

ORIGINAL RESEARCH

Clinical Relevance of Fractional Flow Reserve-Guided Percutaneous Coronary Intervention According to Left Ventricular Ejection Fraction in Patients With Acute Myocardial Infarction and Multivessel Disease

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BACKGROUND: Fractional flow reserve (FFR)-guided or angiography-guided complete revascularization has not been evaluated in patients with acute myocardial infarction (AMI) with multivessel disease and reduced left ventricular ejection fraction (LVEF). This study sought to evaluate the impact of FFR-guided percutaneous coronary intervention (PCI) for patients with AMI with multivessel disease according to left ventricular systolic function.

METHODS: We performed a prespecified analysis of the FRAME-AMI (Fractional Flow Reserve Versus Angiography-Guided Strategy in Acute Myocardial Infarction With Multivessel Disease) trial, which randomly allocated 562 patients to undergo either FFR-guided PCI (FFR ≤ 0.80) or angiography-guided PCI (diameter stenosis $>50\%$) for non-infarct-related arteries. Patients were classified into preserved ($\geq 50\%$) and reduced ($<50\%$) LVEF groups. Primary end point was major adverse cardiovascular events, a composite of death, myocardial infarction, and repeat revascularization.

RESULTS: Overall, 187 patients (33.3%) had reduced LVEF. During a median 3.5-year follow-up, patients with AMI with reduced LVEF showed an increased risk of major adverse cardiovascular events compared with those with preserved LVEF ($P < 0.001$). FFR-guided PCI for non-infarct-related arteries significantly reduced major adverse cardiovascular events among patients

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with preserved LVEF (3.3% versus 19.0%; hazard ratio [HR], 0.26 [95% CI, 0.11–0.66]; $P=0.004$). Conversely, there was no significant difference in major adverse cardiovascular events between the FFR and angiography-guided PCI among patients with reduced LVEF (17.0% versus 21.0%; HR, 0.64 [95% CI, 0.31–1.31]; $P=0.225$). In the exploratory analysis, the clinical benefit of FFR-guided PCI was more evident with an increased LVEF (interaction $P=0.028$).

CONCLUSIONS: In patients with AMI with multivessel disease, FFR-guided PCI for a non–infarct-related artery had differential clinical impact according to left ventricular systolic function. The beneficial effect of FFR-guided PCI might be maximized among patients with preserved LVEF rather than reduced LVEF.

REGISTRATION: URL: <https://clinicaltrials.gov>. Unique identifier: NCT02715518.

Key Words: acute myocardial infarction ■ complete revascularization ■ fractional flow reserve ■ left ventricular ejection fraction ■ percutaneous coronary intervention

CLINICAL PERSPECTIVE

What Is New?

- Fractional flow reserve–guided percutaneous coronary intervention for non–infarct-related artery lesions significantly reduced major adverse cardiovascular events in the preserved left ventricular ejection fraction (LVEF) group but not the reduced LVEF group.
- In the exploratory analysis, the clinical benefit of fractional flow reserve–guided percutaneous coronary intervention tended to increase with an increase in LVEF (adjusted hazard ratios for major adverse cardiovascular events, 0.69 versus 0.66 versus 0.25 versus 0.20 for the LVEF $\leq 40\%$ versus 40%–50% versus 50%–60% versus $\geq 60\%$; interaction $P=0.028$).

What Are the Clinical Implications?

- These results support the use of fractional flow reserve–guided treatment decision making for non–infarct-related artery lesions, but caution is warranted in patients with acute myocardial infarction with multivessel disease and reduced LVEF.

FULL REVASC	FFR-Guidance for Complete Nonculprit Revascularization
IRA	infarct-related artery
MACE	major adverse cardiac event
TIMI	Thrombolysis in Myocardial Infarction

Acute myocardial infarction (AMI) remains the leading cause of death and major health problems in the world.¹ Multivessel disease is present in approximately half of patients with AMI and is associated with adverse outcomes.² Based on consistent results from randomized controlled trials, the current guidelines recommend complete revascularization for patients with AMI with multivessel disease, except in cases complicated by cardiogenic shock.^{1,3,4} Either fractional flow reserve (FFR)-guided or angiography-guided lesion assessment is able to support decision making for revascularization of non–infarct-related artery (IRA) lesions.^{5–9} However, debates about whether FFR-guided percutaneous coronary intervention (PCI) can improve clinical outcomes compared with angiography-guided PCI continue to occur.

In the FLOWER-MI (Flow Evaluation to Guide Revascularization in Multivessel ST-Elevation Myocardial Infarction) trial,¹⁰ there was no significant difference between the FFR-guided and angiography-guided PCI groups regarding the risk of a composite of death, myocardial infarction (MI), or unplanned urgent revascularization in patients with ST-segment-elevation MI, despite the lower rates of non-IRA PCI with fewer stents in the FFR-guided PCI group. On the contrary, the FRAME-AMI (Fractional Flow Reserve Versus Angiography-Guided Strategy in Acute Myocardial Infarction With Multivessel Disease) trial showed that FFR-guided PCI significantly reduced the risk of a composite of death, MI, or repeat revascularization at a median 3.5 years of follow-up, compared with angiography-guided PCI in patients with

Nonstandard Abbreviations and Acronyms

FFR	fractional flow reserve
FLOWER-MI	Flow Evaluation to Guide Revascularization in Multivessel ST-Elevation Myocardial Infarction
FRAME-AMI	Fractional Flow Reserve Versus Angiography-Guided Strategy in Acute Myocardial Infarction With Multivessel Disease

ST-segment-elevation MI or non-ST-segment-elevation MI.¹¹ Considering that FFR-guided decision making resulted in fewer interventions, the beneficial effect of FFR-guided PCI might be more evident in patients with multivessel disease and reduced left ventricular ejection fraction (LVEF).¹² Nevertheless, the prognostic impact of FFR-guided PCI for non-IRA lesions has not been fully evaluated in patients with reduced LVEF.

In this regard, the current prespecified substudy of the FRAME-AMI trial sought to evaluate the differential prognostic impact of FFR-guided PCI according to LVEF compared with angio-guided PCI in patients with AMI and multivessel disease.

METHODS

The FRAME-AMI trial is planning to continue analysis, including post hoc subgroup analysis. Until then, no individual participant data will be available. Any relevant inquiry should be emailed to Dr Joo Myung Lee (email: drone80@hanmail.net) or Dr Joo-Yong Hahn (email: jy-hahn@skku.edu).

Study Design

This substudy of the FRAME-AMI trial sought to evaluate clinical outcomes according to LVEF. The FRAME-AMI trial was an investigator-initiated, randomized, open-label, multicenter trial conducted at 14 sites in Korea. Patients aged ≥ 19 years with ST-segment-elevation MI or non-ST-segment-elevation MI undergoing successful primary or urgent PCI of an IRA were candidates for enrollment. Successful PCI for IRA was defined as a TIMI (Thrombolysis in Myocardial Infarction) flow grade ≥ 2 and residual angiographic stenosis $< 30\%$. Eligible patients also had to have at least 1 non-IRA lesion with diameter stenosis $> 50\%$ in a major epicardial coronary artery or major side branch with a vessel diameter ≥ 2.0 mm judged to be amenable to PCI by operators on visual estimation. An IRA was identified by electrocardiography and angiography. If needed, echocardiography or intravascular imaging was additionally performed to assess the IRA, especially in patients with non-ST-segment-elevation MI. Key exclusion criteria were single-vessel disease, flow-limiting stenosis with a TIMI flow grade ≤ 2 in the non-IRA, target lesion located in the left main coronary artery, cardiogenic shock, and chronic total occlusion in the non-IRA. The trial protocol was approved by the institutional review board at each participating site and has been previously published.¹¹

All patients provided written informed consent before randomization. An independent clinical event-adjudication committee whose members were masked to the study group assignments assessed all clinical

outcomes. Concealment of results according to allocation was maintained for the executive committee until the end of scheduled follow-up of the final enrolled patient and the completion of blinded clinical event adjudication. An independent data and safety monitoring board monitored the trial, and all board members were informed of the number of enrolled patients per group allocation. All participating centers, trial personnel, and detailed inclusion and exclusion criteria are described in [Data S1](#).

Randomization and Treatment

Eligible patients were randomly assigned in a 1:1 ratio to undergo either FFR-guided PCI or angiography-guided PCI ([Figure 1](#)). In patients presenting with conditions that precluded their understanding of the trial process, informed consent was obtained after stabilization by revascularization of the IRA, and subsequent procedures for non-IRAs were performed in a staged manner during the index hospitalization. Randomization was performed using a web-based randomization program (S-Soft, Seoul, Korea), in permuted blocks with block sizes of 4 and was stratified by the presence of ST-segment elevation in initial electrocardiography, participating center, and type of stents used.

In the FFR group, FFR was measured in all non-IRAs with lesions $> 50\%$ stenosis on visual estimation using a pressure-sensor guidewire (Certus, Abbott Vascular or Prestige, Philips Volcano). Hyperemia was induced by intravenous infusion of adenosine ($140 \mu\text{g/kg}$ per min) or intracoronary nicorandil (2 mg).¹³ The protocol specified that only stenoses with an FFR ≤ 0.80 were to be treated with PCI. In the angiography group, any lesions with diameter stenosis $> 50\%$ on visual estimation were treated with PCI. In both groups, complete revascularization during the index procedure was recommended. However, staged procedures during the index hospitalization were permitted at operators' discretion. In both groups, PCI was performed using zotarolimus-eluting stents with biocompatible polymer (Resolute Onyx, Medtronic Vascular) or sirolimus-eluting stents with bioresorbable polymer (Orsiro, Biotronik). Regardless of group allocation, guideline-directed medical treatment was performed, and dual antiplatelet therapy was recommended for at least 12 months.¹⁴ All angiograms and raw data of FFR measurement were analyzed in an independent core laboratory at Samsung Medical Center. Procedural success was defined by a final in-stent diameter stenosis $< 30\%$ by quantitative coronary angiography over the entire target vessel with TIMI grade 3 flow and no more than type C dissection with or without any adjunctive devices and without cardiac death, spontaneous target-vessel MI, or repeat revascularization of the target lesion during the index hospitalization.

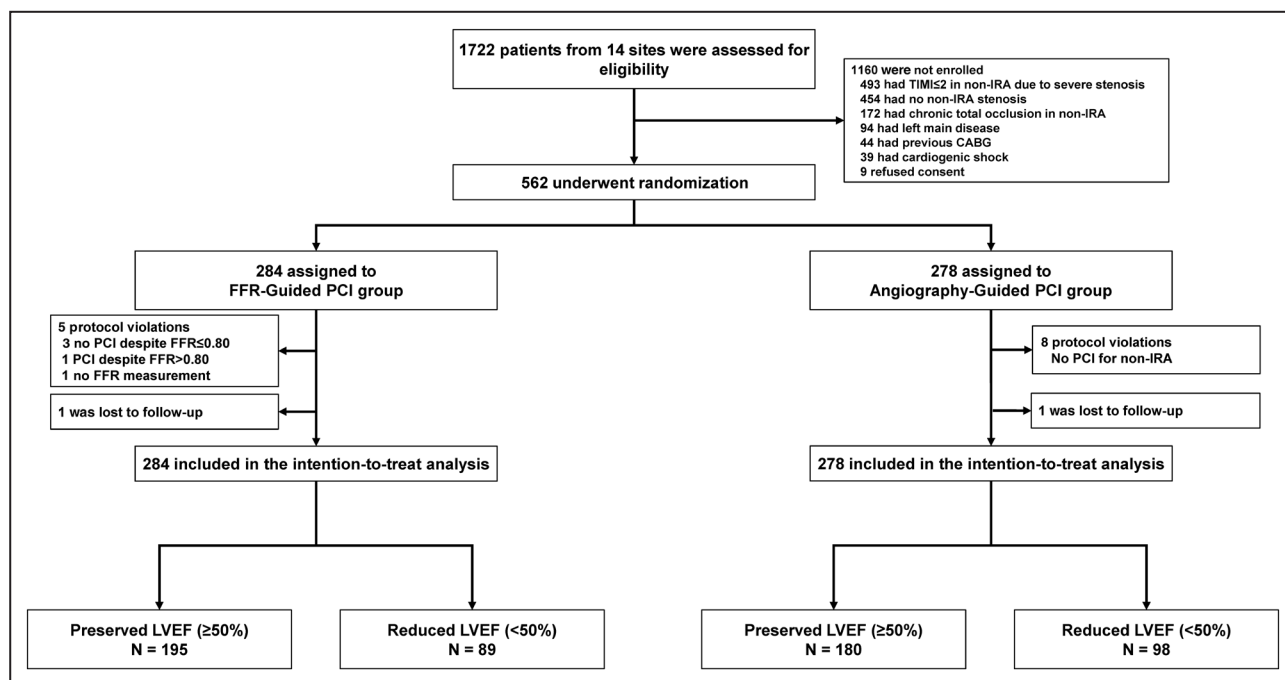


Figure 1. Study flow of LVEF substudy of the FRAME-AMI trial.

Between August 2016 and December 2020, 562 patients with AMI and multivessel disease were enrolled in the FRAME-AMI trial. These patients were classified into preserved ($\geq 50\%$) and reduced ($< 50\%$) LVEF groups and used to compare the clinical benefits of FFR- and angiography-guided PCI. CABG indicates coronary artery bypass graft; FFR, fractional flow reserve; FRAME-AMI, Fractional Flow Reserve Versus Angiography-Guided Strategy in Acute Myocardial Infarction With Multivessel Disease; IRA, infarct-related artery; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction.

Echocardiography

All patients underwent 2-dimensional echocardiography for evaluating left ventricular systolic function during periprocedural periods using commercially available ultrasound systems (Vivid 7, GE Medical Systems, Milwaukee, WI; Acuson 512, Siemens Medical Solution, Mountain View, CA; or Sonos 5500, Philips Medical System, Andover, MA). The median timing for echocardiography was 1.0 day (interquartile range, 0.0–3.0 days). LVEF was assessed using the biplane Simpson technique, M-mode, or visual estimation.¹⁵ The distribution of LVEF values is shown in Figure S1. Patients with LVEF $\geq 50\%$ were defined as the preserved LVEF group, while those with LVEF $< 50\%$ were defined as the reduced LVEF group (Figure 1).

Clinical Events and Definitions

The primary outcome was major adverse cardiac events (MACEs), a composite of all-cause death, MI, or repeat revascularization. Secondary outcomes were all-cause death, cardiac death, procedure-related MI, spontaneous MI, repeat revascularization, definite stent thrombosis, and cerebrovascular accident. Clinical events were defined according to criteria from the Academic Research Consortium,¹⁶ which provides standardized definitions of end points used in coronary device trials.

Cardiac death was defined as any death due to a proximate cardiac cause (eg, MI, low-output failure, fatal arrhythmia), unwitnessed death and death of unknown cause, and all procedure-related deaths including those related to concomitant treatment. MI was defined on the basis of the third universal definition.¹⁷ PCI-related MI was defined as an elevation of cardiac troponin values in patients with normal baseline values or a $> 20\%$ increase in cardiac troponin values if the baseline values were elevated but they are stable or falling. In addition, either (1) symptoms suggestive of myocardial ischemia, (2) new ischemic electrocardiographic changes, (3) angiographic findings consistent with a procedural complication, or (4) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality were required. For procedure-related MIs from PCI for non-IRA lesions, angiographic findings consistent with a procedural flow-limiting complication like coronary dissection, occlusion of a major epicardial artery or a side branch occlusion/thrombus, disruption of collateral flow, or distal embolization needed to be confirmed. Detailed definitions of each clinical event are given in Data S1.

Clinical follow-up was conducted during outpatient clinic visits scheduled at 1, 6, and 12 months and yearly thereafter. Patients unable to attend outpatient clinical visits were contacted by telephone. For patients lost to follow-up,

cross-validation of survival status was performed using the Korean National Health Insurance database.

Statistical Analysis

The full statistical analysis plan, including sample-size calculation in the FRAME-AMI trial, has been previously published.¹¹ All analyses were performed on an intention-to-treat basis, under which all patients were analyzed as part of their assigned treatment group. All categorical or discrete variables were expressed as numbers and relative frequencies (percentages). Continuous variables were presented as means±SDs or medians with interquartile ranges, contingent upon their distributions, which were assessed by the Kolmogorov–Smirnov test and visual inspection of Q–Q plots. For per-lesion evaluations of FFR, a generalized estimating equation with independent correlation structure was used to adjust for intrasubject variability among lesions from the same patient. Kaplan–Meier analyses were performed for time-to-event outcomes with treatment effects estimated by Cox proportional hazard regression models, and results are presented as hazard ratios (HRs) with 95% CIs. The proportional hazards assumption was evaluated with a 2-sided score test of the scaled Schoenfeld residuals over time at the 0.05 level.

To adjust the baseline differences, multivariable Cox proportional hazards models were constructed using all variables with $P < 0.1$ from univariable analyses with backward elimination based on an information criterion. The final model included the variables of age, sex, body mass index, initial presentation, and chronic renal insufficiency. As sensitivity analyses, inverse probability treatment weighting analyses were performed using the propensity score from a multivariable logistic regression model with a good balance.

All probability values were 2-sided, and $P < 0.05$ were considered statistically significant. There was no pre-defined plan to adjust for multiple comparisons in this trial. Secondary end points are reported with the use of 95% CIs that have not been adjusted for multiple comparisons and should not be used to infer definitive treatment effects. Statistical analyses were performed using SPSS 25.0 (SPSS-PC, Chicago, IL) and R version 4.2.3 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study Population and Overall Clinical Outcomes According to LVEF

Among 562 patients with AMI and multivessel disease who were randomly allocated to either FFR-guided or angiography-guided PCI, 375 had preserved LVEF, and 187 had reduced LVEF (Figure 1 and Table S1). Patients in the reduced LVEF group were older and showed a greater

incidence of chronic renal insufficiency. Considering procedural findings (Table S2), the reduced LVEF group had higher SYNTAX scores (median, 17.5 versus 15.0 points; $P < 0.001$) and more frequent designation of the left anterior descending artery as the IRA (51.9% versus 26.1%; $P < 0.001$). Although there was no significant difference in the rate of complications during hospitalization, the hospital stay was longer among patients with reduced LVEF than those with preserved LVEF (median, 3.0 versus 2.0 days; $P < 0.001$). At a median follow-up of 3.5 (interquartile range, 2.7–4.1) years, MACEs frequently occurred in the reduced LVEF group than in the preserved LVEF group (18.9% versus 10.8%; adjusted HR, 2.65 [95% CI, 1.53–4.58]; $P < 0.001$; Figure 2 and Table S3). The significantly higher risk of MACEs in patients with reduced LVEF than in those with preserved LVEF was similarly observed in both ST-segment-elevation MI and non-ST-segment-elevation MI population (Table S4).

Clinical Characteristics According to LVEF and Treatment for Non-IRA Lesions

Patients were classified into 4 groups according to LVEF and treatment strategy for non-IRA lesions, as follows: (1) preserved LVEF and FFR-guided PCI (N=195), (2) preserved LVEF and angiography-guided PCI (N=180), (3) reduced LVEF and FFR-guided PCI (N=89), and (4) reduced LVEF and angiography-guided PCI (N=98). Table 1 shows the baseline clinical characteristics. There were no significant differences in demographics and comorbidities among patients with preserved LVEF. The angiography-guided PCI subgroup showed slightly higher LVEF (59.7% versus 58.4%; $P = 0.032$) and less frequent 3-vessel disease (30.0% versus 43.6%; $P = 0.009$) than the FFR-guided PCI subgroup among patients with preserved LVEF. Similarly, there were no significant differences in the baseline characteristics according to the treatment strategy for non-IRAs among patients with reduced LVEF. Table 2 summarizes procedural characteristics. FFR-guided PCI was significantly related to reduced numbers of non-IRA PCI procedures and stents used, regardless of LVEF status. By generalized estimating equation analysis, the estimated mean value of FFR was 0.78 in the preserved LVEF group and 0.81 in the reduced LVEF group, indicating a tendency toward higher values in the reduced LVEF group. Among 89 patients with FFR-guided PCI and reduced LVEF, 8 patients (9.0%) had pre-PCI FFRs of 0.75–0.80.

Differential Clinical Impact of FFR-Guided PCI for Non-IRA Lesions According to LVEF

Among patients with preserved LVEF, FFR-guided PCI reduced the risk of MACEs compared with

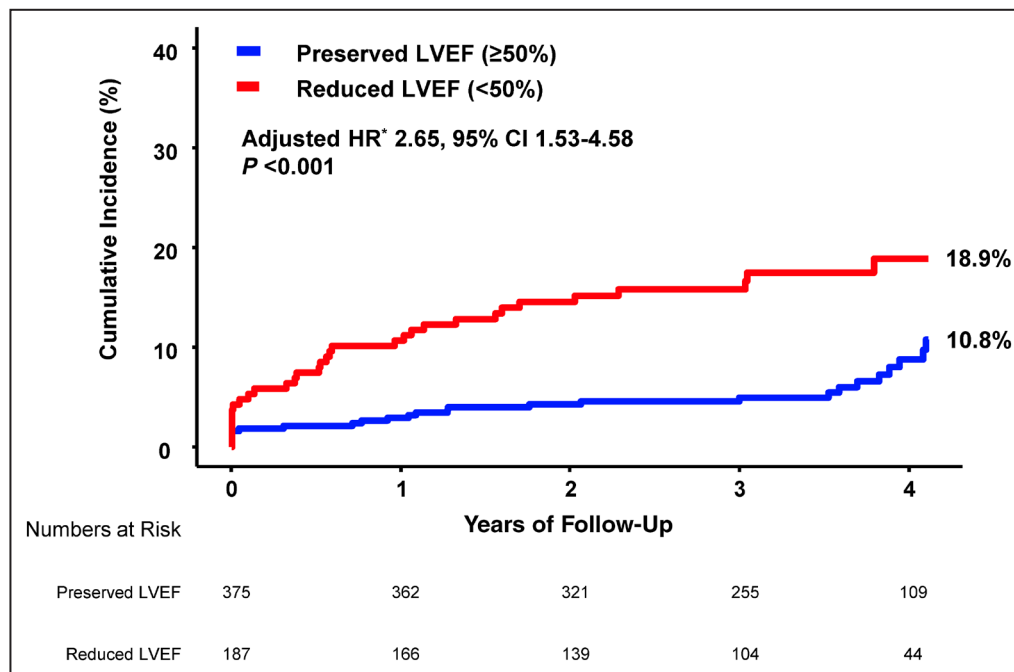


Figure 2. Kaplan–Meier curves for MACEs according to LVEF status.

MACEs include a composite of time to death, MI, or repeat revascularization during the overall study period (median, 3.5 years). *Multivariable model included the variables of age, sex, body mass index, initial presentation (ST-segment-elevation MI vs non-ST-segment-elevation MI), diabetes, chronic renal insufficiency, and non-IRA treatment strategy (FFR- vs angiography-guided). FFR indicates fractional flow reserve; HR, hazard ratio; LVEF, left ventricular ejection fraction; MACE, major adverse cardiac event; and MI, myocardial infarction.

angiography-guided PCI (3.3% versus 19.0%; HR, 0.26 [95% CI, 0.11–0.66]; $P=0.004$; Table 3 and Figure 3). Conversely, there was no significant difference in the risk of MACEs between the FFR-guided and angiography-guided strategies among patients with reduced LVEF (17.0% versus 21.0%; HR, 0.64 [95% CI, 0.31–1.31]; $P=0.225$). Interaction P value of this binary subgroup was 0.128. These results remained consistent even in the sensitivity analysis, which excluded periprocedural MI (Figure S2). Meanwhile, there was also no significant difference between the FFR-guided and angiography-guided strategies according to procedural timing (immediate versus staged PCI) among patients with reduced LVEF (Figure S3). The clinical benefits of FFR-guided PCI for non-IRA lesions might be driven by decreased risks of cardiac death (0.5% versus 8.6%; HR, 0.11 [95% CI, 0.01–0.89]) and MI (0.5% versus 7.3%; HR, 0.09 [95% CI, 0.01–0.70]) among patients with preserved LVEF. Multivariable Cox regression and inverse probability treatment weighting-adjusted analyses also demonstrated consistent results (Table S5). For clinical outcomes that did not include all-cause death, competing risk analyses showed similar results to those of the main analyses (Table S6).

As exploratory analysis, when we stratified patients according to 10% intervals of LVEF, the clinical benefit

of FFR-guided decision making was evident for patients with LVEF 50% to 60% (adjusted HR, 0.25 [95% CI, 0.08–0.81]) and $\geq 60\%$ (adjusted HR, 0.20 [95% CI, 0.04–0.95]), compared with angiography-guided decision making (interaction $P=0.028$; Figure S4).

DISCUSSION

This prespecified analysis of the FRAME-AMI trial assessed the differential prognostic impact of FFR-guided PCI for non-IRA lesions among patients with AMI and multivessel disease during a median 3.5 years of follow-up. The major findings are as follows. First, in patients with AMI with multivessel disease, only 33% had reduced LVEF ($<50\%$), which was associated with an increased risk of MACE compared with patients with preserved LVEF ($\geq 50\%$). Second, FFR-guided PCI significantly reduced the risk of MACEs compared with angiography-guided PCI among patients with preserved LVEF, a trend that was mainly driven by cardiac death and MI. Conversely, FFR-guided PCI did not significantly reduce MACEs in patients with reduced LVEF. There was a trend of more evident clinical benefit of FFR-guided PCI for non-IRA lesions with an increase in LVEF.

The goals of revascularization for IRA lesions in patients with AMI are to restore coronary flow and

Table 1. Baseline Characteristics

Characteristic	Preserved LVEF (N=375)		Reduced LVEF (N=187)	
	FFR-guided (n=195)	Angiography-guided (n=180)	FFR-guided (n=89)	Angiography-guided (n=98)
Age, y	62.3±11.1	60.8±11.4	67.3±11.2	66.1±10.9
Male sex	165 (84.6)	156 (86.7)	75 (84.3)	78 (79.6)
Body mass index, kg/m ²	25.1±3.1	24.9±3.1	23.8±2.7	24.8±3.8
Initial presentation				
ST-segment–elevation MI	74 (37.9)	79 (43.9)	57 (64.0)	55 (56.1)
Non–ST-segment–elevation MI	121 (62.1)	101 (56.1)	32 (36.0)	43 (43.9)
Hemodynamic data				
Systolic blood pressure, mm Hg	130.1±20.6	128.6±22.7	124.5±23.1	132.8±23.2
Diastolic blood pressure, mm Hg	78.4±13.9	77.3±15.2	77.0±17.2	78.3±14.5
Heart rate, beats/min	73.5±13.7	74.9±15.5	82.1±19.0	80.2±15.4
Medical history				
Hypertension	99 (50.8)	97 (53.9)	52 (58.4)	55 (56.1)
Diabetes	67 (34.4)	52 (28.9)	30 (33.7)	34 (34.7)
Dyslipidemia	86 (44.1)	69 (38.3)	35 (39.3)	38 (38.8)
Current smoking	65 (33.3)	72 (40.0)	26 (29.2)	33 (33.7)
Family history of premature coronary artery disease	16 (8.2)	17 (9.4)	3 (3.4)	5 (5.1)
Chronic renal insufficiency	3 (1.5)	2 (1.1)	5 (5.6)	6 (6.1)
Previous stroke	4 (2.1)	8 (4.4)	5 (5.6)	7 (7.1)
Previous MI	3 (1.5)	6 (3.3)	4 (4.5)	1 (1.0)
Previous PCI	10 (5.1)	14 (7.8)	7 (7.9)	6 (6.1)
Peripheral-vessel disease	1 (0.5)	1 (0.6)	4 (4.5)	0 (0.0)
Atrial fibrillation	7 (3.6)	2 (1.1)	4 (4.5)	6 (6.1)
LVEF, %	58.4±6.1	59.7±6.2	41.8±6.2	42.4±5.4
Arteries with stenosis				
2	110 (56.4)	126 (70.0)	47 (52.8)	62 (63.3)
3	85 (43.6)	54 (30.0)	42 (47.2)	36 (36.7)
Laboratory data				
Hemoglobin, g/dL	14.4±2.0	14.3±1.8	13.8±2.2	13.8±2.1
Creatinine, mg/dL	1.0±0.6	1.0±0.5	1.4±1.8	1.4±1.9
Glycated hemoglobin, %	6.7±1.6	6.3±1.1	6.4±1.1	6.5±1.1
Total cholesterol, mg/dL	184.5±46.0	180.1±44.5	175.1±47.0	175.6±46.9
HDL cholesterol, mg/dL	43.9±10.7	43.1±13.7	41.0±9.8	44.8±11.4
LDL cholesterol, mg/dL	122.9±41.4	119.2±40.4	117.8±40.6	119.1±55.3
NT-proBNP, pg/mL	113.0 (34.1–768.9)	240.9 (71.9–579.7)	1533.5 (258.6–5172.2)	1771.0 (417.0–3831.5)
Discharge medication				
Aspirin	192 (98.5)	180 (100.0)	87 (97.8)	97 (99.0)
P2Y ₁₂ inhibitor				
- Any	193 (99.0)	179 (99.4)	87 (97.8)	97 (99.0)
- Clopidogrel	47 (24.1)	39 (21.7)	38 (42.7)	35 (35.7)
- Ticagrelor	51 (26.2)	46 (25.6)	22 (24.7)	23 (23.5)
- Prasugrel	95 (48.7)	94 (52.2)	27 (30.3)	39 (39.8)
Cilostazol	1 (0.5)	1 (0.6)	1 (1.1)	2 (2.0)
Oral anticoagulant	3 (1.5)	4 (2.2)	9 (10.1)	3 (3.1)
Statin	186 (95.4)	177 (98.3)	87 (97.8)	95 (96.9)

(Continued)

Table 1. Continued

Characteristic	Preserved LVEF (N=375)		Reduced LVEF (N=187)	
	FFR-guided (n=195)	Angiography-guided (n=180)	FFR-guided (n=89)	Angiography-guided (n=98)
β Blocker	142 (72.8)	142 (78.9)	68 (76.4)	79 (80.6)
ACE inhibitor or ARB	126 (64.6)	132 (73.3)	65 (73.0)	62 (63.3)
Calcium channel blocker	18 (9.2)	12 (6.7)	4 (4.5)	6 (6.1)

Data presented as mean±SD, median (interquartile range), or as n (%). ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; FFR, fractional flow reserve; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; and PCI, percutaneous coronary intervention.

prevent acute pump failure, avoid cardiac remodeling, and improve long-term outcomes. It has been well documented that the risk of non-IRA events after index AMI events is responsible for a substantial portion of future cardiac events.^{18,19} Considering non-IRA lesions in patients with AMI and multivessel disease, previous trials have consistently demonstrated the clinical benefit of complete revascularization over IRA-only revascularization, regardless of FFR-guided or angiography-guided decision making.^{5–9,20} Based on these results, the latest updated guideline from the European Society recommends complete revascularization as a class I indication in ST-segment–elevation MI and a class IIa indication in non-ST-segment–elevation MI.¹ However, the recent FULL REVASC (FFR-Guidance for Complete Nonculprit Revascularization) trial showed that FFR-guided complete revascularization did not improve clinical outcomes compared with culprit-only PCI during a median 4.8-year follow-up.²¹ The authors attributed their results to (1) a greater incidence of restenosis, stent thrombosis, and target-vessel revascularization in the FFR-guided complete revascularization group than the culprit-only PCI group and (2) limitations of the FFR in differentiating vulnerable plaques, which might be associated with hard end points. Although these conflicting data do not deny the role of FFR-guided complete revascularization in contemporary practice, the proper selection of lesions and patients may be crucial for better clinical outcomes.

The methods for evaluating non-IRA stenosis severity include angiography- and physiology-guided lesion selection. To date, only 2 trials, the FLOWER-MI and the FRAME-AMI trials, have directly compared these methods.^{10,11} The FLOWER-MI trial evaluated patients with ST-segment–elevation MI and multivessel disease and found no significant difference in clinical outcomes between the FFR-guided and angiography-guided strategies at 1- and 3-year follow-up.^{10,22} Conversely, the FRAME-AMI trial evaluated patients with ST-segment–elevation MI and non-ST-segment–elevation MI and multivessel disease and determined that FFR-guided PCI significantly reduced the risk of adverse events compared with angiography-guided PCI over a median follow-up of 3.5 years.¹¹ Although

the superiority of FFR-guided PCI for patients with AMI with multivessel disease is debatable on the basis of these results, FFR-guided PCI was associated with the use of fewer stents in both trials, which should result in potentially favorable long-term outcomes.

It is well known that reduced LVEF is significantly associated with poor clinical outcomes after patients with AMI undergo successful PCI.^{23,24} Furthermore, research shows that patients with AMI with multivessel disease have substantially lower LVEF and demonstrate an increased risk of death, reinfarction, and MACEs than those with single-vessel disease.²⁵ Reduced LVEF increases the risk of arrhythmic events, thrombotic events, and the development of heart failure.^{26–28} The beneficial effects of PCI for non-IRA lesions include preventing future adverse cardiovascular events from vulnerable plaques in non-IRAs and improving left ventricular systolic function by restoring flow to functionally significant stenosis. Although FFR-guided decision making has been linked to lower rates of cardiovascular events among stable patients and the values of FFR were not influenced unless the stenoses were very tight,^{12,29} the role of FFR-guided PCI for non-IRA lesions in the AMI remains questionable.

In the current analysis, reduced LVEFs were identified in one third of the study population and associated with an increased risk of adverse events. For those patients with AMI with reduced LVEF, there was no significant difference the clinical outcomes between FFR-guided and angiography-guided decision making for non-IRA lesions. Although the FFR-guided strategy used fewer stents, which was related to improvements in stent-related events, this relationship did not exist for patients with reduced LVEF. Our findings present the opposite results from the study conducted by Di Gioia et al,¹² which demonstrated that an FFR-guided strategy in patients with reduced LVEF significantly reduced adverse cardiovascular and cerebrovascular events at 5 years compared with angiography-guided treatment. The discrepancies in outcomes may be attributed to differences in study populations, as Di Gioia et al included patients with chronic coronary artery disease and excluded those with acute coronary syndromes. In contrast, our study focused on patients with AMI

Table 2. Baseline Procedural Characteristics

Characteristics	Preserved LVEF (N=375)			Reduced LVEF (N=187)		
	FFR-guided (n=195)	Angiography-guided (n=180)	P value	FFR-guided (n=89)	Angiography-guided (n=98)	P value
Index procedure						
Symptom to door time, min						
ST-segment-elevation MI	119.5 (56.0–405.0)	95.0 (42.0–210.0)	0.263	143.0 (66.0–260.0)	121.0 (61.0–285.0)	0.604
Non-ST-segment-elevation MI	806.0 (612.0–971.0)	824.0 (588.0–965.0)	0.979	778.0 (624.0–1061.5)	790.0 (696.0–1107.0)	0.664
Door to balloon time, min						
ST-segment-elevation MI	68.5 (52.0–89.0)	65.0 (50.0–78.0)	0.221	73.0 (58.5–88.5)	73.0 (61.0–88.5)	0.802
Non-ST-segment-elevation MI	581.0 (208.0–1143.0)	373.0 (166.0–1057.0)	0.096	804.0 (310.5–1124.0)	660.0 (201.5–1151.0)	0.713
SYNTAX score						
Baseline score, including IRA	15.0 (11.0–20.8)	14.0 (10.0–21.0)	0.331	17.5 (14.0–25.5)	17.2 (13.0–24.5)	0.309
Residual score, after non-IRA PCI	3.2 (0.0–5.5)	0.0 (0.0–2.0)	<0.001	3.0 (0.0–6.0)	0.0 (0.0–3.0)	<0.001
Pre-PCI FFR	0.78±0.11 0.79 (0.16–0.97)	NA	NA	0.81±0.13 0.82 (0.36–0.99)	NA	NA
PCI of infarct related artery						
Location of IRA			0.881			0.083
Left anterior descending artery	51 (26.2)	47 (26.1)		39 (43.8)	58 (59.2)	
Circumflex artery	54 (27.7)	46 (25.6)		15 (16.9)	15 (15.3)	
Right coronary artery	90 (46.2)	87 (48.3)		35 (39.3)	25 (25.5)	
Radial access	168 (86.2)	150 (83.3)	0.538	74 (83.1)	79 (80.6)	0.796
Thrombus aspiration	30 (15.4)	29 (16.1)	0.959	22 (24.7)	16 (16.3)	0.214
Glycoprotein IIb/IIIa inhibitor use	38 (19.5)	23 (12.8)	0.105	23 (25.8)	22 (22.4)	0.711
Treatment method			0.254			0.115
Drug-eluting stent	191 (97.9)	179 (100.0)		86 (96.6)	97 (99.0)	
Drug-coated balloon angioplasty	3 (1.5)	0 (0)		0 (0)	1 (1.0)	
Aspiration thrombectomy only	1 (0.5)	0 (0)		3 (3.4)	0 (0)	
Intravascular imaging used	49 (25.3)	34 (18.9)	0.175	14 (15.7)	25 (25.5)	0.178
Direct stenting	15 (7.7)	16 (8.9)	0.816	8 (9.0)	11 (11.2)	0.793
Mean no. of stents used per patient	1.2±0.5	1.2±0.5	0.750	1.3±0.7	1.2±0.4	0.350
Dimensions of stents, mm						
Mean diameter	3.2±0.5	3.2±0.6	0.584	3.1±0.4	3.1±0.4	0.482
Total length	34.4±15.6	34.1±15.6	0.850	40.6±22.6	35.9±15.0	0.103
Procedural success	195 (100.0)	179 (99.4)	0.480	89 (100.0)	98 (100.0)	1.000
PCI of non-IRA						
Timing of non-IRA PCI			0.692			0.889
Immediate PCI during same procedure	123 (63.1)	109 (60.6)		49 (55.1)	56 (57.1)	
Staged intervention during same hospitalization	72 (36.9)	71 (39.4)		40 (44.9)	42 (42.9)	
At least 1 non-IRA treated	127 (65.1)	173 (96.1)	<0.001	55 (61.8)	97 (99.0)	<0.001
Treatment method			0.311			1.000
Drug-eluting stent	125 (98.4)	166 (96.0)		52 (94.5)	90 (92.8)	
Drug-coated balloon angioplasty	2 (1.6)	7 (4.0)		3 (5.5)	6 (6.2)	
Plain balloon angioplasty	0 (0)	0 (0)		0 (0)	1 (1.0)	
Intravascular imaging used	43 (33.9)	52 (30.1)	0.566	14 (25.5)	25 (25.8)	1.000
Mean no. of stents used per patient	0.9±0.9	1.3±0.7	<0.001	0.9±1.0	1.4±0.7	<0.001

(Continued)

Table 2. Continued

Characteristics	Preserved LVEF (N=375)			Reduced LVEF (N=187)		
	FFR-guided (n=195)	Angiography-guided (n=180)	P value	FFR-guided (n=89)	Angiography-guided (n=98)	P value
Dimensions of stents, mm						
Mean diameter	3.0±0.4	3.0±0.5	0.725	3.0±0.4	3.1±0.5	0.169
Total length	40.9±19.2	37.0±19.3	0.085	40.6±25.8	36.8±22.8	0.343
Procedural success	127 (100.0)	172 (99.4)	1.000	53 (96.4)	94 (96.9)	0.525
Procedural characteristics						
Total no. of stents used per patient	2.1±1.0	2.5±0.9	<0.001	2.2±1.2	2.6±0.9	0.015
Volume of contrast media used, mL						
During index procedure	187.6±75.4	195.9±80.5	0.316	181.9±85.9	193.4±81.5	0.365
During staged procedure	136.7±73.8	146.2±57.9	0.390	113.0±64.5	140.7±68.2	0.058
Total amount during hospitalization	294.1±108.4	307.1±110.8	0.483	246.1±81.5	303.4±105.8	0.006
Complications during hospitalization						
Any complications	8 (4.1)	10 (5.6)	0.678	4 (4.5)	6 (6.1)	0.750
Congestive heart failure	0 (0)	3 (1.7)	0.110	0 (0)	2 (2.0)	0.498
Cardiogenic shock	2 (1.0)	4 (2.2)	0.433	2 (2.2)	0 (0%)	0.225
Resuscitated cardiac arrest	0 (0)	2 (1.1)	0.230	0 (0)	0 (0)	1.000
Anaphylactic reaction to contrast agent	1 (0.5)	0 (0)	1.000	0 (0)	0 (0)	1.000
Access-site bleeding	2 (1.0)	2 (1.1)	1.000	0 (0)	0 (0)	1.000
Non-access-site bleeding	1 (0.5)	2 (1.1)	0.610	1 (1.1)	1 (1.0)	1.000
Hospital-acquired infection	1 (0.5)	0 (0)	1.000	1 (1.1)	2 (2.0)	1.000
Arrhythmia	2 (1.0)	1 (0.6)	1.000	0 (0)	0 (0)	1.000
Median length of hospital stay, d	2.0 (1.5–4.0)	2.0 (1.0–4.0)	0.989	4.0 (2.0–5.0)	3.0 (2.0–5.0)	0.157

Data presented as mean±SD, median (interquartile range), or as n (%). FFR indicates fractional flow reserve; IRA, infarct-related artery; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NA, not available; and PCI, percutaneous coronary intervention.

with multivessel disease, which inherently represents a more dynamic clinical scenario with distinct physiological and pathological considerations. Additionally, one plausible explanation for this finding is that the potential underestimation of FFR values in the setting of nonviable myocardium and heterogeneous microvascular impairment could diminish its prognostic utility in patients with reduced LVEF. Meanwhile, the beneficial effect of FFR-guided PCI for non-IRA lesions was more evident than that of angiography-guided PCI among patients with preserved LVEF in terms of a reduced risk of hard end points like cardiac death and MI. Additionally, the clinical benefits of FFR-guided PCI were increased with an increase in LVEF. Interestingly, Kang et al³⁰ analyzed 1314 cases of ST-segment-elevation MI with multivessel disease and reported that complete revascularization did not reduce the number of clinical events during a 3-year follow-up among patients with reduced LVEF. Despite the current analysis and previous study, however, more evidence is needed to confirm the role of FFR-guided decision making for non-IRAs in patients with AMI with reduced LVEF. More importantly, since our fundamental goal of treating AMI is saving myocardium and lives, the importance of appropriate intensive

medical treatment should also be considered beyond the local therapy of vessels.

STUDY LIMITATIONS

There are several limitations in the current analysis that need to be addressed. First, although this was a prespecified substudy of the FRAME-AMI randomized controlled trial, it might not have had enough power to conclude our findings. Furthermore, due to the relatively small sample size in the reduced LVEF group, there is a possibility of a type II error. Therefore, further studies with larger cohorts are needed to confirm our results. Second, follow-up echocardiograms were not collected for the study population. Therefore, the changes in LVEF could not be evaluated in the current study. Third, treatments with sodium-glucose cotransporter 2 and angiotensin receptor-neprylisin inhibitors have been recommended as guideline-directed medical therapy. However, prescription rates of these medications were not available because they were not covered by national health insurance and were not recommended as part of routine practice during the study enrollment

Table 3. Primary and Secondary End Points

End Point	FFR-guided	Angiography-guided	Hazard ratio (95% CI)	P value
Preserved LVEF ($\geq 50\%$)	N=195	N=180		
Primary end point				
Major adverse cardiovascular events Death, myocardial infarction, and repeat revascularization	6 (3.3)	20 (19.0)	0.26 (0.11–0.66)	0.004
Secondary end point [†]				
All-cause death	2 (1.0)	8 (8.6)	0.22 (0.04–1.05)	
Cardiac death	1 (0.5)	8 (8.6)	0.11 (0.01–0.89)	
Myocardial infarction	1 (0.5)	10 (7.3)	0.09 (0.01–0.70)	
- Procedure-related myocardial infarction	1 (0.5)	5 (2.8)	0.18 (0.02–1.57)	
- Spontaneous myocardial infarction	0 (0)	5 (4.6)	NA	
Repeat revascularization	3 (1.8)	9 (9.5)	0.30 (0.08–1.09)	
- Infarct-related artery	1 (0.7)	5 (5.7)	0.18 (0.02–1.53)	
- Non-infarct related artery	3 (1.8)	6 (5.2)	0.45 (0.11–1.81)	
Definite stent thrombosis	0 (0)	1 (0.6)	NA	
Cerebrovascular accident	1 (0.5)	2 (1.1)	0.46 (0.04–5.05)	
Contrast induced nephropathy [‡]	0 (0)	0 (0)	NA	
Reduced LVEF ($< 50\%$)	N=89	N=98		
Primary end point				
Major adverse cardiovascular events Death, myocardial infarction, and repeat revascularization	12 (17.0)	20 (21.0)	0.64 (0.31–1.31)	0.225
Secondary end point [*]				
All-cause death	3 (5.0)	8 (8.3)	0.41 (0.11–1.55)	
Cardiac death	2 (3.9)	7 (7.3)	0.31 (0.07–1.52)	
Myocardial infarction	6 (6.7)	11 (11.8)	0.58 (0.21–1.57)	
- Procedure-related myocardial infarction	2 (2.2)	6 (6.1)	0.36 (0.07–1.79)	
- Spontaneous myocardial infarction	4 (4.5)	5 (5.7)	0.87 (0.23–3.25)	
Repeat revascularization	7 (10.1)	7 (8.0)	1.12 (0.39–3.18)	
- Infarct-related artery	3 (5.8)	3 (3.3)	1.12 (0.23–5.54)	
- Non-infarct-related artery	4 (4.5)	6 (7.0)	0.73 (0.21–2.58)	
Definite stent thrombosis	0 (0)	0 (0)	NA	
Cerebrovascular accident	3 (3.4)	1 (1.0)	3.28 (0.34–31.57)	
Contrast induced nephropathy [‡]	2 (2.2)	1 (1.0)	2.23 (0.20–24.56)	

Data presented as n (%). The database for the analysis presented here was locked on April 12, 2022. Clinical end points were evaluated in the intention-to-treat population during the overall study period (ie, beginning from the time of randomization to the day of the first occurrence of a primary end-point event, the day of the last office or phone visit, or the day of death during follow-up). Percentages are 4-year Kaplan–Meier estimates. FFR indicates fractional flow reserve; IPTW, inverse probability treatment-weighting; LVEF, left ventricular ejection fraction; and NA, not applicable.

^{*}The individual end points listed are the first occurrence of that event.

[†]Contrast-induced nephropathy is defined as an increase in serum creatinine of ≥ 0.5 mg/dL or $\geq 25\%$ from baseline within 48 to 72 hours after contrast agent exposure.

period. Fourth, data on myocardial viability for non-IRA lesions were not available in this study. Fifth, identifying the IRA lesions for non-ST-segment-elevation MI is sometimes questionable. Although the study protocol recommended echocardiography and intravascular imaging for assessing the IRA lesions, data on the frequency of adjunctive examinations were not available.

CONCLUSIONS

In a population of patients with AMI with multivessel disease, one third had reduced LVEF, which was associated with an increased 3.5-year MACE risk compared with those with preserved LVEF. FFR-guided PCI for non-IRA lesions significantly reduced future

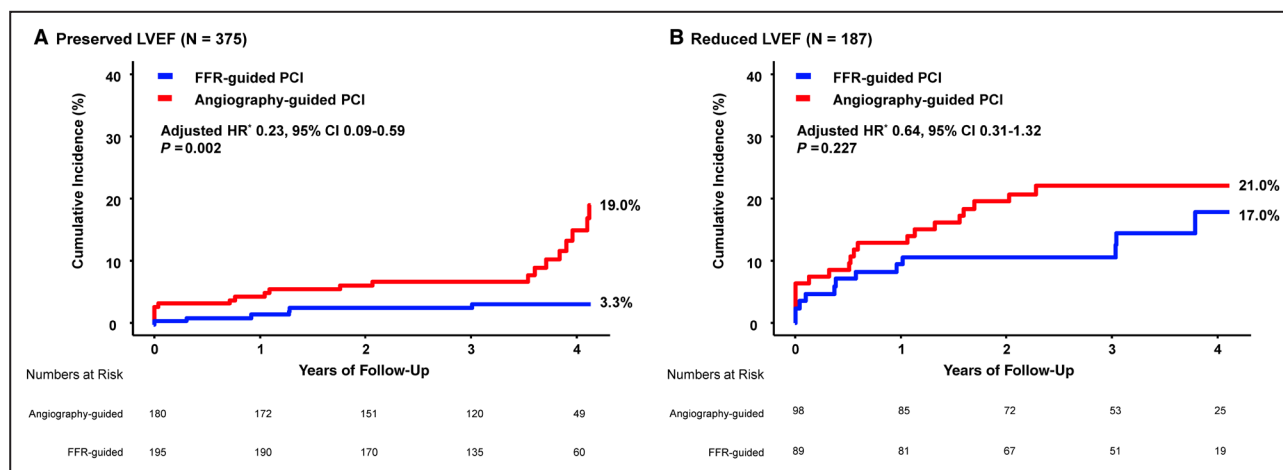


Figure 3. Kaplan–Meier curves for MACEs according to the treatment strategy for non-IRAs.

MACEs, a composite of time to death, MI, or repeat revascularization, were compared in patients with (A) preserved LVEF ($\geq 50\%$) and (B) reduced LVEF ($< 50\%$) during the overall study period (median, 3.5 years). *Multivariable model included the variables of age, sex, body mass index, initial presentation (ST-segment-elevation MI vs non-ST-segment-elevation MI), diabetes, and chronic renal insufficiency. FFR indicates fractional flow reserve; HR, hazard ratio; IRA, infarct-related artery; LVEF, left ventricular ejection fraction; MACE, major adverse cardiac event; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

adverse events compared with angiography-guided PCI among patients with preserved LVEF. Conversely, there was no significant difference in clinical outcomes between FFR-guided and angiography-guided PCI among patients with reduced LVEF. These results support the notion that the clinical impact of FFR-guided decision making differs according to the left ventricular systolic function among patients with AMI with multi-vessel disease.

ARTICLE INFORMATION

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Supplemental Material

Data S1
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REFERENCES

- Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, Claeys MJ, Dan GA, Dweck MR, Galbraith M, et al. 2023 ESC guidelines for the management of acute coronary syndromes. *Eur Heart J*. 2023;44:3720–3826. doi: [10.1093/eurheartj/ehad191](https://doi.org/10.1093/eurheartj/ehad191)
- Secemsky EA, Butala N, Raja A, Khera R, Wang Y, Curtis JP, Maddox TM, Virani SS, Armstrong EJ, Shunk KA, et al. Temporal changes and institutional variation in use of percutaneous coronary intervention for ST-elevation myocardial infarction with multivessel coronary artery disease in the United States: an NCDR research to practice project. *JAMA Cardiol*. 2021;6:574–580. doi: [10.1001/jamacardio.2020.5354](https://doi.org/10.1001/jamacardio.2020.5354)
- Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J*. 2019;40:87–165. doi: [10.1093/eurheartj/ehy394](https://doi.org/10.1093/eurheartj/ehy394)

4. Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM, Bischoff JM, Bittl JA, Cohen MG, DiMaio JM, Don CW, et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *Circulation*. 2022;145:e18–e114. doi: [10.1161/cir.0000000000001038](https://doi.org/10.1161/cir.0000000000001038)
5. Wald DS, Morris JK, Wald NJ, Chase AJ, Edwards RJ, Hughes LO, Berry C, Oldroyd KG. Randomized trial of preventive angioplasty in myocardial infarction. *N Engl J Med*. 2013;369:1115–1123. doi: [10.1056/NEJMoa1305520](https://doi.org/10.1056/NEJMoa1305520)
6. Gershlick AH, Khan JN, Kelly DJ, Greenwood JP, Sasikaran T, Curzen N, Blackman DJ, Dalby M, Fairbrother KL, Banya W, et al. Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease: the CvLPRIT trial. *J Am Coll Cardiol*. 2015;65:963–972. doi: [10.1016/j.jacc.2014.12.038](https://doi.org/10.1016/j.jacc.2014.12.038)
7. Engstrom T, Kelbaek H, Helqvist S, Hofsten DE, Klovgaard L, Holmvang L, Jorgensen E, Pedersen F, Saunamaki K, Clemmensen P, et al. Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3-PRIMULTI): an open-label, randomised controlled trial. *Lancet*. 2015;386:665–671. doi: [10.1016/s0140-6736\(15\)60648-1](https://doi.org/10.1016/s0140-6736(15)60648-1)
8. Smits PC, Abdel-Wahab M, Neumann FJ, Boxma-de Klerk BM, Lunde K, Schotborgh CE, Piroth Z, Horak D, Wlodarczak A, Ong PJ, et al. Fractional flow reserve-guided multivessel angioplasty in myocardial infarction. *N Engl J Med*. 2017;376:1234–1244. doi: [10.1056/NEJMoa1701067](https://doi.org/10.1056/NEJMoa1701067)
9. Mehta SR, Wood DA, Storey RF, Mehran R, Bainey KR, Nguyen H, Meeks B, Di Pasquale G, Lopez-Sendon J, Faxon DP, et al. Complete revascularization with multivessel PCI for myocardial infarction. *N Engl J Med*. 2019;381:1411–1421. doi: [10.1056/NEJMoa1907775](https://doi.org/10.1056/NEJMoa1907775)
10. Puymirat E, Cayla G, Simon T, Steg PG, Montalescot G, Durand-Zaleski I, le Bras A, Gallet R, Khalife K, Morelle JF, et al. Multivessel PCI guided by FFR or angiography for myocardial infarction. *N Engl J Med*. 2021;385:297–308. doi: [10.1056/NEJMoa2104650](https://doi.org/10.1056/NEJMoa2104650)
11. Lee JM, Kim HK, Park KH, Choo EH, Kim CJ, Lee SH, Kim MC, Hong YJ, Ahn SG, Doh JH, et al. Fractional flow reserve versus angiography-guided strategy in acute myocardial infarction with multivessel disease: a randomized trial. *Eur Heart J*. 2023;44:473–484. doi: [10.1093/eurheartj/ehac763](https://doi.org/10.1093/eurheartj/ehac763)
12. Di Gioia G, De Bruyne B, Pellicano M, Bartunek J, Colaiori I, Fiordelisi A, Cancelli G, Xaplanteris P, Fournier S, Katbeh A, et al. Fractional flow reserve in patients with reduced ejection fraction. *Eur Heart J*. 2020;41:1665–1672. doi: [10.1093/eurheartj/ehz571](https://doi.org/10.1093/eurheartj/ehz571)
13. Toth GG, Johnson NP, Jeremias A, Pellicano M, Vranckx P, Fearon WF, Barbato E, Kern MJ, Pijls NH, De Bruyne B. Standardization of fractional flow reserve measurements. *J Am Coll Cardiol*. 2016;68:742–753. doi: [10.1016/j.jacc.2016.05.067](https://doi.org/10.1016/j.jacc.2016.05.067)
14. Levine GN, Bates ER, Bittl JA, Brindis RG, Fihn SD, Fleisher LA, Granger CB, Lange RA, Mack MJ, Mauri L, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention, 2011 ACCF/AHA guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and Management of Patients with Stable Ischemic Heart Disease, 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction, 2014 AHA/ACC guideline for the Management of Patients with non-ST-elevation acute coronary syndromes, and 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and Management of Patients Undergoing Noncardiac Surgery. *Circulation*. 2016;134:e123–e155. doi: [10.1161/cir.0000000000000404](https://doi.org/10.1161/cir.0000000000000404)
15. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, Flachskampf FA, Gillebert TC, Klein AL, Lancellotti P, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2016;29:277–314. doi: [10.1016/j.echo.2016.01.011](https://doi.org/10.1016/j.echo.2016.01.011)
16. Garcia-Garcia HM, McFadden EP, Farb A, Mehran R, Stone GW, Spertus J, Onuma Y, Morel MA, van Es GA, Zuckerman B, et al. Standardized end point definitions for coronary intervention trials: the academic research Consortium-2 consensus document. *Circulation*. 2018;137:2635–2650. doi: [10.1161/CIRCULATIONAHA.117.029289](https://doi.org/10.1161/CIRCULATIONAHA.117.029289)
17. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, Katus HA, Lindahl B, Morrow DA, Clemmensen PM, et al. Third universal definition of myocardial infarction. *Circulation*. 2012;126:2020–2035. doi: [10.1161/CIR.0b013e31826e1058](https://doi.org/10.1161/CIR.0b013e31826e1058)
18. Stone GW, Maehara A, Lansky AJ, de Bruyne B, Cristea E, Mintz GS, Mehran R, McPherson J, Farhat N, Marso SP, et al. A prospective natural-history study of coronary atherosclerosis. *N Engl J Med*. 2011;364:226–235. doi: [10.1056/NEJMoa1002358](https://doi.org/10.1056/NEJMoa1002358)
19. Lee SH, Hong D, Shin D, Kim HK, Park KH, Choo EH, Kim CJ, Kim MC, Hong YJ, Ahn SG, et al. QFR assessment and prognosis after nonculprit PCI in patients with acute myocardial infarction. *JACC Cardiovasc Interv*. 2023;16:2365–2379. doi: [10.1016/j.jcin.2023.08.032](https://doi.org/10.1016/j.jcin.2023.08.032)
20. Biscaglia S, Guiducci V, Escaned J, Moreno R, Lanzillotti V, Santarelli A, Cerrato E, Sacchetta G, Jurado-Roman A, Menozzi A, et al. Complete or culprit-only PCI in older patients with myocardial infarction. *N Engl J Med*. 2023;389:889–898. doi: [10.1056/NEJMoa2300468](https://doi.org/10.1056/NEJMoa2300468)
21. Böhm F, Mogensen B, Engström T, Stankovic G, Srdanovic I, Lønborg J, Zwackman S, Hamid M, Kellerth T, Lauermann J, et al. FFR-guided complete or culprit-only PCI in patients with myocardial infarction. *N Engl J Med*. 2024;390:1481–1492. doi: [10.1056/NEJMoa2314149](https://doi.org/10.1056/NEJMoa2314149)
22. Puymirat E, Cayla G, Simon T, Steg PG, Montalescot G, Durand-Zaleski I, Ngaleu Siahia F, Gallet R, Khalife K, Morelle JF, et al. Three-year outcomes with fractional flow reserve-guided or angiography-guided multivessel percutaneous coronary intervention for myocardial infarction. *Circ Cardiovasc Interv*. 2024;17:e013913. doi: [10.1161/circinterventions.123.013913](https://doi.org/10.1161/circinterventions.123.013913)
23. Sobel BE, Bresnahan GF, Shell WE, Yoder RD. Estimation of infarct size in man and its relation to prognosis. *Circulation*. 1972;46:640–648. doi: [10.1161/01.cir.46.4.640](https://doi.org/10.1161/01.cir.46.4.640)
24. Thanavaro S, Kleiger RE, Province MA, Hubert JW, Miller JP, Krone RJ, Oliver GC. Effect of infarct location on the in-hospital prognosis of patients with first transmural myocardial infarction. *Circulation*. 1982;66:742–747. doi: [10.1161/01.cir.66.4.742](https://doi.org/10.1161/01.cir.66.4.742)
25. Sorajja P, Gersh BJ, Cox DA, McLaughlin MG, Zimetbaum P, Costantini C, Stuckey T, Tcheng JE, Mehran R, Lansky AJ, et al. Impact of multivessel disease on reperfusion success and clinical outcomes in patients undergoing primary percutaneous coronary intervention for acute myocardial infarction. *Eur Heart J*. 2007;28:1709–1716. doi: [10.1093/eurheartj/ehm184](https://doi.org/10.1093/eurheartj/ehm184)
26. Henkel DM, Witt BJ, Gersh BJ, Jacobsen SJ, Weston SA, Meverden RA, Roger VL. Ventricular arrhythmias after acute myocardial infarction: a 20-year community study. *Am Heart J*. 2006;151:806–812. doi: [10.1016/j.ahj.2005.05.015](https://doi.org/10.1016/j.ahj.2005.05.015)
27. Jenča D, Melenovský V, Stehlík J, Staněk V, Kettner J, Adámková V, Wohlfahrt P. Heart failure after myocardial infarction: incidence and predictors. *ESC Heart Failure*. 2021;8:222–237. doi: [10.1002/ehf2.13144](https://doi.org/10.1002/ehf2.13144)
28. Camaj A, Fuster V, Giustino G, Bienstock SW, Sternheim D, Mehran R, Dangas GD, Kini A, Sharma SK, Halperin J, et al. Left ventricular thrombus following acute myocardial infarction: JACC state-of-the-art review. *J Am Coll Cardiol*. 2022;79:1010–1022. doi: [10.1016/j.jacc.2022.01.011](https://doi.org/10.1016/j.jacc.2022.01.011)
29. Kobayashi Y, Tonino PA, De Bruyne B, Yang HM, Lim HS, Pijls NH, Fearon WF. The impact of left ventricular ejection fraction on fractional flow reserve: insights from the FAME (fractional flow reserve versus angiography for multivessel evaluation) trial. *Int J Cardiol*. 2016;204:206–210. doi: [10.1016/j.ijcard.2015.11.169](https://doi.org/10.1016/j.ijcard.2015.11.169)
30. Kang J, Zheng C, Park KW, Park J, Rhee T, Lee HS, Han JK, Yang HM, Kang HJ, Koo BK, et al. Complete revascularization of multivessel coronary artery disease does not improve clinical outcome in ST-segment elevation myocardial infarction patients with reduced left ventricular ejection fraction. *J Clin Med*. 2020;9:9. doi: [10.3390/jcm9010232](https://doi.org/10.3390/jcm9010232)
31. Pijls NH, Fearon WF, Tonino PA, Siebert U, Ikeno F, Bornschein B, van't Veer M, Klauss V, Manoharan G, Engstrom T, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention in patients with multivessel coronary artery disease: 2-year follow-up of the FAME (fractional flow reserve versus angiography for multivessel evaluation) study. *J Am Coll Cardiol*. 2010;56:177–184. doi: [10.1016/j.jacc.2010.04.012](https://doi.org/10.1016/j.jacc.2010.04.012)
32. Sels JW, Tonino PA, Siebert U, Fearon WF, Van't Veer M, De Bruyne B, Pijls NH. Fractional flow reserve in unstable angina and non-ST-segment elevation myocardial infarction experience from the FAME (fractional flow reserve versus angiography for multivessel evaluation) study. *JACC Cardiovasc Interv*. 2011;4:1183–1189. doi: [10.1016/j.jcin.2011.08.008](https://doi.org/10.1016/j.jcin.2011.08.008)
33. Sardella G, Lucisano L, Garbo R, Pennacchi M, Cavallo E, Stio RE, Calcagno S, Ugo F, Boccuzzi G, Fedele F, et al. Single-staged compared with multi-staged PCI in multivessel NSTEMI patients: the SMILE trial. *J Am Coll Cardiol*. 2016;67:264–272. doi: [10.1016/j.jacc.2015.10.082](https://doi.org/10.1016/j.jacc.2015.10.082)