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Routine Stress Testing After PCI in Patients With and Without Acute Coronary Syndrome

A Secondary Analysis of the POST-PCI Randomized Clinical Trial

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IMPORTANCE The appropriate follow-up surveillance strategy for patients with acute coronary syndrome (ACS) who have undergone percutaneous coronary intervention (PCI) remains unknown.

OBJECTIVE To assess clinical outcomes in patients with and without ACS who have undergone high-risk PCI according to a follow-up strategy of routine stress testing at 12 months after PCI vs standard care alone.

DESIGN, SETTING, AND PARTICIPANTS The POST-PCI (Pragmatic Trial Comparing Symptom-Oriented vs Routine Stress Testing in High-Risk Patients Undergoing Percutaneous Coronary Intervention) trial was a randomized clinical trial that compared follow-up strategies of routine functional testing vs standard care alone 12 months after high-risk PCI. Patients were categorized as presenting with or without ACS. Patients were enrolled in the trial from November 2017 through September 2019, and patients were randomized from 11 sites in South Korea; data analysis was performed in 2022.

INTERVENTION Patients categorized as presenting with or without ACS were randomized to either a routine functional testing or standard care alone follow-up strategy 12 months after high-risk PCI.

MAIN OUTCOMES AND MEASURES The primary outcome was a composite of death from any cause, myocardial infarction, or hospitalization for unstable angina at 2 years following randomization. Kaplan-Meier event rates through 2 years and Cox model hazard ratios (HRs) were generated, and interactions were tested.

RESULTS Of 1706 included patients, 350 patients (20.5%) were female, and the mean (SD) patient age was 64.7 (10.3) years. In total, 526 patients (30.8%) presented with ACS. Compared with those without ACS, patients with ACS had a 55% greater risk of the primary outcome (HR, 1.55; 95% CI, 1.03-2.33; *P* = .03) due to higher event rates in the first year. The 2-year incidences of the primary outcome were similar between strategies of routine functional testing or standard care alone in patients with ACS (functional testing: 16 of 251 [6.6%]; standard care: 23 of 275 [8.5%]; HR, 0.76; 95% CI, 0.40-1.44; *P* = .39) and in patients without ACS (functional testing: 30 of 598 [5.1%]; standard care: 28 of 582 [4.9%]; HR, 1.04; 95% CI, 0.62-1.74; *P* = .88) (*P* for interaction for ACS = .45). Although a landmark analysis suggested that the rates of invasive angiography and repeat revascularization were higher after 1 year in the routine functional testing group, the formal interactions between ACS status and either invasive angiography or repeat revascularization were not significant.

CONCLUSION AND RELEVANCE Despite being at higher risk for adverse clinical events in the first year after PCI than patients without ACS, patients with ACS who had undergone high-risk PCI did not derive incremental benefit from routine surveillance stress testing at 12 months compared with standard care alone during follow-up.

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Visual Abstract

Supplemental content

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Patients presenting with acute coronary syndrome (ACS) who are undergoing percutaneous coronary intervention (PCI) are among a very common and high-risk group of patients with atherosclerosis.[1] Although remarkable improvements have been made in ACS management with evolving PCI devices and antithrombotic therapies,[2] the residual ischemic risk and the recurrence of ischemic cardiovascular events in patients with ACS undergoing PCI remain of major concern. Furthermore, the appropriate follow-up surveillance strategy for patients with ACS who have undergone PCI remains debated, and theoretical arguments have been made to support an active surveillance follow-up strategy to reduce the risk of future ischemic events.[3] In real-world clinical practice, routine surveillance stress testing has commonly been implemented as part of post-PCI management,[3-5] but its prognostic value is still uncertain in high-risk patients presenting with ACS who have undergone PCI.

In this clinical context, given that patients with ACS have a higher incidence of recurrent cardiovascular events and mortality compared with patients with stable coronary artery disease (CAD),[6,7] it should be determined whether such high-risk patients with ACS undergoing PCI could benefit from routine surveillance stress testing to reduce the risk of adverse cardiovascular events during follow-up. Therefore, we used data from the POST-PCI (Pragmatic Trial Comparing Symptom-Oriented vs Routine Stress Testing in High-Risk Patients Undergoing Percutaneous Coronary Intervention) trial, a randomized clinical trial evaluating follow-up strategy in high-risk patients who have undergone PCI,[8] to examine clinical outcomes according to a randomized follow-up strategy of routine functional testing at 12 months vs standard care alone in patients presenting initially with vs without ACS.

Key Points

Question Is stress testing 12 months after percutaneous coronary intervention (PCI) among high-risk patients with or without acute coronary syndrome (ACS) associated with beneficial long-term outcomes compared with standard care alone?

Findings In this prespecified analysis of the POST-PCI randomized clinical trial including 1706 patients, patients with ACS had higher rates of major cardiovascular events than those without ACS in the first year after PCI. A follow-up strategy of functional testing at 12 months did not improve clinical outcomes during long-term follow-up compared with standard care, regardless of initial ACS status.

Meaning In high-risk patients who had undergone PCI presenting with or without ACS, there was no incremental benefit from surveillance stress testing at 12 months compared with standard care alone.

Methods

Study Design and Patients

The POST-PCI trial was a multicenter, pragmatic, randomized clinical trial that compared an active follow-up strategy of routine functional testing vs standard care alone in high-risk patients with complex anatomical or clinical characteristics who had undergone PCI.[8] This trial was conducted at 11 hospitals in South Korea from November 2017 to September 2019. Enrolled participants had 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, or bypass graft disease. Clinical high-risk characteristics included medically treated diabetes, chronic kidney failure, and enzyme-positive ACS. All patients underwent successful PCI with contemporary drug-eluting stents, bioabsorbable scaffolds, or drug-coated balloons (only for instent restenosis). Patient race was determined by trial investigators; the POST-PCI randomized clinical trial was conducted in South Korea, where more than 99% of the population is Asian. The trial was approved by the institutional review board or ethics committee at each of the 11 participating centers. All patients provided written informed consent before enrollment. The POST-PCI trial was conducted in accordance with Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines. The POST-PCI trial protocol can be found in Supplement 1, and the statistical analysis plan can be found in Supplement 2.

For this prespecified secondary analysis, patients were categorized according to whether or not they presented with ACS as the clinical indication for PCI. The cohort with ACS had unstable angina or myocardial infarction (MI) with ST-segment elevation (STEMI) or without ST-segment elevation (non-STEMI), and the cohort without ACS had stable angina or silent ischemia.

Trial Procedures and Functional Testing

The trial procedures and randomized follow-up strategies have been previously described.[8] Patients in the routine functional testing group were subjected to routine cardiac stress testing, including exercise electrocardiography (ECG), nuclear stress testing, or stress echocardiography, at 12 months after randomization. Due to the high likelihood of false-positive findings on exercise ECG tests 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 pragmatic design of the POST-PCI trial, the test findings were based on real-time, site-specific interpretation of all functional test results, thereby ensuring the timely availability of results for patient management. All clinical decisions regarding further diagnostic or therapeutic procedures and subsequent treatment decisions were made at the discretion of the treating physician at each participating center.

Clinical Outcomes and Follow-Up

The primary outcome was a composite of major cardiovascular events, consisting of death from any cause, MI, or hospitalization for unstable angina, within 2 years of randomization. Secondary outcomes included individual components of the primary composite outcome; a composite of death or MI;

hospitalization for any reason (for either cardiac or noncardiac causes); invasive coronary angiography; and repeat revascularization procedures (target lesion or non-target lesion revascularization). Definitions of each clinical end point have been described previously,[8] and all components of the primary and secondary clinical outcomes were independently adjudicated by a clinical events committee, the members of which were unaware of the treatment assignments.

Clinical follow-up was performed at 6, 12, 18, and 24 months after randomization as scheduled. During the follow-up period, participating treating physicians were strongly advised to follow contemporary clinical guidelines for guideline-directed medical therapy and the management of risk factors to achieve intensive secondary prevention. All information on clinical events and cardiovascular medicines was systematically obtained at each clinical visit. To ensure accuracy, patient vital status was verified by crosschecking with the national death registry of the Korean National Health Insurance Service database.

Statistical Analysis

To compare patients with vs without ACS, baseline characteristics were compared using the χ^2 or Fisher exact test for categorical variables and the Kruskal-Wallis test for continuous variables. Time-to-event estimates for clinical outcomes, including the primary composite outcome and secondary outcomes, were obtained by Kaplan-Meier estimates and compared using the log-rank test.

A comparison between the groups randomized to different follow-up strategies (routine functional testing vs standard care alone) among patients with or without ACS was performed using a Cox proportional hazards model. Hazard ratios (HRs) and 95% CIs were calculated. The proportional hazards assumption was tested for each outcome using Schoenfeld residuals and visual inspection. Interactions between the randomized follow-up strategy and ACS status were also tested.

Although the proportional hazards assumption was met for most of the primary outcomes and key secondary outcomes, it was not met for the secondary outcome of invasive coronary angiography and repeat revascularization. Therefore, prespecified landmark analyses were performed using a 1-year cutoff, which corresponded to the planned period of routine functional testing, during which proportional hazards were preserved.[8] All tests were 2-tailed, and $P < .05$ was considered statistically significant for all end points with no adjustment for multiple testing. Therefore, all findings of this study should be interpreted as exploratory given the potential for a type I error due to multiple comparisons. Analyses were performed by independent statisticians using commercially available software (SAS version 9.4 [SAS Institute] and Stata version 16.1 [StataCorp LLC]).

Results

Study Population and Baseline Characteristics

Baseline characteristics of the study population categorized by the clinical presentation (with or without ACS) and the randomized post-PCI follow-up strategies are summarized in **Table 1**. Of 1706 total patients randomized in the POST-PCI trial, 350 pa-

Table 1. Baseline Characteristics of Patients According to Randomized Follow-Up Strategy in Patients With or Without Acute Coronary Syndrome (ACS)[a]

Characteristic	No. (%)					
	With ACS			Without ACS		
	Functional testing (n = 251)	Standard care (n = 275)	*P* value	Functional testing (n = 598)	Standard care (n = 582)	*P* value
Demographic characteristics						
Age, mean (SD), y	64.7 (11.4)	64.1 (11.6)	.56	64.6 (9.8)	65.1 (9.6)	.32
Sex						
Female	57 (22.7)	49 (17.8)	.19	126 (21.1)	118 (20.3)	.79
Male	194 (77.3)	226 (82.2)		472 (78.9)	464 (79.7)	
Body mass index, mean (SD)[b]	24.4 (3.1)	24.9 (3.2)	.09	25.0 (2.9)	25.0 (3.2)	.74
Cardiac risk factors and comorbidities						
Hypertension	155 (61.8)	173 (62.9)	.86	428 (71.6)	422 (72.5)	.77
Current smoker	85 (33.9)	99 (36.0)	.67	139 (23.2)	139 (23.9)	.85
Dyslipidemia	202 (80.5)	233 (84.7)	.24	532 (89.0)	520 (89.3)	.91
History of MI	14 (5.6)	24 (8.7)	.22	36 (6.0)	39 (6.7)	.72
Previous PCI	40 (15.9)	55 (20.0)	.27	147 (24.6)	133 (22.9)	.53
Previous CABG	1 (0.4)	1 (1.8)	.26	21 (3.5)	15 (2.6)	.45
History of stroke	12 (4.8)	21 (7.6)	.24	33 (5.5)	43 (7.4)	.23
History of heart failure	3 (1.2)	12 (4.4)	.06	10 (1.7)	15 (2.6)	.38
Peripheral artery disease	3 (1.2)	5 (1.8)	.82	16 (2.7)	15 (2.6)	>.99
Chronic lung disease	3 (1.2)	10 (3.6)	.13	10 (1.7)	23 (4.0)	.03
Atrial fibrillation or atrial flutter	5 (2.0)	9 (3.3)	.52	15 (2.5)	14 (2.4)	>.99
Left ventricular ejection fraction, mean (SD), %	55.3 (10.5)	55.8 (11.1)	.61	60.4 (7.8)	59.6 (9.4)	.16

(continued)

Table 1. Baseline Characteristics of Patients According to Randomized Follow-Up Strategy in Patients With or Without Acute Coronary Syndrome (ACS)[a] (continued)

Characteristic	No. (%)					
	With ACS			Without ACS		
	Functional testing (n = 251)	Standard care (n = 275)	*P* value	Functional testing (n = 598)	Standard care (n = 582)	*P* value
Criteria for high risk after PCI[c]						
High-risk anatomical characteristics						
Left main disease	40 (15.9)	49(17.8)	.65	141 (23.6)	129 (22.2)	.61
Bifurcation disease	68 (27.1)	80 (29.1)	.68	284 (47.5)	270 (46.4)	.75
Ostial lesion	20 (8.0)	29 (10.5)	.39	108 (18.1)	98 (16.8)	.63
Chronic total occlusion	10 (4.0)	31 (11.3)	.003	91 (15.2)	96 (16.5)	.60
Restenotic lesion	15 (6.0)	22 (8.0)	.46	53 (8.9)	57 (9.8)	.65
Diffuse long lesion[d]	106 (42.2)	128 (46.5)	.37	385 (64.4)	383 (65.8)	.65
Bypass graft disease	0	1 (0.4)	>.99	2 (0.3)	1 (0.2)	>.99
High-risk clinical characteristics						
Diabetes	97 (38.6)	98 (35.6)	.53	224 (37.5)	241 (41.4)	.18
Use of insulin	8 (3.2)	11 (4.0)	.79	24 (4.0)	30 (5.2)	.43
Chronic kidney failure[e]	12 (4.8)	16 (5.8)	.74	30 (5.0)	29 (5.0)	>.99
Receipt of dialysis	5 (2.0)	8 (2.9)	.69	18 (3.0)	18 (3.1)	>.99
Procedural characteristics						
Diseased lesions per patient, mean (SD)	2.0 (1.1)	2.1 (1.2)	.33	2.3 (1.2)	2.3 (1.1)	.61
Treated lesions per patient, mean (SD)	1.4 (0.7)	1.5 (0.7)	.45	1.4 (0.7)	1.5 (0.7)	.38
Stents per patient, mean (SD)	1.7 (1.0)	1.8 (1.1)	.54	2.0 (1.1)	2.1 (1.2)	.30
Stent length per patient, mean (SD), mm	48.5 (30.7)	50.6 (30.2)	.42	59.3 (34.1)	61.7 (35.4)	.26
Use of drug-eluting stents	242 (96.4)	269 (97.8)	.48	582 (97.3)	552 (94.8)	.04
Use of bioabsorbable scaffold	3 (1.2)	0	.22	3 (0.5)	10 (1.7)	.09
Use of drug-coated balloon	11 (4.4)	14 (5.1)	.86	35 (5.9)	45 (7.7)	.24
Intravascular ultrasound guidance	157 (62.5)	196 (71.3)	.04	465 (77.8)	451 (77.5)	.97
Fractional flow reserve assessed	37 (14.7)	49 (17.8)	.40	268 (44.8)	255 (43.8)	.77
Medication at hospital discharge						
DAPT[f]	246 (98.0)	264 (96.0)	.28	586 (98.0)	576 (99.0)	.26
Aspirin or P2Y12 inhibitors	249 (99.2)	272 (98.9)	>.99	596 (99.7)	580 (99.7)	>.99
Oral anticoagulants	6 (2.4)	10 (3.6)	.56	22 (3.7)	12 (2.1)	.14
β-Blockers	177 (70.5)	203 (73.8)	.46	405 (67.7)	371 (63.7)	.17
ACE inhibitor or ARB	128 (51.0)	135 (49.1)	.73	184 (30.8)	202 (34.7)	.17
Calcium-channel blockers	108 (43.0)	98 (35.6)	.10	431 (72.1)	448 (77.0)	.06
Statins	244 (97.2)	267 (97.1)	>.99	585 (97.8)	574 (98.6)	.41

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CABG, coronary artery bypass grafting; DAPT, dual antiplatelet therapy; MI, myocardial infarction; PCI, percutaneous coronary intervention.

[a] Percentages may not total 100 because of rounding.

[b] Calculated as weight in kilograms divided by height in meters squared.

[c] To be eligible for participation in the trial, patients had to have ≥1 high-risk anatomical or clinical characteristic associated with an increased risk of ischemic or thrombotic events during follow-up.

[d] Diffuse long lesions were defined as lesions with a length of ≥30 mm or a stent length of ≥32 mm.

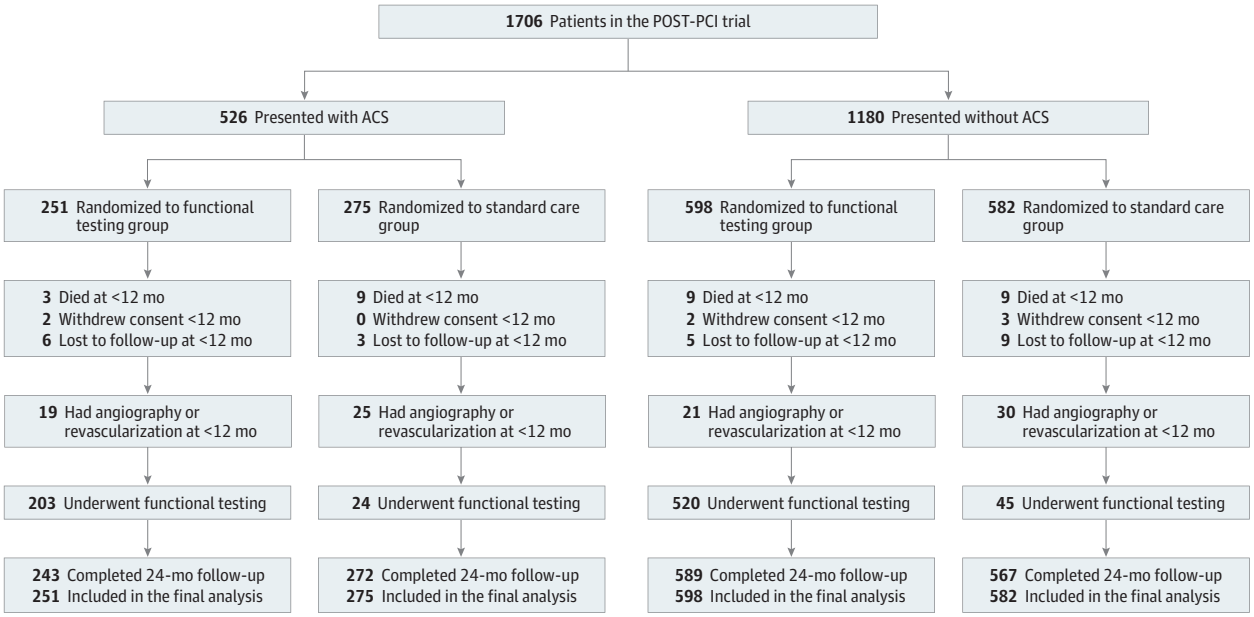
[e] Chronic kidney failure was defined as a serum creatinine level of ≥2.0 mg/dL or long-term receipt of hemodialysis.

[f] DAPT includes both aspirin and any P2Y12 inhibitors (clopidogrel, ticagrelor, or prasugrel).

tients (20.5%) were female, and mean (SD) patient age was 64.7 (10.3) years. A total of 526 patients (30.8%) presented with ACS. Among these, 331 patients (62.9%) presented with STEMI or non-STEMI and 195 patients (37.1%) presented with unstable angina. Among 526 patients with ACS, 251 patients (47.7%) were randomized to the routine functional testing strategy and 275 patients (52.5%) were randomized to the standard care strategy. Among 1180 patients without ACS, 598 patients were randomized to the routine functional testing group (50.6%) and 582 patients were randomized to the standard care group (49.3%) (**Figure 1**). Most baseline characteristics were not significantly different between groups randomized to the routine stress testing and standard care alone strategies in each cohort of patients with and without ACS.

Baseline characteristics according to ACS status are shown in eTable 1 in Supplement 3. Compared to those without ACS, patients with ACS were more likely to currently smoke and to have a lower left ventricular ejection fraction. However, patients without ACS were more likely to have higher risk profiles of clinical comorbidities or anatomical or procedural characteristics.

Figure 1. CONSORT Flow Diagram



ACS indicates acute coronary syndrome.

Functional Testing and Follow-Up

At a mean (SD) of 12 (2) months following randomization, 203 of 243 eligible patients with ACS in the routine functional testing group (91.8%) underwent testing. This total excludes 3 patients who died, 2 who withdrew consent, 6 who were lost to follow-up, and 19 who underwent angiography or revascularization before 12 months following randomization. Twenty-four of 238 eligible patients in the standard care group (10.1%) also underwent functional testing as clinically needed. This total excludes 9 patients who died, 3 who were lost to follow-up, and 25 who underwent angiography or revascularization before 12 months following randomization (Figure 1). Among patients without ACS, 520 of 598 patients in the functional testing group (92.7%) and 45 of 582 patients in the standard care group (8.5%) underwent functional testing. Since guideline-directed medical therapy was equally emphasized in both treatment groups, the use of cardioactive medications was well-balanced between the functional testing group and the standard care group at baseline (Table 1) and during follow-up in each stratum of patients with and without ACS (eTable 2 and eFigure 2 in Supplement 3).

Clinical Outcomes

Data for the primary and secondary outcomes at 2 years were complete for 1671 of 1706 overall patients (97.9%), 515 of 526 patients in the ACS cohort (97.9%), and 1156 of 1180 patients in the non-ACS cohort (98.0%) (Figure 1). Data on vital status were obtained for all patients.

Patients With vs Without ACS

Clinical outcomes in patients with and without ACS are presented in eTable 3 in Supplement 3. Despite being at lower risk for clinical risk factors or high-risk anatomical characteristics, the primary composite outcome of death from any cause, MI, or hospitalization for unstable angina at 2 years was 55% more likely in patients with ACS than in patients without ACS (with ACS: 39 of 526 patients [7.6%]; without ACS: 58 of 1180 patients [5.0%]; HR, 1.55; 95% CI, 1.03-2.33; P = .03) (eFigure 3 in Supplement 3). In addition, the 2-year incidence of death or MI was nonsignificantly higher (with ACS: 26 of 526 patients [5.0%]; without ACS: 39 of 1180 patients [3.4%]; HR, 1.53; 95% CI, 0.93-2.51; P = .09) and the rate of rehospitalization owing to cardiac causes was significantly higher (with ACS: 87 of 526 patients [17.2%]; without ACS: 145 of 1180 patients [12.7%]; HR, 1.42; 95% CI, 1.09-1.86; P = .009) in patients with ACS than in patients without ACS. These higher event rates at 2 years were driven by higher event rates in the first year before the 12-month intervention.

Routine Stress Testing vs Standard Care Alone in Groups of Patients With and Without ACS

When outcomes were compared by randomized follow-up strategy, the rate of the primary composite outcome through 2 years was 6.6% in the functional testing group (16 of 251 patients) compared with 8.5% in the standard care group (23 of 275 patients) among patients presenting with ACS (HR, 0.76; 95% CI, 0.40-1.44; P = .39), whereas the rates of the primary composite outcome were 5.1% in the functional testing group (30 of 598 patients) and 4.9% in the standard care group (28 of 582 patients) in patients without ACS (HR, 1.04; 95% CI, 0.62-1.74; P = .88) (P for interaction = .45) (eFigure 1 and eTable 4 in Supplement 3). The pattern of nonsignificant difference was similar for each individual component of the primary outcome and other key secondary outcomes according to the pres-

ence or absence of ACS and the randomized follow-up strategy. Rates of invasive coronary angiography and repeat revascularization according to randomized follow-up strategy in patients with and without ACS are illustrated in eFigure 4 in Supplement 3.

To assess the time-dependent pattern of clinical outcomes, prespecified landmark analyses were performed at 1 year (the prespecified point of intervention with functional testing or no testing for the standard care group) (**Table 2**; **Figure 2**; **Figure 3**). Within the first year, there were no significant differences in the primary composite outcome, its individual components, or other secondary outcomes between the functional testing and standard care groups in patients with ACS (Figure 2) and in those without ACS (Figure 3). From 1 year to 2 years, there were also no significant between-group differences in the primary composite outcome and several secondary outcomes, including death, MI, or rehospitalization. The incidences of invasive coronary angiography and repeat revascularization beyond 1 year were numerically higher in the functional testing group than the standard care group among patients with ACS (eFigure 5 in Supplement 3), but incidences were significantly higher in the functional testing group among patients without ACS (eFigure 6 in Supplement 3). Nevertheless, in these landmark analyses beyond 1 year, there were no significant interactions between ACS status and randomized follow-up strategy with respect to primary composite outcome and key secondary outcomes, including coronary angiography or repeat revascularization (Table 2).

Discussion

In this prespecified analysis of the POST-PCI trial, outcomes were compared according to randomized follow-up strategies of routine functional testing or standard care alone in patients with or without ACS. The major findings can be summarized as follows. First, patients presenting with ACS had fewer comorbidities and a lower risk of anatomical or procedural complexity compared to patients without ACS. However, patients with ACS had higher rates of the primary composite outcome through the duration of follow-up, which were driven by higher event rates before the 12-month intervention. Second, the 2-year rates of the primary composite outcome were not significantly different between the routine functional testing group and the standard care group in patients with or without ACS. Third, although invasive angiography and repeat revascularization after 1 year occurred at higher rates in the functional testing group, there were no significant interactions between ACS status and randomized follow-up strategy for the 2-year end points of coronary angiography and repeat revascularization. Fourth, regardless of ACS status, the maintenance of and compliance with optimal medical therapy, including antiplatelet and statin therapy, during follow-up may have a positive effect on improving outcomes. This positive effect could mitigate the effect of an active surveillance follow-up strategy after high-risk PCI.

The findings of this analysis address a clinically important gap in the evidence base necessary to guide decisions about the follow-up strategy of patients with ACS undergoing PCI. Prior clinical studies evaluating patients with ACS undergoing PCI have been conducted almost entirely in observational studies or small clinical trials.[4,5,9-11] Moreover, to our knowledge, no randomized clinical trials to date have been powered to explore whether there is a relationship between the follow-up surveillance strategy and clinical outcomes specifically among patients with ACS undergoing PCI. Therefore, the current study may provide important insights into such unaddressed issues.

The patients with ACS enrolled in our trial were naturally different from those with stable CAD. Although patients with ACS have fewer comorbidities and less complex anatomical or procedural characteristics than those without ACS, patients with ACS have a higher incidence of major cardiovascular events. These differences in clinical outcomes may be related to the myocardial injury occurring during ACS,[12] as well as to the difference in atherosclerotic burden of vulnerable plaque among patients presenting with vs without ACS.[13,14] A 2023 study[15] also showed that patients with ACS have higher rates of long-term cardiovascular mortality or MI after coronary revascularization compared with those without ACS.

Cardiac stress testing has been widely implemented as an important part of the follow-up surveillance strategy after myocardial revascularization, including either PCI or coronary artery bypass grafting.[3-5] Nevertheless, it remains unclear whether this type of active surveillance strategy can improve clinical outcomes. It is well established that patients undergoing PCI have a substantial (approximately 10%) risk of restenosis at the target lesion.[16] Among patients with target lesion failure after PCI, most require repeat revascularization, and a certain proportion of patients presents with spontaneous MI.[16,17] Moreover, atherosclerotic plaque characteristics in patients with ACS differ from those with stable CAD, particularly concerning nonculprit vulnerable plaques, which contribute to distinct clinical outcomes.[18,19] Given the heightened risk for recurrent events across the coronary tree after ACS, one might anticipate a protective benefit of active follow-up surveillance with routine stress testing 12 months following PCI in the ACS setting. However, the findings in this prespecified analysis from the POST-PCI trial do not support this concept. The key findings of the POST-PCI trial were adopted in the 2023 clinical guidelines for chronic CAD.[20] The current data, if supported by additional larger trials of functional testing after PCI of patients with ACS, might inform future recommendations for management after ACS.

It should be noted that the overall event rates in the cohorts both with and without ACS in this trial were quite low and most likely reflect adherence to guideline recommendations for medical therapy after PCI for patients presenting with ACS or chronic CAD. In addition, current guidelines recommend intravascular imaging (class IIa) for procedural guidance, particularly during high-risk PCI.[21,22] The use of intravascular imaging is associated with lower risks of major cardiovascular events[23-25]; thus, the high proportion of imaging-guided PCI in our study might be associated with favorable

Table 2. Landmark Analyses for Clinical Outcomes Occurring Within 1 Year, and Between 1 and 2 Years in Patients With or Without Acute Coronary Syndrome (ACS) According to Randomized Follow-Up Strategy[a]

Outcome	With ACS				Without ACS				
	Events, No. (estimated %)				Events, No. (estimated %)				
	Functional testing (n = 251)	Standard care (n = 275)	HR (95% CI)	*P* value	Functional testing (n = 598)	Standard care (n = 582)	HR (95% CI)	*P* value	*P* value for interaction[b]
From randomization to 1 y									
Primary composite end point[c]	9 (3.7)	19 (6.9)	0.52 (0.23-1.14)	.10	16 (2.7)	15 (2.6)	1.03 (0.51-2.08)	.94	.20
Death from any cause	3 (1.2)	9 (3.3)	0.36 (0.10-1.36)	.13	9 (1.5)	9 (1.6)	0.97 (0.38-2.43)	.94	.24
MI	2 (0.8)	3 (1.1)	0.78 (0.13-4.95)	.80	0	2 (0.4)	0.19 (0.01-6.03)	.35	.48
Hospitalization for unstable angina	4 (1.7)	8 (2.9)	0.55 (0.16-1.81)	.32	7 (1.2)	4 (0.7)	1.69 (0.49-5.78)	.40	.20
Secondary end points									
Death or MI	5 (2.0)	12 (4.4)	0.46 (0.16-1.30)	.14	9 (1.5)	11 (1.9)	0.79 (0.33-1.90)	.60	.44
Hospitalization									
Any reason	41 (16.9)	48 (17.9)	0.93 (0.61-1.41)	.72	66 (11.1)	68 (11.9)	0.94 (0.67-1.32)	.71	.96
Cardiac reason	24 (9.9)	29 (10.9)	0.90 (0.53-1.55)	.71	27 (4.68)	34 (5.9)	0.76 (0.46-1.26)	.29	.65
Noncardiac reason	17 (7.0)	19 (7.1)	0.98 (0.51-1.88)	.95	39 (6.6)	34 (5.9)	1.12 (0.71-1.77)	.64	.75
Invasive CAG	16 (6.3)	24 (8.7)	0.83 (0.42-1.65)	.60	21 (3.5)	28 (4.8)	0.86 (0.48-1.53)	.61	.82
Showing restenosis or obstructive CAD	9 (56.2)	13 (54.1)	0.92 (0.38-2.21)	.85	13 (61.9)	19 (67.9)	0.97 (0.47-1.99)	.93	.74
Showing no restenosis or obstructive CAD	7 (43.7)	11 (45.8)	0.72 (0.24-2.15)	.56	8 (38.1)	9 (32.1)	0.69 (0.26-1.82)	.45	.95
Repeat revascularization	11 (4.6)	12 (4.5)	1.00 (0.44-2.27)	.99	9 (1.5)	17 (2.9)	0.51 (0.23-1.14)	.10	.25
TLR	5 (2.1)	5 (1.9)	1.09 (0.32-3.78)	.88	6 (1.0)	9 (1.6)	0.64 (0.23-1.80)	.40	.52
Non-TLR	6 (2.5)	7 (2.6)	0.94 (0.32-2.81)	.91	3 (0.5)	8 (1.4)	0.36 (0.10-1.36)	.13	.27
PCI	11 (100)	12 (100)	1.01 (0.44-2.31)	.99	9 (100)	15 (88.2)	0.98 (0.42-2.28)	.98	.98
CABG	0	0	NA	NA	0	2 (11.8)	NA	NA	NA

(continued)

Table 2. Landmark Analyses for Clinical Outcomes Occurring Within 1 Year, and Between 1 and 2 Years in Patients With or Without Acute Coronary Syndrome (ACS) According to Randomized Follow-Up Strategy[a] (continued)

Outcome	With ACS				Without ACS				
	Events, No. (estimated %)				Events, No. (estimated %)				
	Functional testing (n = 251)	Standard care (n = 275)	HR (95% CI)	*P* value	Functional testing (n = 598)	Standard care (n = 582)	HR (95% CI)	*P* value	*P* value for interaction[b]
From 1-2 y									
Primary composite end point[c]	7 (3.0)	4 (1.6)	1.91 (0.56-6.52)	.30	14 (2.4)	13 (2.4)	1.04 (0.49-2.20)	.93	.41
Death from any cause	5 (2.1)	2 (0.8)	2.76 (0.54-14.26)	.22	6 (1.0)	8 (1.4)	0.72 (0.25-2.07)	.54	.18
MI	0	2 (0.8)	0.22 (0.01-6.86)	.39	2 (0.3)	3 (0.5)	0.68 (0.11-4.29)	.68	.57
Hospitalization for unstable angina	2 (0.8)	0	5.49 (0.20-152.68)	.32	6 (1.1)	2 (0.4)	2.51 (0.51-12.42)	.26	.68
Secondary end points									
Death or MI	5 (2.1)	4 (1.6)	1.37 (0.37-5.11)	.64	8 (1.4)	11 (2.0)	0.69 (0.28-1.73)	.43	.40
Hospitalization									
Any reason	28 (11.1)	18 (6.5)	1.71 (0.95-3.09)	.07	76 (14.6)	56 (11.3)	1.34 (0.95-1.89)	.10	.48
Cardiac reason	20 (9.3)	14 (5.9)	1.56 (0.79-3.09)	.20	51 (9.2)	33 (6.3)	1.48 (0.96-2.29)	.08	.89
Noncardiac reason	8 (3.6)	4 (1.6)	2.21 (0.67-7.36)	.19	25 (4.6)	23 (4.4)	1.07 (0.61-1.88)	.82	.28
Invasive CAG	13 (5.2)	8 (2.9)	1.76 (0.73-4.24)	.21	51 (8.5)	17 (2.9)	2.92 (1.69-5.06)	<.001	.33
Showing restenosis or obstructive CAD	8 (61.5)	6 (75.0)	1.43 (0.49-4.14)	.50	39 (76.4)	8 (47.0)	4.74 (2.21-10.13)	<.001	.53
Showing no restenosis or obstructive CAD	5 (38.5)	2 (25.0)	2.72 (0.07-1.90)	.23	12 (23.5)	9 (52.9)	1.30 (0.55-3.09)	.55	.44
Repeat revascularization	11 (4.9)	7 (2.8)	1.74 (0.68-4.50)	.25	35 (6.1)	12 (2.2)	2.82 (1.46-5.43)	.002	.41
TLR	6 (2.6)	2 (0.8)	3.34 (0.68-16.56)	.14	17 (2.9)	10 (1.8)	1.63 (0.75-3.57)	.22	.43
Non-TLR	5 (2.0)	5 (2.0)	1.10 (0.32-3.79)	.88	18 (3.1)	2 (0.4)	8.65 (2.01-37.30)	.004	.04
PCI	9 (81.8)	7 (100)	1.43 (0.53-3.83)	.48	35 (100)	11 (91.6)	3.07 (1.56-6.05)	.001	.64
CABG	2 (18.2)	0	NA	NA	0	1 (8.4)	NA	NA	NA

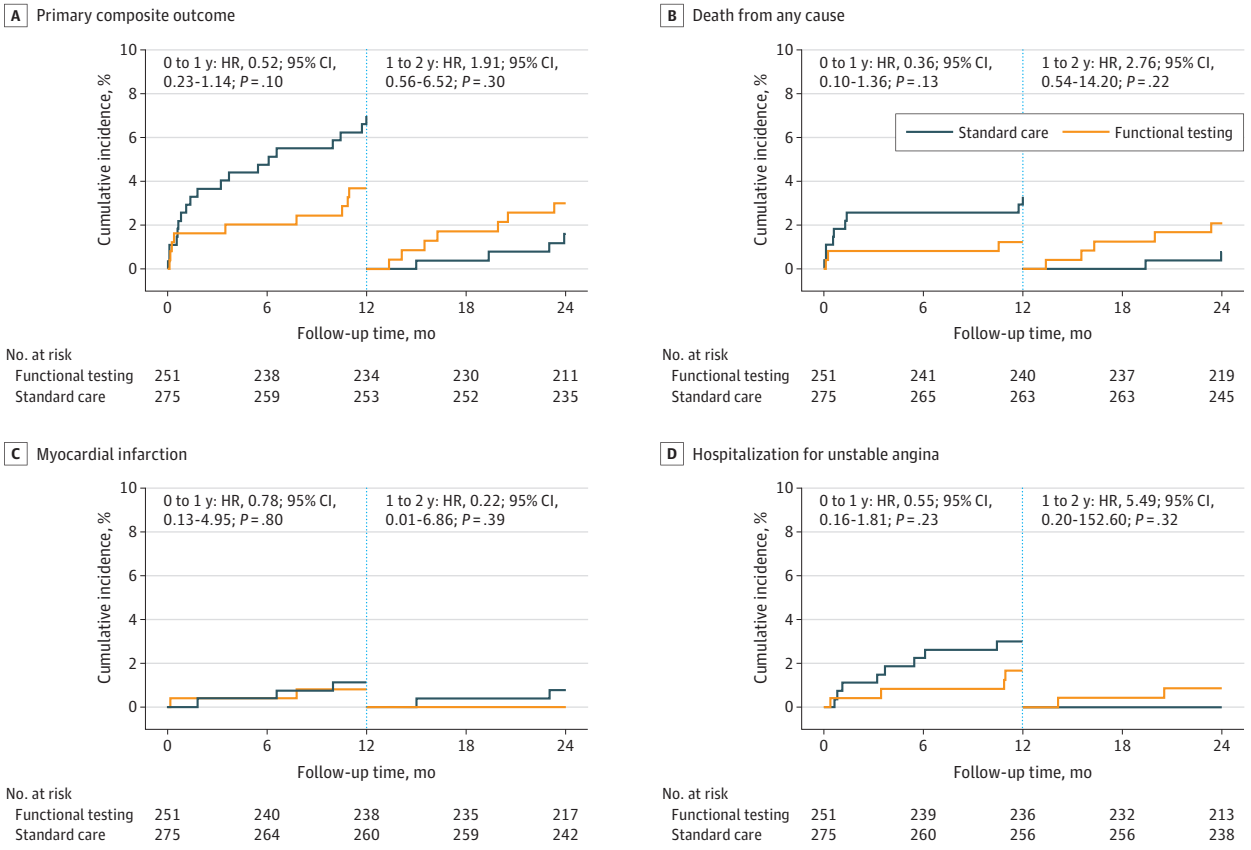
Abbreviations: CABG, coronary artery bypass grafting; CAD, coronary artery disease; CAG, coronary angiography; HR, hazard ratio; MI, myocardial infarction; NA, not applicable; PCI, percutaneous coronary intervention; TLR, target lesion revascularization.

[a] Event rate percentages are shown as the number of incidences estimated with a Kaplan-Meier survival analysis of data from 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. The 95% CIs for secondary end points have not been adjusted for multiple comparisons; therefore inferences drawn from these intervals may not be reproducible.

[b] *P* value for interaction between the ACS status (with vs without ACS) and the randomization group (functional testing vs standard care).

[c] The primary composite end point was death from any cause, MI, or hospitalization for unstable angina.

Figure 2. Landmark Analysis at Time of Intervention for the Primary Composite End Point and its Components in Patients With Acute Coronary Syndrome



Kaplan-Meier curves of landmark analysis of the cumulative incidence of the primary composite outcome of death from any cause, myocardial infarction, or hospitalization for unstable angina (A) in patients with acute coronary syndrome, and the cumulative incidence of the components of the primary composite: death from any cause (B), myocardial infarction (C), and hospitalization for unstable angina (D). The vertical dotted line indicates the intervention. The *P* values were determined by log-rank tests. HR indicates hazard ratio.

long-term outcomes. These factors underscore the importance of proper procedural techniques and aggressive secondary prevention to improve outcomes after PCI, which mitigate the clinical impact of routine surveillance stress testing after PCI among patients with and without ACS.

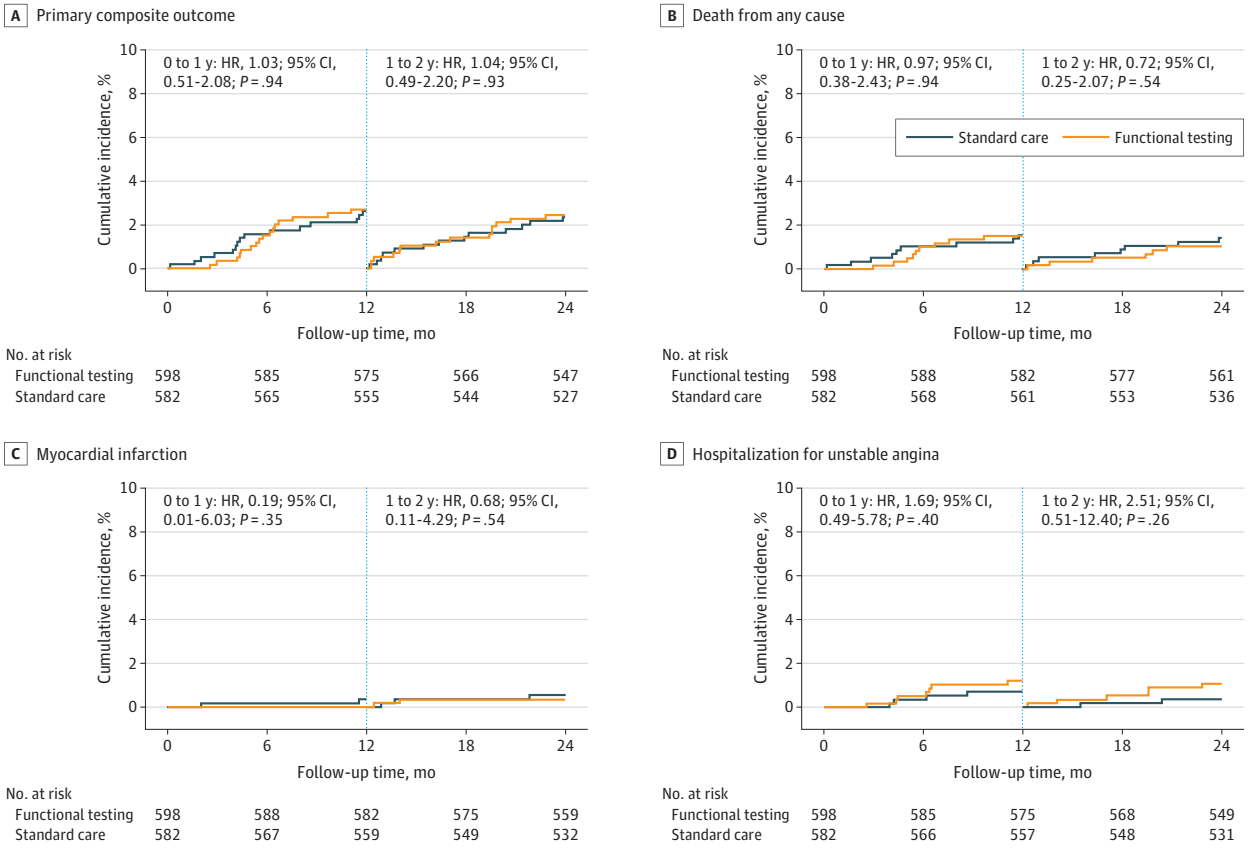
Limitations

This study has several limitations. First, while patients with ACS were a prespecified subgroup of interest for the original POST-PCI trial, there was no adjustment for multiple testing, and thus these findings should be interpreted as hypothesis-generating. Second, given this subgroup analysis had insufficient statistical power to allow for a firm conclusion, the results cannot be considered clinically actionable. Thus, these data warrant further investigation and should be confirmed or refuted through large randomized clinical trials with long-term follow-up. Third, exact information on the status of complete revascularization for nonculprit lesions in patients with ACS was lacking. This uncertainty could have influenced the clinical outcomes in patients with ACS. Fourth, this study was based on an Asian cohort and women were underrepresented in this study cohort, both factors of which could potentially impact the generalizability of the study results. Lastly, clinical outcomes in this study were measured based on a 2-year follow-up period (1 year after the intervention of stress testing at 12 months vs standard care with no testing), which might limit the assessment of long-term effects and potential changes in clinical outcomes beyond this timeframe. Additionally, there are limitations regarding the loss of study power after 1 year, due to relatively few cardiac events occurring beyond 1 year after the intervention.

Conclusions

In high-risk patients presenting with ACS who had undergone PCI, a follow-up strategy of routine surveillance functional testing 12 months after PCI did not reduce the risk of the primary composite outcome of death from any cause, MI, or hospitalization for unstable angina at 2 years compared with standard care alone. These findings were consistent regardless of ACS status, though the study had insufficient statistical power to allow for firm conclusions.

Figure 3. Landmark Analysis at Time of Intervention for the Primary Composite End Point and its Components in Patients Without Acute Coronary Syndrome



Kaplan-Meier curves of landmark analysis of the cumulative incidence of the primary composite outcome of death from any cause, myocardial infarction, or hospitalization for unstable angina (A) in patients without acute coronary syndrome, and the cumulative incidence of the components of the primary composite: death from any cause (B), myocardial infarction (C), and hospitalization for unstable angina (D). The vertical dotted line indicates the intervention. The *P* values were determined by log-rank tests. HR indicates hazard ratio.

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