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Surveillance Stress Testing After Percutaneous Intervention for Patients With Multivessel or Left Main Coronary Disease

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ABSTRACT

BACKGROUND The optimal surveillance strategy after percutaneous coronary intervention (PCI) for high-risk patients with multivessel or left main coronary artery disease (CAD) remains uncertain.

OBJECTIVES This study aims to determine the prognostic role of routine functional testing in patients with multivessel or left main CAD who underwent PCI.

METHODS The POST-PCI (Pragmatic Trial Comparing Symptom-Oriented Versus Routine Stress Testing in High-Risk Patients Undergoing Percutaneous Coronary Intervention) trial randomized high-risk PCI patients to routine functional testing at 1 year or standard care alone during follow-up. This analysis focused on participants with multivessel or left main CAD. The primary outcome was a composite of death from any cause, myocardial infarction, or hospitalization for unstable angina at 2 years.

RESULTS Among 1,706 initially randomized patients, 1,192 patients with multivessel (n = 833) or left main (n = 359) were identified, with 589 in the functional testing group and 603 in the standard care group. Two-year incidences of primary outcome were similar between the functional testing group and the standard care group (6.2% vs 5.7%, respectively; HR: 1.09; 95% CI: 0.68-1.74; $P = 0.73$). This trend persisted in both groups of multivessel (6.2% vs 5.7%; HR: 1.09; 95% CI: 0.62-1.89; $P = 0.78$) and left main disease (6.2% vs 5.7%; HR: 1.09; 95% CI: 0.46-2.56; $P = 0.85$) (P for interaction = 0.90). Routine surveillance functional testing was associated with increased rates of invasive angiography and repeat revascularization beyond 1 year.

CONCLUSIONS In high-risk patients with multivessel or left main CAD who underwent PCI, there was no incremental clinical benefit from routine surveillance functional-testing compared with standard care alone during follow-up. (Pragmatic Trial Comparing Symptom-Oriented Versus Routine Stress Testing in High-Risk Patients Undergoing Percutaneous Coronary Intervention [POST-PCI]; NCT03217877) (J Am Coll Cardiol 2024;83:890-900) © 2024 by the American College of Cardiology Foundation.

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Although coronary artery bypass grafting is recommended as the standard revascularization strategy for patients with multivessel or left main coronary artery disease (CAD),[1,2] percutaneous coronary intervention (PCI) with the advancement of drug-eluting stents (DES), procedural techniques, and adjunctive pharmacology has also been widely performed for these high-risk patients in the daily clinical practice.[3,4] However, despite aggressive secondary prevention with guideline-directed medical therapy, comprehensive lifestyle changes and attainment of multiple, specific risk factor goals, the incidence of death, myocardial infarction (MI), or repeat revascularization remains substantial after multivessel or left main PCI during follow-up.[5-8] The optimal follow-up surveillance strategy after PCI in high-risk patients with multivessel or left main disease remains undefined. Although cardiac stress testing has been commonly performed after complex PCI in routine clinical practice,[9-12] whether patients with multivessel or left main disease who underwent PCI could benefit from routine functional testing after myocardial revascularization remains undetermined.

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In the clinical context, given that more aggressive forms of CAD, complex PCI procedures, and incomplete revascularization and residual ischemia are common in patients with multivessel or left main disease, clinicians should determine whether such high-risk PCI patients could benefit from routine surveillance testing in a reduction of adverse cardiovascular events during follow-up. Therefore, using contemporary data from the POST-PCI (Pragmatic Trial Comparing Symptom-Oriented Versus Routine Stress Testing in High-Risk Patients Undergoing Percutaneous Coronary Intervention) study, a randomized trial of follow-up evaluation strategies in high-risk patients who had undergone PCI,[13,14] we assessed whether the risk of cardiovascular outcomes differed between an active follow-up strategy of routine functional testing and standard care alone in patients with multivessel or left main CAD who underwent PCI.

METHODS

STUDY DESIGN AND PATIENT POPULATION. The study design, methods, and primary results of the POST-PCI trial have been described previously.[13] In brief, the POST-PCI trial was an investigator-initiated, multicenter, pragmatic, and randomized trial conducted at 11 hospitals in South Korea from November 2017 to September 2019. A total of 1,706 patients with high-risk anatomical or clinical characteristics who had undergone PCI were randomly assigned in a 1:1 ratio to undergo an active follow-up strategy of routine functional testing at 1 year after PCI (n = 849) or to undergo a conservative follow-up strategy of standard care (n = 857). The trial was approved by the Investigational Review Board or ethics committee at each participating center. All patients provided written informed consent before enrollment.

In the POST-PCI trial, participants were required to have at least 1 high-risk anatomical or clinical characteristic associated with an increased risk of ischemic or thrombotic events. Anatomical high-risk characteristics included multivessel CAD (requiring stenting of at least 2 vessels), left main disease, bifurcation disease, an ostial lesion, chronic total occlusion, a restenosis lesion, a long diffuse lesion, and bypass graft disease. Clinical high-risk characteristics included medically treated diabetes mellitus, chronic renal failure, and enzyme-positive acute coronary syndrome. All patients underwent successful PCI with contemporary DES, bioresorbable scaffolds, or drug-coated balloons (only for in-stent restenosis).

In the present subgroup analysis, we focused on high-risk patients with either multivessel or left main CAD who had undergone PCI. We conducted separate analyses for the entire group of patients with multivessel or left main CAD and individually for those with multivessel disease and those with left main disease. The multivessel disease group comprised patients with multivessel disease without left main disease. In contrast, the left main disease group included patients with any left main disease irrespective of the number of diseased vessels as previously classified.[15]

TRIAL PROCESSES AND FOLLOW-UP. Detailed trial processes and follow-up plans of the POST-PCI trial have been reported.[13,14] Patients in the routine functional testing group were subjected to routine cardiac stress testing comprising exercise electrocardiography (ECG), nuclear stress testing, or stress echocardiography at 12 months after randomization. Because of the high likelihood of false-positive exercise ECG test results indicating myocardial ischemia, simple exercise ECG testing only was discouraged; thus, a combined noninvasive imaging strategy was strongly recommended. In the standard care group, stress testing was only performed when clinically indicated during follow-up. In keeping with the

ABBREVIATIONS AND ACRONYMS

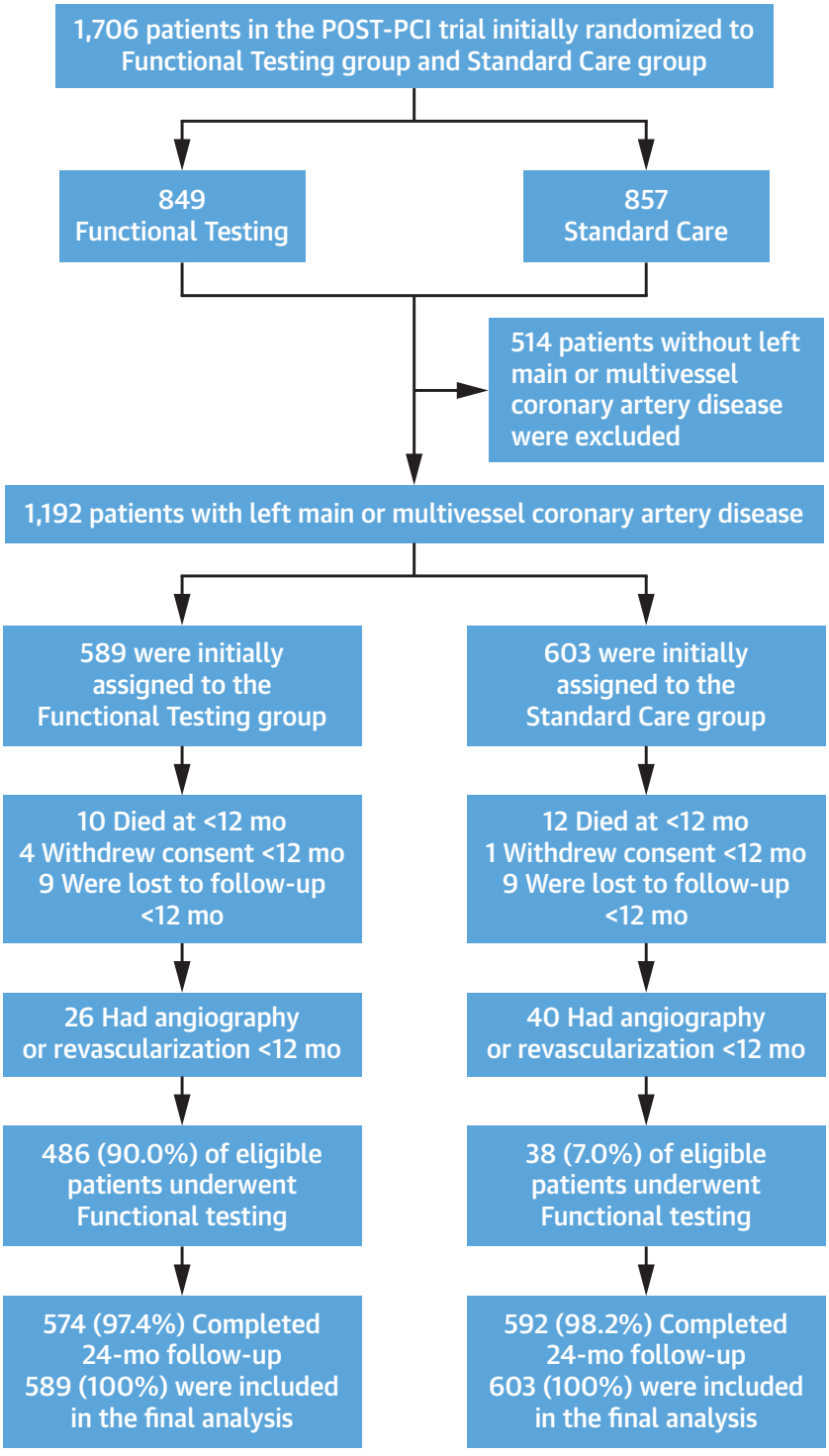
CAD = coronary artery disease

ECG = exercise electrocardiography

MI = myocardial infarction

PCI = percutaneous coronary intervention

FIGURE 1 **Study Flow Chart**



Patients who were eligible to undergo functional testing included those who at 1 year after randomization had not died, had not withdrawn, were not lost to follow-up, and had not had clinically driven angiography or revascularization. Percentages may not total 100 because of rounding. POST-PCI = Pragmatic Trial Comparing Symptom-Oriented Versus Routine Stress Testing in High-Risk Patients Undergoing Percutaneous Coronary Intervention.

pragmatic design of the POST-PCI trial, the test findings were based on real-time, site-based interpretation of all functional test results, thereby ensuring the timely availability of the results for patient management. All clinical decisions regarding further diagnostic or therapeutic procedures and subsequent management were made at the discretion of the treating physician at each participating center.

STUDY OUTCOMES AND FOLLOW-UP. The primary outcome of the POST-PCI trial was a composite of major cardiovascular events consisting of death from any cause, MI, or hospitalization for unstable angina at 2 years after randomization. Secondary outcomes included the following: individual components of the primary composite outcome; a composite of death or myocardial infarction; hospitalization for any reason (for either cardiac causes or noncardiac causes); invasive coronary angiography; and repeat revascularization procedures (target-lesion or nontarget-lesion revascularization). Definitions of each clinical endpoint have been described previously,[13] and all components of clinical endpoints were independently adjudicated by a clinical events committee, the members of which were unaware of the treatment assignments.

Enrolled patients underwent routine clinical follow-up at 6, 12, 18, and 24 months. During follow-up, guideline-directed medical therapy and management of risk factors for comprehensive secondary prevention were highly emphasized. All information on clinical events and cardiovascular medicines was systematically obtained at each clinical visit. Vital status was reconfirmed by checking the national death registry of the Korean National Health Insurance Service database.

STATISTICAL ANALYSIS. All statistical analyses were performed on an intention-to-treat basis. For baseline characteristics and procedural data, continuous variables are presented as mean ± SD and were compared with Student's *t*-tests; discrete data are presented as frequencies and were compared with chi-square or Fisher exact test, as appropriate.

Kaplan-Meier estimates of the cumulative incidence of primary and secondary outcomes by randomized follow-up strategy in the entire cohort and in each cohort of multivessel or left main disease were plotted in which the log-rank test was used to assess differences of outcomes. Cumulative event probabilities were estimated using the Kaplan-Meier method for outcomes. HRs and 95% CIs were

TABLE 1 Baseline Characteristics of Patients According to Randomized Follow-Up Strategy

	Functional Testing Group (n = 589)	Standard Care Group (n = 603)
Age, y	65.3 ± 9.9	65.2 ± 10.0
Male	456 (77.4)	490 (81.3)
Body mass index, kg/m^2	24.9 ± 2.9	25.0 ± 3.2
Cardiac risk factors and comorbidities[a]		
Hypertension	421 (71.5)	430 (71.3)
Diabetes	236 (40.1)	247 (41.0)
Dyslipidemia	511 (86.8)	535 (88.7)
Current smoker	154 (26.1)	168 (27.9)
Family history of premature CAD	37 (6.3)	35 (5.8)
Previous MI	31 (5.3)	41 (6.8)
Previous heart failure	10 (1.7)	18 (3.0)
Previous PCI	130 (22.1)	127 (21.1)
Previous CABG	19 (3.2)	18 (3.0)
History of cerebrovascular disease	36 (6.1)	52 (8.6)
History of peripheral artery disease	18 (3.1)	14 (2.3)
Atrial fibrillation or atrial flutter	18 (3.1)	11 (1.8)
Criteria for high risk after PCI		
High-risk anatomical characteristics		
Bifurcation disease	278 (47.2)	263 (43.6)
Ostial lesion	105 (17.8)	101 (16.7)
Chronic total occlusion	72 (12.2)	93 (15.4)
Restenotic lesion	46 (7.8)	57 (9.5)
Diffuse long lesion[b]	364 (61.8)	372 (61.7)
Bypass graft disease	2 (0.3)	1 (0.2)
High-risk clinical characteristics		
Diabetes on insulin	24 (4.1)	31 (5.1)
Chronic renal failure[c]	31 (5.3)	31 (5.1)
On dialysis	18 (3.1)	16 (2.7)
Enzyme-positive ACS	91 (15.4)	100 (16.6)
Clinical indication for index PCI		
Stable angina or silent ischemia	444 (75.4)	436 (72.3)
Unstable angina	54 (9.2)	67 (11.1)
NSTEMI	60 (10.2)	62 (10.3)
STEMI	31 (3.1)	38 (6.3)
Procedural characteristics		
Total diseased lesions per patient	2.7 ± 1.1	2.7 ± 1.0
Total treated lesions per patient	1.6 ± 0.8	1.6 ± 0.7
Total stents per patient	2.2 ± 1.1	2.2 ± 1.3
Total stent length per patient, mm	64.5 ± 35.0	65.6 ± 36.1
Use of drug-eluting stents	575 (97.6)	582 (96.5)
Use of bioabsorbable scaffold	4 (0.7)	5 (0.8)
Use of drug-coated balloon	37 (6.3)	49 (8.1)
Intravascular ultrasound guidance	459 (77.9)	469 (77.8)
Fractional flow reserve assessed	255 (43.3)	257 (42.6)

Values are mean ± SD or n (%) unless otherwise indicated. Percentages may not total 100 because of rounding.
[a]Patients who were eligible for participation in the trial were required to have at least 1 high-risk anatomical or clinical characteristic associated with an increased risk of ischemic or thrombotic events during follow-up.
[b]Diffuse long lesions were defined as lesions with a length of at least 30 mm or a stent length of at least 32 mm.
[c]Chronic renal failure was defined as a serum creatinine level of at least 2.0 mg/dL (177 μmol/L) or long-term receipt of hemodialysis.

ACS = acute coronary syndrome; CABG = coronary artery bypass grafting; CAD = coronary artery disease; MI = myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction.

TABLE 2 Concomitant Cardiac-Related Medications According to Randomized Follow-Up Strategy

	Functional Testing Group	Standard Care Group
At hospital discharge	589	603
Aspirin	580 (98.5)	598 (99.2)
$P2Y_{12}$ inhibitors	583 (99.0)	598 (99.2)
Oral anticoagulants[a]	18 (3.1)	15 (2.5)
Beta-blockers	408 (69.3)	411 (68.2)
ACE inhibitor or ARB	208 (35.3)	229 (38.0)
Calcium-channel blockers	390 (66.2)	407 (67.5)
Statins	577 (98.0)	593 (98.3)
6 months after randomization	576	590
Aspirin	491 (85.2)	509 (86.3)
$P2Y_{12}$ inhibitors	550 (95.5)	562 (95.3)
Oral anticoagulants[a]	20 (3.5)	14 (2.4)
Beta-blockers	391 (67.9)	395 (66.9)
ACE inhibitor or ARB	202 (35.1)	228 (38.6)
Calcium-channel blockers	339 (58.9)	348 (59.0)
Statins	557 (96.7)	575 (97.5)
12 months after randomization	568	584
Aspirin	362 (63.7)	373 (63.9)
$P2Y_{12}$ inhibitors	496 (87.3)	506 (86.6)
Oral anticoagulants[a]	23 (4.0)	15 (2.6)
Beta-blockers	381 (67.1)	390 (66.8)
ACE inhibitor or ARB	205 (36.1)	236 (40.4)
Calcium-channel blockers	339 (59.7)	338 (57.9)
Statins	554 (97.5)	568 (97.3)
18 months after randomization	558	576
Aspirin	320 (57.3)	319 (55.4)
$P2Y_{12}$ inhibitors	443 (79.4)	463 (80.4)
Oral anticoagulants[a]	28 (5.0)	22 (3.8)
Beta-blockers	371 (66.5)	385 (66.8)
ACE inhibitor or ARB	210 (37.6)	234 (40.6)
Calcium-channel blockers	331 (59.3)	327 (56.8)
Statins	552 (98.9)	568 (98.6)
24 months after randomization	557	573
Aspirin	312 (56.0)	310 (54.1)
$P2Y_{12}$ inhibitors	440 (79.0)	462 (80.6)
Oral anticoagulants[a]	28 (5.0)	22 (3.8)
Beta-blockers	374 (67.1)	381 (66.5)
ACE inhibitor or ARB	209 (37.5)	235 (41.0)
Calcium-channel blockers	326 (58.5)	323 (56.4)
Statins	552 (99.1)	566 (98.8)

Values are n or n (%). Percentages are from the intention-to-treat analysis. A window period (±2 months) was allowed at each time point during follow-up. [a]Oral anticoagulants were vitamin K antagonists or non-vitamin K antagonist oral anticoagulants.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker.

generated with Cox proportional hazards models. The proportional hazards assumption regarding the treatment assignments was confirmed using Schoenfeld residual tests.[16] Although the proportional hazards assumption was met for most of the primary and key secondary outcomes, it was not met for the secondary outcomes of invasive coronary angiography and repeat revascularization ($P < 0.05$ for Schoenfeld residuals test). Therefore, prespecified landmark analyses were performed using a 1-year cutoff corresponding to the planned period of routine functional testing—intervals during which the proportional hazards were preserved.[13]

All reported P values were 2-sided, and $P < 0.05$ was considered significant for all tests. No adjustment for multiple testing was undertaken; thus, all findings of this study should be interpreted as exploratory given the potential for type I error due to multiple comparisons. All statistical analyses were performed using SAS software version 9.4 and R software version 4.2.1.

RESULTS

STUDY POPULATION AND BASELINE CHARACTERISTICS. Of the 1,706 patients initially randomized in the POST-PCI trial, 1,192 (69.9%) had either multivessel or left main CAD; among them, 833 (69.9%) had multivessel disease without left main involvement, and 359 (30.1%) had any left main disease. A total of 1,192 patients with multivessel or left main disease was stratified by original randomized follow-up strategy: 589 (49.4%) in the routine functional testing group and 603 (50.6%) in the standard care group (**Figure 1**).

The baseline characteristics of the study participants with multivessel or left main disease are summarized in **Table 1**. Baseline characteristics including comorbidities, coronary anatomical, and procedural characteristics were well balanced between the routine functional testing group and the standard care group. Similarly, there was no difference in baseline characteristics between the functional testing and the standard care groups in each cohort of multivessel or left main disease (Supplemental Table 1).

FUNCTIONAL TESTING AND FOLLOW-UP. At 12 ± 2 months after randomization, 486 (90.0%; n = 540) eligible patients in the routine functional testing group (excluding those who died [n = 10], withdrew [n = 4], were lost to follow-up [n = 9], or underwent angiography or revascularization [n = 26] before 12 months) underwent functional testing as did 38 (7.0%) patients in the standard care group as clinically needed (excluding those who died [n = 12], withdrew [n = 1], were lost to follow-up [n = 9], or underwent angiography or revascularization [n = 40] before 12 months) (**Figure 1**). Among 524 patients who underwent any stress testing, 248 (47.3%) had a single stress test and 276 (52.7%) had multiple stress tests.

Because guideline-directed medical therapy was equally emphasized in both groups, the use of cardioactive medications was well-balanced between the

functional testing group and the standard care group at baseline and during follow-up (Table 2). This finding was consistent in each cohort of multivessel or left main disease (Supplemental Table 2).

PRIMARY AND SECONDARY ENDPOINTS. Ascertainment of the primary and secondary endpoints at 2 years was completed in 97.8% of patients (97.4% of the functional testing group and 98.2% of the standard care group) (Figure 1). Data on vital status were obtained for all patients.

Primary and secondary clinical outcomes in patients with multivessel or left main disease are presented in Table 3. At 2 years after randomization, the incidences of primary composite outcome were similar between the routine functional testing group and the standard care group (6.2% vs 5.7%, respectively; HR: 1.09; 95% CI: 0.68-1.74; $P = 0.73$) (Figure 2). The incidences of individual component of death, MI, or hospitalization for unstable angina were also similar. This trend was consistent in each cohort of multivessel or left main disease (Supplemental Table 3, Supplemental Figure 1). Therefore, there was no significant interaction between multivessel and left main disease (P for interaction = 0.90).

In patients with multivessel or left main disease, the rates of invasive coronary angiography (13.5% vs 9.6%) tended to be higher in the functional testing group compared with the standard care group and repeat revascularization (9.6% vs 6.0%) was more frequent in the functional testing group than in the standard care group (Table 3, Figure 3). This trend was similar in each cohort of multivessel or left main disease (Supplemental Table 3, Supplemental Figure 2).

LANDMARK ANALYSES. To assess the time-dependent pattern of the clinical outcomes, landmark analyses at 1 year were performed in the overall cohort and in each cohort of multivessel or left main disease (Supplemental Tables 4 and 5). From randomization to 1 year, there were no differences in the primary and secondary endpoints between the functional testing group and the standard care group. After 1 year, the rate of primary composite endpoint and its components were also not significantly different between these 2 groups (Supplemental Figure 3) and in the multivessel or left main disease cohorts (Supplemental Figures 4 and 5). However, after 1 year, the rates of invasive coronary angiography and repeat revascularization were higher in the functional testing group than in the standard care group in the entire study cohort (Supplemental Figure 6) and in each cohort of multivessel or left main disease (Supplemental Figures 7 and 8).

TABLE 3 Clinical Outcomes After Multivessel or Left Main PCI According to Randomized Follow-Up Strategy

	No. of Events (%) at 2 Years			
	Functional Testing Group (n = 589)	Standard Care Group (n = 603)	HR (95% CI)	*P* Value
Primary composite outcome[a]	36 (6.2)	34 (5.7)	1.09 (0.68-1.74)	0.73
Secondary outcomes				
Death from any cause	18 (3.1)	18 (3.0)	1.03 (0.53-1.97)	0.94
Myocardial infarction	2 (0.3)	7 (1.2)	0.29 (0.06-1.41)	0.13
Hospitalization for unstable angina	16 (2.8)	9 (1.5)	1.83 (0.81-4.13)	0.15
Death or myocardial infarction	20 (3.5)	25 (4.2)	0.82 (0.46-1.47)	0.50
Hospitalization				
Any reason	156 (27.3)	133 (22.6)	1.23 (0.97-1.54)	0.09
Cardiac reason	91 (16.0)	73 (12.5)	1.27 (0.94-1.73)	0.12
Noncardiac reason	65 (11.4)	60 (10.2)	1.13 (0.80-1.61)	0.50
Invasive coronary angiography	76 (13.5)	56 (9.6)	1.39 (0.98-1.96)	0.06
Showing restenosis or obstructive CAD	54 (71.1)	34 (60.7)		
Showing no restenosis or obstructive CAD	22 (28.9)	22 (39.3)		
Repeat revascularization	54 (9.6)	35 (6.0)	1.59 (1.04-2.43)	0.03
Target lesion revascularization	25 (4.6)	15 (2.6)	1.72 (0.91-3.27)	0.10
Nontarget lesion revascularization	29 (5.3)	20 (3.5)	1.50 (0.85-2.64)	0.17
PCI	52 (96.3)	33 (94.3)		
CABG	2 (3.7)	2 (5.7)		

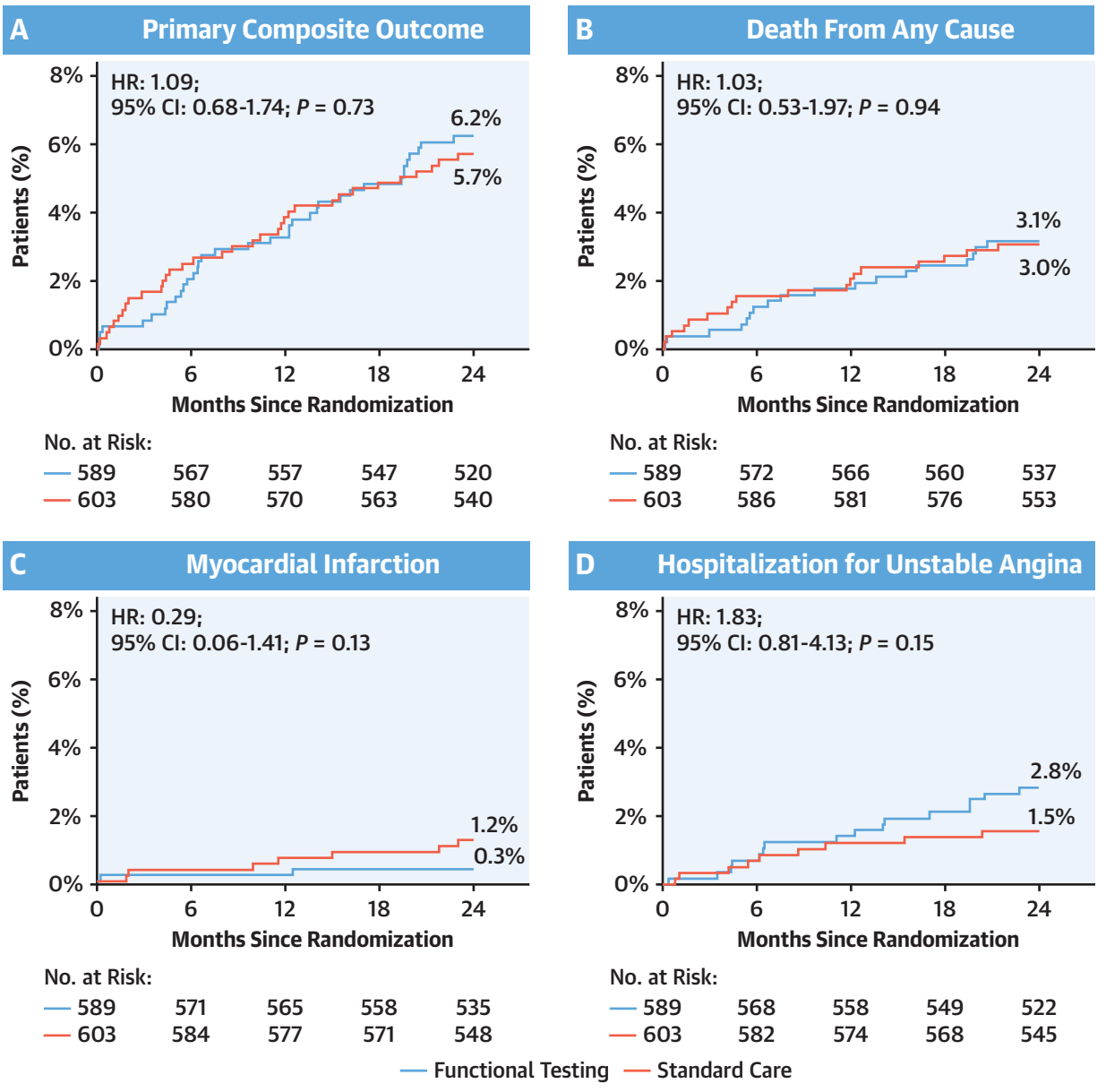
Values are n (%) unless otherwise indicated. The number of events and estimated percentages were calculated with the use of a Kaplan-Meier survival analysis of data in the intention-to-treat population; therefore, the percentages may not reflect the ratio of the numerator and the denominator. HRs are for the routine functional testing follow-up strategy compared with the standard care follow-up strategy. No corrections for multiple testing were applied. [a]The primary composite outcome was death from any cause, myocardial infarction, or hospitalization for unstable angina.

Abbreviations as in Table 1.

DISCUSSION

In this key subgroup analysis of the POST-PCI trial, we evaluated the clinical role and the prognostic impact of routine surveillance stress testing on major clinical outcomes in high-risk patients with multivessel or left main CAD who had undergone PCI. The key findings can be summarized as follows (Central Illustration): 1) the incidences of the primary composite outcome of death from any cause, MI, or hospitalization for unstable angina at 2 years were similar between strategies of routine functional testing or standard care alone; 2) this trend was consistent in each cohort of multivessel or left main disease; and 3) in landmark analyses performed at 1 year (the period when routine testing was planned to be performed), the incidences of coronary angiography and revascularization were more than 2 times higher in the functional testing group than in the standard care group but did not translate into a reduction in primary outcome events or mortality.

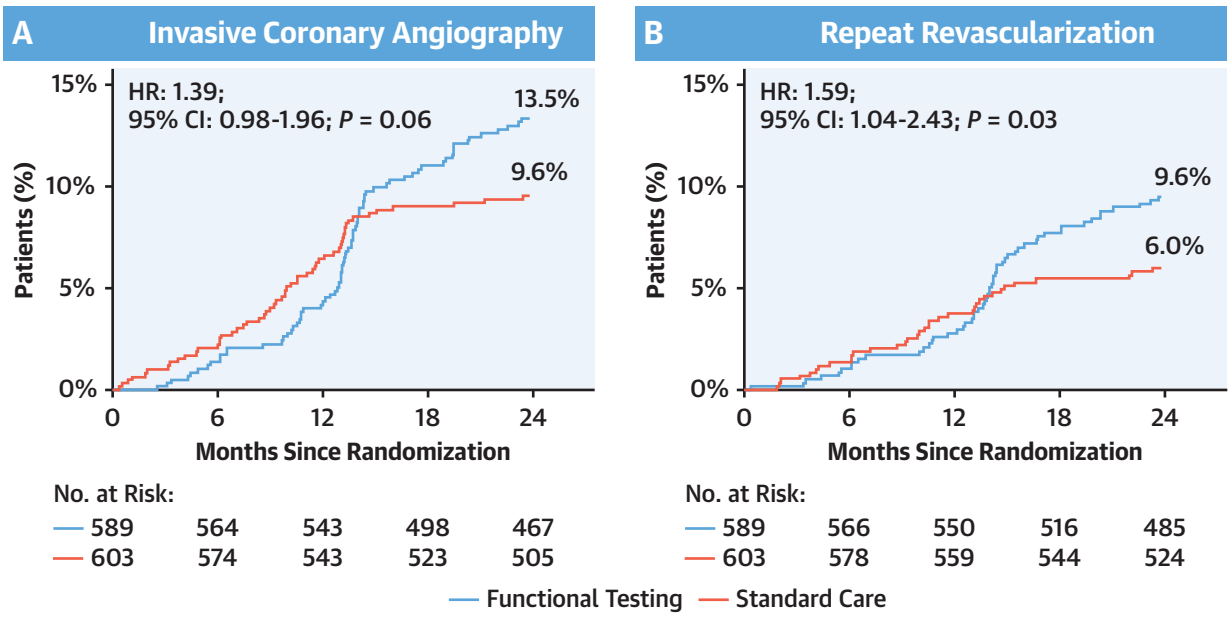
FIGURE 2 Kaplan-Meier Curves for the Primary Composite Outcome by Randomized Follow-Up Strategy



Kaplan-Meier curves for the cumulative incidence of the (A) primary composite outcome of (B) death from any cause, (C) myocardial infarction, or (D) hospitalization for unstable angina in patients. The shown percentages are Kaplan-Meier estimates. The *P* value was calculated using the log-rank test. No corrections for multiple testing were applied.

In patients diagnosed with obstructive CAD, noninvasive functional stress testing is clinically useful in deciding on coronary revascularization, assessing residual ischemia after an acute MI or incomplete revascularization, or treating symptomatic patients who have had previous revascularization. However, until recently, little has been known about the clinical role of routine surveillance functional testing in high-risk patients with multivessel or left main disease after complex PCI. In contemporary PCI practice, functional stress testing after revascularization has been widely used[9,11,12,17,18] with a substantially high rate of repeat revascularization noted in hospitals with the highest frequency of stress testing

FIGURE 3 Rates of Coronary Angiography and Repeat Revascularization by Randomized Follow-Up Strategy



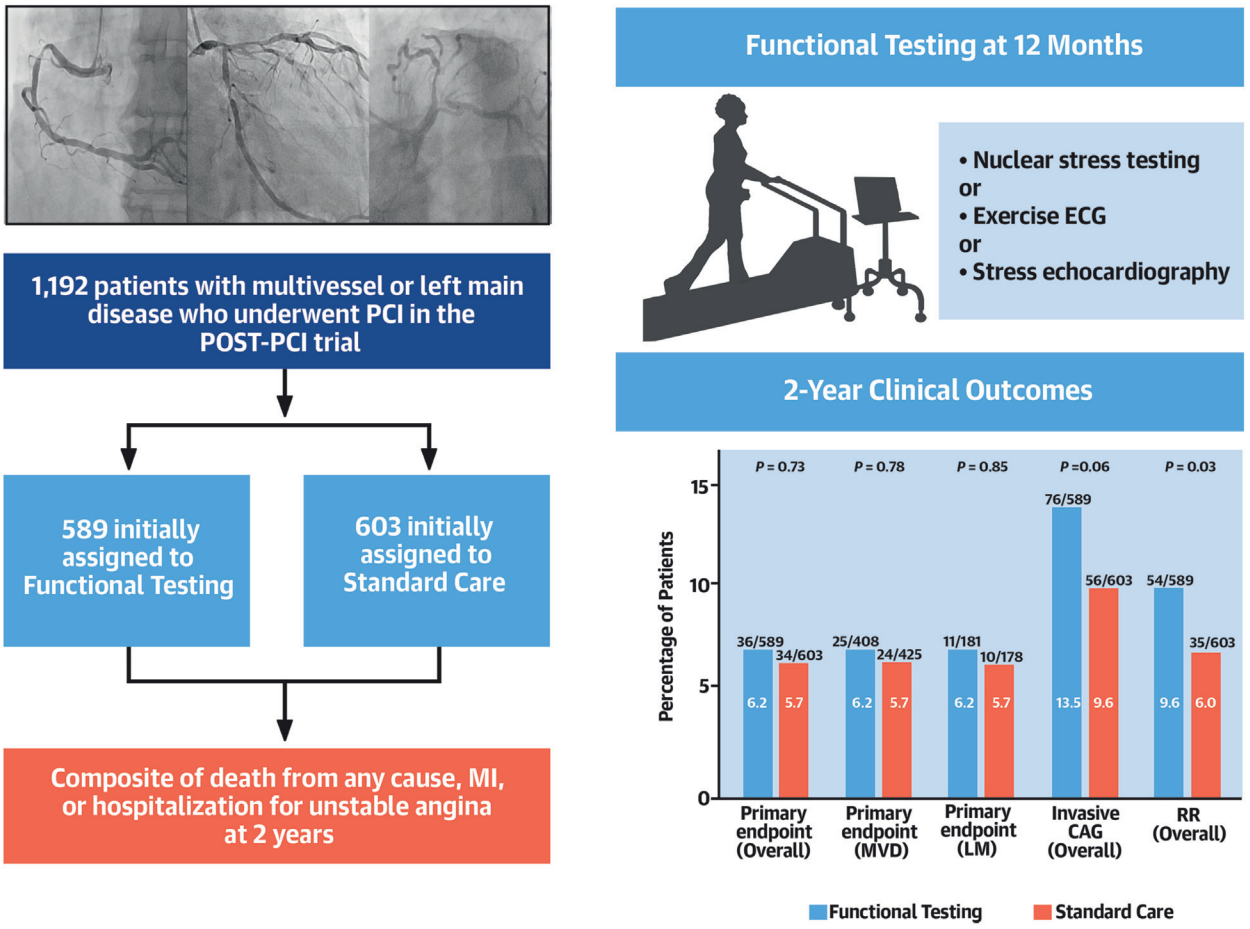
Kaplan-Meier curves for the cumulative incidence of (A) invasive coronary angiography and (B) repeat revascularization in patients with multivessel or left main disease. The shown percentages are Kaplan-Meier estimates. The *P* value was calculated using the log-rank test. No corrections for multiple testing were applied.

after PCI.[9] However, this has not translated into a lower risk of MI or death during long-term follow-up.[19,20] Therefore, because of the lack of valid evidence based on solid randomized clinical trials, the 2021 American College of Cardiology-American Heart Association-Society of Cardiovascular Angiography and Interventions guideline for coronary artery revascularization and the 2018 European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines on myocardial revascularization do not provide a recommendation for routine stress testing after revascularization, and the European Society of Cardiology guidelines provide a weak (Class IIb) recommendation for surveillance stress testing after PCI.[1,2]

In this clinical context, the POST-PCI trial provided compelling clinical evidence for a Class III recommendation for routine surveillance testing after PCI, which was recently adopted in the updated 2023 clinical practice guidelines for managing patients with chronic coronary disease.[21] The current key subgroup analysis of the POST-PCI may reemphasize that stringent follow-up surveillance with routine functional testing has no clinical benefit compared with standard care alone after multivessel or left main PCI, which is frequently performed in the routine clinical practice. Surveillance stress testing might increase the rates of invasive procedures (ie, invasive angiography and repeat revascularization) and related complications without affecting the hard clinical endpoint. These rates might be indicative of the interventionalists' responses to the extra diagnostic information that was obtained from routing functional testing around year 1, which is commonly known as the oculostenotic reflex. Moreover, increased unnecessary procedures may lead to an elevated radiation exposure, potentially harming both patients and medical staff members, and invasive procedures can bring unexpected additional complications, potentially causing further detriment to patients. Therefore, without any clinical signs or symptoms suggestive of stent failure or disease progression, routine surveillance stress testing should be avoided in patients who underwent multivessel or left main PCI.

The key findings of the POST-PCI trial and such subgroup analyses can build on the major findings of the ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) trial, in which patients with moderate-to-

CENTRAL ILLUSTRATION **Impact of Routine Surveillance Stress Testing After Multivessel or Left Main Percutaneous Coronary Intervention**



Lee JM, et al. J Am Coll Cardiol. 2024;83(9):890-900.

In the POST-PCI (Pragmatic Trial Comparing Symptom-Oriented Versus Routine Stress Testing in High-Risk Patients Undergoing Percutaneous Coronary Intervention) trial, a subgroup with multivessel or left main disease was extracted for evaluation. Of these, 589 were initially allocated to the functional testing group and 603 to the standard care group. At 24 months postrandomization, primary composite outcomes were comparable between the groups. However, the incidences of invasive angiography and repeat revascularization were more frequent in the functional testing group after 12 months. CAG = coronary angiography; ECG = electrocardiogram; LM = left main disease; MI = myocardial infarction; MVD = multivessel disease; PCI = percutaneous coronary intervention; RR = repeat revascularization.

severe ischemia on stress testing were randomly assigned to an initial invasive or conservative strategy.[22] In the ISCHEMIA trial, approximately 20% of patients had previously undergone PCI, and approximately one-third had no symptoms of angina in the 4 weeks before randomization. Although only high-risk patients (ie, those with high-risk findings on stress testing) were included in the ISCHEMIA, there was no substantial difference between the 2 strategies in the primary endpoint at 5 years. Furthermore, the extent of ischemia on stress testing did not identify a subgroup of patients that derived benefit from an invasive strategy.[23] Although the ISCHEMIA trial primarily focused on the initial treatment strategy and the POST-PCI trial focused on the follow-up surveillance strategy; both highlight the lack of benefit of routine functional stress testing in asymptomatic patients after PCI.

STUDY LIMITATIONS. First, as the POST-PCI trial suffered from lower-than-expected primary endpoint events,[13] this prespecified subgroup analysis might have an inherent limitation of statistical underpower

to detect clinically relevant events. Therefore, observed findings of the present study should be interpreted as being hypothesis-generating. Second, because such a subgroup analysis was not prespecified, the possibility of baseline imbalance exists. However, most of baseline characteristics were well-balanced among groups of randomized strategies, and overall findings were consistent in the adjusted analyses. Third, women were underrepresented in this study. Considering sex-specific difference in post-PCI outcomes,[24] it could potentially impact the generalizability of the study results. Last, the present trial only evaluated the prognostic impact of routine stress-testing at 1 year after PCI; therefore, whether annual cardiac stress testing could improve patient outcomes remains undetermined. Further trials are warranted to evaluate the prognostic impact of the annual or specific time interval cardiac stress testing on major cardiovascular events in high-risk PCI patients.

CONCLUSIONS

In high-risk patients with multivessel or left main disease who have undergone PCI, a follow-up strategy of routine functional testing, compared with standard care alone, did not reduce the risk of primary composite outcome of death from any causes, MI, or hospitalization for unstable angina at 2 years. These findings were consistent in each cohort of multivessel or left main disease. Although the present study had insufficient statistical power to allow for a firm conclusion, our findings do not support an active follow-up surveillance strategy with routine functional testing after multivessel or left main PCI.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS:

Compared with standard care, little or no incremental benefit accrues from routine surveillance stress testing after percutaneous intervention for multivessel or left main CAD.

TRANSLATIONAL OUTLOOK:

Further research is needed to define optimal follow-up strategies for high-risk patients who have undergone multivessel or left main PCI.

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KEY WORDS coronary artery disease, percutaneous coronary intervention, prognosis, stress testing

APPENDIX For supplemental tables and figures, please see the online version of this paper.