

Three-year outcomes following non-ST-segment elevation myocardial infarction and new-generation drug-eluting stent implantation, stratified by patient age (under and over 75 years) and left ventricular ejection fraction

A prospective cohort study

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Abstract

Due to limited published data, we investigated 3-year outcomes according to left ventricular ejection fraction (LVEF) in patients older and younger than 75 years with non-ST-segment elevation myocardial infarction (NSTEMI) who underwent successful newer-generation drug-eluting stent (DES) implantation. This research analyzed the data of 4558 patients (1032 older adults [≥ 75 years] and 3526 younger adults [< 75 years]) from the Korea Acute MI Registry-NIH. We further divided the older group based on LVEF: heart failure (HF) with reduced EF (HFrEF, $\leq 40\%$, $n = 196$; group A), HF with mildly reduced EF (HFmrEF, 41–49%, $n = 228$; group B), and HF with preserved EF (HFpEF, $\geq 50\%$, $n = 608$; group C). Similarly, the younger group was divided into HFrEF (group D, $n = 353$), HFmrEF (group E, $n = 577$), and HFpEF (group F, $n = 2596$). The primary outcome was a composite of major adverse cardiac events (MACE) at 3 years, including all-cause death, recurrent MI, any repeat revascularization, or hospitalization for HF. MACE rates were highest in the HFrEF groups (A and D), followed by the HFmrEF groups (B and E), and lowest in the HFpEF groups (C and F) for both age groups. All-cause death, cardiac death (CD), all-cause death or MI, and hospitalization for HF rates were higher in group A than in groups B and C, and higher in group D than in groups E and F. Across all LVEF categories, MACE, all-cause death, CD, and non-CD, and all-cause death or MI rates were higher in the older group. This multicenter cohort study demonstrates that older patients have higher mortality rates compared to younger patients. Additionally, MACE rates were highest in the HFrEF group, followed by the HFmrEF group, and lowest in the HFpEF group across both age groups. Further research is needed to confirm these findings.

Abbreviations: 1G-DES = first-generation drug-eluting stents, ACS = acute coronary syndrome, BMS = bare-metal stents, CPR = cardiopulmonary resuscitation, DBT = door-to-balloon time, DES = drug-eluting stents, DM = diabetes mellitus, HF = heart failure, HFmrEF = heart failure with mildly reduced ejection fraction, HFpEF = heart failure with preserved EF, HFrEF = heart failure with reduced ejection fraction, IHD = ischemic heart disease, IRA = infarct-related artery, KAMIR-NIH = Korea Acute Myocardial Infarction Registry-National Institute of Health, LVEF = left ventricular ejection fraction, MACE = major adverse cardiac events, MI = myocardial infarction, NSTEMI = non-ST-segment-elevation myocardial infarction, PCI = percutaneous coronary intervention, SDT = symptom-to-door time, STEMI = ST-segment-elevation myocardial infarction.

Keywords: heart failure, non-ST-segment-elevation myocardial infarction, outcomes

YHK and A-YH contributed equally to the writing.

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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1. Introduction

Aging is a significant risk factor for heart failure (HF), leading to poorer outcomes in elderly individuals, with an incidence of HF as high as 20% among those over 75 years old.^[1] In a global registry,^[2] patients with ischemic heart disease (IHD) were older, had more comorbidities, and were more likely to have a left ventricular ejection fraction (LVEF) < 40% (indicating HF with reduced ejection fraction [HFrEF]). This group also showed higher one-year mortality (hazard ratio [HR]: 1.12, $P = .010$) compared to those without IHD.

The 2016 European Society of Cardiology guidelines for acute and chronic HF^[3] introduced a new category for patients with LVEF ranging from 41% to 49%: HF with mildly reduced EF (HFmrEF). Compared to HF with preserved EF (HFpEF), HFmrEF shares more similarities with HFrEF, including a higher prevalence of IHD and a greater risk of developing new IHD events.^[4] While the long-term prognosis of HFrEF is known to be worse than HFpEF, the prognosis for HFmrEF remains unclear and under debate.^[5,6] Additionally, bare-metal stents (BMS) and first-generation drug-eluting stents (1G-DES) are rarely used in real-world percutaneous coronary intervention (PCI) procedures. Studies show that patients receiving newer-generation drug-eluting stents (DES) have better outcomes compared to those using BMS or 1G-DES.^[7] Although short-term mortality is higher in patients with ST-segment-elevation myocardial infarction (STEMI),^[8] long-term mortality is higher in non-STEMI (NSTEMI) patients.^[9] Considering that PCI rates exceed 60% in NSTEMI patients, investigating the long-term prognosis of HFmrEF in this population would be valuable for interventional cardiologists. However, existing research has primarily focused on patients with acute coronary syndrome (ACS)^[6] or specifically on STEMI patients.^[10] Notably, no studies have examined the prognosis of HFmrEF patients aged 75 years and older who underwent newer-generation DES implantation for NSTEMI. Therefore, in this study, we aimed to compare the 3-year outcomes in patients with NSTEMI who underwent successful newer-generation DES implantation, based on age (≥ 75 years and < 75 years) and LVEF (HFrEF, HFmrEF, and HFpEF).

2. Methods

2.1. Study population selection and data collection

We analyzed data from the Korea Acute Myocardial Infarction Registry-National Institute of Health (KAMIR-NIH)^[11] for patients enrolled between November 2011 and December 2015. KAMIR-NIH is a prospective, open, observational online registry that includes 20 high-volume university or community hospitals offering primary PCI and onsite cardiac surgery in South Korea. A total of 13,104 patients aged 18 years or older were enrolled in KAMIR-NIH during the study period. We excluded patients who did not undergo PCI ($n = 1369$, 10.4%), had unsuccessful PCI ($n = 152$, 1.2%), received plain old balloon angioplasty ($n = 739$, 5.6%), underwent coronary artery bypass graft ($n = 44$, 0.3%), had a history of HF ($n = 69$, 0.5%), received BMS or 1G-DES ($n = 678$, 5.2%), were diagnosed with STEMI ($n = 5337$, 40.7%), or lacked follow-up data ($n = 158$, 1.2%).

This resulted in a final study population of 4558 patients with NSTEMI who underwent successful PCI with newer-generation DES. We divided them into 2 groups based on age: ≥ 75 years ($n = 1032$) and < 75 years ($n = 3526$). These groups were further divided based on LVEF into HFrEF (group A, $n = 196$; group D, $n = 353$), HFmrEF (group B, $n = 228$; group E, $n = 577$), and HFpEF groups (group C, $n = 608$; group F, $n = 2596$) (Fig. 1). All participants provided written informed consent before enrollment. This non-randomized study was approved by the ethics committees of each participating center, including the Korea University Guro Hospital Institutional Review Board Ethics Committee (#KUGH MD11024). The study adhered to the ethical principles outlined in the 2004 Declaration of Helsinki. Clinical research coordinators independently collected data using a web-based case report form integrated into the Internet-based Clinical Research and Trial Management System (iCReaT) developed by the Centers for Disease Control and Prevention, Ministry of Health and Welfare, Republic of Korea. This system functions as a data management infrastructure (iCReaT Study No. C110016; KCT-0000863). We completed the 3-year follow-up through outpatient visits, telephone surveys, and medical record reviews. The event adjudication process has been described in detail in previous studies.^[11] An independent committee within KAMIR-NIH rigorously monitored and evaluated all events for accuracy.

2.2. PCI and medical treatment

Coronary angiography and PCI were performed according to established, standardized techniques.^[12] Patients younger than 75 years scheduled for PCI received a loading dose of one of the following medications: aspirin (200–300 mg), clopidogrel (300–600 mg), ticagrelor (180 mg), or prasugrel (60 mg). Following PCI, these patients were recommended to take daily aspirin (100 mg) along with clopidogrel (75 mg), ticagrelor (90 mg), or prasugrel (5–10 mg) for at least 1 year. For patients aged ≥ 75 years, prasugrel was used neither for the initial loading dose nor for the medications administered after PCI.^[13]

2.3. Study definitions

In this study, we compared outcomes between 2 age groups to investigate outcomes in older and younger patients. The definition of elderly in the cardiology literature has shifted over time, with recent studies using 75 years old as the cut-off. We adopted this definition (≥ 75 years old) to reflect the improved health and increased independence observed in older adults.^[13] Acute MI (AMI) was defined according to the Fourth Universal Definition of MI.^[14] Because LVEF is a key tool for categorizing HF patients in randomized controlled trials and observational studies.^[15] LVEF was assessed using the Simpson method.^[6] Successful PCI was defined as achieving thrombolysis in myocardial infarction flow grade 3 or residual stenosis less than 30% in the infarct-related artery (IRA) after PCI. Symptom-to-door time (SDT) was defined as the time between the last sustained chest pain experienced by the patient and their arrival at the PCI-capable center.^[15] Door-to-balloon time (DBT) was defined as the time between patient's arrival at the PCI-capable center and the first balloon inflation during PCI.^[16]

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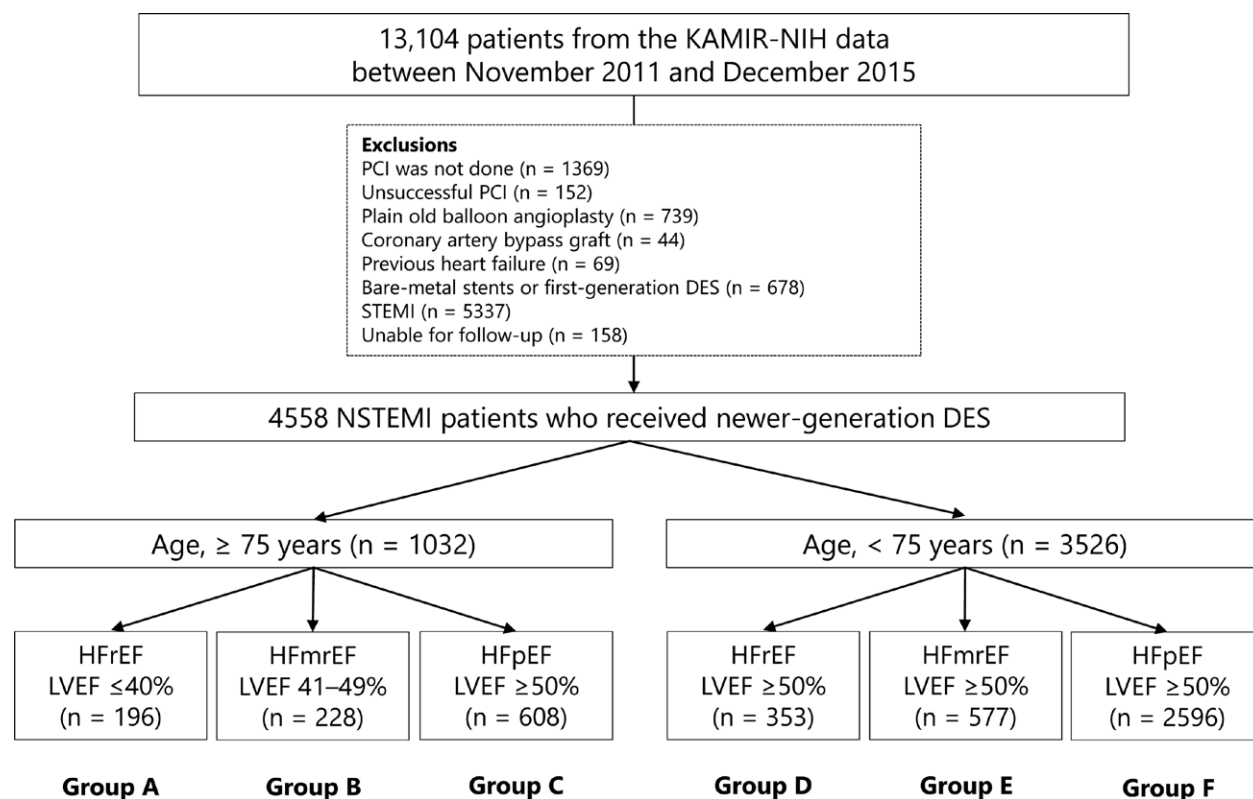


Figure 1. Flowchart.

2.4. Clinical outcomes

The primary outcome of this study was the occurrence of major adverse cardiac events (MACE), a composite endpoint encompassing all-cause death, recurrent MI, any repeat coronary revascularization, and hospitalization for HF. The individual components of MACE served as the secondary outcomes.

In the absence of compelling evidence to the contrary, all deaths were classified as cardiac deaths (CD) by default.^[17] Recurrent MI was diagnosed based on a combination of factors: recurrence of symptoms, characteristic electrocardiogram changes, an increase in cardiac troponin levels, with at least one measurement exceeding the upper reference limit of the 99th percentile.^[14] Periprocedural MI was excluded as a clinical outcome. Clinically necessary revascularization procedures performed after discharge from the initial hospitalization were considered repeat revascularization events, following criteria established by the Academic Research Consortium.^[18]

2.5. Statistical analyses

Differences in continuous variables among the 3 groups were evaluated using analysis of variance or the Jonckheere-Terpstra test. post hoc comparisons were conducted using the Hochberg or Dunnnett-T3 tests, with results reported as mean ± standard deviation or median (interquartile range) depending on normality. Discrete variables were compared among the 3 groups using either the chi-square or Fisher's exact test, as appropriate. Results for discrete variables were expressed as counts and percentages. Kaplan-Meier estimates were used to depict the cumulative incidence of adverse events during follow-up, and statistical significance was determined using a log-rank test. HRs and their corresponding 95% confidence intervals (CIs) were calculated using Cox proportional hazards regression models. Statistical significance was set at a threshold of $P < .05$. In this study, we performed multicollinearity tests^[19] for MACE within various LVEF categories to ensure there were no issues

among all significant confounding variables ($P < .05$) (Table S1, Supplemental Digital Content, <http://links.lww.com/MD/N527>). We used the Variance Inflation Factor, tolerance index, and condition index to determine collinearity. Collinearity was judged to be present if the Variance Inflation Factor exceeded 5,^[20] the tolerance was below 0.1, or the condition index exceeded 10.^[20]

The variables ultimately included in the multivariable Cox proportional hazards regression analysis are listed in Table S1, Supplemental Digital Content, <http://links.lww.com/MD/N527>. These include male sex, systolic blood pressure, diastolic blood pressure, heart rate, body mass index, Killip class II/III, cardiogenic shock, cardiopulmonary resuscitation (CPR) on admission, SDT, DBT, hypertension, diabetes mellitus (DM), dyslipidemia, previous MI, previous PCI, previous coronary artery bypass graft, previous stroke, current smoker, peak creatine kinase myocardial band, peak troponin-I, hemoglobin, blood glucose, serum creatinine, triglyceride, and low-density lipoprotein (LDL)-cholesterol (Table S1, Supplemental Digital Content, <http://links.lww.com/MD/N527>). The results of collinearity testing for MACE between the age groups ≥ 75 years and < 75 years are presented in Table S2, Supplemental Digital Content, <http://links.lww.com/MD/N527>. All statistical analyses were conducted using the IBM Statistical Package for the Social Sciences software version 20 (Armonk).

3. Results

3.1. Baseline characteristics

Table 1; Tables S3, Supplemental Digital Content, <http://links.lww.com/MD/N527>, and S4, Supplemental Digital Content, <http://links.lww.com/MD/N527> summarize the baseline clinical, laboratory, angiographic, and procedural characteristics of the study participants. Table 1 presents a comparison of baseline characteristics within each LVEF group for both age groups (≥ 75 years and < 75 years). In both age groups (≥ 75 years and < 75

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Table 1
Baseline characteristics.

Variables	Age, ≥ 75 years (n = 1032)				Age, < 75 years (n = 3526)			
	Group A HFREF LVEF ≤ 40% (n = 196)	Group B HFmrEF LVEF 41–49% (n = 228)	Group C HFpEF LVEF ≥ 50% (n = 608)	P	Group D HFREF LVEF ≤ 40% (n = 353)	Group E HFmrEF LVEF 41–49% (n = 577)	Group F HFpEF LVEF ≥ 50% (n = 2956)	P
Male, n (%)	89 (45.4)	111 (48.7)	299 (49.2)	.652	267 (75.6)	451 (78.2)	2085 (80.3)	.085
Age, years	80.2 ± 3.9	79.8 ± 3.9	79.4 ± 3.8	.033	63.2 ± 8.8	61.2 ± 9.4	59.1 ± 9.8	<.001
SBP, mm Hg	132.2 ± 29.0	132.0 ± 26.1	134.9 ± 26.8	.266	131.0 ± 27.6	131.8 ± 24.9	137.7 ± 25.5	<.001
DBP, mm Hg	78.7 ± 16.6	77.1 ± 14.0	78.5 ± 14.0	.420	80.1 ± 17.1	80.6 ± 16.4	83.0 ± 15.2	<.001
Heart rate, beats/min	91.5 ± 18.2	81.3 ± 18.8	77.9 ± 17.4	<.001	92.6 ± 20.2	80.1 ± 17.1	76.6 ± 15.5	<.001
Body mass index, kg/m ²	22.6 ± 4.0	22.6 ± 3.0	22.7 ± 3.3	.833	23.7 ± 3.6	24.1 ± 3.1	24.7 ± 3.1	<.001
LVEF, %	33.0 ± 6.0	45.7 ± 2.5	59.5 ± 6.5	<.001	32.7 ± 6.6	45.9 ± 2.4	59.5 ± 6.1	<.001
Killip class I/II/III	106 (54.1)	69 (30.3)	111 (18.3)	<.001	149 (42.4)	89 (15.4)	209 (8.1)	<.001
Cardiogenic shock	7 (3.6)	4 (1.8)	14 (2.3)	.458	15 (4.2)	9 (1.6)	30 (1.2)	<.001
CPR on admission	18 (9.2)	14 (6.1)	17 (2.8)	.001	49 (13.9)	14 (2.4)	16 (0.6)	<.001
Symptom-to-door time, hours	17.7 (4.0–72.0)	9.9 (4.0–30.7)	9.0 (3.0–37.4)	.065	8.9 (3.0–28.8)	6.9 (2.3–24.0)	5.9 (2.1–23.6)	.590
Door-to-balloon time, hours	16.6 (3.5–40.7)	15.8 (3.8–30.7)	14.6 (4.0–26.3)	.006	14.0 (3.5–39.1)	11.3 (3.1–23.0)	13.2 (3.8–23.9)	<.001
Risk factors								
Hypertension, n (%)	147 (75.0)	148 (64.9)	421 (69.2)	.080	190 (53.8)	256 (44.4)	1264 (48.7)	.018
Diabetes mellitus, n (%)	85 (43.4)	73 (32.0)	201 (33.1)	.019	178 (50.4)	188 (32.6)	672 (25.9)	<.001
Dyslipidemia, n (%)	16 (8.2)	15 (6.6)	54 (8.9)	.559	33 (9.3)	53 (9.2)	382 (14.7)	<.001
Previous MI, n (%)	26 (13.3)	19 (8.3)	40 (6.6)	.012	54 (15.3)	52 (9.0)	121 (4.7)	<.001
Previous PCI, n (%)	35 (17.9)	22 (9.6)	76 (12.5)	.038	57 (16.1)	64 (11.1)	195 (7.5)	<.001
Previous CABG, n (%)	4 (2.0)	1 (0.4)	3 (0.5)	.080	8 (2.3)	7 (1.2)	13 (0.5)	.001
Previous stroke, n (%)	30 (15.3)	30 (13.2)	44 (7.2)	.001	33 (9.3)	28 (4.9)	114 (4.4)	<.001
Current smokers, n (%)	21 (10.7)	30 (13.2)	84 (13.8)	.534	129 (36.4)	239 (41.4)	1141 (44.0)	.024
Laboratory results								
Peak CK-MB, mg/dL	21.9 (7.8–67.8)	29.3 (9.3–102.9)	14.3 (5.2–56.9)	.183	21.3 (5.8–68.8)	35.7 (7.5–132.8)	21.8 (5.9–81.6)	<.001
Peak troponin-I, ng/mL	9.0 (2.1–31.3)	10.4 (2.4–27.5)	4.5 (1.0–17.8)	<.001	8.4 (2.2–33.3)	10.9 (2.5–34.3)	6.6 (1.5–23.0)	<.001
Hemoglobin, mg/dL	11.5 ± 2.1	12.3 ± 2.0	12.5 ± 1.8	<.001	12.9 ± 2.4	13.8 ± 2.1	14.3 ± 1.8	<.001
Blood glucose, mg/dL	191.6 ± 99.1	160.6 ± 76.3	159.9 ± 79.6	<.001	200.0 ± 89.4	165.9 ± 93.5	149.9 ± 66.1	<.001
Serum creatinine, mg/dL	1.59 ± 0.84	1.07 ± 0.95	1.14 ± 0.87	<.001	1.80 ± 0.72	1.21 ± 0.88	1.02 ± 0.57	<.001
Total cholesterol, mg/dL	159.9 ± 47.3	169.5 ± 48.1	172.0 ± 43.7	.007	172.9 ± 45.4	179.0 ± 45.3	183.9 ± 43.8	<.001
Triglyceride, mg/dL	93.2 ± 39.5	97.6 ± 38.8	114.8 ± 67.5	.005	122.3 ± 72.3	129.8 ± 71.4	144.0 ± 80.2	.001
HDL-cholesterol, mg/dL	43.4 ± 13.1	43.8 ± 12.2	43.2 ± 12.1	.873	41.5 ± 13.0	42.3 ± 11.7	42.8 ± 11.2	.119
LDL-cholesterol, mg/dL	96.6 ± 38.7	106.3 ± 40.3	107.6 ± 41.2	.006	108.2 ± 40.6	112.0 ± 38.3	116.9 ± 37.9	<.001
Discharge medications								
Aspirin, n (%)	192 (98.0)	224 (98.2)	603 (99.2)	.310	344 (97.5)	572 (99.1)	2574 (99.2)	.011
Clopidogrel, n (%)	177 (90.3)	202 (88.6)	512 (84.2)	.051	259 (73.4)	403 (69.8)	1735 (66.8)	.027
Ticagrelor, n (%)	19 (9.7)	26 (11.4)	96 (15.8)	.051	60 (17.0)	114 (19.8)	541 (20.8)	.228
Prasugrel, n (%)	0 (0)	0 (0)	0 (0)	–	34 (9.6)	60 (10.3)	320 (11.7)	.414
Beta-blocker, n (%)	154 (78.6)	180 (78.9)	500 (82.2)	.379	279 (79.0)	502 (87.0)	2249 (86.6)	<.001
RASI, n (%)	153 (78.1)	173 (75.9)	496 (81.6)	.157	276 (78.2)	470 (81.5)	2184 (84.1)	.010
Statin, n (%)	166 (84.7)	213 (93.4)	574 (94.4)	<.001	309 (87.5)	549 (95.1)	2495 (96.1)	<.001
Anticoagulant, n (%)	6 (3.1)	10 (4.4)	16 (2.6)	.427	34 (9.6)	9 (1.6)	20 (0.8)	<.001
Infarct-related artery								
Left main, n (%)	7 (3.6)	5 (2.2)	27 (4.4)	.311	23 (6.5)	15 (2.6)	60 (2.3)	<.001
LAD, n (%)	93 (47.4)	127 (55.7)	231 (38.0)	<.001	186 (52.7)	290 (50.3)	1020 (39.3)	<.001

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Table 1
(Continued)

Variables	Age, ≥ 75 years (n = 1032)				Age, < 75 years (n = 3526)			
	Group A HFREF LVEF ≤ 40% (n = 196)	Group B HFmrEF LVEF 41–49% (n = 228)	Group C HFpEF LVEF ≥ 50% (n = 608)	P	Group D HFREF LVEF ≤ 40% (n = 353)	Group E HFmrEF LVEF 41–49% (n = 577)	Group F HFpEF LVEF ≥ 50% (n = 2956)	P
LCx, n (%)	38 (19.4)	45 (19.7)	145 (23.8)	.265	49 (13.9)	135 (23.4)	751 (28.9)	<.001
RCA, n (%)	58 (29.6)	51 (22.4)	205 (33.7)	.006	95 (26.9)	137 (23.7)	765 (29.5)	.018
Treated vessel								
Left main, n (%)	12 (6.1)	14 (6.1)	36 (5.9)	.990	30 (8.5)	24 (4.2)	93 (3.6)	<.001
LAD, n (%)	131 (66.8)	160 (70.2)	342 (56.3)	<.001	252 (71.4)	362 (62.7)	1388 (53.5)	<.001
LCx, n (%)	67 (34.2)	87 (38.2)	223 (36.7)	.694	117 (33.1)	200 (34.7)	1073 (41.3)	<.001
RCA, n (%)	73 (37.2)	74 (32.5)	257 (42.3)	.029	143 (40.5)	198 (34.3)	982 (37.8)	.137
Multivessel disease, n (%)	142 (72.4)	157 (68.9)	359 (59.0)	.001	242 (68.6)	320 (55.5)	1323 (51.0)	<.001
IVUS/OCT, n (%)	31 (15.8)	47 (20.6)	132 (21.7)	.203	66 (18.7)	159 (27.6)	706 (27.2)	.002
FFR, n (%)	1 (0.5)	1 (0.4)	11 (1.8)	.166	5 (1.4)	12 (2.1)	72 (2.8)	.237
Drug-eluting stents								
ZES, n (%)	43 (21.9)	54 (23.7)	136 (22.4)	.896	82 (23.2)	135 (23.4)	615 (23.7)	.974
EES, n (%)	105 (53.6)	122 (53.5)	317 (52.1)	.906	210 (59.5)	304 (52.7)	1294 (49.8)	.002
BES, n (%)	36 (18.4)	39 (17.2)	135 (22.2)	.197	45 (12.7)	113 (19.6)	551 (21.2)	.001
Others, n (%)	12 (6.1)	13 (5.7)	20 (3.3)	.128	16 (4.5)	25 (4.3)	136 (5.2)	.604
Stent diameter, mm	3.04 ± 0.41	3.01 ± 0.38	3.01 ± 0.40	.704	3.08 ± 0.41	3.06 ± 0.39	3.09 ± 0.43	.188
Stent length, mm	33.1 ± 16.6	33.5 ± 16.5	29.7 ± 13.7	<.001	31.4 ± 14.5	30.1 ± 14.1	28.8 ± 13.6	.001
Number of stents	1.30 ± 0.53	1.29 ± 0.54	1.22 ± 0.44	.048	1.21 ± 0.46	1.19 ± 0.44	1.19 ± 0.44	.759

The P values for categorical data from chi-square or Fisher's exact test. The P values for continuous data obtained from the analysis of variance or Jonckheere-Terpstra test. Values are means ± standard deviation or median (interquartile range) or numbers and percentages. BES = biolimus-eluting stent, CABG = coronary artery bypass graft, CK-MB = creatine kinase myocardial band, CPR = cardiopulmonary resuscitation, DBP = diastolic blood pressure, DBT = door-to-balloon time, EES = everolimus-eluting stent, FFR = fractional flow reserve, HDL = high-density lipoprotein, HFmrEF = heart failure with mildly reduced ejection fraction, HFpEF = heart failure with preserved ejection fraction, HFREF = heart failure with reduced ejection fraction, IVUS = intravascular ultrasound, LAD = left anterior descending artery, LCx = left circumflex artery, LDL = low-density lipoprotein, LVEF = left ventricular ejection fraction, MI = myocardial infarction, OCT = optical coherence tomography, PCI = percutaneous coronary intervention, RASI = renin-angiotensin system inhibitor, RCA = right coronary artery, SBP = systolic blood pressure, SDT = symptom-to-door time, ZES = zotarolimus-eluting stent.

years), patients in the HF_rEF group (groups A and D) were older on average and had higher heart rates, DBT, blood glucose, and serum creatinine levels compared to those in other LVEF groups. Additionally, they had the highest prevalence of comorbidities such as DM, previous MI, previous PCI, and previous stroke. These patients also showed the highest rates of Killip class II/III, CPR on admission, and multivessel disease. In the HF_mrEF group (groups B and E), peak troponin-I levels were the highest, whereas, in the HF_prEF group (groups C and F), patients had the highest mean hemoglobin, total cholesterol, triglyceride, and LDL cholesterol levels, as well as the highest proportion of patients discharged on statin medications.

Tables S3 and S4, Supplemental Digital Content, <http://links.lww.com/MD/N527> compare characteristics between the 2 age groups (≥ 75 years and < 75 years) within the total study population (Table S3, Supplemental Digital Content, <http://links.lww.com/MD/N527>) and further stratified by LVEF groups (Table S4, Supplemental Digital Content, <http://links.lww.com/MD/N527>). Compared to the younger group (< 75 years), the older group (≥ 75 years) had a higher proportion of women, Killip class II/III, CPR on admission, hypertension, DM, previous PCI, and previous stroke. They were also more likely to be discharged on clopidogrel medication and have the left main coronary artery or left anterior descending coronary artery as the culprit lesion and treated vessel (Table S3, Supplemental Digital Content, <http://links.lww.com/MD/N527>). Additionally, the older group had higher average values for SDT, DBT, blood glucose, total cholesterol, total length of deployed stents, and total number of stents implanted (Table S3, Supplemental Digital Content, <http://links.lww.com/MD/N527>).

3.2. Clinical outcomes

Tables 2 and 3 and Figure 2A–H, depict the major outcomes observed during the 3-year follow-up period.

3.2.1. HF_rEF versus HF_mrEF versus HF_prEF. For patients aged ≥ 75 years, the MACE rate was significantly higher in the HF_rEF group (group A) compared to both the HF_mrEF group (group B, adjusted HR [aHR]: 1.836, 95% confidence interval [CI]: 1.351–2.495, $P < .001$) and HF_prEF group (group C, aHR: 2.451, 95% CI: 1.878–3.199, $P < .001$). Looking at the individual components of MACE, patients in group A also had significantly higher rates of all-cause death ($P < .001$ for both comparisons with groups B and C), CD ($P < .001$ for both comparisons), and all-cause death or MI ($P < .001$ for both comparisons). Additionally, hospitalization rates for HF were significantly higher in group A compared to group B ($P = .027$) and group C ($P < .001$). Furthermore, group A had a higher rate of non-CD (NCD) compared to group C ($P = .005$). They also had a significantly higher rate of recurrent MI ($P = .025$ compared to group C) and any repeat revascularization ($P = .005$ compared to group C). Comparing groups B and C within the older age group, the MACE rate was significantly higher in group B (aHR: 1.556, 95% CI: 1.181–2.050, $P = .002$) (Table 2).

In the younger age group (less than 75 years old), patients in the HF_rEF group (group D) had significantly higher rates of MACE ($P < .001$ and $P < .001$, respectively), all-cause death ($P < .001$ and $P < .001$, respectively), CD ($P < .001$ and $P < .001$, respectively), NCD ($P < .001$ and $P < .001$, respectively), recurrent MI ($P = .039$ and $P = .002$, respectively), all-cause death or MI ($P < .001$ and $P < .001$, respectively), and hospitalization for HF ($P < .001$ and $P < .001$, respectively) compared to both the HF_mrEF group (group E) and HF_prEF group (group F). Additionally, the any repeat revascularization rate in group D was significantly higher compared to group F ($P = .015$). Group E (HF_mrEF) also showed a significantly higher MACE ($P = .004$), all-cause death ($P < .001$), CD ($P < .001$), NCD

($P = .036$), and all-cause death or MI ($P < .001$) rates compared to group F (Table 2).

3.2.2. Aged ≥ 75 years group versus Aged < 75 years group. Patients in the older age group (≥ 75 years group, groups A–C) consistently had significantly higher rates of MACE ($P < .001$ for all LVEF groups), all-cause death ($P < .001$ for all LVEF groups), CD ($P = .005$, $P = .001$, and $P < .001$, respectively), NCD ($P = .032$, $P < .001$, and $P < .001$, respectively), and all-cause death or MI ($P < .001$ for all LVEF groups) compared to their younger counterparts (groups D–F) (Table 3).

Additionally, in both the HF_mrEF and HF_prEF groups, the older age group had a significantly higher hospitalization rate for HF compared to the younger group ($P < .001$ for both). Within the HF_prEF group, the older age group had a significantly higher rate of any repeat revascularization compared to the younger group ($P = .026$) (Table 3).

3.2.3. In-hospital mortality. Table S5, Supplemental Digital Content, <http://links.lww.com/MD/N527> details the in-hospital mortality rates within the study population. The in-hospital mortality rates for the older age group (≥ 75 years) showed significantly higher rates of all-cause death ($P = .024$ and $P < .001$, respectively) in the HF_rEF group (group A) compared to both HF_mrEF group (group B) and the HF_prEF group (group C). In the younger age group (< 75 years), the HF_rEF group (group D) had a significantly higher rate of in-hospital mortality compared to the HF_mrEF group (group E) for both all-cause death ($P < .001$) and CD ($P < .001$). However, comparisons between groups D and F, and between groups E and F, could not be made due to the low frequency of in-hospital mortality or the excessively wide confidence intervals.

3.2.4. Independent predictors for MACE. Table S6, Supplemental Digital Content, <http://links.lww.com/MD/N527> summarizes the independent predictors for MACE identified in this study. Both for patients aged ≥ 75 years and those < 75 years, several factors emerged as significant independent predictors of MACE: Killip class II/III, CPR on admission, nonuse of renin-angiotensin system inhibitor (RASi), nonuse of statins, and multivessel disease.

4. Discussion

The main findings of this cohort study are as follows: First, within the older age group (≥ 75 years), the MACE rate was highest in the HF_rEF group (group A), followed by the HF_mrEF group (group B), and then the HF_prEF group (group C). All-cause death, CD, all-cause death or MI, hospitalization for HF rates were higher in group A than in groups B and C. Additionally, group A had higher rates of NCD, recurrent MI, any repeat revascularization compared to group C. Second, in the younger age group (< 75 years), the MACE, all-cause death, CD, NCD, all-cause death or MI rates were highest in the HF_rEF group (group D), intermediate in the HF_mrEF group (group E), and lowest in the HF_prEF group (group F). Group D had higher rates of recurrent MI and hospitalization for HF compared to groups E and F. Additionally, group D had a higher rate of any repeat revascularization compared to group F. Third, across all LVEF categories, patients aged ≥ 75 years (groups A–C) had significantly higher rates of MACE, all-cause death, CD, NCD, all-cause death, or MI compared to their younger counterparts (groups D–F). Hospitalization for HF was significantly higher in the older age group (≥ 75 years) within both the HF_mrEF and HF_prEF groups compared to the younger age group. Fourth, Killip class II/III, CPR on admission, not being on RASi, and not being on statin medications were significant independent predictors for MACE.

With the rising prevalence of NSTEMI compared to all MIs,^[21] understanding the consequences of HF in patients

Table 2**Comparison of clinical outcomes based on LVEF groups in patients aged ≥ 75 years and < 75 years.**

	Age, ≥ 75 years, n = 1032						
	Group A HFrEF (n = 196)	Group B HFmrEF (n = 228)	Log-Rank	Unadjusted		Adjusted*	
				HR (95% CI)	P value	HR (95% CI)	P value
MACE	97 (49.5)	81 (35.5)	.001	1.655 (1.232–2.223)	.001	1.836 (1.351–2.495)	<.001
All-cause death	64 (32.7)	42 (18.4)	<.001	1.990 (1.348–2.937)	.001	2.175 (1.448–3.268)	<.001
Cardiac death	44 (22.5)	22 (10.1)	<.001	2.498 (1.457–4.234)	<.001	2.679 (1.571–4.568)	<.001
Non-cardiac death	20 (10.2)	20 (8.3)	.382	1.308 (0.609–2.449)	.383	1.650 (0.861–3.159)	.131
Recurrent MI	13 (8.1)	11 (5.4)	.252	1.592 (0.713–3.555)	.256	1.954 (0.850–4.489)	.115
All-cause death or MI	71 (36.2)	49 (21.5)	<.001	1.926 (1.338–2.772)	<.001	2.102 (1.436–3.076)	<.001
Any repeat revascularization	19 (12.0)	19 (9.3)	.368	1.338 (0.708–2.527)	.370	1.588 (0.807–3.125)	.181
Hospitalization for HF	26 (16.0)	20 (9.7)	.054	1.760 (0.983–3.154)	.057	1.987 (1.082–3.651)	.027
	Group A HFrEF (n = 196)	Group C HFpEF (n = 608)	Log-Rank	Unadjusted		Adjusted*	
				HR (95% CI)	P value	HR (95% CI)	P value
MACE	97 (49.5)	150 (24.7)	<.001	2.492 (1.929–3.218)	<.001	2.451 (1.878–3.199)	<.001
All-cause death	64 (32.7)	80 (13.2)	<.001	2.866 (2.063–3.982)	<.001	2.792 (1.979–3.938)	<.001
Cardiac death	44 (22.5)	43 (7.1)	<.001	3.536 (2.388–5.437)	<.001	3.273 (2.111–5.075)	<.001
Non-cardiac death	20 (10.2)	37 (6.1)	.013	1.861 (1.108–3.380)	.015	2.271 (1.289–4.001)	.005
Recurrent MI	13 (8.1)	22 (3.9)	.024	2.159 (1.087–4.287)	.028	2.233 (1.105–4.511)	.025
All-cause death or MI	71 (36.2)	97 (16.0)	<.001	2.663 (1.960–3.617)	<.001	2.599 (1.887–3.579)	<.001
Any repeat revascularization	19 (12.0)	32 (5.6)	.005	2.202 (1.248–3.885)	.006	2.304 (1.289–4.120)	.005
Hospitalization for HF	26 (16.0)	37 (6.5)	<.001	2.653 (1.606–4.384)	<.001	2.709 (1.613–4.550)	<.001
	Group B HFmrEF (n = 228)	Group C HFpEF (n = 608)	Log-Rank	Unadjusted		Adjusted*	
				HR (95% CI)	P value	HR (95% CI)	P value
MACE	81 (35.5)	150 (24.7)	.002	1.521 (1.161–1.993)	.002	1.556 (1.181–2.050)	.002
All-cause death	42 (18.4)	80 (13.2)	.053	1.442 (0.993–2.096)	.055	1.470 (0.996–2.171)	.053
Cardiac death	22 (10.1)	43 (7.1)	.192	1.406 (0.841–2.350)	.194	1.426 (0.837–2.429)	.191
Non-cardiac death	20 (8.3)	37 (6.1)	.152	1.485 (0.862–2.559)	.154	1.514 (0.852–2.690)	.157
Recurrent MI	11 (5.4)	22 (3.9)	.387	1.375 (0.667–2.835)	.389	1.438 (0.681–3.037)	.341
All-cause death or MI	49 (21.5)	97 (16.0)	.061	1.386 (0.983–1.954)	.063	1.425 (0.997–2.039)	.052
Any repeat revascularization	19 (9.3)	32 (5.6)	.079	1.655 (0.938–2.920)	.082	1.764 (0.992–3.139)	.053
Hospitalization for HF	20 (9.7)	37 (6.5)	.130	1.518 (0.881–2.616)	.133	1.616 (0.930–2.808)	.089
	Group D HFrEF (n = 353)	Group E HFmrEF (n = 577)	Log-Rank	Unadjusted		Adjusted*	
				HR (95% CI)	P value	HR (95% CI)	P value
MACE	138 (39.1)	101 (17.5)	<.001	2.626 (2.031–3.394)	<.001	2.453 (1.879–3.201)	<.001
All-cause death	85 (24.1)	37 (6.4)	<.001	4.244 (2.885–6.245)	<.001	4.195 (2.807–6.269)	<.001
Cardiac death	59 (16.7)	21 (3.6)	<.001	4.935 (3.020–8.452)	<.001	4.790 (2.877–7.976)	<.001
Non-cardiac death	26 (7.4)	16 (2.8)	<.001	2.964 (1.643–5.712)	<.001	3.317 (1.706–6.450)	<.001
Recurrent MI	19 (6.2)	16 (2.8)	.014	2.246 (1.155–4.368)	.017	2.014 (1.018–3.986)	.039
All-cause death or MI	94 (26.7)	50 (8.7)	<.001	3.511 (2.491–4.948)	<.001	3.382 (2.367–4.831)	<.001
Any repeat revascularization	38 (12.7)	49 (8.8)	.066	1.485 (0.972–2.268)	.068	1.398 (0.905–2.158)	.131
Hospitalization for HF	35 (11.7)	11 (2.0)	<.001	6.193 (3.145–12.20)	<.001	5.721 (2.859–11.45)	<.001
	Group D HFrEF (n = 353)	Group F HFpEF (n = 2596)	Log-Rank	Unadjusted		Adjusted*	
				HR (95% CI)	P value	HR (95% CI)	P value
MACE	138 (39.1)	343 (13.2)	<.001	3.620 (2.971–4.412)	<.001	3.415 (2.786–4.192)	<.001
All-cause death	85 (24.1)	66 (2.5)	<.001	10.86 (7.874–14.99)	<.001	9.735 (6.885–13.57)	<.001
Cardiac death	59 (16.7)	31 (1.2)	<.001	14.75 (9.270–23.34)	<.001	13.92 (8.911–21.74)	<.001
Non-cardiac death	26 (7.4)	35 (1.3)	<.001	6.145 (3.780–10.71)	<.001	6.016 (3.543–10.21)	<.001
Recurrent MI	19 (6.2)	68 (2.7)	<.001	2.451 (1.473–4.076)	.001	2.248 (1.334–3.789)	.002
All-cause death or MI	94 (26.7)	128 (4.9)	<.001	6.336 (4.854–8.270)	<.001	5.729 (4.343–7.556)	<.001
Any repeat revascularization	38 (12.7)	225 (8.8)	.022	1.490 (1.056–2.101)	.023	1.543 (1.087–2.188)	.015
Hospitalization for HF	35 (11.7)	25 (1.0)	<.001	12.52 (7.491–20.92)	<.001	11.14 (6.581–18.86)	<.001

(Continued)

Table 2
(Continued)

	Group E HFmrEF (n = 577)	Group F HFpEF (n = 2596)	Log-Rank	Unadjusted		Adjusted*	
				HR (95% CI)	P value	HR (95% CI)	P value
MACE	101 (17.5)	343 (13.2)	.006	1.365 (1.093–1.704)	.006	1.389 (1.107–1.742)	.004
All-cause death	37 (6.4)	66 (2.5)	<.001	2.565 (1.715–3.836)	<.001	2.566 (1.699–3.874)	<.001
Cardiac death	21 (3.6)	31 (1.2)	<.001	3.093 (1.777–5.382)	<.001	3.342 (1.908–5.856)	<.001
Non-cardiac death	16 (2.8)	35 (1.3)	.012	2.097 (1.160–3.788)	.014	1.898 (1.124–3.519)	.036
Recurrent MI	16 (2.8)	68 (2.7)	.781	1.080 (0.627–1.862)	.782	1.108 (0.639–1.924)	.714
All-cause death or MI	50 (8.7)	128 (4.9)	<.001	1.792 (1.293–2.485)	<.001	1.800 (1.297–2.514)	<.001
Any repeat revascularization	49 (8.8)	225 (8.8)	.998	1.000 (0.734–1.362)	.999	1.045 (0.764–1.430)	.783
Hospitalization for HF	11 (2.0)	25 (1.0)	.047	2.021 (0.995–4.107)	.052	1.751 (0.852–3.596)	.127

BMI = body mass index, CABG = coronary artery bypass graft, CI = confidence interval, CK-MB = creatine kinase myocardial band, CPR = cardiopulmonary resuscitation, DBP = diastolic blood pressure, DBT = door-to-balloon time, DM = diabetes mellitus, HFmrEF = heart failure with mildly reduced ejection fraction, HFpEF = heart failure with preserved ejection fraction, HFrEF = heart failure with reduced ejection fraction, HR = hazard ratio, LDL = low-density lipoprotein, MACE = major adverse cardiac events, MI = myocardial infarction, PCI = percutaneous coronary intervention, SBP = systolic blood pressure, SDT = symptom-to-door time.

*Adjusted by male, SBP, DBP, heart rate, BMI, Killip class II/III, cardiogenic shock, CPR on admission, SDT, DBT, hypertension, DM, dyslipidemia, previous MI, previous PCI, previous CABG, previous stroke, current smoker, peak CK-MB, peak troponin-I, hemoglobin, blood glucose, serum creatinine, triglyceride, and LDL-cholesterol (Table S1, Supplemental Digital Content, <http://links.lww.com/MD/N527>).

with NSTEMI becomes increasingly important. A previous report^[22] found that NSTEMI patients who develop HF have a significantly higher risk of death (odds ratio [OR]: 3.4, 95% CI: 2.7–4.3) or MI (OR: 2.8, 95% CI: 2.2–3.6) compared to those without HF. HFmrEF, a category of HF with characteristics between HFrEF and HFpEF,^[3] presents uncertainties in patient prognosis. Studies not limited to NSTEMI patients suggest similar mortality rates^[23] for HFmrEF and HFrEF, but a higher prevalence of IHD as HFrEF.^[4] However, other studies report similar mortality rates across HF subtypes (HFrEF, HFmrEF, and HFpEF).^[24] Further research is needed to definitively determine the prognosis of patients with HFmrEF, particularly within the context of NSTEMI. According to a report by Puymirat et al,^[25] PCI during the initial hospital stay of patients with NSTEMI was as high as 67%. The 2021 American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions guidelines for coronary artery revascularization^[26] recommend the use of newer-generation DES in the treatment of patients with AMI due to their lower rates of target vessel revascularization and stent thrombosis compared to BMS. Lin et al^[27] showed that the 5-year risk of hospitalization for HF was lower in the newer-generation DES group than in the BMS group among 8644 pairs of patients with NSTEMI (8.89% vs 11.9%, $P < .001$). Although the results of long-term outcomes for HF patients among all ACS^[6] or STEMI^[10] patients provide useful information, we believe that presenting the results of a 3-year study focusing on NSTEMI patients who underwent newer-generation DES implantation would better reflect the current real-world practice and offer insights into long-term outcomes. This could be highly beneficial for interventional cardiologists, particularly given the poorer long-term outcomes in NSTEMI^[9] compared to STEMI patients.

In our study, in the < 75 years age group, mortality (all-cause death, CD, and NCD) was highest in the HFrEF group, intermediate in the HFmrEF group, and lowest in the HFpEF group. However, in the older age group, while all-cause death and CD were still highest in the HFrEF group (group A) compared to the HFmrEF (group B) and HFpEF (group C) groups, there was no significant difference in these outcomes between groups B and C ($P = .053$ and $P = .191$) (Table 2). A previous study on chronic HF patients^[28] reported similar findings, with the highest one-year all-cause death rate in the HFrEF group (8.8%), followed by the HFpEF group (7.6%), and then the HFmrEF group (6.3%) ($P = .005$). Unfortunately, for patients specifically with NSTEMI, there is a lack of research comparing mortality rates based on LVEF categories. Two single-center studies^[29,30] conducted on STEMI patients showed that the HFmrEF group

had higher mortality compared to the HFpEF group. In another single-center study involving all ASC patients,^[6] the HFrEF group had a higher 10-year mortality compared to the HFpEF group (aHR: 1.64, 95% CI: 1.36–1.96; $P < .001$). Similarly, the HFmrEF group had a higher 10-year mortality compared to the HFpEF group (aHR: 1.33, 95% CI: 1.05–1.68; $P = .019$). Therefore, it is necessary to conduct additional studies that focus on patients with NSTEMI.

Despite advancements in treating ACS patients, optimal treatment strategies for older NSTEMI patients remain uncertain.^[30] Clinical trials for ACS often underrepresent this population, even though they carry a high burden of risk factors for ischemic events.^[31] Furthermore, older adults (≥ 75 years) constitute a significant portion (30–40%) of NSTEMI hospital admissions and account for most NSTEMI-related deaths.^[32,33] While our study included 1032 patients aged ≥ 75 years (22.6%), this number is likely lower than real-world prevalence due to our focus on patients who received newer-generation DES procedures. It is expected that this number would increase without the exclusion criteria. Consistent with previous research, our study found that patients aged ≥ 75 years had poorer baseline characteristics compared to younger patients.^[32,33] These characteristics likely contribute to the higher mortality rates observed in the older group across all HF categories, even after adjusting for other variables (Table 3).

Aging itself is a risk factor for both acute and chronic HF in patients with coronary artery disease.^[1] Reduced responsiveness to beta-blockers and lower peak cardiac output in response to stress are physiological changes that occur with age.^[34] Additionally, increased collagen deposition and impaired myocardial relaxation can lead to higher LV end-diastolic pressure in older patients.^[34] These factors likely contribute to poorer long-term outcomes in the older age group. A systematic review suggests that frailty is associated with an increased risk of death in NSTEMI patients (HR, 2.63; 95% CI: 1.51–4.60).^[35] Unfortunately, our study could not analyze frailty due to its absence as a mandatory variable in the dataset. Therefore, the potential impact of frailty on mortality in the older age group remains unclear.

Several factors are well-documented to increase mortality risk in NSTEMI patients, including age^[9,31,33] and requiring CPR upon admission.^[9] Additionally, Killip classification^[36] is a strong independent predictor of death in NSTEMI-ACS. Our study confirmed these findings, showing that Killip class II/III and CPR on admission were significant independent predictors of MACE in both younger and older age groups (Table S6, Supplemental Digital Content, <http://links.lww.com/MD/N527>).

Table 3**Comparison of clinical outcomes between the older and younger groups based on LVEF groups.**

HFREF (LVEF ≤ 40%), n = 549							
Outcomes	Group A		Log-rank	Unadjusted		Adjusted*	
	Age, ≥ 75 years (n = 196)	Age, < 75 years (n = 353)		HR (95% CI)	P value	HR (95% CI)	P value
MACE	97 (49.5)	138 (39.1)	.010	1.404 (1.083–1.821)	.010	1.709 (1.285–2.271)	<.001
All-cause death	64 (32.7)	85 (24.1)	.037	1.411 (1.020–1.951)	.038	1.901 (1.331–2.715)	<.001
Cardiac death	44 (22.5)	59 (16.7)	.096	1.391 (0.941–2.055)	.098	1.857 (1.207–2.856)	.005
Non-cardiac death	20 (10.2)	26 (7.4)	.204	1.456 (0.813–2.609)	.206	2.015 (1.061–3.827)	.032
Recurrent MI	13 (8.1)	19 (6.2)	.463	1.301 (0.643–2.635)	.465	1.373 (0.645–2.919)	.411
All-cause death or MI	71 (36.2)	94 (26.7)	.022	1.429 (1.050–1.944)	.023	1.841 (1.314–2.580)	<.001
Any repeat revascularization	19 (12.0)	38 (12.7)	.866	0.954 (0.550–1.654)	.866	1.102 (0.609–1.991)	.749
Hospitalization for HF	26 (16.0)	35 (11.7)	.128	1.480 (0.891–2.458)	.130	1.584 (0.915–2.742)	.100
HFmrEF (LVEF 41–49%), n = 805							
Outcomes	Group B		Log-rank	Unadjusted		Adjusted*	
	Age, ≥ 75 years (n = 228)	Age, < 75 years (n = 577)		HR (95% CI)	P value	HR (95% CI)	P value
MACE	81 (35.5)	101 (17.5)	<.001	2.267 (1.692–3.038)	<.001	2.106 (1.528–2.903)	<.001
All-cause death	42 (18.4)	37 (6.4)	<.001	3.090 (1.986–4.807)	<.001	3.368 (2.067–5.488)	<.001
Cardiac death	22 (10.1)	21 (3.6)	<.001	2.861 (1.573–5.203)	.001	3.102 (1.605–5.996)	.001
Non-cardiac death	20 (8.3)	16 (2.8)	<.001	3.390 (1.756–6.542)	<.001	3.716 (1.790–7.711)	<.001
Recurrent MI	11 (5.4)	16 (2.8)	.096	1.899 (0.881–4.093)	.102	2.248 (0.975–5.185)	.057
All-cause death or MI	49 (21.5)	50 (8.7)	<.001	2.680 (1.807–3.975)	<.001	2.823 (1.829–4.358)	<.001
Any repeat revascularization	19 (9.3)	49 (8.8)	.832	1.059 (0.624–1.799)	.832	1.008 (0.569–1.785)	.978
Hospitalization for HF	20 (9.7)	11 (2.0)	<.001	5.133 (2.459–11.72)	<.001	4.491 (2.229–10.953)	<.001
HFpEF (≥50%), n = 3204							
Outcomes	Group C		Log-rank	Unadjusted		Adjusted*	
	Age, ≥ 75 years (n = 608)	Age, < 75 years (n = 2596)		HR (95% CI)	P value	HR (95% CI)	P value
MACE	150 (24.7)	343 (13.2)	<.001	2.030 (1.675–2.459)	<.001	1.705 (1.387–2.096)	<.001
All-cause death	80 (13.2)	66 (2.5)	<.001	5.472 (3.950–7.581)	<.001	3.988 (2.795–5.691)	<.001
Cardiac death	43 (7.1)	31 (1.2)	<.001	6.219 (3.919–9.870)	<.001	3.993 (2.419–6.589)	<.001
Non-cardiac death	37 (6.1)	35 (1.3)	<.001	4.806 (3.027–7.630)	<.001	4.019 (2.425–6.662)	<.001
Recurrent MI	22 (3.9)	68 (2.7)	.109	1.478 (0.914–2.390)	.111	1.301 (0.780–2.172)	.314
All-cause death or MI	97 (16.0)	128 (4.9)	<.001	3.454 (2.653–4.496)	<.001	2.764 (2.073–3.684)	<.001
Any repeat revascularization	32 (5.6)	225 (8.8)	.016	0.637 (0.440–0.923)	.017	1.548 (1.054–2.274)	.026
Hospitalization for HF	37 (6.5)	25 (1.0)	<.001	6.857 (4.128–11.39)	<.001	4.832 (2.771–8.425)	<.001

BMI = body mass index, CI = confidence interval, CPR = cardiopulmonary resuscitation, DBP = diastolic blood pressure, DBT = door-to-balloon time, DM = diabetes mellitus, HFmrEF = heart failure with mildly reduced ejection fraction, HFpEF = heart failure with preserved ejection fraction, HFREF = heart failure with reduced ejection fraction, HR = hazard ratio, LDL = low-density lipoprotein, MACE = major adverse cardiac events, MI = myocardial infarction, PCI = percutaneous coronary intervention, SBP = systolic blood pressure, SDT = symptom-to-door time.

*Adjusted by male, SBP, DBP, heart rate, BMI, Killip class II/III, cardiogenic shock, CPR on admission, SDT, DBT, hypertension, DM, dyslipidemia, previous PCI, previous stroke, current smoker, peak troponin-I, hemoglobin, blood glucose, serum creatinine, triglyceride, LDL-cholesterol, and clopidogrel (Table S2, Supplemental Digital Content, <http://links.lww.com/MD/N527>).

Due to the lack of specific randomized controlled trials for HFmrEF patients, current guidelines recommend beta-blockers and RASIs with a Class IIb/Level of Evidence C for this condition.^[15] Our study found that in the entire patient (including HFREF, HFmrEF, and HFpEF), not using RASI emerged as a significant independent predictor of MACE in both age groups (≥75 years and < 75 years). Additionally, not using beta-blocker was a significant predictor in the younger age group (Table S6, Supplemental Digital Content, <http://links.lww.com/MD/N527>).

Recent studies^[37,38] suggest that NSTEMI patients with a symptom duration of ≥ 24 hours (delayed hospitalization) have higher mortality rates compared to those with a shorter symptom duration (<24 hours) (aHR: 1.284, 95% CI: 1.015–1.625, *P* = .037 and aHR: 1.35, 95% CI: 1.17–1.56, *P* < .001, respectively). Furthermore, these studies indicate that being aged ≥ 75 years is an independent risk factor for delayed hospitalization.^[38] Our study aligns with these observations, demonstrating a significantly longer SDT in the older age group compared to the younger age group (*P* = .001) (Table S3, Supplemental Digital Content, <http://links.lww.com/MD/N527>). To account for this potential bias and achieve more

accurate outcomes, this study included SDT in the multivariable-adjusted analyses (Tables 2 and 3; Tables S1 and S2, Supplemental Digital Content, <http://links.lww.com/MD/N527>).

Although Table S5, Supplemental Digital Content, <http://links.lww.com/MD/N527> shows that in the ≥ 75 years cohort, in-hospital all-cause death and CD rates were higher in group A compared to both groups B and C, in the < 75 years cohort, these outcomes were higher in group D compared to group E, the overall number of patients might be insufficient to definitively establish these trends. A larger study would be necessary to overcome this limitation. Despite the limitations in sample size, this study benefitted from the participation of 20 high-volume hospitals across the Republic of Korea, making the results representative of a broader real-world setting (KAMIR-NIH registry). Therefore, we believe the findings offer valuable insights for interventional cardiologists.

Our study has some limitations. First, as with many registry-based studies, our data may be affected by underreporting or missing information. Second, our multivariate analysis addressed some confounding factors, but the KAMIR-NIH dataset may lack other relevant variables, potentially introducing bias.

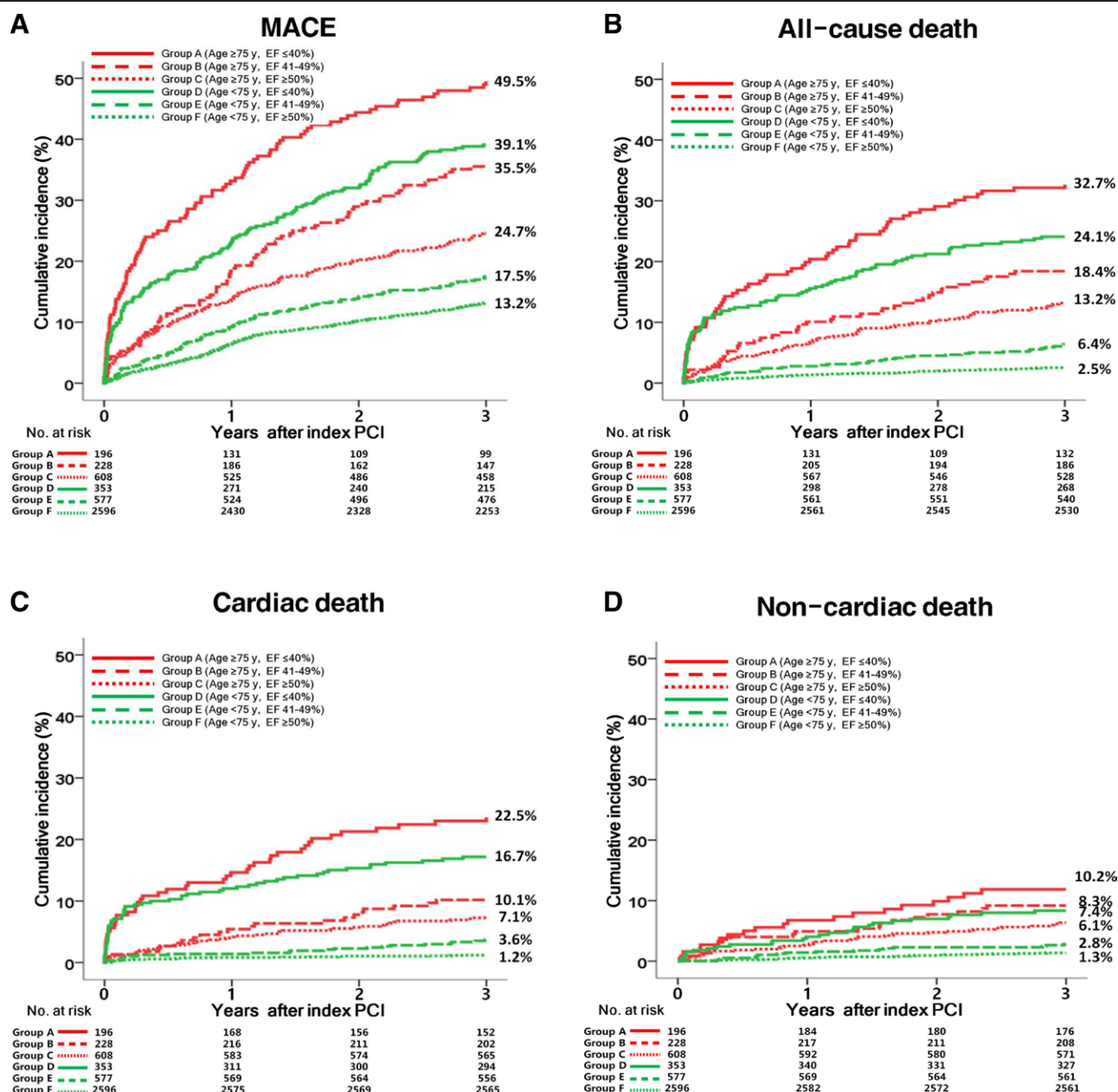


Figure 2. Kaplan-Meier analysis for MACE (A), all-cause death (B), cardiac death (C), non-cardiac death (D), all-cause death or MI (E), recurrent MI (F), any repeat revascularization (G), and hospitalization for HF (H) during a 3-year follow-up period. HF = heart failure, MACE = major adverse cardiac events, MI = myocardial infarction.

Third, the in-hospital mortality results highlight limitations due to a smaller sample size in certain groups. Fourth, the 3-year follow-up period might not fully capture long-term outcomes. A longer study duration could provide more conclusive results. Finally, this study focused solely on the Korean population, limiting generalizability to other ethnicities. Future research should include diverse populations across multiple countries.

5. Conclusions

This multicenter, prospective cohort study suggests that patients aged ≥ 75 years have higher mortality rates compared to younger patients. Additionally, within both age groups, the MACE rate appears to be highest in the HFrEF group, followed by HFmrEF and then HFpEF. However, due to the limitations mentioned above, further studies are warranted to confirm these results.

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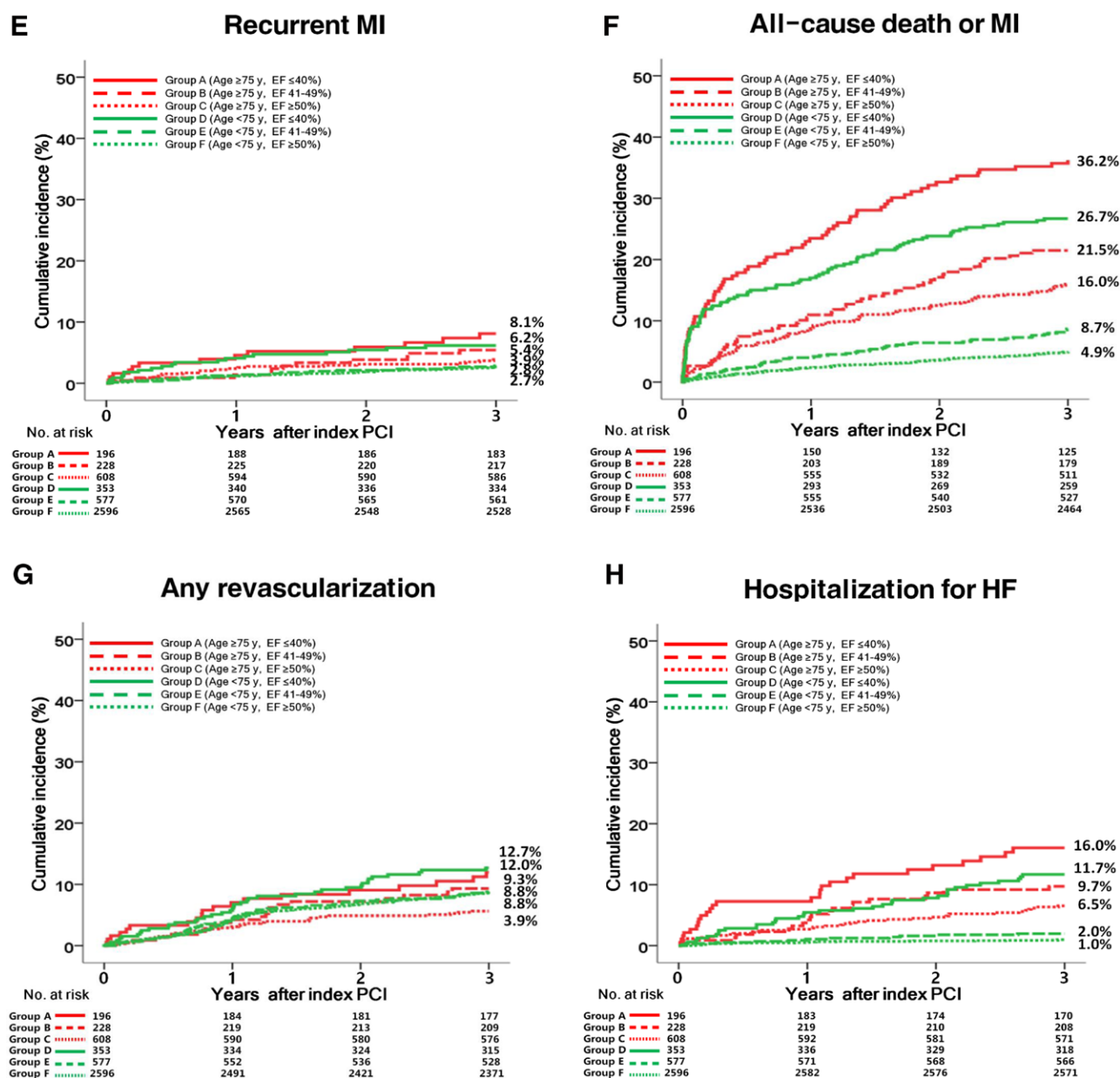


Figure 2. Continued

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