117 (9.1%)		< 0.001	3.064	2.290	4.099	< 0.001	1.441	1.019	2.036	0.039
	Group 4	94 (18.8%)		< 0.001	6.847	5.048	9.287	< 0.001	2.174	1.469	3.216	< 0.001
Cardiac death			< 0.001	< 0.001								
	Group 1	35 (1.5%)			1.000				1.000			
	Group 2	46 (3.5%)		< 0.001	2.431	1.566	3.774	< 0.001	1.567	0.985	2.493	0.058
	Group 3	85 (6.6%)		< 0.001	4.625	3.120	6.856	< 0.001	1.808	1.140	2.869	0.012
	Group 4	77 (15.4%)		< 0.001	11.294	7.573	16.843	< 0.001	2.707	1.636	4.480	< 0.001
Myocardial infarction			0.009	0.002								
	Group 1	17 (0.7%)			1.000				1.000			
	Group 2	21 (1.6%)		0.016	2.319	1.223	4.395	0.010	1.778	0.899	3.515	0.098
	Group 3	16 (1.2%)		0.017	1.855	0.937	3.671	0.076	1.160	0.516	2.607	0.719
	Group 4	11 (2.2%)		< 0.001	3.645	1.707	7.782	< 0.001	1.892	0.725	4.940	0.193
Target vessel revascularization			0.649	0.693								
	Group 1	12 (0.5%)			1.000				1.000			
	Group 2	9 (0.7%)		0.321	1.406	0.593	3.337	0.439	1.166	0.448	3.034	0.752
	Group 3	6 (0.5%)		0.877	0.990	0.372	2.639	0.985	0.779	0.236	2.574	0.682
	Group 4	2 (0.4%)		0.730	0.959	0.215	4.287	0.957	0.420	0.063	2.818	0.372
Cerebrovascular events			0.006	0.002								
	Group 1	9 (0.4%)			1.000				1.000			
	Group 2	12 (0.9%)		0.017	2.500	1.053	5.932	0.038	2.335	0.953	5.725	0.064
	Group 3	15 (1.2%)		< 0.001	3.305	1.446	7.552	0.005	2.181	0.836	5.695	0.111
	Group 4	7 (1.4%)		< 0.001	4.454	1.658	11.960	0.003	2.985	0.899	9.914	0.074

Data are presented as *n* (%). Group was stratified according to age (Group I , *n* = 2405, < 60 years; Group II , *n* = 1310, 60–70 years; Group III, *n* = 1291, 70–80 years; Group IV, *n* = 499, ≥ 80 years). STEMI: ST segment elevation myocardial infarction.

Table 2S. 1-Year primary clinical outcomes in NSTEMI patients stratified by age.

	Group		*P*-value	Log-rank *P*-value	HR	95.0% CI		95.0% CI	Adjusted HR	95.0% CI		*P*-value
						Lower	Upper			Lower	Upper	
1-year primary end-point			< 0.001	< 0.001								
	Group 1	71 (4.0%)			1.000				1.000			
	Group 2	72 (5.7%)		< 0.001	1.453	1.047	2.017	0.026	1.034	0.734	1.457	0.846
	Group 3	128 (8.6%)		< 0.001	2.275	1.702	3.041	< 0.001	1.197	0.859	1.667	0.288
	Group 4	78 (15.0%)		< 0.001	4.272	3.097	5.893	< 0.001	1.749	1.184	2.584	0.005
Cardiac death			< 0.001	< 0.001								
	Group 1	27 (1.5%)			1.000				1.000			
	Group 2	32 (2.5%)		0.002	1.695	1.016	2.829	0.044	1.025	0.597	1.759	0.929
	Group 3	63 (4.2%)		< 0.001	2.892	1.842	4.539	< 0.001	1.261	0.761	2.090	0.368
	Group 4	61 (11.8%)		< 0.001	8.495	5.399	13.365	< 0.001	2.764	1.600	4.775	< 0.001
Myocardial infarction			0.039	< 0.001								
	Group 1	27 (1.5%)			1.000				1.000			
	Group 2	20 (1.6%)		0.481	1.063	0.596	1.896	0.835	0.616	0.333	1.140	0.123
	Group 3	39 (2.6%)		0.003	1.822	1.116	2.977	0.017	0.774	0.431	1.388	0.390
	Group 4	12 (2.3%)		0.042	1.724	0.873	3.403	0.117	0.574	0.259	1.271	0.171
Target vessel revascularization			< 0.001	< 0.001								
	Group 1	13 (0.7%)			1.000				1.000			
	Group 2	16 (1.3%)		0.093	1.773	0.853	3.687	0.125	1.638	0.737	3.641	0.226
	Group 3	7 (0.5%)		0.705	0.680	0.271	1.706	0.412	0.521	0.180	1.509	0.229
	Group 4	2 (0.4%)		0.949	0.614	0.139	2.721	0.521	0.472	0.090	2.468	0.374
Cerebrovascular events			< 0.001	< 0.001								
	Group 1	7 (0.4%)			1.000				1.000			
	Group 2	13 (1.0%)		0.017	2.671	1.066	6.694	0.036	2.137	0.820	5.570	0.120
	Group 3	29 (2.0%)		< 0.001	5.208	2.282	11.889	< 0.001	3.529	1.389	8.968	0.008
	Group 4	9 (1.7%)		< 0.001	4.982	1.855	13.378	0.001	3.235	1.022	10.245	0.046

Data are presented as *n* (%). Group was stratified according to age (Group I, *n* = 1794, < 60 years; Group II, *n* = 1267, 60–70 years; Group III, *n* = 1483, 70–80 years; Group IV, *n* = 519, ≥ 80 years). NSTEMI: non-ST segment elevation myocardial infarction.