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ORIGINAL RESEARCH

Optimal Revascularization Strategy in Non–ST-Segment–Elevation Myocardial Infarction With Multivessel Coronary Artery Disease: Culprit-Only Versus One-Stage Versus Multistage Revascularization

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BACKGROUND: Few studies have investigated optimal revascularization strategies in non–ST-segment–elevation myocardial infarction with multivessel disease. We investigated 3-year clinical outcomes according to revascularization strategy in patients with non–ST-segment–elevation myocardial infarction and multivessel disease.

METHODS AND RESULTS: This retrospective, observational, multicenter study included patients with non–ST-segment–elevation myocardial infarction and multivessel disease without cardiogenic shock. Data were analyzed at 3 years according to the percutaneous coronary intervention strategy: culprit-only revascularization (COR), 1-stage multivessel revascularization (MVR), and multistage MVR. The primary outcome was major adverse cardiac events (MACE: a composite of all-cause death, nonfatal spontaneous myocardial infarction, or any repeat revascularization). The COR group had a higher risk of MACE than those involving other strategies (COR versus 1-stage MVR; hazard ratio, 0.65; 95% CI, 0.54–0.77; $P<0.001$; and COR versus multistage MVR; hazard ratio, 0.74; 95% CI, 0.57–0.97; $P=0.027$). There was no significant difference in the incidence of MACE between 1-stage and multistage MVR (hazard ratio, 1.14; 95% CI, 0.86–1.51; $P=0.355$). The results were consistent after multivariate regression, propensity score matching, inverse probability weighting, and Bayesian proportional hazards modeling. In subgroup analyses stratified by the Global Registry of Acute Coronary Events score, 1-stage MVR lowered the risk of MACE compared with multistage MVR in low-to-intermediate risk patients but not in patients at high risk.

CONCLUSIONS: MVR reduced 3-year MACE in patients with non–ST-segment–elevation myocardial infarction and multivessel disease compared with COR. However, 1-stage MVR was not superior to multistage MVR for reducing MACE except in low-to-intermediate risk patients.

Key Words: multivessel coronary artery disease ■ myocardial infarction ■ percutaneous coronary intervention

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CLINICAL PERSPECTIVE

What Is New?

- Previous studies have shown the benefit of multivessel revascularization in patients with non–ST-segment–elevation myocardial infarction and multivessel coronary artery disease. However, few studies have focused on staged percutaneous coronary intervention strategies in these patients.
- Although 1-stage multivessel revascularization was not superior to multistage multivessel revascularization for reducing major adverse cardiac events, it was associated with a lower rate of major adverse cardiac events in low-to-intermediate risk patients but not in patients at high risk.

What Are the Clinical Implications?

- Our results provide information for optimal timing of staged percutaneous coronary intervention non-infarct-related artery stenosis using the large nationwide registry data.
- Additional clinical studies, including randomized trials, are needed to determine the optimal timing of staged percutaneous coronary intervention for non-infarct-related artery stenosis.

Nonstandard Abbreviations and Acronyms

COR	culprit-only revascularization
GRACE	Global Registry of Acute Coronary Events
HR	hazard ratio
KAMIR-NIH	Korea Acute Myocardial Infarction Registry-National Institutes of Health
MACE	major adverse cardiac events
MI	myocardial infarction
MVD	multivessel coronary artery disease
MVR	multivessel revascularization
NSTEMI	non–ST-segment–elevation myocardial infarction
PCI	percutaneous coronary intervention
STEMI	ST–segment–elevation myocardial infarction

Many patients with non–ST-segment–elevation myocardial infarction (NSTEMI) have multivessel coronary artery disease (MVD), which is associated with poor clinical outcomes.[1,2] In cases of hemodynamically stable ST-segment–elevation myocardial infarction (STEMI) and MVD, many studies demonstrated the superiority of complete revascularization by both 1-stage and multistage procedures compared with culprit-only revascularization (COR).[3–7] The 2017 European Society of Cardiology guidelines for STEMI recommend routine revascularization for nonculprit lesions before hospital discharge in patients without cardiogenic shock.[8] However, there have been few studies of revascularization strategy in patients with NSTEMI and MVD. Only 1 randomized controlled trial, the SMILE (Impact of One Stage Compared With Multistaged PCI Complete Revascularization on Clinical Outcome in Multivessel NSTEMI Patients) trial, compared 1-stage and multistage multivessel revascularization (MVR) in these patients.[9] Although the results of most studies analyzing interventional strategies in patients with NSTEMI and MVD showed superior results of MVR compared with COR,[10–12] they did not provide information about staged revascularization. One-stage MVR was associated with better clinical outcomes compared with multistage MVR in the SMILE trial, whereas 1-stage and multistage MVR had similar incidences of adverse outcomes in large registry data.[9,13] Although the 2018 European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines for myocardial revascularization recommend complete 1-stage revascularization in NSTEMI and MVD, it emphasizes individualization based on clinical status and comorbidities, as well as disease severity.[14]

Therefore, we compared the long-term clinical outcomes among COR, 1-stage MVR, and multistage MVR in hemodynamically stable patients with NSTEMI and MVD using a Korean multicenter registry.

METHODS

Study Protocols and Patient Selection

We used data from the prospective, multicenter, web-based KAMIR-NIH (Korea Acute Myocardial Infarction Registry-National Institutes of Health), which includes patients from 20 major cardiovascular centers admitted between November 2011 and December 2015. The data that support the findings of this study are available from the corresponding author upon reasonable request. The details of the study protocols have been published previously.[15] The study protocols were approved by the ethics committees at each participating center, and all followed the principles of the Declaration of Helsinki (institutional review board approval number: CNUH-2011-172). All patients provided written informed consent to participate in the registry.

Among 13 104 patients with acute myocardial infarction (MI), we analyzed 2872 patients with NSTEMI

and MVD (Figure 1). The exclusion criteria were STEMI, patients who did not receive percutaneous coronary intervention (PCI), cardiogenic shock, single-vessel disease, failed PCI, and loss to follow-up. The patients were divided into 3 groups according to the PCI strategy: COR was defined as culprit-only PCI (N=1294), 1-stage MVR was defined as the simultaneous treatment of culprit and nonculprit arteries during index PCI (N=1244), and multistage MVR was defined as PCI for the culprit artery followed by staged PCI for the nonculprit artery during initial hospitalization (N=334).

The diagnosis of NSTEMI was based on the criteria for a fourth universal definition of MI.[16] MVD was defined as having additional ≥70% diameter stenosis in at least 1 major non-infarct-related artery or ≥50% diameter stenosis in the left main coronary artery. We assessed the clinical and diagnostic parameters of all subjects. Coronary angiography was performed through the femoral or radial artery. After PCI, dual antiplatelet therapy was prescribed daily as a maintenance dose. Angiographic data were obtained visually by PCI operators at the investigative site. Patients were managed according to current guidelines.[14,17] Stent type, diameter, and length and the choice of therapeutic strategy, including the use of medication, a glycoprotein IIb/IIIa inhibitor, thrombus aspiration, intravascular imaging, or hemodynamic support devices, were left to the discretion of the operator. Successful PCI was defined as final residual stenosis <30% with thrombolysis in myocardial infarction grade 3 blood flow.

Study Outcomes

The primary outcome was major adverse cardiac events (MACE: a composite of all-cause mortality, nonfatal spontaneous MI, or any repeat revascularization). The secondary outcome was all-cause mortality, cardiac mortality, nonfatal spontaneous MI, any repeat revascularization, nontarget vessel revascularization repeat PCI, definite or probable stent thrombosis, and all-cause death or nonfatal spontaneous MI during 3 years of clinical follow-up. All deaths were considered cardiac deaths unless there was a definite noncardiac cause. Nonfatal spontaneous MI was defined as the development of recurrent angina symptoms accompanied by changes in the 12-lead electrocardiogram or increased levels of cardiac-specific biomarkers. Repeat revascularization was defined as the need for clinically driven revascularization that occurred after discharge from the index hospitalization, according to Academic Research Consortium definitions.

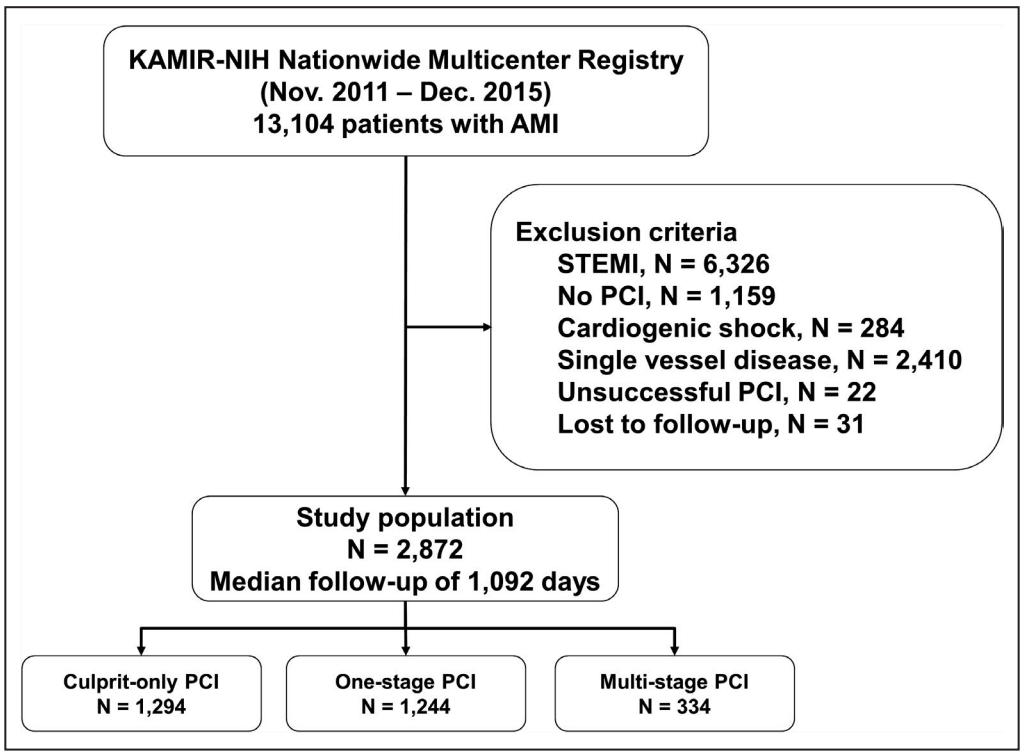

Figure 1. Study flowchart.
AMI indicates acute myocardial infarction; KAMIR-NIH, Korea Acute Myocardial Infarction Registry-National Institutes of Health; PCI, percutaneous coronary intervention; and STEMI, ST-segment–elevation myocardial infarction.

Statistical Analysis

Continuous variables are presented as means±SD or as medians with interquartile ranges and were compared by the unpaired *t* test, the Mann–Whitney rank-sum test or 1-way analysis of variance. Discrete variables are expressed as counts with percentages and were compared using Pearson's chi-square test or Fisher's exact test. We prepared Kaplan-Meier curves of the primary and secondary outcomes according to the interventional strategy. As differences in baseline characteristics could significantly affect outcomes, sensitivity analyses were performed to adjust for confounding factors as much as possible. First, a multivariate Cox regression model was used for each of the above cutoffs, with covariates that had $P<0.05$ on univariate analysis. Second, we performed propensity score matching between groups. The percent standardized mean difference after propensity score matching was within 10% across nearly all matched covariates, demonstrating a successful balance between the groups (Tables S1 through S6). Third, for inverse probability weighting adjustment, the inverse of the propensity score was assessed by calculating the percent standardized mean differences in the covariate used to generate the propensity score. The values after inverse probability weighting adjustment were within ±10% across all matched covariates, demonstrating successful balance between the groups (Figures S1 through S3). Fourth, we performed Bayesian modeling, with internal validation data as an additional sensitivity analysis to assess the effects of unmeasured

Table 1. Baseline Clinical Characteristics

	Culprit-Only PCI (N=1294)	One-Stage MVR (N=1244)	Multistage MVR (N=334)	*P* Value
Age, y	66.4±12.0	66.1±11.5	64.9±11.7	0.111
Male	938 (72.5%)	847 (68.1%)	254 (76.0%)	0.005
Body mass index	23.9±3.3	24.1±3.5	23.9±3.4	0.182
Killip class 3	143 (11.1%)	120 (9.6%)	37 (11.1%)	0.473
GRACE score ≥140	462 (35.7%)	429 (34.5%)	125 (37.4%)	0.575
Process of care index				
Symptom-to-door time, h	46.1±143.1	45.6±114.8	49.3±121.3	0.896
Door-to-balloon time, min	27.0±55.1	27.1±47.9	19.3±33.0	0.028
Past medical history				
Hypertension	755 (58.3%)	738 (59.3%)	190 (56.9%)	0.702
Diabetes mellitus	459 (35.5%)	436 (35.0%)	111 (33.2%)	0.747
Dyslipidemia	151 (11.7%)	157 (12.6%)	38 (11.4%)	0.704
Current smoker	449 (34.7%)	367 (29.5%)	126 (37.7%)	0.003
Previous history of myocardial infarction	119 (9.2%)	92 (7.4%)	23 (6.9%)	0.169
Previous history of PCI	113 (8.7%)	77 (6.2%)	14 (4.2%)	0.004
Previous history of CVA	114 (8.8%)	102 (8.2%)	26 (7.8%)	0.776
LVEF, %	52.6±11.2	53.7±11.0	51.2±11.7	0.001
Laboratory findings				
eGFR, mL/min per 1.73 m^2	83.3±38.8	85.5±38.9	85.0±31.7	0.350
Peak level of troponin I, ng/mL	24.2±50.6	21.1±69.2	30.6±53.0	0.032
Peak level of CK-MB, ng/mL	61.9±115.1	56.8±173.7	73.5±93.8	0.153
Medications at discharge				
Aspirin	1293 (99.9%)	1244 (100.0%)	332 (99.4%)	0.100
P2Y12 inhibitor	1287 (99.5%)	1241 (99.8%)	332 (99.4%)	0.434
Ticagrelor	266 (20.6%)	263 (21.1%)	92 (27.5%)	
Prasugrel	85 (6.6%)	117 (9.4%)	43 (12.9%)	
Clopidogrel	937 (72.4%)	861 (69.2%)	199 (59.6%)	
ACEI or ARB	1058 (81.8%)	1003 (80.6%)	296 (88.6%)	0.003
Beta-blocker	1104 (85.3%)	1072 (86.2%)	287 (85.9%)	0.823
Statin	1216 (94.0%)	1181 (94.9%)	319 (95.5%)	0.407

Values are mean±SD, median (interquartile range), or n (%). ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; CK-MB, creatine kinase-myocardial band; CVA, cerebrovascular accident; eGFR, estimated glomerular filtration rate; GRACE, Global Registry of Acute Coronary Events; LVEF, left ventricular ejection fraction; MVR, multivessel revascularization; and PCI, percutaneous coronary intervention.

confounders on the summary estimates. The Bayesian estimators were adjusted by combining internal validation and study data for unmeasured confounding factors, as described previously.[18] In Bayesian analysis, the hazard ratio (HR) and 95% CI were calculated by Cox regression. All analyses were 2 tailed, and $P<0.05$ was taken to indicate significance. Comparisons of primary outcome among the different interventional strategies were stratified by the GRACE (Global Registry of Acute Coronary Events) score, and the interaction between the treatment effect and these covariates was assessed using a Cox regression model.[19]

All statistical analyses were performed using the R statistical package (version 3.3.2, R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org).

Table 2. Coronary Angiographic and Procedural Characteristics

	Culprit-Only PCI (N=1294)	One-Stage MVR (N=1244)	Multistage MVR (N=334)	*P* Value
Culprit lesion profiles				
Culprit vessel				<0.001
Left main coronary artery	62 (4.8%)	83 (6.7%)	7 (2.1%)	
Left anterior descending artery	484 (37.4%)	449 (36.1%)	104 (31.1%)	
Left circumflex artery	346 (26.7%)	365 (29.3%)	68 (20.4%)	
Right coronary artery	402 (31.1%)	347 (27.9%)	155 (46.4%)	
ACC/AHA B2/C lesion	1098 (84.9%)	1054 (84.7%)	306 (91.6%)	0.004
Small vessel*	485 (37.5%)	467 (37.5%)	103 (30.8%)	0.059
Long lesion†	577 (44.6%)	559 (44.9%)	177 (53.0%)	0.017
Overall-lesion profiles				
Left main disease	123 (9.5%)	156 (12.5%)	30 (9.0%)	0.026
Triple vessel disease	428 (33.1%)	456 (36.7%)	185 (55.4%)	<0.001
Procedural characteristics				
Transradial approach	609 (47.1%)	600 (48.2%)	180 (53.9%)	0.213
Use of glycoprotein IIb/IIIa inhibitor	88 (6.8%)	84 (6.8%)	46 (13.8%)	<0.001
Thrombus aspiration	154 (11.9%)	80 (6.4%)	65 (19.5%)	<0.001
IRA treatment				0.022
Bare metal stent	37 (2.9%)	23 (1.8%)	5 (1.5%)	
First-generation DES	15 (1.2%)	8 (0.6%)	4 (1.2%)	
Second-generation DES	1137 (87.9%)	1140 (91.6%)	310 (92.8%)	
Plain balloon angioplasty	105 (8.1%)	73 (5.9%)	15 (4.5%)	
Total number of stents	1.2±0.6	2.3±0.9	2.6±1.1	<0.001
Pre-PCI TIMI flow 0–1 in culprit lesion	525 (40.6%)	441 (35.5%)	174 (52.1%)	<0.001
IVUS guided PCI	337 (26.0%)	326 (26.2%)	59 (17.7%)	0.004
OCT guided PCI	33 (2.6%)	38 (3.1%)	0	0.006
Hemodynamic support device				
IABP	5 (0.4%)	10 (0.8%)	0	0.128
ECMO	1 (0.1%)	0	0	0.543
Interval between index and second stage PCI, d			5.0 (4.0–7.0)	
Complete revascularization		922 (74.1%)	207 (62.0%)	
Complications during hospitalization				
Heart failure	51 (3.9%)	48 (3.9%)	21 (6.3%)	0.122
Atrioventricular block	10 (0.8%)	6 (0.5%)	4 (1.2%)	0.342
Ventricular tachycardia	14 (1.1%)	6 (0.5%)	6 (1.8%)	0.053
Ventricular fibrillation	4 (0.3%)	3 (0.2%)	2 (0.6%)	0.583
Length of hospital stay, d	4.0 (3.0–6.0)	4.0 (3.0–6.0)	7.0 (6.0–9.0)	<0.001

Values are mean±SD, median (interquartile range), or n (%). ACC/AHA indicates American College of Cardiology/American Heart Association; DES, drug-eluting stent; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; IRA, infarct-related artery; IVUS, intravascular ultrasound; MVR, multivessel revascularization; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; and TIMI, thrombolysis in myocardial infarction.

*Small vessel: reference diameter ≤2.75 mm.

†Long lesion: length ≥28 mm.

RESULTS

Baseline Characteristics

Three years of follow-up were completed for all patients; the median follow-up duration was 1092 days. The patients' baseline clinical characteristics, and lesion- and procedure-related profiles are described in Tables 1 and 2. The patients in the multistage MVR group were mostly male. They also had a shorter door-to-balloon time and lower left ventricular ejection fraction. The COR group had a higher rate of a history of PCI. There were no significant differences in other atherosclerotic risk factors among the groups except for a lower rate of current smokers in the 1-stage MVR group. The enzymatic infarction size by peak level of troponin I was larger in the multistage MVR group. With regard to medications at discharge, patients in the multistage MVR group had a slightly lower rate of treatment with aspirin (99.9% versus 100% versus 99.4%; *P*=0.010) and a slightly higher rate of treatment with renin-angiotensin-aldosterone system inhibitors. Other evidence-based medications for MI had similar rates of prescription among the 3 groups. The proportion of patients with the left main coronary artery as the culprit vessel was 6.7% in the 1-stage MVR group. The prevalence of American College of Cardiology/American Heart Association-defined complex lesions, long lesions, and triple vessel disease was higher in the multistage MVR group. Patients in the COR group received second-generation drug-eluting stents less frequently than those in the MVR group (87.9% versus 91.6% versus 92.8%; *P*=0.022). The multistage MVR group had lower baseline thrombolysis in myocardial infarction flow in the culprit artery and a lower rate of imaging-guided PCI. In the multistage MVR group, the median interval between the index and second-stage PCI was 5.0 (4.0–7.0) days. The length of hospital stay was longer in the multistage MVR group (median 4.0 versus 4.0 versus 7.0 days; *P*<0.001). There were no significant differences in in-hospital complication rates among the groups.

Clinical Outcomes According to Treatment Strategy

At 3 years, the patients in the COR group had a higher risk of MACE (COR versus 1-stage MVR; 25.0% versus 17.1%; HR, 0.63; 95% CI, 0.53–0.75; *P*<0.001; and COR versus multistage MVR; 25.0% versus 19.5%; HR, 0.73; 95% CI, 0.56–0.96; *P*=0.027), mainly driven by a significantly higher risk of all and nontarget vessel revascularization repeat PCI. The risk of all-cause death was also significantly higher in the COR group compared with 1-stage MVR (Figures 2 and 3).

Sensitivity analyses using multivariate Cox regression, propensity score matching, inverse probability weighting, and Bayesian modeling showed a significantly higher risk of MACE in the COR group than in the 1-stage and multistage MVR groups, and a lower risk of all-cause death in the 1-stage MVR group than in the COR group. There

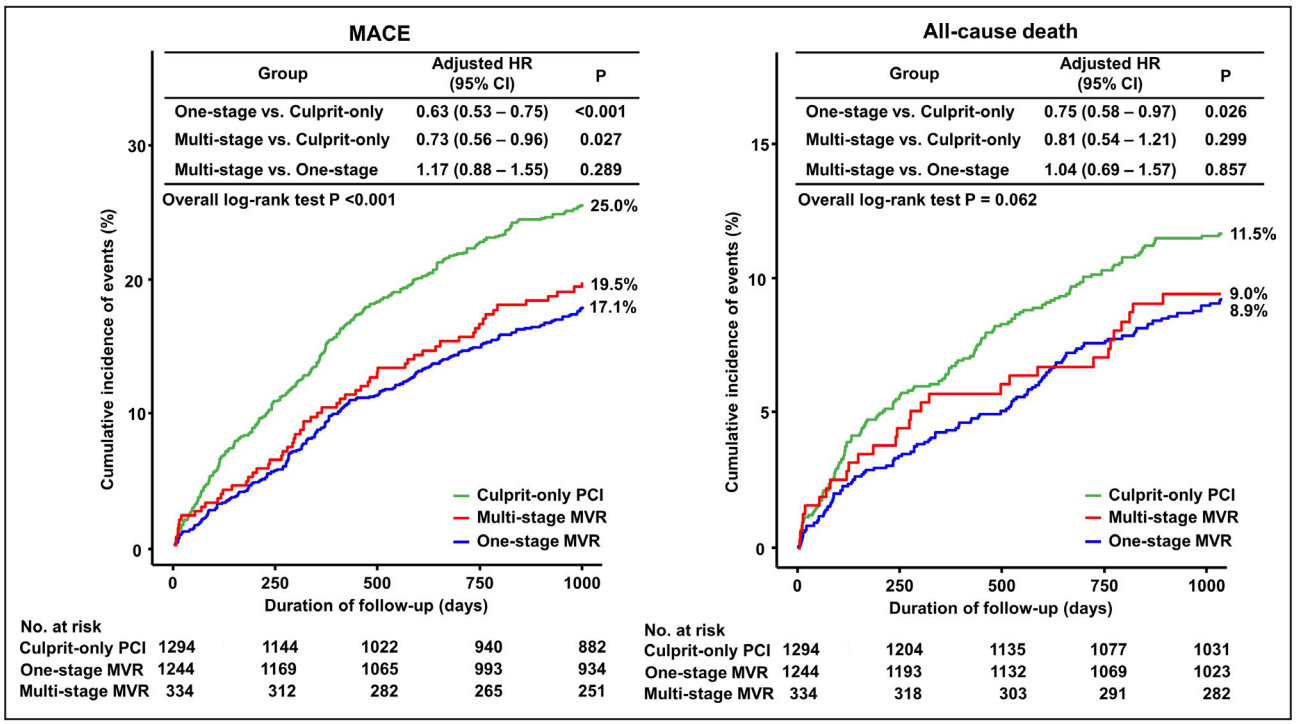

Figure 2. Cumulative incidence of MACE and all-cause death.
HR indicates hazard ratio; MACE, major adverse cardiac events; MVR, multivessel revascularization; and PCI, percutaneous coronary intervention.

were no significant differences in MACE or all-cause death between the 1-stage and multistage MVR groups (Table 3).

Independent Predictors of MACE and All-Cause Death

A multivariate Cox proportional hazard model identified independent predictors of the primary and secondary outcomes (Table 4). The multivessel (1-stage and multistage) MVR group was associated with lower incidences of all-cause death (HR, 0.742; 95% CI, 0.578–0.951; *P*=0.019) and MACE (HR, 0.643; 95% CI, 0.540–0.765; *P*<0.001) than COR at 3 years.

Subgroup Analyses

In subgroup analyses stratified by GRACE score, 1-stage and multistage MVR reduced MACE in both

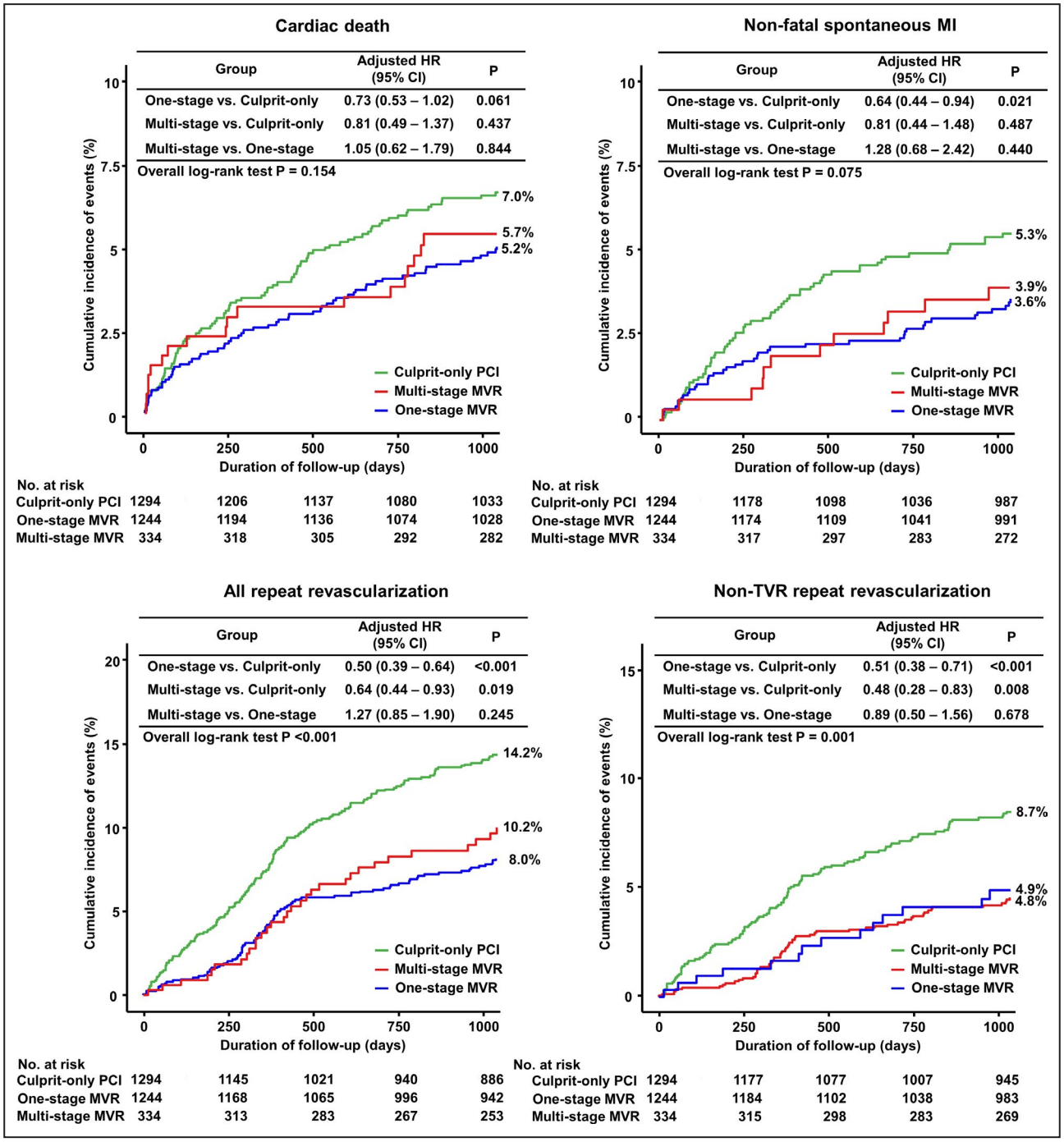

Figure 3. Cumulative incidence of cardiac death, nonfatal spontaneous MI, all repeat revascularization and non-TVR repeat PCI.
HR indicates hazard ration; MI, myocardial infarction; MVR, multivessel revascularization; PCI, percutaneous coronary intervention; and TVR, target-vessel revascularization.

Table 3. Comparison of 3-year Clinical Outcomes According to Interventional Strategy

	Culprit-Only PCI (N=1294)	Multistage MVR (N=334)	Unadjusted	Adjusted	PS-Matched	IPW-Adjusted	Bayesian Model
			HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
All-cause death	149 (11.5%)	30 (9.0%)	0.76 (0.52–1.13)	0.81 (0.54–1.21)	0.73 (0.48–1.10)	0.89 (0.54–1.48)	0.73 (0.52–1.09)
Cardiac death	90 (7.0%)	19 (5.7%)	0.80 (0.49–1.31)	0.82 (0.49–1.37)	0.74 (0.44–1.25)	0.87 (0.45–1.71)	0.84 (0.55–1.31)
Nonfatal spontaneous MI	69 (5.3%)	13 (3.9%)	0.71 (0.39–1.28)	0.80 (0.44–1.48)	0.72 (0.39–1.36)	0.66 (0.31–1.39)	0.78 (0.41–1.26)
Any repeat revascularization	184 (14.2%)	34 (10.2%)	0.67 (0.47–0.97)	0.64 (0.44–0.93)	0.66 (0.45–0.97)	0.61 (0.39–0.94)	0.69 (0.48–0.93)
Non-TVR repeat PCI	112 (8.7%)	16 (4.8%)	0.53 (0.31–0.89)	0.48 (0.28–0.83)	0.52 (0.30–0.90)	0.48 (0.26–0.89)	0.51 (0.32–0.86)
Definite/probable ST	5 (0.4%)	2 (0.6%)	1.52 (0.29–7.82)	1.81 (0.31–10.4)	2.14 (0.30–15.2)	1.73 (0.11–26.1)	2.09 (0.58–4.71)
All-cause death or MI	198 (15.3%)	41 (12.3%)	0.78 (0.56–1.01)	0.85 (0.60–1.20)	0.76 (0.53–1.08)	0.81 (0.52–1.26)	0.80 (0.60–1.01)
MACE*	323 (25.0%)	65 (19.5%)	0.74 (0.57–0.97)	0.73 (0.56–0.96)	0.71 (0.54–0.94)	0.71 (0.51–0.99)	0.73 (0.56–0.98)
	One-Stage MVR (N=1244)	Multistage MVR (N=334)	Unadjusted	Adjusted	PS-Matched	IPW-Adjusted	Bayesian Model
			HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
All-cause death	111 (8.9%)	30 (9.0%)	1.01 (0.67–1.50)	1.04 (0.69–1.57)	0.99 (0.65–1.50)	1.01 (0.61–1.67)	1.01 (0.72–1.77)
Cardiac death	65 (5.2%)	19 (5.7%)	1.08 (0.65–1.81)	1.05 (0.62–1.79)	0.99 (0.59–1.67)	1.07 (0.55–2.05)	1.24 (0.82–1.74)
Nonfatal spontaneous MI	45 (3.6%)	13 (3.9%)	1.07 (0.58–1.98)	1.28 (0.68–2.42)	0.91 (0.49–1.70)	1.32 (0.58–3.03)	1.13 (0.82–1.66)
Any repeat revascularization	99 (8.0%)	34 (10.2%)	1.28 (0.87–1.89)	1.27 (0.85–1.90)	1.19 (0.80–1.77)	1.47 (0.87–2.49)	1.30 (0.86–1.99)
Non-TVR repeat PCI	61 (4.9%)	16 (4.8%)	0.97 (0.56–1.69)	0.89 (0.50–1.56)	0.89 (0.51–1.56)	1.05 (0.52–2.13)	0.83 (0.57–1.46)
Definite/probable ST	7 (0.6%)	2 (0.6%)	1.06 (0.22–5.09)	1.01 (0.20–5.06)	0.99 (0.20–4.89)	1.30 (0.15–11.4)	2.57 (1.39–7.43)
All-cause death or MI	147 (11.8%)	41 (12.3%)	1.03 (0.73–1.46)	1.13 (0.79–1.61)	0.98 (0.69–1.39)	1.08 (0.69–1.68)	1.01 (0.76–1.48)
MACE*	213 (17.1%)	65 (19.5%)	1.14 (0.86–1.51)	1.17 (0.88–1.55)	1.08 (0.81–1.44)	1.23 (0.85–1.76)	1.13 (0.89–1.47)
	Culprit-Only PCI (N=1294)	One-Stage MVR (N=1244)	Unadjusted	Adjusted	PS-Matched	IPW-Adjusted	Bayesian Model
			HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
All-cause death	149 (11.5%)	111 (8.9%)	0.76 (0.59–0.97)	0.75 (0.58–0.97)	0.76 (0.60–0.98)	0.77 (0.61–0.99)	0.73 (0.60–0.92)
Cardiac death	90 (7.0%)	565 (5.2%)	0.74 (0.53–1.01)	0.73 (0.53–1.02)	0.73 (0.53–1.01)	0.79 (0.56–1.11)	0.73 (0.54–1.09)
Nonfatal spontaneous MI	69 (5.3%)	45 (3.6%)	0.66 (0.45–0.96)	0.64 (0.44–0.94)	0.67 (0.47–0.99)	0.63 (0.43–0.93)	0.71 (0.53–0.88)
Any repeat revascularization	184 (14.2%)	99 (8.0%)	0.53 (0.41–0.67)	0.50 (0.39–0.64)	0.53 (0.42–0.68)	0.49 (0.38–0.62)	0.50 (0.36–0.63)
Non-TVR repeat PCI	112 (8.7%)	61 (4.9%)	0.54 (0.40–0.74)	0.51 (0.37–0.71)	0.56 (0.41–0.76)	0.49 (0.36–0.66)	0.62 (0.44–0.92)
Definite/probable ST	5 (0.4%)	7 (0.6%)	1.43 (0.45–4.51)	1.48 (0.47–4.71)	1.47 (0.47–4.64)	2.09 (0.55–7.94)	2.30 (1.72–4.72)
All-cause death or MI	198 (15.3%)	147 (11.8%)	0.75 (0.61–0.93)	0.74 (0.60–0.92)	0.76 (0.61–0.94)	0.76 (0.61–0.95)	0.75 (0.62–0.91)
MACE*	323 (25.0%)	213 (17.1%)	0.75 (0.54–0.77)	0.63 (0.53–0.75)	0.65 (0.55–0.78)	0.63 (0.53–0.75)	0.65 (0.55–0.77)

Values are n (%) unless otherwise indicated. HR indicates hazard ratio; IPW, inverse probability weight; IRA, infarct-related artery; MACE, major adverse cardiovascular event; MI, myocardial infarction; MVR, multivessel revascularization; PCI, percutaneous coronary intervention; PS, propensity score; ST, stent thrombosis; and TVR, target-vessel revascularization.

*MACE was defined as a composite of all-cause death, nonfatal spontaneous myocardial infarction, or any repeat revascularization.

high-risk (GRACE score ≥140) patients and low-to-intermediate risk (GRACE score <140) patients. However, there was no significant difference in the incidence of MACE between the 1-stage and multistage MVR groups in high-risk patients. Interestingly, 1-stage MVR was associated with a lower risk of MACE compared with the multistage MVR (HR for multistage MVR, 1.55; 95% CI, 1.06–2.27; *P*=0.023) and COR groups (HR, 0.56; 95% CI, 0.44–0.72; *P*<0.001) in low-to-intermediate risk patients (Figures 4 and 5).

DISCUSSION

The present study compared 3 years of clinical outcomes among different treatment strategies in patients with NSTEMI and MVD using data from a nationwide, multicenter, prospective registry. As the main findings, we found that the multivessel MVR strategy (1-stage and multistage MVR) was associated with significantly lower incidences of MACE and all-cause death than the COR strategy. In addition, there were no significant differences in the incidences of any of the primary or secondary outcomes between the 1-stage and multistage MVR groups. However, subgroup analyses stratified by GRACE score revealed a significantly lower risk of MACE in 1-stage MVR in low-to-intermediate risk patients (GRACE score <140) compared with multistage MVR but not in high-risk patients (GRACE score ≥140).

MVD is common in NSTEMI patients, and it adversely affects clinical outcomes.[1,2] However, there have been few studies of the impacts of different interventional strategies in these patients. Earlier studies using the registry or single-center data have reported significant benefits of MVR compared with COR. Shishehbor et al showed that MVR was significantly associated with a lower revascularization rate, but not hard clinical end points, compared with COR.[10] In addition, a Korean study using the KAMIR registry reported that MVR was associated with a 42% reduction in all-cause death or nonfatal MI and a 56% reduction in nontarget vessel revascularization repeat PCI during a 1-year follow-up period.[11] In hemodynamically stable patients with STEMI and MVD, complete revascularization is more beneficial than COR.[3–7] Complete revascularization also appears to be useful in patients with NSTEMI with MVD. A recently published large-scale study using British Cardiac Intervention Society data showed that 1-stage complete revascularization was superior to COR in terms of long-term mortality.[12] However, the impact of staged PCI in patients with NSTEMI and MVD is uncertain. Data from 1 registry showed comparable 3-year mortality rates between 1-stage and multistage MVR in NSTEMI and MVD.[13] To our knowledge, only 1 randomized controlled trial has been performed about this issue. The SMILE trial compared 1-stage and multistage MVR, and all patients in the multistage MVR group received staged PCI at 3

Table 4. Independent Predictors of Clinical Outcomes at 3 Years

	Hazard Ratio	95% CI	*P* Value
All-cause death			
Multivessel (1- and multistage) MVR*	0.742	0.578–0.951	0.019
Multistage MVR*	0.771	0.519–1.144	0.197
Age> 60 y	3.569	2.372–5.370	<0.001
Killip class ≥3	1.859	1.409–2.453	<0.001
eGFR <60 mL/min per 1.73 m^2	2.619	2.052–3.342	<0.001
LVEF <50%	2.196	1.706–2.825	<0.001
Left main disease	1.605	1.101–2.339	0.014
Previous history of MI	1.518	1.097–2.100	0.012
MACE			
Multivessel (1- and multistage) MVR*	0.643	0.540–0.765	<0.001
Multistage MVR*	0.747	0.571–0.975	0.032
Age >60 y	1.426	1.169–1.737	<0.001
Killip class ≥3	1.613	1.295–2.008	<0.001
eGFR <60 mL/min per 1.73 m^2	1.960	1.644–2.335	<0.001
LVEF <50%	1.355	1.138–1.611	0.001
Left main disease	1.654	1.272–2.150	<0.001
Previous history of MI	1.453	1.139–1.853	0.003

Hazard rations and their 95% CIs were calculated using multivariate Cox regression analysis. eGFR indicates estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; MACE, major adverse cardiac events; MI, myocardial infarction; and MVR, multivessel revascularization.

*Reference is a culprit-only percutaneous coronary intervention.

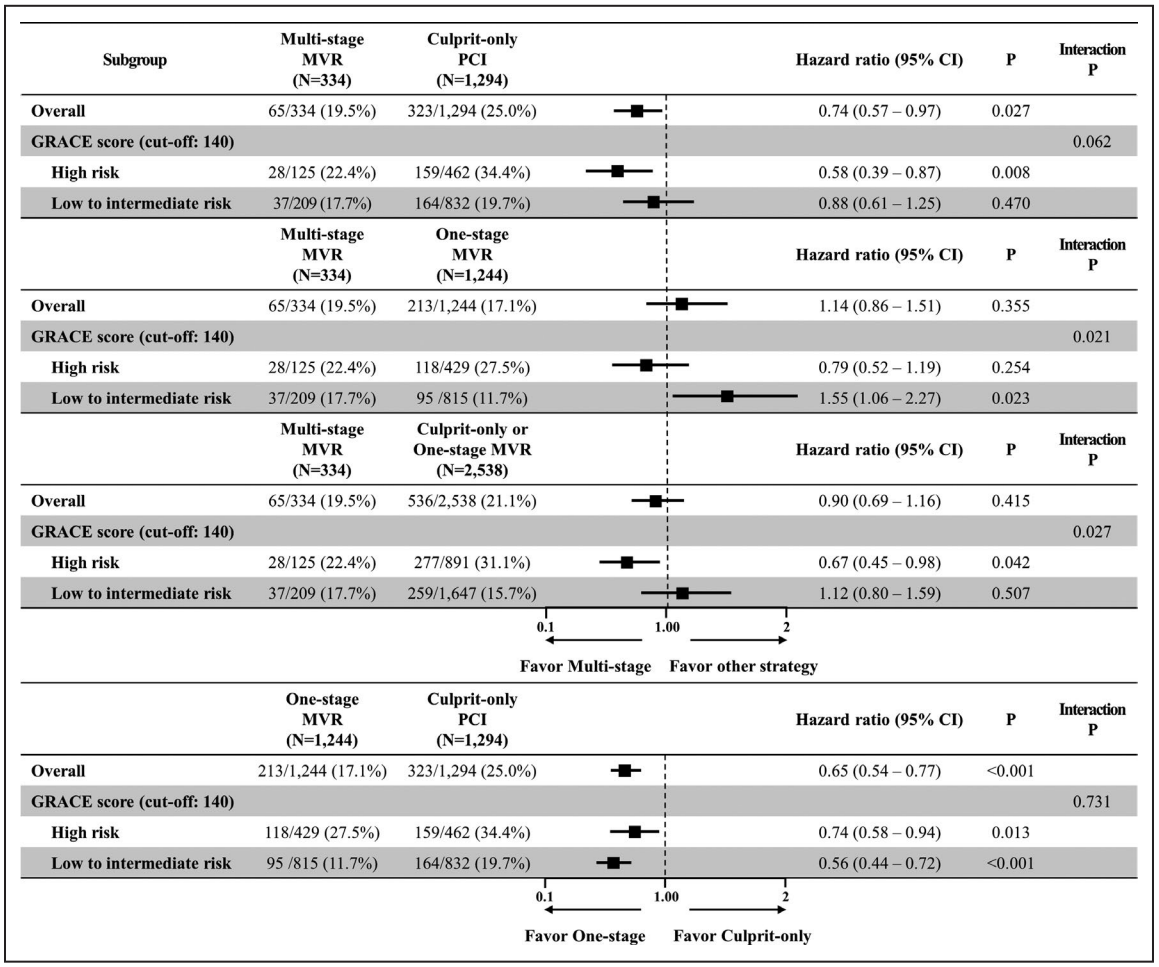

Figure 4. Cumulative incidence of MACE according to interventional strategies stratified by GRACE score.
GRACE indicates Global Registry of Acute Coronary Events; HR, hazard ratio; MACE, major adverse cardiac events; MVR, multivessel revascularization; and PCI, percutaneous coronary intervention.

to 7 days after index PCI.[9] The results indicated that 1-stage MVR was superior in terms of lower 1-year composite outcomes, mainly because of lower target vessel revascularization and lower mortality rates, compared with multistage MVR. Based on these results, the 2018 European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines for myocardial revascularization recommend complete 1-stage MVR over multistage MVR in NSTEMI and MVD. However, the guidelines emphasize the importance of individualization of interventional strategy based on clinical status and comorbidities, as well as disease severity.[14] That is, various subgroup analyses are needed to define an optimal interventional strategy for these patients. Our study investigated which strategy (1-stage or multistage MVR) was more beneficial and which patients could be integrated to determine the revascularization approach.

In the present study, there was a significantly lower risk of MACE and all-cause death at 3 years in the multivessel PCI (1-stage and multistage MVR) group compared with the COR group. These findings are consistent with other studies indicating the superiority of MVR over COR. However, both 1-stage and multistage MVR had comparable incidences of primary and secondary outcomes on analyses using various statistical methods. The results are different from those of the SMILE trial; that large registry data study comparing 1-stage and multistage MVR also investigated only mortality.[13] The patients enrolled in the SMILE trial were at low risk, but 35.9% of all patients in the present study were at high risk (GRACE score ≥140).

A potentially important finding of the present study is that subgroup analyses stratified by GRACE score showed a significantly lower risk of MACE for 1-stage MVR in patients at low-to-intermediate risk (GRACE score <140) but not in patients at high risk (GRACE score ≥140). The main reasons for the differences in interventional strategy between STEMI and NSTEMI are heterogeneity and more comorbidities in NSTEMI. Therefore, we stratified the study patients into

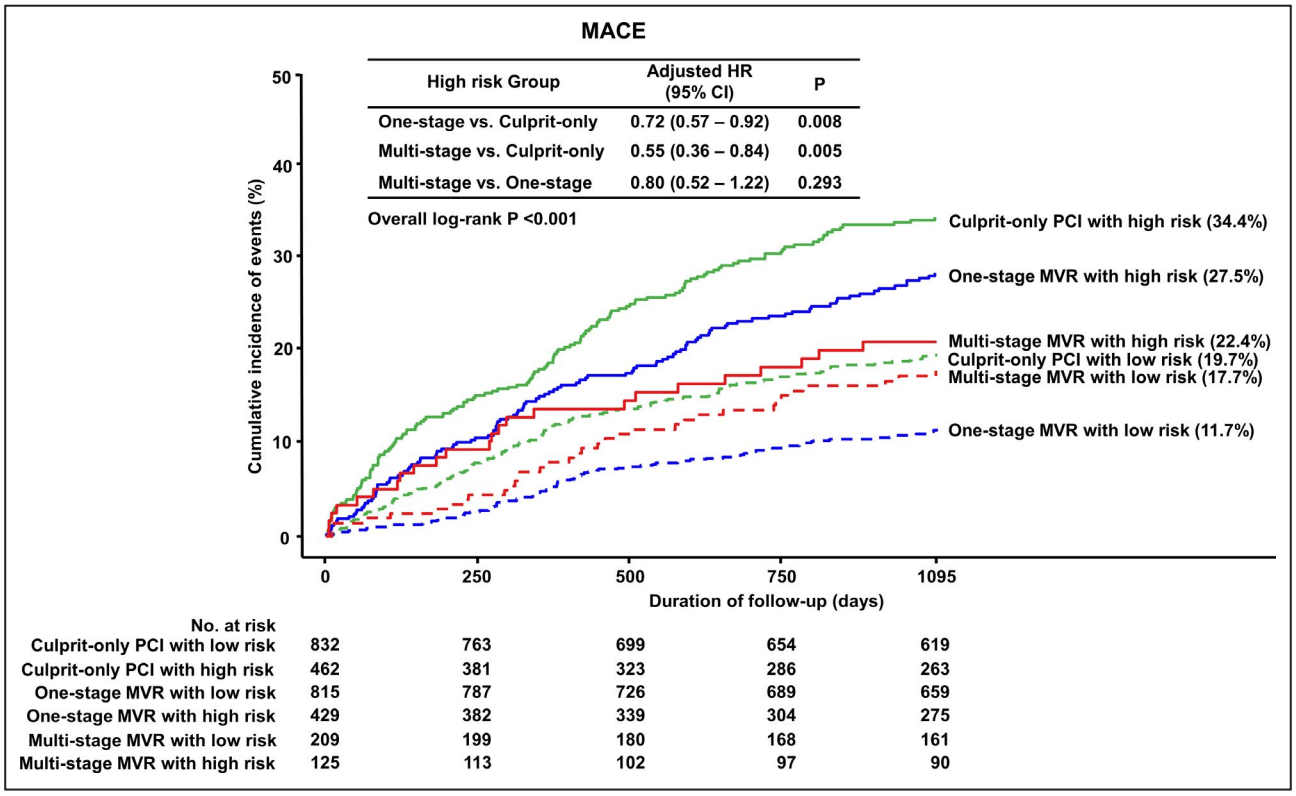

Figure 5. Subgroup analysis for MACE stratified by GRACE score.
GRACE indicates Global Registry of Acute Coronary Events; HR, hazard ratio; MACE, major adverse cardiac events; MVR, multivessel revascularization; and PCI, percutaneous coronary intervention.

2 groups by GRACE risk score to reflect their clinical status. Although the incidence of MACE in multistage MVR was not significantly different from that in 1-stage MVR, it showed a lower trend of MACE in high-risk patients (22.4% versus 27.5%). Furthermore, the Kaplan-Meier curve showed definite separation among the 3 interventional strategies in high-risk patients (Figure 4). The main reason for the insufficient statistical power of this analysis was the small number of patients with multistage MVR. In the present study, a low proportion (11.6% of all patients) of patients received multistage MVR. In South Korea, patients with NSTEMI and MVD should be revascularized for both culprit and nonculprit arteries simultaneously because of the national insurance system, and in special cases with NSTEMI and MVD, such as patients with renal insufficiency or the use of large amounts of contrast media, which is covered by national insurance. In aforementioned registry data, 1-stage MVR was also associated with a higher short-term mortality despite of lower long-term mortality compared with COR.[12] A large-scale randomized trial is needed to confirm this issue.

This study has some limitations. First, we used observational registry data. Therefore, selection bias was inevitable. However, we attempted to perform various sensitivity analyses to adjust for measured or unmeasured confounders of different clinical characteristics between the groups. Second, we conducted an angiographic assessment of non-infarct-related artery stenosis. Although there was insufficient evidence, fractional flow-guided and imaging-guided PCI are useful to assess the nonculprit artery. Third, we did not collect data on procedure-related risks, including procedure time, radiation dose, total amount of contrast dye, and incidence of contrast media-induced nephropathy.

In conclusion, MVR reduced 3-year MACE in patients with NSTEMI and MVD compared with COR. Although 1-stage MVR was not superior to multistage MVR for reducing MACE, it was associated with fewer MACE in patients at low-to-intermediate risk but not in patients at high risk. These findings were based on retrospective studies; thus, additional large-scale randomized trials are required for verification.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Materials

Tables S1–S6
Figures S1–S3

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Supplemental Material

Table S1. Baseline Clinical Characteristics Between Culprit-Only PCI and Multi-stage MVR after Propensity-Score Matching.

	Culprit-only PCI vs. Multi-stage MVR				
	Culprit-only PCI (N=689)	Multi-stage MVR (N=311)	Total (N=1000)	*P* Value	SMD (%)
Demographics					
Age, years	66.3±12.3	65.0±11.6	65.9±12.1	0.109	-8.43
Male	492 (71.4)	237 (76.2)	729 (72.9)	0.133	9.15
Body mass index	24.0±3.4	23.9±3.3	23.9±3.4	0.824	0.11
Killip class 3	75 (10.9)	32 (10.3)	107 (10.7)	0.864	-2.39
Process of care index					
Symptom-to-door time, h	53.0±166.0	49.1±118.8	51.8±152.8	0.674	-2.65
Door-to-balloon time, min	24.1±42.8	19.9±33.9	22.8±40.3	0.092	-9.65
Cardiovascular risk factors					
Hypertension	405 (58.8)	176 (56.6)	581 (58.1)	0.562	-1.84
Diabetes mellitus	250 (36.3)	105 (33.8)	355 (35.5)	0.484	-7.38
Dyslipidemia	72 (10.4)	35 (11.3)	107 (10.7)	0.787	0.67
Current smoker	238 (34.5)	116 (37.3)	354 (35.4)	0.44	-2.21
Previous history of MI	61 (8.9)	23 (7.4)	84 (8.4)	0.518	-3.17
Previous history of PCI	62 (9.0)	24 (7.7)	86 (8.6)	0.589	-2.69
Previous history of CVA	60 (8.7)	25 (8.0)	85 (8.5)	0.819	-1.20
Familial history	44 (6.4)	16 (5.1)	60 (6.0)	0.534	-2.92
LVEF, %	52.4±11.5	51.3±11.4	52.1±11.5	0.177	-4.21
eGFR	82.0±39.1	85.3±31.2	83.0±36.9	0.151	9.17
Peak cardiac enzyme levels					
Troponin I, ng/ml	25.4±53.2	30.6±54.5	27.0±53.6	0.157	9.99
CK-MB, ng/ml	59.2±88.7	72.1±94.0	63.2±90.5	0.036	14.76
Medication at discharge					
Aspirin	689 (100)	309 (99.4)	998 (99.8)	0.179	-8.32
P2Y12 inhibitor	686 (99.6)	309 (99.4)	995 (99.5)	1.000	-4.16
ACEI or ARB	576 (83.6)	279 (89.7)	855 (85.5)	0.015	12.64
Beta-blocker	596 (86.5)	265 (85.2)	861 (86.1)	0.654	-3.85
Statin	657 (95.4)	296 (95.2)	953 (95.3)	1.000	-1.03

Values are mean ± SD, median (interquartile range), or n (%). ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; CK-MB, creatine kinase-myocardial band; CVA, cerebrovascular accident; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; MVR, multivessel revascularization; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.

Table S2. Procedural-Related Characteristics Between Culprit-Only PCI and Multi-stage MVR after Propensity-Score Matching.

	Culprit-only PCI vs. Multi-stage MVR				
	Culprit-only PCI (N=689)	Multi-stage MVR (N=311)	Total (N=1,000)	*P* Value	SMD (%)
Culprit lesion profiles					
Culprit vessel				0.002	
Left main artery	29 (4.2)	7 (2.3)	36 (3.6)		18.48
LAD	258 (37.4)	99 (31.8)	357 (35.7)		-
LCX	171 (24.8)	63 (20.3)	234 (23.4)		-1.59
RCA	231 (33.5)	142 (45.7)	373 (37.3)		14.81
Type B2/C lesion	594 (86.2%)	284 (91.3)	878 (87.8)	0.029	10.62
Small vessel*	248 (36.0)	97 (31.2)	345 (34.5)	0.159	-8.57
Long lesion†	309 (44.8)	163 (52.4)	472 (47.2)	0.032	13.62
Overall-lesion profiles					
Left main artery disease	68 (9.9)	30 (9.6)	98 (9.8)	1	0.00
3-vessel disease	260 (37.7)	170 (54.7)	430 (43.0)	0.001	13.52
Procedural characteristics					
Trans-radial approach	334 (48.5)	166 (53.4)	500 (50.0)	0.336	5.58
GP IIb/IIIa inhibitor	57 (8.3)	43 (13.8)	100 (10.0)	0.009	13.51
Thrombus aspiration	103 (14.9)	57 (18.3)	160 (16.0)	0.209	8.38
IRA treatment				0.582	
Bare metal stent	18 (2.6)	5 (1.6)	23 (2.3)		-
1st generation DES	7 (1.0)	3 (1.0)	10 (1.0)		0
2nd generation DES	621 (90.1)	289 (92.9)	910 (91.0)		6.84
POBA	43 (6.2)	14 (4.5)	57 (5.7)		-2.84
Total number of stents	1.3±0.6	2.0±0.9	1.5±0.8	<0.001	84.87
Pre-PCI TIMI 0-1 flow	295 (42.8)	160 (51.4)	455 (45.5)	0.014	-14.35
IVUS guided PCI	181 (26.3)	53 (17.0)	234 (23.4)	0.002	10.81
OCT guided PCI	11 (1.6)	0	11 (1.1)	0.056	8.91
Hemodynamic support					
IABP	3 (0.4)	0	3 (0.3)	0.589	5.67
ECMO	0	0	0	1.000	0.00
In-hospital complications					
Acute heart failure	26 (3.8)	20 (6.4)	46 (4.6)	0.09	9.26
Atrioventricular block	5 (0.7)	4 (1.3)	9 (0.9)	0.612	4.92
Ventricular tachycardia	9 (1.3)	5 (1.6)	14 (1.4)	0.932	1.61
Ventricular fibrillation	2 (0.3)	2 (0.6)	4 (0.4)	0.782	2.77

Values are mean ± SD, median [interquartile range], or n (%). ACC/AHA indicates American College of Cardiology/American Heart Association; DES, drug-eluting stent; ECMO, extracorporeal membrane oxygenation; GP, glycoprotein; IABP, intra-aortic balloon pump; IRA, infarct-related artery; IVUS, intravascular ultrasound; LAD, left anterior descending artery; LCX, left circumflex artery; OCT, optical coherence tomography; POBA, plain balloon angioplasty; RCA, right coronary artery; TIMI, Thrombolysis in Myocardial Infarction. *Small vessel: reference diameter ≤ 2.75 mm. †long lesion: length ≥ 28mm.

Table S3. Baseline Clinical Characteristics Between One-stage and Multi-stage MVR after Propensity-Score Matching.

	One-stage vs. Multi-stage MVR				
	One-stage MVR (N=818)	Multi-stage MVR (N=327)	Total (N=1145)	*P* Value	SMD (%)
Demographics					
Age, years	65.6±11.5	65.1±11.6	65.4±11.6	0.583	-1.31
Male	579 (70.8)	247 (75.5)	826 (72.1)	0.122	5.72
Body mass index	24.0±3.6	23.8±3.4	24.0±3.5	0.389	-2.95
Killip class 3	82 (10.0)	37 (11.3)	119 (10.4)	0.59	2.43
Process of care index					
Symptom-to-door time, h	49.9±118.6	49.1±121.4	49.7±119.4	0.921	-0.51
Door-to-balloon time, min	22.8±31.4	19.6±33.3	21.9±31.9	0.133	-6.48
Cardiovascular risk factors					
Hypertension	490 (59.9)	188 (57.5)	678 (59.2)	0.495	-1.95
Diabetes mellitus	276 (33.7)	109 (33.3)	385 (33.6)	0.95	-0.11
Dyslipidemia	104 (12.7)	38 (11.6)	142 (12.4)	0.684	-2.08
Current smoker	552 (67.5)	204 (62.4)	756 (66.0)	0.115	-6.09
Previous history of MI	66 (8.1)	23 (7.0)	89 (7.8)	0.639	-4.42
Previous history of PCI	41 (5.0)	14 (4.3)	55 (4.8)	0.712	-3.3
Previous history of CVA	71 (8.7)	26 (8.0)	97 (8.5)	0.778	-1.71
Familial history	49 (6.0)	17 (5.2)	66 (5.8)	0.705	-0.69
LVEF, %	52.9±10.9	51.1±11.7	52.4±11.2	0.016	-9.05
eGFR	85.2±37.2	85.1±31.9	85.2±35.7	0.967	-1.19
Peak cardiac enzyme levels					
Troponin I, ng/ml	22.7±80.4	30.2±53.2	24.9±73.7	0.066	6.83
CK-MB, ng/ml	62.4±207.3	73.0±93.7	65.4±182.3	0.235	6.77
Medication at discharge					
Aspirin	818 (100)	327 (100)	1145 (100)	1.000	0
P2Y12 inhibitor	818 (100)	327 (100)	1145 (100)	1.000	0
ACEI or ARB	686 (83.9)	289 (88.4)	975 (85.2)	0.064	9.46
Beta-blocker	713 (87.2)	280 (85.6)	993 (86.7)	0.551	-4.54
Statin	783 (95.7)	312 (95.4)	1095 (95.6)	0.944	-1.97

Values are mean ± SD, median (interquartile range), or n (%). ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; CK-MB, creatine kinase-myocardial band; CVA, cerebrovascular accident; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; MVR, multivessel revascularization; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.

Table S4. Procedural-Related Characteristics Between One-stage and Multi-stage MVR after Propensity-Score Matching.

	One-stage vs. Multi-stage MVR				
	One-stage MVR (N=818)	Multi-stage MVR (N=327)	Total (N=1145)	*P* Value	SMD (%)
Culprit lesion profiles					
Culprit vessel	26 (3.2)	7 (2.1)	33 (2.9)	0.004	
Left main artery	300 (36.7)	104 (31.8)	404 (35.3)		-3.91
LAD	212 (25.9)	67 (20.5)	279 (24.4)		-
LCX	280 (34.2)	149 (45.6)	429 (37.5)		-7.58
RCA	26 (3.2)	7 (2.1)	33 (2.9)		12.86
Type B2/C lesion	718 (87.8)	299 (91.4)	1017 (88.8)	0.094	8.26
Small vessel*	290 (35.5)	103 (31.5)	393 (34.3)	0.229	-4.63
Long lesion†	393 (48.0)	172 (52.6)	565 (49.3)	0.184	5.4
Overall-lesion profiles					
Left main artery disease	72 (8.8)	29 (8.9)	101 (8.8)	1	1.07
3-vessel disease	359 (43.9)	179 (54.7)	538 (47.0)	0.001	13.41
Procedural characteristics					
Trans-radial approach	411 (50.2)	176 (53.8)	587 (51.3)	0.545	4.19
GP IIb/IIIa inhibitor	70 (8.6)	44 (13.5)	114 (10.0)	0.017	7.68
Thrombus aspiration	76 (9.3)	60 (18.3)	136 (11.9)	0	11.83
IRA treatment				0.992	
Bare metal stent	11 (1.3)	5 (1.5)	16 (1.4)		-
1st generation DES	5 (0.6)	2 (0.6)	7 (0.6)		0.47
2nd generation DES	762 (93.2)	305 (93.3)	1067 (93.2)		0.99
POBA	40 (4.9)	15 (4.6%)	55 (4.8)		-1.72
Total number of stents	2.4±1.0	2.6±1.1	2.5±1.0	0.015	10.48
Pre-PCI TIMI 0-1 flow	342 (41.8)	168 (51.4)	510 (44.5)	0.004	-12.73
IVUS guided PCI	179 (21.9)	59 (18.0)	238 (20.8)	0.172	-7.61
OCT guided PCI	4 (0.5)	0	4 (0.3)	0.476	6.38
Hemodynamic support					
IABP	2 (0.2)	0	2 (0.2)	0.911	4.51
ECMO	0	0	0	1.000	0.00
In-hospital complications					
Acute heart failure	32 (3.9)	21 (6.4)	53 (4.6)	0.095	6.5
Atrioventricular block	3 (0.4)	4 (1.2)	7 (0.6)	0.208	6.08
Ventricular tachycardia	5 (0.6)	5 (1.5)	10 (0.9)	0.248	5.36
Ventricular fibrillation	3 (0.4)	2 (0.6)	5 (0.4)	0.943	3.3

Values are mean ± SD, median [interquartile range], or n (%). ACC/AHA indicates American College of Cardiology/American Heart Association; DES, drug-eluting stent; ECMO, extracorporeal membrane oxygenation; GP, glycoprotein; IABP, intra-aortic balloon pump; IRA, infarct-related artery; IVUS, intravascular ultrasound; LAD, left anterior descending artery; LCX, left circumflex artery; OCT, optical coherence tomography; POBA, plain balloon angioplasty; RCA, right coronary artery; TIMI, Thrombolysis in Myocardial Infarction. *Small vessel: reference diameter ≤ 2.75 mm. †long lesion: length ≥ 28mm.

Table S5. Baseline Clinical Characteristics Between Culprit-only PCI and One-stage MVR after Propensity-Score Matching.

	Culprit-only PCI vs. One-stage MVR				
	Culprit-only PCI (N=969)	One-stage MVR (N=969)	Total (N=1938)	*P* Value	SMD (%)
Demographics					
Age, years	66.1±12.0	66.3±11.5	66.2±11.8	0.715	1.7
Male	681 (70.3)	671 (69.2)	1352 (69.8)	0.656	-2.21
Body mass index	24.0±3.3	24.1±3.5	24.1±3.4	0.420	3.55
Killip class 3	98 (10.1)	91 (9.4)	189 (9.8)	0.646	-2.45
Process of care index					
Symptom-to-door time, h	41.2±111.7	45.3±115.0	43.3±113.3	0.421	3.61
Door-to-balloon time, min	29.1±60.4	27.5±47.3	28.3±54.2	0.515	-3.37
Cardiovascular risk factors					
Hypertension	575 (59.3)	574 (59.2)	1149 (59.3)	1.000	-0.21
Diabetes mellitus	352 (36.3)	342 (35.3)	694 (35.8)	0.670	-2.16
Dyslipidemia	117 (12.1)	117 (12.1)	234 (12.1)	1.000	0
Current smoker	658 (67.9)	690 (71.2)	1348 (69.6)	0.126	7.24
Previous history of MI	97 (10.0)	75 (7.7)	172 (8.9)	0.093	-8.67
Previous history of PCI	87 (9.0)	61 (6.3)	148 (7.6)	0.032	-9.13
Previous history of CVA	82 (8.5)	82 (8.5)	164 (8.5)	1.000	0
Familial history	62 (6.4)	63 (6.5)	125 (6.4)	1.000	0.41
LVEF, %	52.8±11.2	53.7±10.7	53.3±11.0	0.076	8.06
eGFR	83.9±39.1	84.8±37.1	84.3±38.1	0.594	2.37
Peak cardiac enzyme levels					
Troponin I, ng/ml	23.0±49.9	18.3±34.4	20.6±42.9	0.016	-6.81
CK-MB, ng/ml	58.2±120.3	52.9±86.6	55.5±104.8	0.264	-3.06
Medication at discharge					
Aspirin	969 (100)	969 (100)	1938 (100)	1.000	0
P2Y12 inhibitor	964 (99.5)	966 (99.7)	1930 (99.6)	0.723	4.21
ACEI or ARB	787 (81.2)	786 (81.1)	1573 (81.2)	1.000	-0.26
Beta-blocker	832 (85.9)	832 (85.9)	1664 (85.9)	1.000	0
Statin	908 (93.7)	928 (95.8)	1836 (94.7)	0.053	9.41

Values are mean ± SD, median (interquartile range), or n (%). ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; CK-MB, creatine kinase-myocardial band; CVA, cerebrovascular accident; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; MVR, multivessel revascularization; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.

Table S6. Procedural-Related Characteristics Between Culprit-only PCI and One-stage MVR after Propensity-Score Matching.

	Culprit-only PCI vs. One-stage MVR				
	Culprit-only PCI (N=969)	One-stage MVR (N=969)	Total (N=1938)	*P* Value	SMD (%)
Culprit lesion profiles					
Culprit vessel				0.347	
Left main artery	55 (5.7)	72 (7.4)	127 (6.6)		7.03
LAD	347 (35.8)	359 (37.0)	706 (36.4)		-
LCX	277 (28.6)	267 (27.6)	544 (28.1)		9.41
RCA	290 (29.9)	271 (28.0)	561 (28.9)		-4.37
Type B2/C lesion	808 (83.4)	828 (85.4)	1636 (84.4)	0.234	5.74
Small vessel*	363 (37.5)	364 (37.6)	727 (37.5)	1.000	0.21
Long lesion†	440 (45.4)	433 (44.7)	873 (45.0)	0.784	-1.45
Overall-lesion profiles					
Left main artery disease	97 (10.0)	128 (13.2)	225 (11.6)	0.33	9.66
3-vessel disease	303 (31.3)	347 (35.8)	650 (33.5)	0.39	9.42
Procedural characteristics					
Trans-radial approach	472 (48.7)	468 (48.3)	940 (48.5)	0.983	-0.83
GP IIb/IIIa inhibitor	49 (5.1)	64 (6.6)	113 (5.8)	0.175	6.17
Thrombus aspiration	101 (10.4)	65 (6.7)	166 (8.6)	0.004	-15.14
IRA treatment				0.002	
Bare metal stent	27 (2.8)	19 (2.0)	46 (2.4)		-
1st generation DES	10 (1.0)	7 (0.7)	17 (0.9)		-3.87
2nd generation DES	838 (86.5)	890 (91.8)	1728 (89.2)		19.38
POBA	94 (9.7)	53 (5.5)	147 (7.6)		-18.0
Total number of stents	1.2±0.7	2.3±1.0	1.8±1.0	<0.001	10.65
Pre-PCI TIMI 0-1 flow	368 (38.0)	356 (36.7)	724 (37.4)	0.605	2.59
IVUS guided PCI	235 (24.3)	262 (27.0)	497 (25.6)	0.176	6.33
OCT guided PCI	29 (3.0)	26 (2.7)	55 (2.8)	0.784	-1.8
Hemodynamic support					
IABP	4 (0.4)	9 (0.9)	13 (0.7)	0.266	5.78
ECMO	1 (0.1)	0	1 (0.1)	1.000	0
In-hospital complications					
Acute heart failure	41 (4.2)	36 (3.7)	77 (4.0)	0.642	-2.68
Atrioventricular block	7 (0.7)	6 (0.6)	13 (0.7)	1.000	-1.49
Ventricular tachycardia	9 (0.9)	6 (0.6)	15 (0.8)	0.604	-4.47
Ventricular fibrillation	3 (0.3)	1 (0.1)	4 (0.2)	0.617	-4.21

Values are mean ± SD, median [interquartile range], or n (%). ACC/AHA indicates American College of Cardiology/American Heart Association; DES, drug-eluting stent; ECMO, extracorporeal membrane oxygenation; GP, glycoprotein; IABP, intra-aortic balloon pump; IRA, infarct-related artery; IVUS, intravascular ultrasound; LAD, left anterior descending artery; LCX, left circumflex artery; OCT, optical coherence tomography; POBA, plain balloon angioplasty; RCA, right coronary artery; TIMI, Thrombolysis in Myocardial Infarction. *Small vessel: reference diameter ≤ 2.75 mm. †long lesion: length ≥ 28mm.

Figure S1. Covariate Balance Between Culprit-Only PCI and Multi-stage MVR – IPW.

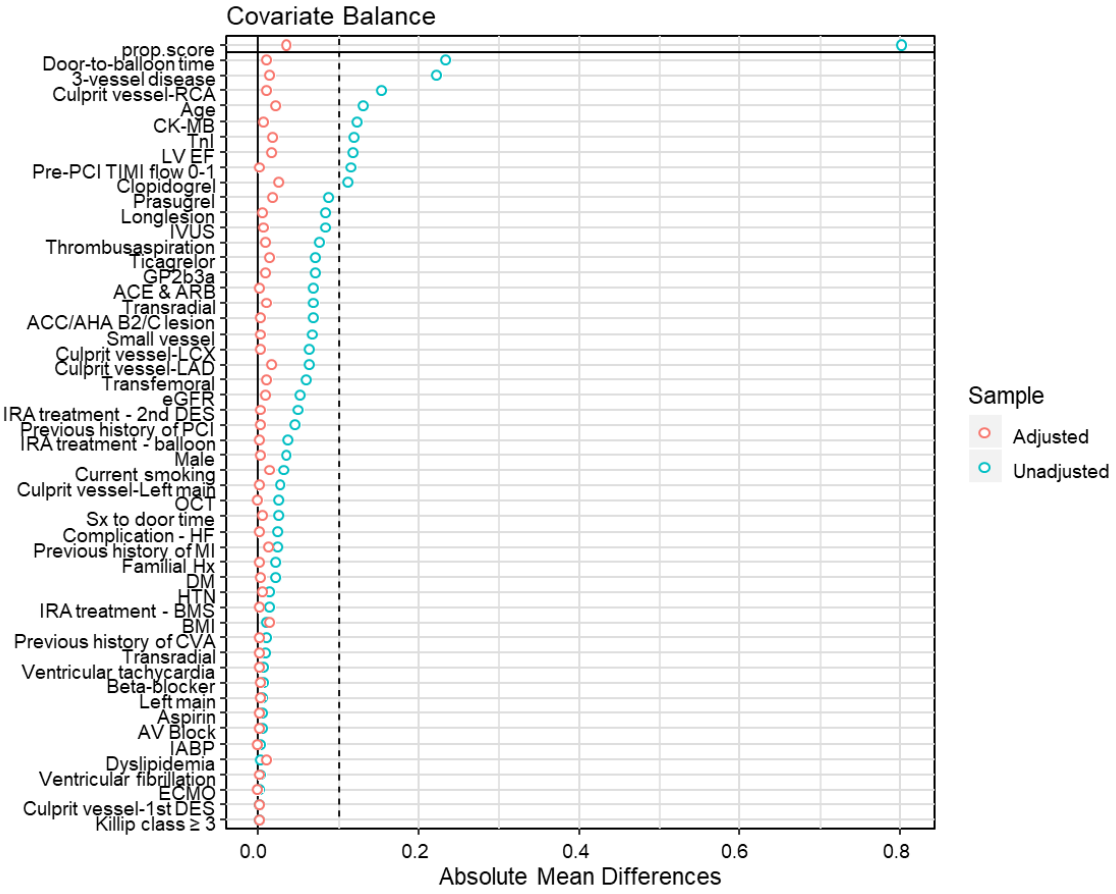

Figure S2. Covariate Balance Between One-stage and Multi-stage MVR – IPW.

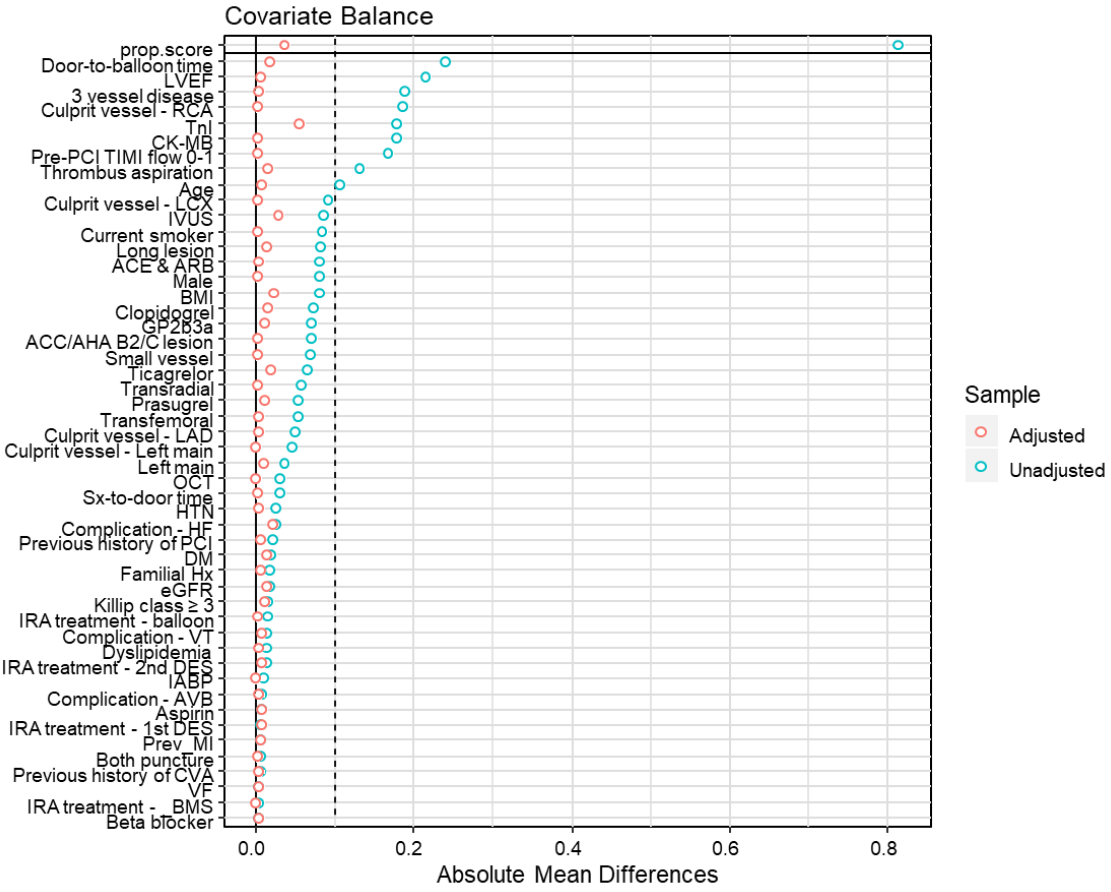

Figure S3. Covariate Balance Between Culprit only PCI and One-stage MVR – IPW.