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ST-segment elevation versus non-ST-segment elevation myocardial infarction in current smokers after newer-generation drug-eluting stent implantation

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Abstract

We compared the 2-year major clinical outcomes between ST-segment elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI) in patients who are current smokers who underwent successful percutaneous coronary intervention (PCI) with newer-generation drug-eluting stents (DESs). The availability of data in this regard is limited.

A total of 8357 AMI patients were included and divided into 2 groups: the STEMI group (n = 5124) and NSTEMI group (n = 3233). The primary endpoint was the occurrence of major adverse cardiac events (MACE), defined as all-cause death, recurrent myocardial infarction (re-MI), or coronary repeat revascularization. The secondary endpoints were the cumulative incidences of the individual components of MACE and stent thrombosis (definite or probable).

After propensity score-matched (PSM) analysis, 2 PSM groups (2250 pairs, C-statistics = 0.795) were generated. In the PSM patients, both for 1 month and at 2 years, the cumulative incidence of MACE ($P = .183$ and $P = .655$, respectively), all-cause death, cardiac death, re-MI, all-cause death or MI, any repeat revascularization, and stent thrombosis ($P = .998$ and $P = .341$, respectively) was not significantly different between the STEMI and NSTEMI groups. In addition, these results were confirmed using multivariate analysis.

In the era of contemporary newer-generation DESs, both during 1 month and at 2 years after index PCI, the major clinical outcomes were not significantly different between the STEMI and NSTEMI groups confined to the patients who are current smokers. However, further research is needed to confirm these results.

Abbreviations: AMI = acute myocardial infarction, CAG = coronary angiography, DES = drug-eluting stents, KAMIR = Korea Acute Myocardial Infarction Registry, MACE = major adverse cardiac events, NSTEMI = non-ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, Re-MI = recurrent myocardial infarction, STEMI = ST-segment elevation myocardial infarction.

Keywords: non-ST-segment elevation myocardial infarction, outcomes, smoking, ST-segment elevation myocardial infarction

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1. Introduction

Cigarette smoking is a significant independent predictor of cardiovascular disease[1] and increases the incidence of myocardial infarction (MI).[2] In cigarette smokers, coronary flow reserve was significantly lower compared to nonsmokers (2.25 vs 2.75, $P < .01$).[3] In addition, cigarette smokers tend to have a more vulnerable atheromatous plaque, including higher extracellular lipid content and increased matrix metalloproteinase activity[4] than nonsmokers. The mortality rate of smokers was significantly higher than that of never smokers [hazard ratio (HR), 1.35; 95% confidence interval (95% CI), 1.04–1.74] in 3133 ST-segment elevation MI (STEMI) patients.[5] In a substudy[6] from the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial, smoking was an independent predictor of higher 1-year mortality (HR, 1.37; 95% CI, 1.07–1.75) in patients with non-STE-acute coronary syndrome (NSTE-ACS). The Global Registry of Acute Coronary Events (GRACE) study[7] showed that the 6-month post-discharge death rate of the STEMI group was better than that of the NSTEMI group (4.8% vs 6.2%, respectively). In the Observatoire sur la Prise en charge hospitalière, l'Evolution à un an et les caRactéristiques de patients présentant un infArctus du myocarde avec ou sans onde Q (OPERA)[8] study, although in-hospital mortality rate was similar between the STEM and NSTEMI groups (4.6% vs 4.3%, respectively), 1-year mortality rate after discharge was higher in NSTEMI group than that in STEMI group (9.0% vs 11.6%, respectively). Recent reports have shown that the major clinical outcomes could differ according to stent generation[9] and individuals who are current smokers.[10] However, direct comparative results between STEMI and NSTEMI in patients with AMI and current smokers in the contemporary newer-generation drug-eluting stent (DES) era are limited. Hence, in this study, we compared the 2-year clinical outcomes between STEMI and NSTEMI in patients who are current smokers who underwent successful percutaneous coronary intervention (PCI) with newer-generation DESs.

2. Methods

2.1. Study design and population

In this retrospective cohort, a total of 45,863 patients with AMI who underwent successful PCI between November 2005 and June 2015 in the Korea Acute Myocardial Infarction Registry (KAMIR)[11] were evaluated. The KAMIR is a nationwide, prospective, observational online registry in South Korea since November 2005 that evaluates the current epidemiology and major clinical outcomes of patients with AMI. Eligible patients were aged ≥ 18 years at the time of hospital admission, and more than 50 high-volume university or teaching hospitals for primary PCI and onsite cardiac surgery participated in this registry. Details of the registry can be found on the KAMIR website (http://www.Kamir.or.kr). Patients who had the following conditions were excluded: bare-metal stent implantation (n = 2084, 4.5%), first-generation DES implantation (n = 9957, 21.7%), incomplete laboratory results (n = 12,440, 27.1%), loss to follow-up (n = 2379, 5.2%), and patients who received coronary artery bypass graft (CABG) after index PCI (n = 53, 0.1%). A total of 18,950 patients who underwent newer-generation DES implantation were eligible. Among these patients, those who were nonsmokers (n = 7448, 39.3%) or ex-smokers (n = 3145, 16.6%) were also excluded. Finally, 8357 AMI patients who were current smokers were included and divided into 2 groups: the STEMI group (n = 5124, 61.3%) and the NSTEMI group (n = 3233, 38.7%) (Fig. 1). The study protocol was approved by the ethics committee at each participating center and the Chonnam National University Hospital Institutional Review Board ethics committee (CNUH-2011-172) according to the ethical guidelines of the Declaration of Helsinki. Informed written consent was obtained from all

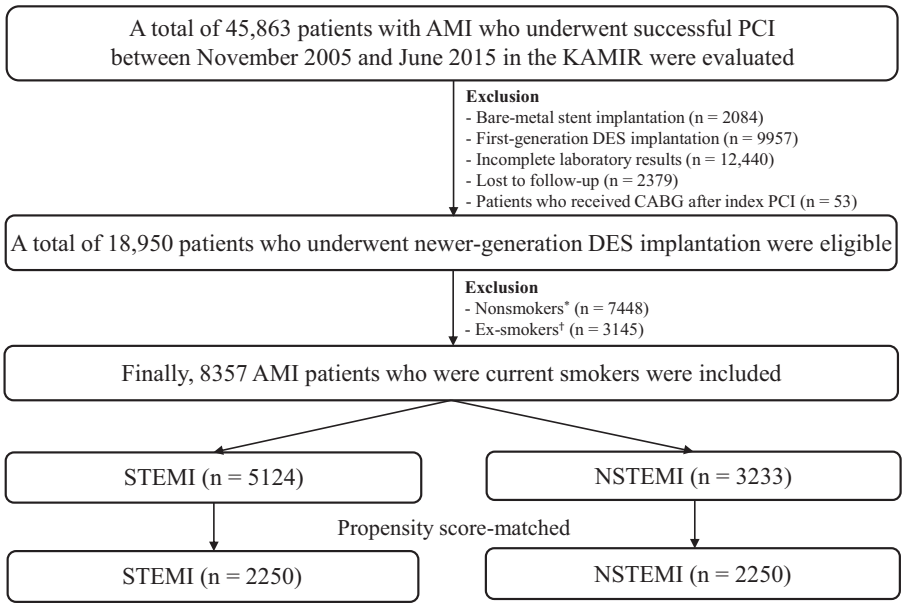

Figure 1. Flowchart. AMI = acute myocardial infarction, PCI = percutaneous coronary intervention, KAMIR = Korea AMI Registry, DES = drug-eluting stent, CABG = coronary artery bypass graft, STEMI = ST-segment elevation myocardial infarction, NSTEMI = non-STEMI. *Nonsmoker was defined as who did not regularly smoke at any time. †Ex-smoker was defined as who stopped smoking for more than 1 year before the index PCI.

patients before inclusion in the study. All 8357 patients completed a 2-year clinical follow-up, and any information concerning adverse events of these participants, including the time intervals and the types of events after the index PCI, which occurred during the follow-up period, was monitored at the outpatient clinic, through phone calls or by reviewing their charts at each participating center on those days. All clinical events were evaluated by an independent event adjudication committee. The processes of event adjudication have been described previously by KAMIR investigators.[12]

2.2. Percutaneous coronary intervention procedure and medical treatment

Diagnostic coronary angiography and PCI were performed according to standard techniques.[13] Successful PCI was defined as residual stenosis < 30% and thrombolysis in myocardial infarction (TIMI) grade 3 flow for the infarct-related artery (IRA) after the procedure.[10] Aspirin 200 to 300 mg and clopidogrel 300 to 600 mg, or alternatively, ticagrelor 180 mg or prasugrel 60 mg, were prescribed as the loading doses before PCI. The recommended total duration of dual antiplatelet therapy was ≥ 12 months for patients who underwent PCI. In addition, triple antiplatelet therapy (TAPT; aspirin + clopidogrel + cilostazol [100 mg twice daily]) was also used based on previous reports,[14,15] and the use of TAPT was left to the discretion of the individual operators.

2.3. Study definitions and clinical outcomes

Smoking status was assessed on the basis of information obtained from hospital medical records at the time of the first medical examination. Nonsmokers were defined as those who did not regularly smoke at any time, and ex-smokers were defined as those who had stopped smoking for more than 1 year before the index PCI[10] (Fig. 1). Current smokers were defined as those who smoke a cigarette within 1 year before the index PCI and currently smoke.[10] STEMI was defined as follows: ongoing chest pain and admission electrocardiogram (ECG) showing STE in at least 2 contiguous leads of ≥ 2 mm (0.2 mV) in men or ≥ 1.5 mm (0.15 mV) in women in leads V2–V3 and/or of ≥ 1 mm (0.1 mV) in other contiguous chest leads or limb leads, or new-onset left bundle branch block (LBBB).[16] NSTEMI was defined as the absence of persistent STE with increased cardiac biomarkers, and the clinical context was appropriate.[17] The primary endpoint was the occurrence of major adverse cardiac events (MACE), defined as all-cause death, recurrent MI (re-MI), or any coronary repeat revascularization. The secondary endpoints were the cumulative incidences of the individual components of MACE and stent thrombosis (definite or probable). All-cause death was considered cardiac death (CD) unless an undisputed noncardiac cause was present.[18] Re-MI was defined as the presence of clinical symptoms, electrocardiographic changes, or abnormal imaging findings of MI combined with an increase in the creatine kinase myocardial band (CK-MB) fraction above the upper normal limits or an increase in troponin-T/troponin-I to greater than the 99th percentile of the upper normal limit after the index PCI.[19] Any coronary repeat revascularization comprised target lesion revascularization, target vessel revascularization, and non-target vessel revascularization. The cumulative incidence of ST was defined according to the Academic Research Consortium.[20]

2.4. Statistical analysis

For continuous variables, differences between groups were evaluated using unpaired t-tests. Data were expressed as mean ± standard deviation. For discrete variables, differences were expressed as counts and percentages and were analyzed using the χ^2 test or Fisher's exact test between groups. To adjust for potential confounders, propensity score matched (PSM) analysis was performed using a logistic regression model. We tested all available variables that could be of potential relevance, such as baseline clinical, angiographic, and procedural factors. The C-statistics for PSM was 0.795 in this study. Patients in the STEMI group were then 1:1 matched to those in the NSTEMI group according to propensity scores with the nearest available pair-matching method. The subjects were matched with a caliper width of 0.01. The procedure yielded well-matched 2250 pairs, except for the serum levels of CK-MB and troponin-I. To overcome these unadjusted variables, we performed another analysis, multivariate analysis, including all variables showing *P*-values < .05 such as age; male sex; left ventricular ejection fraction (LVEF); systolic blood pressure (SBP); diastolic blood pressure (DBP); Killip classification III/IV; cardiopulmonary resuscitation (CPR) on admission; previous history of cardiogenic shock, hypertension, diabetes mellitus, dyslipidemia, MI, PCI, CABG, and stroke; serum peak levels of CK-MB and troponin-I; N-terminal pro-brain natriuretic peptide (NT-ProBNP), blood glucose, and high-density lipoprotein (HDL)-cholesterol levels; use of beta-blocker, angiotensin-converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), calcium channel blocker, or lipid-lowering agents; PCI within 24 hours, pre-PCI TIMI flow grade 0/1, IRA and treated vessels (left main [LM], left anterior descending artery [LAD], left circumflex artery, and right coronary artery [RCA]), American College of Cardiology/American Heart Association (ACC/AHA) type B2/C lesions; 1-vessel, 2-vessel, or ≥ 3-vessel disease; intravascular ultrasound (IVUS); optical coherence tomography (OCT); fractional flow reserve (FFR); zotarolimus-eluting stent (ZES); biolimus-eluting stent (BES); stent diameter; stent length; and number of stents. Cox proportional-hazards models were used to assess the adjusted hazard ratio (aHR) by comparing the 2 groups in the PSM population. All probability values were 2-sided, and *P*-values < .05, were considered statistically significant. All statistical analyses were performed using SPSS software, version 20 (IBM, Armonk, NY).

3. Results

3.1. Baseline characteristics

The baseline characteristics of the study population are presented in Table 1. In the total study population, the mean age of the patients in the NSTEMI group was older than that in the STEMI group (58.2 ± 11.4 vs 56.7 ± 11.5 years, respectively, $P < .001$). The mean LVEF was higher than 50% in both the STEMI and NSTEMI groups and higher in the NSTEMI group than that in the STEMI group (55.0 ± 10.2% vs 51.4 ± 10.5%, respectively, $P < .001$). The mean value of peak CK-MB, troponin-I, blood glucose, and HDL-cholesterol levels and mean diameter of deployed stents and the number of patients who had experienced cardiogenic shock and Killip classification III/IV, who received CPR on admission or PCI within 24 hours, who received beta-blockers and ACEIs as discharge medications, and with pre-PCI TIMI flow grade 0/1, LAD and RCA as the IRA and treated

Table 1

Baseline clinical, laboratory, and procedural characteristics.

Variables	All patients			Propensity score-matched patients		
	STEMI (n = 5124)	NSTEMI (n = 3233)	*P*	STEMI (n = 2250)	NSTEMI (n = 2250)	*P*
Age, yr	56.7 ± 11.5	58.2 ± 11.4	< .001	57.8 ± 11.5	57.6 ± 11.5	.700
Male, n (%)	4830 (94.3)	3016 (93.3)	.070	2114 (94.0)	2105 (93.6)	.579
LVEF (%)	51.4 ± 10.5	55.0 ± 10.2	< .001	53.9 ± 10.1	54.04 ± 10.4	.602
< 40%, n (%)	564 (11.0)	220 (6.8)	< .001	165 (7.3)	177 (7.9)	.536
BMI, kg/m^2	24.3 ± 3.1	24.4 ± 3.1	.187	24.3 ± 3.2	24.4 ± 3.1	.525
SBP, mm Hg	128.5 ± 28.0	134.2 ± 26.3	< .001	132.1 ± 28.4	131.9 ± 25.7	.873
DBP, mm Hg	79.6 ± 17.3	81.7 ± 15.7	< .001	80.6 ± 16.9	80.8 ± 15.5	.776
Cardiogenic shock	278 (5.4)	65 (2.0)	< .001	62 (2.8)	55 (2.4)	.574
CPR on admission	256 (5.0)	74 (2.3)	< .001	75 (3.3)	64 (2.8)	.345
Killip class III/IV, n (%)	495 (9.7)	210 (6.5)	< .001	172 (7.6)	163 (7.2)	.650
Hypertension, n (%)	1813 (35.4)	1333 (41.2)	< .001	872 (38.8)	886 (39.4)	.691
Diabetes mellitus, n (%)	1068 (20.8)	794 (24.6)	< .001	530 (23.6)	508 (22.6)	.457
Dyslipidemia, n (%)	531 (10.4)	416 (12.9)	< .001	252 (11.2)	265 (11.8)	.575
Previous MI, n (%)	133 (2.6)	112 (3.5)	.022	73 (3.2)	69 (3.1)	.798
Previous PCI, n (%)	195 (3.8)	180 (5.6)	< .001	99 (4.4)	111 (4.9)	.437
Previous CABG, n (%)	7 (0.1)	12 (0.4)	.034	5 (0.2)	6 (0.3)	.763
Previous HF, n (%)	21 (0.4)	22 (0.7)	.092	12 (0.5)	13 (0.6)	.841
Previous stroke, n (%)	156 (3.0)	162 (5.0)	< .001	98 (4.4)	96 (4.3)	.942
Peak CK-MB (mg/dL)	188.2 ± 267.6	78.1 ± 198.0	< .001	169.2 ± 317.8	82.7 ± 228.6	< .001
Peak troponin-I, ng/mL	69.9 ± 394.7	29.1 ± 57.6	< .001	57.2 ± 138.6	30.4 ± 60.1	< .001
NT-ProBNP, pg/mL	1004.1 ± 2194.0	1349.3 ± 3281.8	< .001	1207.4 ± 2993.3	1200.1 ± 2669.0	.931
hs-CRP, mg/dL	7.6 ± 35.0	8.6 ± 39.5	.227	9.5 ± 47.4	8.9 ± 37.4	.613
Serum creatinine, mg/L	1.06 ± 1.26	1.04 ± 1.10	.522	1.04 ± 0.89	1.04 ± 1.16	.874
eGFR (mL/min/1.73 m^2)	87.3 ± 37.2	88.3 ± 45.3	.215	88.1 ± 45.9	88.8 ± 45.9	.402
<60 mL/min/1.73 m^2, n (%)	713 (13.9)	460 (14.2)	.688	288 (12.8)	264 (11.7)	.296
Blood glucose, mg/dL	171.6 ± 75.5	153.6 ± 70.2	< .001	159.2 ± 62.9	157.2 ± 74.1	.332
Total cholesterol, mg/dL	188.4 ± 43.7	187.8 ± 43.4	.568	188.0 ± 44.5	187.8 ± 43.0	.893
Triglyceride, mg/L	153.0 ± 123.9	156.7 ± 136.9	.207	151.2 ± 121.4	155.2 ± 138.3	.294
HDL cholesterol, mg/L	42.4 ± 13.8	41.7 ± 11.7	.009	42.4 ± 13.9	41.8 ± 11.9	.083
LDL cholesterol, mg/L	119.5 ± 36.5	119.7 ± 42.3	.814	119.0 ± 36.4	119.0 ± 35.8	.950
Discharge medications						
Aspirin, n (%)	4855 (94.8)	3082 (95.3)	.238	2122 (94.3)	2136 (94.9)	.355
Clopidogrel, n (%)	4447 (86.8)	2772 (85.7)	.433	1871 (83.2)	1879 (83.5)	.749
Ticagrelor, n (%)	388 (7.6)	273 (8.4)	.150	182 (8.1)	178 (7.9)	.869
Prasugrel, n (%)	289 (5.6)	188 (5.8)	.737	129 (5.7)	129 (5.7)	1.000
Cilostazole, n (%)	919 (17.9)	573 (17.7)	.806	402 (17.9)	398 (17.7)	.907
BB, n (%)	4220 (82.4)	2585 (80.0)	.006	1820 (80.9)	1807 (80.3)	.624
ACEI, n (%)	3024 (59.0)	1703 (52.7)	< .001	1229 (54.6)	1253 (55.7)	.472
ARB, n (%)	1088 (21.2)	884 (27.3)	< .001	560 (24.9)	556 (24.7)	.918
CCB, n (%)	157 (3.1)	255 (7.9)	< .001	109 (4.8)	123 (5.5)	.381
Lipid-lowering agents, n (%)	4222 (82.4)	2772 (85.7)	< .001	1877 (83.4)	1910 (84.9)	.178
PCI within 24 hours	4988 (97.3)	2802 (86.7)	< .001	2126 (94.5)	2117 (94.1)	.563
Pre-PCI TIMI flow grade 0/1, n (%)	3687 (72.0)	1407 (43.5)	< .001	1202 (53.4)	1197 (53.2)	.881
Infarct-related artery						
Left main, n (%)	72 (1.4)	73 (2.3)	.004	38 (1.7)	40 (1.8)	.909
LAD, n (%)	2712 (52.9)	1273 (39.4)	< .001	1014 (45.1)	1004 (44.6)	.764
LCx, n (%)	494 (9.6)	943 (29.2)	< .001	422 (18.8)	453 (20.1)	.258
RCA, n (%)	1846 (36.0)	944 (29.2)	< .001	772 (34.3)	750 (33.3)	.508
Treated vessel						
Left main, n (%)	83 (1.6)	114 (3.5)	< .001	48 (2.1)	56 (2.5)	.488
LAD, n (%)	2991 (58.4)	1643 (50.8)	< .001	1209 (53.7)	1203 (53.5)	.858
LCx, n (%)	786 (15.3)	1275 (39.4)	< .001	617 (27.4)	640 (28.4)	.445
RCA, n (%)	2066 (40.3)	1214 (37.6)	.012	921 (40.9)	897 (39.9)	.485
ACC/AHA lesion type						
Type B1, n (%)	712 (13.9)	497 (15.4)	.062	333 (14.8)	334 (14.8)	.967
Type B2, n (%)	1540 (30.1)	1143 (35.4)	< .001	752 (33.4)	757 (33.6)	.875
Type C, n (%)	2369 (46.2)	1310 (40.5)	< .001	970 (43.1)	965 (42.9)	.904
Extent of CAD						
1-vessel, n (%)	2922 (57.0)	1534 (47.4)	< .001	1136 (50.5)	1133 (50.4)	.929
2-vessel, n (%)	1395 (27.2)	1062 (32.8)	< .001	689 (30.6)	698 (31.0)	.772
≥ 3-vessel, n (%)	807 (15.7)	637 (19.7)	< .001	417 (18.5)	411 (18.3)	.847

(*continued*)

Table 1
(continued).

Variables	All patients			Propensity score-matched patients		
	STEMI (n = 5124)	NSTEMI (n = 3233)	*P*	STEMI (n = 2250)	NSTEMI (n = 2250)	*P*
IVUS, n (%)	984 (19.2)	720 (22.3)	.001	465 (20.7)	472 (21.0)	.826
OCT, n (%)	18 (0.4)	34 (1.1)	< .001	10 (0.4)	13 (0.6)	.677
FFR, n (%)	51 (1.0)	48 (1.5)	.049	28 (1.2)	26 (1.2)	.891
Stents*						
ZES, n (%)	1963 (38.3)	1160 (35.9)	< .001	840 (37.3)	839 (37.3)	.975
EES, n (%)	2415 (47.1)	1527 (48.6)	.183	1090 (48.4)	1090 (48.4)	1.000
BES, n (%)	670 (13.1)	501 (15.5)	.002	320 (14.2)	321 (14.3)	.966
Others, n (%)	76 (1.5)	45 (1.4)	.878	33 (1.5)	32 (1.4)	.900
Mitral regurgitation						
Grade 1	1450 (28.3)	931 (28.8)	.623	621 (27.6)	649 (28.8)	.371
Grade 2	353 (6.9)	252 (7.8)	.120	159 (7.1)	184 (8.2)	.177
Grade 3	46 (0.9)	39 (1.2)	.170	25 (1.1)	24 (1.1)	.886
Grade 4	5 (0.1)	4 (0.1)	.741	5 (0.2)	4 (0.2)	.739
Stent diameter, mm	3.25 ± 0.43	3.12 ± 0.44	< .001	3.17 ± 0.42	3.17 ± 0.44	.605
Stent length, mm	25.8 ± 9.33	26.5 ± 11.5	.008	26.2 ± 10.1	26.1 ± 10.5	.685
Number of stent	1.34 ± 0.65	1.54 ± 0.84	< .001	1.46 ± 0.76	1.46 ± 0.78	.982

Values are means ± SD or numbers and percentages. The *P* values for categorical data were obtained from the chi-square or Fisher's exact test. For continuous variables, differences between the 2 groups evaluated with independent samples *t* test.

ACC/AHA = American College of Cardiology/American Heart Association, ACEI = angiotensin converting enzyme inhibitors, ARB = angiotensin receptor blocker, BB = beta-blocker, BMI = body mass index, CABG = coronary artery bypass graft, CAD = coronary artery disease, CCB = calcium channel blockers, CK-MB = creatine kinase myocardial band, CPR = cardiopulmonary resuscitation, DBP = diastolic blood pressure, eGFR = estimated glomerular filtration rate, FFR = fractional flow reserve, HDL = high-density lipoprotein, HF = heart failure, hs-CRP = high-sensitivity C-reactive protein, IVUS = intravascular ultrasound, LAD = left anterior descending coronary artery, LCx = left circumflex coronary artery, LDL = low-density lipoprotein, LVEF = left ventricular ejection fraction, NSTEMI = non-STEMI, NT-ProBNP = N-terminal pro-brain natriuretic peptide, OCT = optical coherence tomography, PCI = percutaneous coronary intervention, RCA = right coronary artery, SBP = systolic blood pressure, STEMI = ST-segment elevation myocardial infarction.

* ZES = zotarolimus-eluting stent (Resolute Integrity stent; Medtronic, Inc., Minneapolis, MN), EES = everolimus-eluting stent (Xience Prime stent, Abbott Vascular, Santa Clara, CA; or Promus Element stent, Boston Scientific, Natick, MA), BES = biolimus-eluting stent (BioMatrix Flex stent, Biosensors International, Morges, Switzerland; or Nobori stent, Terumo Corporation, Tokyo, Japan).

vessel, ACC/AHA type C lesion, 1-vessel disease, and ZES as a deployed stents were significantly higher in the STEMI group than that in the NSTEMI group. In contrast, the mean values of SBP, DBP, and NT-ProBNP, mean length of deployed stents, and mean number of deployed stents; the number of patients who had a history of hypertension, diabetes mellitus, dyslipidemia, MI, PCI, CABG, and stroke; who received ARB, calcium channel blockers, and lipid-lowering agents as discharge medications; with LM and LCx as the IRA and treated vessel; with ACC/AHA type B2 lesion and 2-vessel/≥ 3-vessel disease; who underwent IVUS, OCT, and FFR; and with BES as a deployed stent were significantly higher in the NSTEMI group than that in the STEMI group. However, these intergroup differences in baseline characteristics were well balanced after PSM adjustment.

3.2. Clinical outcomes

The primary and secondary endpoints are shown in Tables 2 and 3 and Figure 2. One month after index PCI, before adjustment, in the total population, the cumulative incidences of MACE (HR, 1.480; 95% CI, 1.114–1.966; *P* = .007), all-cause death (HR, 1.499; 95% CI, 1.091–2.061; *P* = .013), CD (HR, 1.500; 95% CI, 1.082–2.081; *P* = .015), and all-cause death or MI (HR, 1.463; 95% CI, 1.089–1.962; *P* = .011) were higher in the STEMI group than that in the NSTEMI group (Table 2). However, the cumulative incidences of re-MI, any repeat revascularization, and ST (HR, 1.124; 95% CI, 0.497–2.544; *P* = .779) were not significantly different between the 2 groups (Table 2). After PSM analysis, the cumulative incidences of MACE (HR, 1.288; 95% CI, 0.887–1.871; *P* = .183), all-cause death (HR, 1.252; 95% CI, 0.826–1.897; *P* = .290), CD (HR, 1.299; 95% CI, 0.846–1.994; *P* = .232), re-MI (HR, 1.002; 95% CI, 0.323–3.108; *P* = .997), all-cause death or MI (HR, 1.198; 95% CI, 0.810–1.772; *P* = .367), any repeat revascularization (HR, 2.010; 95% CI, 0.605–6.774; *P* = .254), and ST (HR, 1.002; 95% CI, 0.251–4.005; *P* = .998) were not significantly different between the two groups (Table 3). After multivariate analysis (Table 2), the cumulative incidences of MACE (HR, 1.283; 95% CI, 0.945–1.743; *P* = .110), all-cause death, CD, re-MI, all-cause death or MI, any repeat revascularization, and ST (HR, 1.204; 95% CI, 0.490–2.958; *P* = .686) were not significantly different between the two groups.

Two years after index PCI, before adjustment, in the total population, the cumulative incidences of MACE (HR, 1.059; 95% CI, 0.896–1.252; *P* = .503), all-cause death, CD, re-MI, all-cause death or MI, any repeat revascularization, and ST (HR, 1.292; 95% CI, 0.724–2.306; *P* = .386) were not significantly different between the 2 groups (Table 2). After PSM analysis (Table 3), the cumulative incidences of MACE (HR, 1.052; 95% CI, 0.843–1.313; *P* = .655), all-cause death (HR, 1.026; 95% CI, 0.746–1.410; *P* = .876), CD (HR, 1.163; 95% CI, 0.811–1.565; *P* = .411), re-MI (HR, 1.296; 95% CI, 0.724–2.322; *P* = .383), all-cause death or MI (HR, 1.085; 95% CI, 0.819–1.438; *P* = .571), any repeat revascularization (HR, 1.029; 95% CI, 0.728–1.456; *P* = .870), and ST (HR, 1.452; 95% CI, 0.674–3.130; *P* = .341) were not significantly different between the 2 groups. After multivariate analysis (Table 2), the cumulative incidences of MACE (aHR, 1.028; 95% CI, 0.848–1.245; *P* = .781), all-cause death, CD, re-MI, all-cause death or MI, any repeat revascularization, and ST (aHR, 1.605; 95% CI, 0.831–

Table 2

Clinical outcomes in the total population.

Outcomes	STEMI (n = 5124)	NSTEMI (n = 3233)	Log-rank	Univariate analysis Hazard ratio (95% CI)	*P*	Multivariate analysis* Hazard ratio (95% CI)	*P*
30 days							
MACE	159 (3.1)	68 (2.1)	0.006	1.480 (1.114–1.966)	.007	1.283 (0.945–1.743)	.110
All-cause death	128 (2.5)	54 (1.7)	0.012	1.499 (1.091–2.061)	.013	1.225 (0.857–1.727)	.249
Cardiac death	121 (2.4)	51 (1.6)	0.014	1.500 (1.082–2.081)	.015	1.238 (0.869–1.765)	.238
Re-MI	23 (0.5)	10 (0.3)	0.319	1.455 (0.692–3.057)	.322	1.860 (0.811–4.264)	.143
All-cause death or MI	148 (2.9)	64 (2.0)	0.010	1.463 (1.089–1.962)	.011	1.247 (0.908–1.713)	.172
Any revascularization	14 (0.3)	5 (0.2)	0.263	1.777 (0.640–4.933)	.270	2.009 (0.662–6.090)	.392
Stent thrombosis (definite or probable)	16 (0.3)	9 (0.3)	0.779	1.124 (0.497–2.544)	.779	1.204 (0.490–2.958)	.686
2 years							
MACE	368 (7.5)	218 (7.2)	0.502	1.059 (0.896–1.252)	.503	1.028 (0.848–1.245)	.781
All-cause death	181 (3.6)	106 (3.4)	0.559	1.074 (0.845–1.365)	.559	1.180 (0.895–1.557)	.240
Cardiac death	155 (3.1)	77 (2.5)	0.087	1.269 (0.965–1.668)	.088	1.082 (0.792–1.480)	.621
Re-MI	66 (1.4)	37 (1.3)	0.594	1.116 (0.746–1.592)	.594	1.314 (0.822–2.098)	.254
All-cause death or MI	243 (4.9)	140 (4.5)	0.413	1.091 (0.886–1.343)	.414	1.059 (0.834–1.345)	.637
Any revascularization	140 (3.0)	91 (3.2)	0.751	0.958 (0.736–1.248)	.751	1.021 (0.752–1.385)	.896
Stent thrombosis (definite or probable)	35 (0.7)	17 (0.6)	0.385	1.292 (0.724–2.306)	.386	1.605 (0.831–3.100)	.159

ACC/AHA = American College of Cardiology/American Heart Association, ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin receptor blocker, BES = biolimus-eluting stents, CABG = coronary artery bypass graft, CCB = calcium channel blockers, CI = confidence interval, CK-MB = creatine kinase myocardial band, CPR = cardiopulmonary resuscitation, DBP = diastolic blood pressure, FFR = fractional flow reserve, HDL = high-density lipoprotein, IRA = infarct-related artery, IVUS = intravascular ultrasound, LAD = left anterior descending coronary artery, LCx = left circumflex coronary artery, LM = left main coronary artery, LVEF = left ventricular ejection fraction, MACE = major adverse cardiac events, MI = myocardial infarction, NSTEMI = non-STEMI, NT-ProBNP = N-terminal pro-brain natriuretic peptide, OCT = optical coherence tomography, PCI = percutaneous coronary intervention, RCA = right coronary artery, Re-MI = recurrent myocardial infarction, SBP = systolic blood pressure, STEMI = ST-segment elevation myocardial infarction, TIMI = Thrombolysis In Myocardial Infarction, ZES = zotarolimus-eluting stents.

* Adjusted by age, male, LVEF, SBP, DBP, cardiogenic shock, CPR on admission, Killip classification III/IV, hypertension, diabetes mellitus, dyslipidemia, previous history of MI, PCI, CABG, and stroke, peak CK-MB, peak troponin-I, NT-ProBNP, blood glucose, HDL-cholesterol, beta-blocker, ACEI, ARB, CCB, lipid-lowering agents, PCI within 24 hours, pre-PCI TIMI flow grade 0/1, IRA & treated vessels (LM, LAD, LCx, and RCA), ACC/AHA type B2/C lesions, 1-vessel, 2-vessel, ≥ 3-vessel, IVUS, OCT, FFR, ZES, BES, stent diameter, stent length, and number of stents.

3.100; *P* = .159) were not significantly different between the 2 groups.

Table 4 shows the independent predictors for MACE of the total study population. After adjustment, old age (≥ 65 years); reduced LVEF (< 40%); cardiogenic shock; CPR on admission; Killip class III/IV; diabetes mellitus; troponin-I and NT-ProBNP level; use of beta-blocker, ACEI, ARB, and lipid-lowering agent, and multivessel disease were independent predictors for MACE in this study.

4. Discussion

The main findings of this study are as follows. First, both during 1 month and at 2 years after index PCI, the cumulative incidences of MACE, all-cause death, CD, re-MI, all-cause death or MI, any repeat revascularization, and ST were not significantly different between the STEMI and NSTEMI groups after PSM analysis or multivariate analysis. Second, old age; reduced LVEF; cardiogenic shock; CPR on admission; Killip class III/IV; diabetes mellitus; troponin-I and NT-ProBNP levels, use of beta-blockers,

Table 3

Clinical outcomes in the propensity score-matched patients.

Outcomes	STEMI (n = 2250)	NSTEMI (n = 2250)	Log-rank	Hazard ratio (95% CI)	*P*
30 days					
MACE	63 (2.8)	49 (2.2)	0.182	1.288 (0.887–1.871)	.183
All-cause death	50 (2.2)	40 (1.8)	0.288	1.252 (0.826–1.897)	.290
Cardiac death	48 (2.1)	37 (1.6)	0.230	1.299 (0.846–1.994)	.232
Re-MI	6 (0.3)	6 (0.3)	0.997	1.002 (0.323–3.108)	.997
All-cause death or MI	55 (2.4)	46 (2.0)	0.365	1.198 (0.810–1.772)	.367
Any revascularization	8 (0.4)	4 (0.2)	0.245	2.010 (0.605–6.674)	.254
Stent thrombosis (definite or probable)	4 (0.2)	4 (0.2)	0.998	1.002 (0.251–4.005)	.998
2 years					
MACE	160 (7.5)	152 (7.2)	0.654	1.052 (0.843–1.313)	.655
All-cause death	77 (3.5)	75 (3.4)	0.876	1.026 (0.746–1.410)	.876
Cardiac death	64 (2.9)	55 (2.5)	0.410	1.163 (0.811–1.565)	.411
Re-MI	26 (1.3)	20 (1.0)	0.381	1.296 (0.724–2.322)	.383
All-cause death or MI	101 (4.7)	93 (4.3)	0.570	1.085 (0.819–1.438)	.571
Any repeat revascularization	65 (3.2)	63 (3.2)	0.870	1.029 (0.728–1.456)	.870
Stent thrombosis (definite or probable)	16 (0.8)	11 (0.5)	0.338	1.452 (0.674–3.130)	.341

CI = confidence interval, MACE = major adverse cardiac events, NSTEMI = non-STEMI, Re-MI = recurrent myocardial infarction, STEMI = ST-segment elevation myocardial infarction.

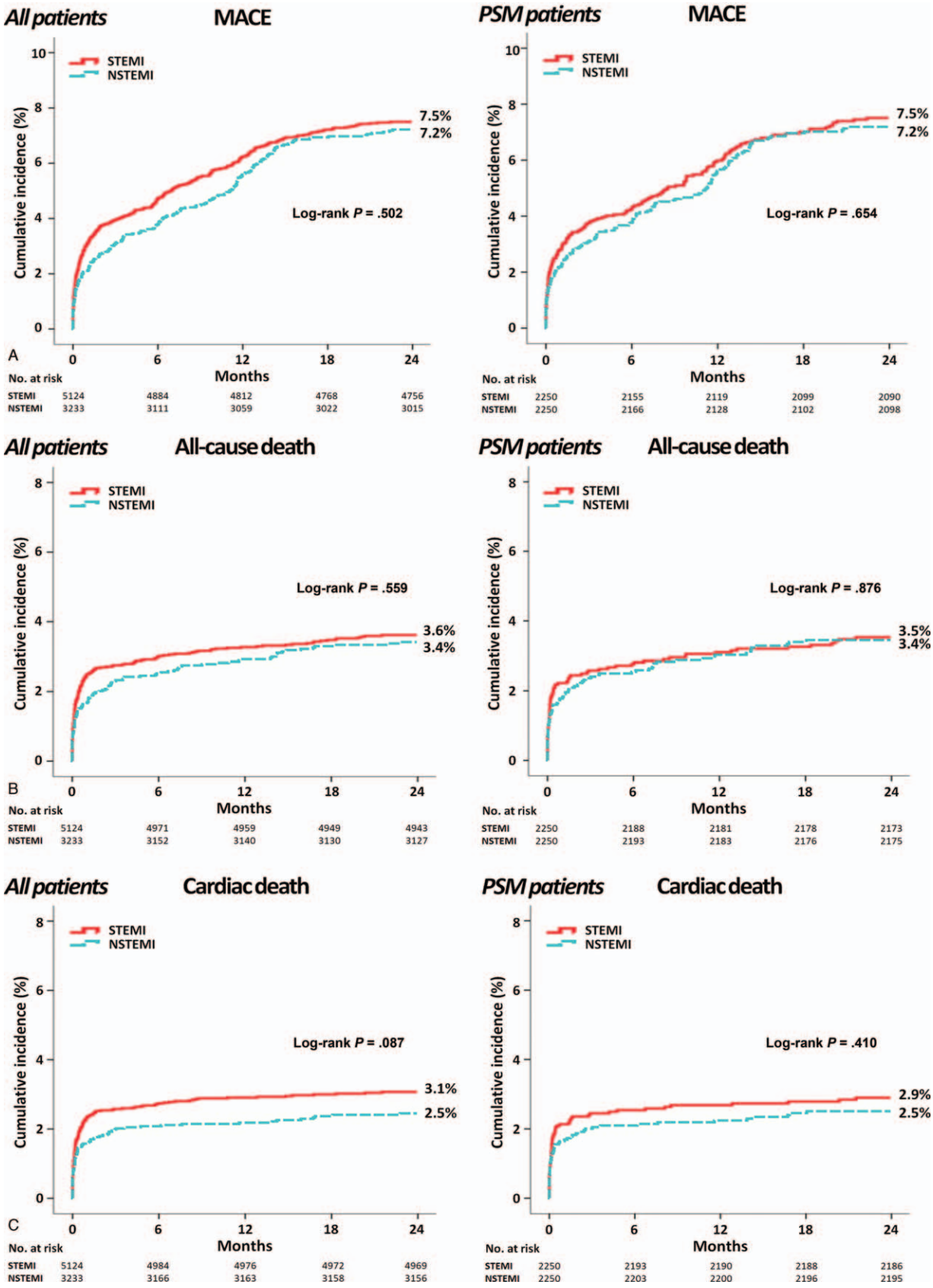

Figure 2. Kaplan–Meier analysis for the MACE (A), all-cause death (B), cardiac death (C), Re-MI (D), All-cause death or MI (E), any repeat revascularization (F), and stent thrombosis (G) during a 2-year follow-up period.

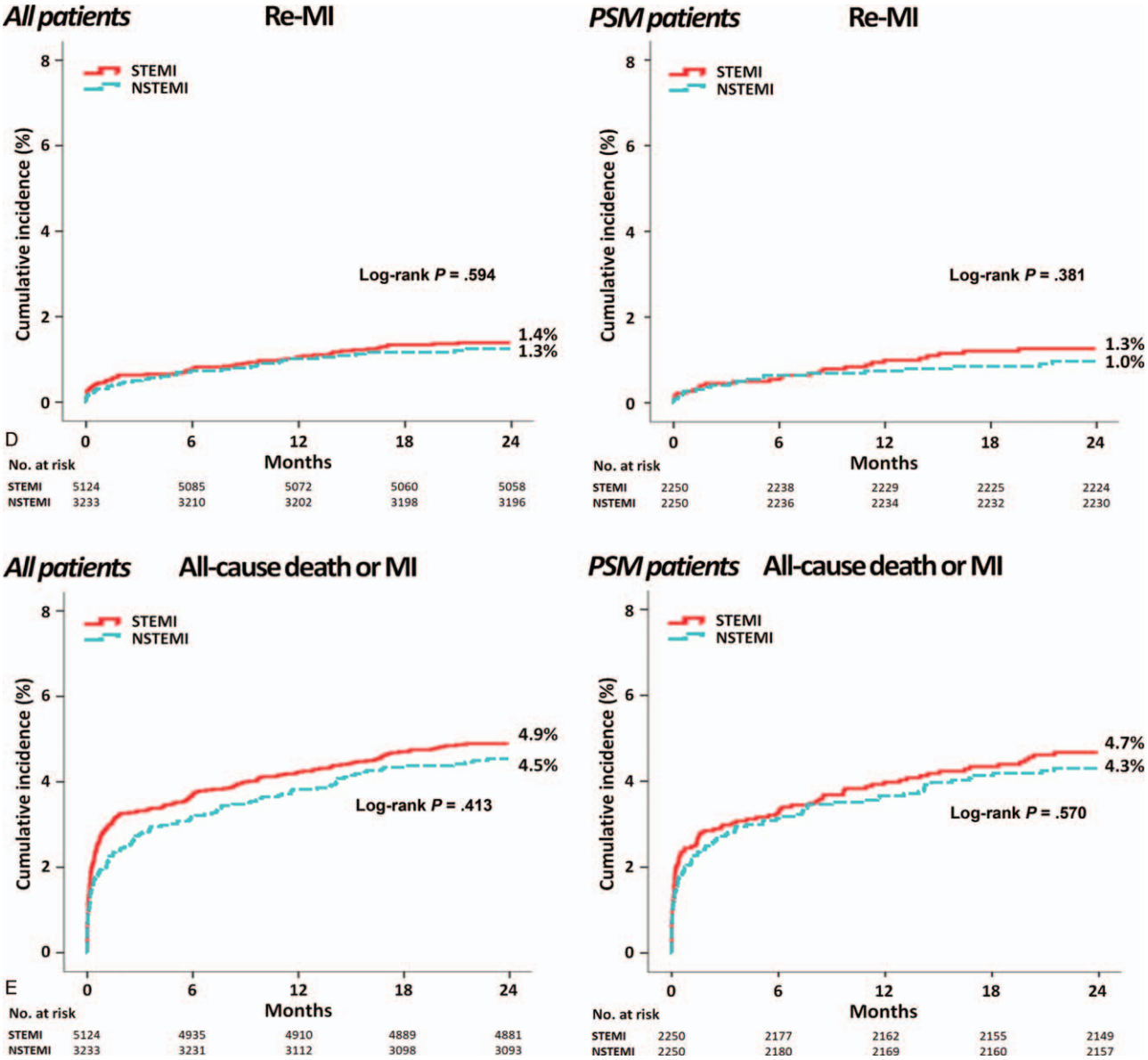

Figure 2. (Continued).

ACEIs, ARBs, and lipid-lowering agents; and multivessel disease were independent predictors of MACE.

Exposure to cigarette smoking has been shown to elicit decreased oxygen-carrying capacity and lead to ischemia, platelet activation, endothelial dysfunction, changes in lipoprotein levels, and thickened arterial walls, which are related to the progression of atherosclerosis and thrombosis.[21] These increased risks of ischemia, atherosclerosis, and thrombosis further increase the risk of MI and other fatal cardiovascular events.[2] Both STEMI and NSTEMI share a common pathophysiology related to coronary plaque erosion or rupture with variable degrees of lumen obstruction and thrombosis. Himbert et al[22] showed that current smokers were more frequently diagnosed with STEMI than NSTEMI. In our study, the number of patients with STEMI was higher than that of patients with NSTEMI (61.3% vs 38.7%, respectively, Fig. 1). Chan et al[23] suggested that STEMI was associated with a higher risk of short-term mortality (≤ 2 months after an index PCI; aHR, 1.85; 95% CI, 1.45–2.38), and NSTEMI was associated with a higher risk of long-term mortality (> 2 months after an index PCI; aHR, 0.68; 95% CI, 0.59–0.83). The worse in-hospital prognosis in STEMI patients could be attributed to a higher incidence of cardiogenic shock.[24] In our study, the number of patients with cardiogenic shock (5.4% vs 2.0%), Killip class III/IV (9.7% vs 6.5%), and CPR on admission (5.0% vs 2.3%) was also higher in STEMI patients than those in NSTEMI patients (Table 1), and these variables were independent predictors of MACE in our study (Table 4). Therefore, 1 month after the index PCI, the cumulative incidences of all-cause death (HR, 1.499; 95% CI, 1.091–2.061; $P = .013$) and CD (HR, 1.500; 95% CI, 1.082–2.081; $P = .015$) were significantly higher in STEMI patients than that in NSTEMI patients before adjustment in our study. However, both after PSM analysis

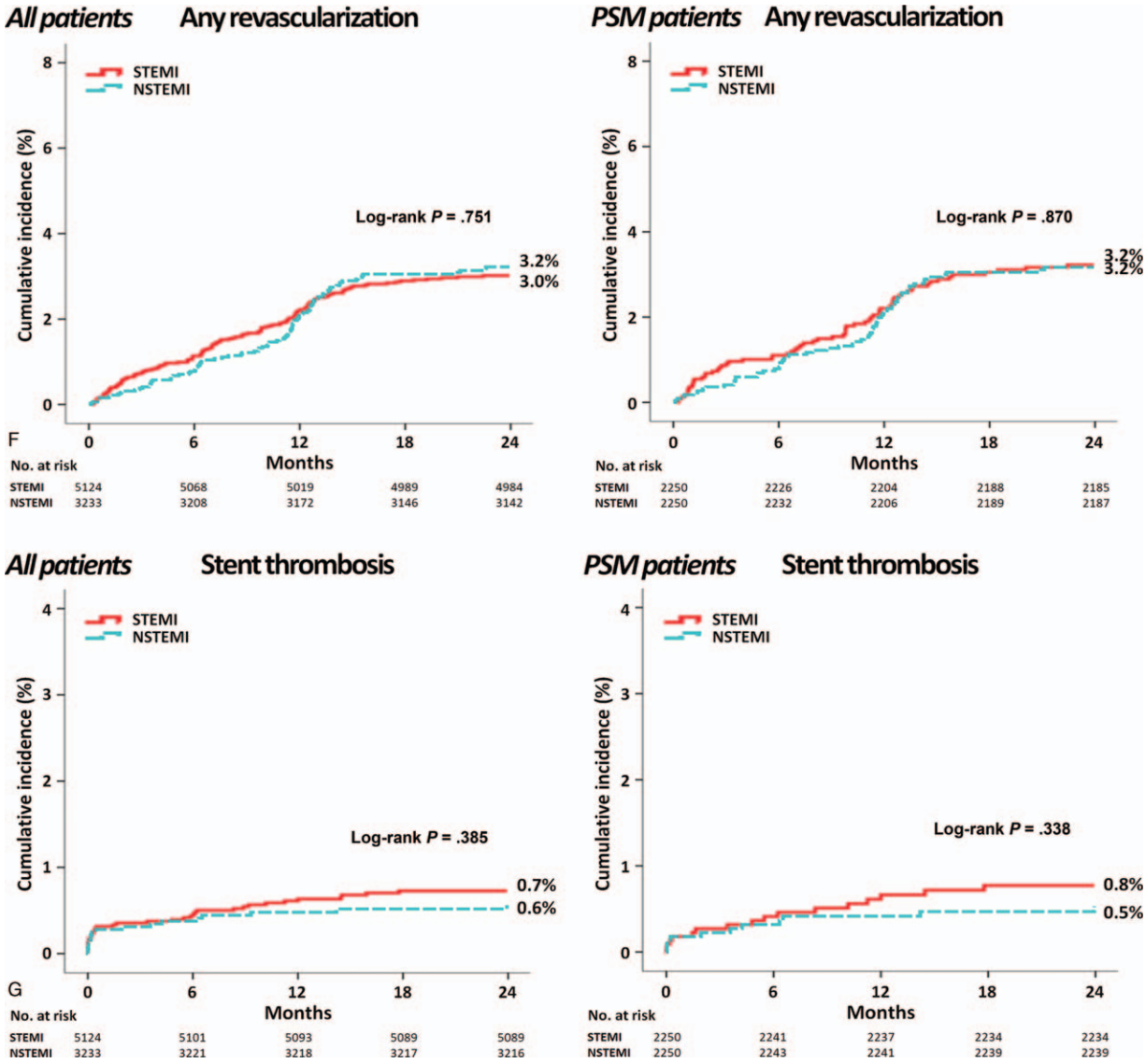

Figure 2. (Continued).

(Table 3) and multivariate analysis (Table 2), the cumulative incidences of all-cause death and CD were not significantly different between the STEMI and NSTEMI groups. Hence, we can speculate that other baseline characteristics may play an important role in determining all-cause death or CD in these 2 groups. In our study, the mean age; the number of patients with hypertension, diabetes mellitus, dyslipidemia, previous history of ischemic heart disease (MI, PCI, and CABG), and multivessel disease; and mean blood level of NT-ProBNP were significantly higher in the NSTEMI group than that in the STEMI group. Therefore, these high-risk profiles may contribute to a higher 1-month mortality rate in patients with NSTEMI. The baseline characteristics of the NSTEMI patients in our study were similar to those of the OPERA[8] and Euro Heart Survey ACS[25] studies. In the OPERA study,[8] in-hospital mortality was similar between the STEMI and NSTEMI groups (4.6% vs 4.3%, respectively). Because timely reperfusion in patients with STEMI could reduce infarction size and improve survival, infarct size is a strong independent predictor of death after STEMI.[26] Recently, Redfors et al[27] reported that infarct size was similar in smokers and nonsmokers (adjusted difference, 0.0%; 95% CI, 3.3–3.3; $P = .99$) when measured at a median of 4 days using either cardiac magnetic resonance imaging or technetium-99m sestamibi single-photon emission computed tomography in patients with STEMI after primary PCI. The extent of microvascular obstruction was not differed between smokers and nonsmokers (adjusted difference, −0.3%; 95% CI, −1.4% to 0.9%; $P = .60$). Furthermore, smoking activates cytochrome P450 isoenzyme 1A2, a key enzyme for converting the clopidogrel prodrug to its active form, thereby increasing its platelet inhibitory effect.[28]

Until now, most previous studies regarding the effect of smoking on long-term outcomes have been confined to STEMI[5,27,29] or NSTEMI[6] separately. Therefore, limited data comparing the long-term clinical outcomes between STEMI and NSTEMI in patients who are current smokers are available.[22] A higher-risk profile of baseline characteristics in patients with

Table 4

Independent predictors for MACE of the total study population.

Variables	Unadjusted		Adjusted	
	HR (95% CI)	P	HR (95% CI)	P
STEMI vs NSTEMI	1.059 (0.896–1.252)	.503	1.068 (0.889–1.282)	.484
Age, ≥ 65 yrs	2.229 (1.893–2.626)	< .001	1.686 (1.414–2.009)	< .001
Male	1.674 (1.237–2.199)	< .001	1.014 (0.761–1.351)	.924
LVEF <40%	2.403 (1.957–2.950)	< .001	1.365 (1.094–1.702)	.006
Cardiogenic shock	2.281 (1.707–3.047)	< .001	2.013 (1.505–2.693)	< .001
CPR on admission	5.594 (4.486–6.976)	< .001	3.673 (2.900–4.651)	< .001
Killip class III/IV	2.939 (2.403–3.594)	< .001	1.651 (1.335–2.041)	< .001
Hypertension	1.231 (1.045–1.451)	.013	1.034 (0.868–1.231)	.710
Diabetes mellitus	1.594 (1.338–1.899)	< .001	1.273 (1.058–1.532)	.011
Dyslipidemia	1.176 (0.897–1.543)	.240	1.036 (0.786–1.366)	.801
CK-MB	1.000 (0.999–1.001)	.864	0.999 (0.998–1.000)	.984
Troponin I	0.997 (0.979–1.001)	.249	1.000 (0.999–1.001)	.039
NT-ProBNP	1.000 (0.999–1.001)	< .001	1.001 (1.000–1.002)	< .001
Beta-blocker	2.847 (2.409–3.365)	< .001	1.753 (1.444–2.129)	< .001
ACEI	1.881 (1.596–2.216)	< .001	1.585 (1.289–1.949)	< .001
ARB	1.204 (0.984–1.472)	.071	1.452 (1.143–1.845)	.002
Lipid lowering agent	2.563 (2.156–3.045)	< .001	1.576 (1.299–1.912)	< .001
PCI within 24 hours	1.070 (0.770–1.486)	.687	1.242 (0.884–1.745)	.211
Pre-PCI TIMI flow grade 0/1	1.151 (0.972–1.363)	.103	1.133 (0.948–1.354)	.171
ACC/AHA type B2/C	1.142 (0.940–1.387)	.180	1.070 (0.873–1.310)	.515
Single-vessel disease	2.138 (1.803–2.535)	< .001	1.769 (0.896–3.496)	.100
Multivessel disease	2.234 (1.882–2.653)	< .001	3.363 (1.687–5.702)	.001
IVUS	1.016 (0.831–1.243)	.877	1.106 (0.901–1.358)	.336
OCT	1.708 (1.764–3.819)	.192	2.123 (0.940–4.792)	.070
ZES	1.035 (0.876–1.223)	.687	1.111 (0.928–1.329)	.252
BES	1.072 (0.843–1.364)	.571	1.014 (0.782–1.315)	.916
Stent diameter, ≤2.75 mm	1.192 (0.991–1.434)	.062	1.007 (0.832–1.218)	.944
Stent length, ≥ 30 mm	1.312 (1.102–1.562)	.002	1.194 (0.989–1.441)	.065
Number of stent	1.220 (1.112–1.339)	< .001	0.969 (0.869–1.080)	.568

ACC/AHA = American College of Cardiology/American Heart Association, ACEI = angiotensin-converting enzyme inhibitors, ARB = angiotensin receptor blocker, BES = biolimus-eluting stent, CI = confidence interval, CK-MB = creatine kinase myocardial band, CPR = cardiopulmonary resuscitation, EES = everolimus-eluting stent, HR = hazard ratio, IVUS = intravascular ultrasound, LVEF = left ventricular ejection fraction, NSTEMI = non-STEMI, NT-ProBNP = N-terminal pro-brain natriuretic peptide, OCT = optical coherence tomography, PCI = percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction, TIMI = Thrombolysis In Myocardial Infarction, ZES = zotarolimus-eluting stent.

NSTEMI could determine long-term clinical outcomes. Chan et al[23] also reported that the greater prevalence of comorbidities among patients with NSTEMI accounts for much of the excess mortality (aHR, 0.84; 95% CI, 0.74–0.97) during a median follow-up of 4 years. The 1-year mortality rate between the STEMI and NSTEMI groups (9.0% vs 11.6%, respectively, $P = .09$) was not significantly different in the OPERA study.[8]

Our study population was confined to patients who were currently smoking. Old age (≥ 65 years); reduced LVEF (< 40%); cardiogenic shock; CPR on admission; Killip class III/IV; diabetes mellitus; troponin-I and NT-ProBNP levels; use of beta-blockers, ACEIs, ARBs, lipid-lowering agents, and multivessel disease were independent predictors of MACE. However, these independent predictors were not significantly different from those in previous studies.[30–32]

The short-term and long-term clinical outcomes of STEMI and NSTEMI remain debatable. Although our results showed that the 1-month and 2-year mortality rates after index PCI were not significantly different between the 2 groups, in the Polonski et al[24] study, in-hospital mortality (11.6% vs 8.7%, respectively) and 2-year mortality rates were higher in the STEMI group (aHR, 0.76; 95% CI, 0.71–0.83; $P < .001$). In the Euro Heart Survey ACS study [25], in-hospital (7.0% vs 2.4%) and 30-day mortalities (8.4% vs 3.5%) were higher in the STEMI group. Most recently, Bouisset et al[33] reported that despite STEMI patients having a worse survival than NSTEMI patients within 28 days after index PCI (adjusted odds ratio, 0.58; 95% CI, 0.38–0.89; $P = .02$), STEMI and NSTEMI patients have a similar survival at the 10-year follow-up (aHR, 1.12; 95% CI, 0.88–1.42; $P = .43$). Fokkema et al[34] showed that mortality was higher in STEMI patients 1 year after PCI (9.6%) than that in NSTEMI patients (4.7%). However, at 1 year after PCI until the end of follow-up, the adjusted mortality risk (1–6 years after PCI) and the risk of MI were comparable between NSTEMI and STEMI patients (aHR, 0.93; 95% CI, 0.86–1.02).

However, most of the previous studies were not confined to patients who received newer-generation DES[7,8,22,25] and patients who were current smokers.[7,8,23–25,33–35] Martins et al[36] suggested that different mortality rates in the registry data are partly due to differences in inclusion criteria and demographic data. In our study, to reflect current trends of PCI, all STEMI and NSTEMI patients were confined to individuals who received newer-generation DESs and who were current smokers. Moreover, more than 50 community and teaching hospitals in South Korea participated in this nationwide registry analysis. Hence, our findings could provide meaningful information to cardiologists in the era of newer-generation DESs.

This study has some limitations. First, because our study was a retrospective registry cohort study, there may have been some

underreporting and/or missing data. Second, the smoking status of the study population was evaluated during initial admission. However, we did not know the quantity and duration of cigarette smoking and smoking status during the follow-up period due to the lack of this information in the registry data. Therefore, this is a major shortcoming of this study. Third, we evaluated all clinical outcomes based on discharge medications, and this registry data did not include detailed information concerning prescription doses, long-term adherence, discontinuation, and drug-related adverse events during the follow-up period. Fourth, despite PSM and multivariate analyses, some variables not included in the KAMIR may have affected the study outcomes. Fifth, more than 50% of patients presenting with acute chest pain and LBBB to the emergency department will be found to have a diagnosis other than MI.[37] Although the diagnosis of STEMI relies primarily on the ECG, the diagnosis of NSTEMI relies primarily on troponin because a significant proportion of patients with AMI presenting with a negative ECG.[38] Some of ECGs in patients with NSTEMI are normal, some have ST-segment depression, and a significant proportion have nonspecific ST/T abnormalities, and there are many confounding preexisting abnormalities (e.g., LBBB, left ventricular hypertrophy). This heterogeneous group has been interpreted simply as NSTEMI.[39] So, in our study, even though we classified the enrolled patients into STEMI or NSTEMI according to the current guidelines,[16,17] there must be patients with incorrect classification in both the STEMI and NSTEMI groups. Sixth, although we included enrolled patient's baseline grade of mitral regurgitation in this study, the information about other valvular dysfunction was not included in the KAMIR data. Moreover, STEMI and NSTEMI are very heterogeneous and there are many other confounders such as comorbidity (e.g., chronic obstructive pulmonary disease, chronic renal failure). In this study, we included the levels of serum creatinine, estimated glomerular filtration rate (eGFR), and number of patients with eGFR < 60 min/min/1.73 m^2 to estimate renal function. However, the major clinical outcomes between the STEMI and NSTEMI groups were not compared according to the grade of chronic kidney disease. Additionally, KAMIR data did not included information about COPD. Hence, these factors were other limitations of our study. Seventh, the 2-year follow-up period in this study was relatively short in determining long-term major clinical outcomes. Finally, because the information concerning time-varying variables including smoking status during a follow-up period was lack or incomplete, we could not provide the results of multivariate analysis using time-varying covariates in our study, unfortunately. Our results could be changed if these time-varying covariates are correctly reflected in this study. This is a big drawback of this study.

In conclusion, in the era of contemporary newer-generation DES, both during 1 month and 2 years after index PCI, the major clinical outcomes were not significantly different between the STEMI and NSTEMI groups in patients who are current smokers. However, further research is needed to confirm these results.

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References

[1] Price JF, Mowbray PI, Lee AJ, et al. Relationship between smoking and cardiovascular risk factors in the development of peripheral arterial disease and coronary artery disease: Edinburgh Artery Study. Eur Heart J 1999;20:344–53.

[2] Iversen B, Jacobsen BK, Løchen ML. Active and passive smoking and the risk of myocardial infarction in 24,968 men and women during 11 year of follow-up: the Tromsø Study. Eur J Epidemiol 2013;28:659–67.

[3] Rooks C, Faber T, Votaw J, et al. Effects of smoking on coronary microcirculatory function: a twin study. Atherosclerosis 2011;215: 500–6.

[4] Csordas A, Bernhard D. The biology behind the atherothrombotic effects of cigarette smoke. Nat Rev Cardiol 2013;10:219–30.

[5] Steele L, Palmer J, Lloyd A, et al. The impact of smoking on mortality after acute ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention: a retrospective cohort outcome study at 3 years. J Thrombosis Thrombolysis 2019;47: 520–6.

[6] Robertson JO, Ebrahimi R, Lansky AJ, et al. Impact of cigarette smoking on extent of coronary artery disease and prognosis of patients with non-ST-segment elevation acute coronary syndromes: an analysis from the ACUITY Trial (Acute Catheterization and Urgent Intervention Triage Strategy). JACC Cardiovasc Interv 2014;7:372–9.

[7] Goldberg RJ, Currie K, White K, et al. Six-month outcomes in a multinational registry of patients hospitalized with an acute coronary syndrome (the Global Registry of Acute Coronary Events [GRACE]). Am J Cardiol 2004;93:288–93.

[8] Montalescot G, Dallongeville J, Van Belle E, et al. STEMI and NSTEMI: are they so different? 1 year outcomes in acute myocardial infarction as defined by the ESC/ACC definition (the OPERA registry). Eur Heart J 2007;28:1409–17.

[9] Kim YH, Her AY, Jeong MH, Kim BK, et al. Impact of stent generation on 2-year clinical outcomes in ST-segment elevation myocardial infarction patients with multivessel disease who underwent culprit-only or multivessel percutaneous coronary intervention. Cath Cardiovasc Interv 2020;95:E40–55.

[10] Kim YH, Her AY, Jeong MH, et al. A comparison of the impact of current smoking on 2-year major clinical outcomes of first- and second-generation drug-eluting stents in acute myocardial infarction: data from the Korea Acute Myocardial Infarction Registry. Medicine 2019;98: e14797.

[11] Kim Y, Ahn Y, Cho MC, et al. Current status of acute myocardial infarction in Korea. Korean J Intern Med 2019;34:1–10.

[12] Kim JH, Chae SC, Oh DJ, et al. Multicenter cohort study of acute myocardial infarction in Korea: interim analysis of the Korea Acute Myocardial Infarction Registry-National Institutes of Health Registry. Circ J 2016;80:1427–36.

[13] Grech ED. ABC of interventional cardiology: percutaneous coronary intervention. II: the procedure. BMJ 2003;326:1137–40.

[14] Chen KY, Rha SW, Li YJ, et al. Triple versus dual antiplatelet therapy in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Circulation 2009;119:3207–14.

[15] Gao W, Zhang Q, Ge H, et al. Efficacy and safety of triple antiplatelet therapy in obese patients undergoing stent implantation. Angiology 2013;64:554–8.

[16] O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2013;127: e362–425.

[17] Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;64:e139–228.

[18] Lee JM, Rhee TM, Hahn JY, et al. Multivessel percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction with cardiogenic shock. J Am Coll Cardiol 2018;71:844–56.

[19] Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. Circulation 2012;126:2020–35.

[20] Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007; 115:2344–51.

[21] Armani C, Landini LJr, Leone A. Molecular and biochemical changes of the cardiovascular system due to smoking exposure. Curr Pharm Des 2009;15:1038–53.

[22] Himbert D, Klutman M, Steg G, et al. Cigarette smoking and acute coronary syndromes: a multinational observational study. Int J Cardiol 2005;100:109–17.

[23] Chan MY, Sun JL, Newby LK, et al. Long-term mortality of patients undergoing cardiac catheterization for ST-elevation and non-ST-elevation myocardial infarction. Circulation 2009;119:3110–7.

[24] Polonski L, Gasior M, Gierlotka M, et al. A comparison of ST elevation versus non-ST elevation myocardial infarction outcomes in a large registry database: are non-ST myocardial infarctions associated with worse long-term prognoses? Int J Cardiol 2011;152:70–7.

[25] Hasdai D, Behar S, Wallentin L, et al. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin; the Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS). Eur Heart J 2002;23:1190–201.

[26] Stone GW, Selker HP, Thiele H, et al. Relationship between infarct size and outcomes following primary PCI: patient-level analysis from 10 randomized trials. J Am Coll Cardiol 2016;67:1674–83.

[27] Redfors B, Furer A, Selker HP, et al. Effect of smoking on outcomes of primary PCI in patients with STEMI. J Am Coll Cardiol 2020;75:1743–54.

[28] Gagne JJ, Bykov K, Choudhry NK, et al. Effect of smoking on comparative efficacy of antiplatelet agents: systematic review, meta-analysis, and indirect comparison. BMJ 2013;347:f5307.

[29] Tolouey M, Ghaffari S, Tajlil A, et al. The impact of cigarette smoking on infarct location and in-hospital outcome following acute ST-elevation myocardial infarction. J Cardiovasc Thorac Res 2019;11:209–15.

[30] Huang X, Redfors B, Chen S, et al. Predictors of mortality in patients with non-anterior ST-segment elevation myocardial infarction: analysis from the HORIZONS-AMI trial. Cath Cardiovasc Interv 2019;94: 172–80.

[31] Acharji S, Baber U, Mehran R, et al. Prognostic significance of elevated baseline troponin in patients with acute coronary syndromes and chronic kidney disease treated with different antithrombotic regimens: a substudy from the ACUITY trial. Circ Cardiovasc Interv 2012;5:157–65.

[32] Lee SJ, Cho JY, Kim BK, et al. Ticagrelor monotherapy versus ticagrelor with aspirin in patients with ST-segment elevation myocardial infarction. JACC Cardiovasc Interv 2021;14:431–40.

[33] Bouisset F, Ruidavets JB, Dallongeville J, et al. Comparison of short- and long-term prognosis between ST-Elevation and non-ST-elevation myocardial infarction. J Clin Med 2021;10:180.

[34] Fokkema ML, James SK, Albertsson P, et al. Outcome after percutaneous coronary intervention for different indications: long-term results from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR). EuroIntervention 2016;12:303–11.

[35] Hirsch A, Verouden NJ, Koch KT, et al. Comparison of long-term mortality after percutaneous coronary intervention in patients treated for acute ST-elevation myocardial infarction versus those with unstable and stable angina pectoris. Am J Cardiol 2009;104:333–7.

[36] Martins E, Magne J, Pradel V, et al. The mortality rates in registries of patients with STEMI are highly affected by inclusion criteria and population characteristics. Acta Cardiol 2021;76:504–12.

[37] Nestelberger T, Cullen L, Lindahl B, et al. Diagnosis of acute myocardial infarction in the presence of left bundle branch block. Heart 2019; 105:1559–67.

[38] Welch RD, Zalenski RJ, Frederick PD, et al. Prognostic value of a normal or nonspecific initial electrocardiogram in acute myocardial infarction. JAMA 2001;286:1977–84.

[39] Miranda DF, Lobo AS, Walsh B, et al. New insights into the use of the 12-lead electrocardiogram for diagnosing acute myocardial infarction in the emergency department. Can J Cardiol 2018;34:132–45.