Routine Functional Testing or Standard Care in High-Risk Patients after PCI

: POST-PCI Trial

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Disclosure

- I, Do-Yoon Kang, DO NOT have a conflict of interest related to this presentation.

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- The funders did not participate in the trial design, data analysis, or manuscript preparation.

Background

- There are limited data from randomized trials to guide a specific follow-up surveillance approach after coronary revascularization.
- Prior studies have reported the widespread use of cardiac stress testing after coronary revascularization in clinical practice;[1-4] more than half of all patients who underwent PCI or CABG had functional testing within 2 years of revascularization.
- It is uncertain whether a follow-up strategy that includes routine functional testing improves clinical outcomes among high-risk patients who undergo PCI.

CABG, coronary-artery bypass grafting; PCI, percutaneous coronary intervention

[1]Shah BR , et al. *J Am Coll Cardiol* 2010;56:1328-34. [2]Shah BR, et al. *J Am Coll Cardiol* 2013;62:439-46. [3]Bagai A, et al. *Circ Cardiovasc Qual Outcomes* 2017;10. [4]Dhoot A, et al. *Am J Cardiol* 2020;136:9-14.

Background: Current Guidelines

- Strategies for follow-up and management in patients after myocardial revascularization

Asymptomatic patients	Class	LOE
Surveillance by non-invasive imaging-based stress testing may be considered in high-risk patient subsets 6 months after revascularization.	IIb	C
After high-risk PCI (e.g. unprotected LM stenosis), late (3–12 months) surveillance angiography may be considered, irrespective of symptoms.	IIb	C
Routine non-invasive imaging-based stress testing may be considered 1 year after PCI and >5 years after CABG.	IIb	C

Neumann FJ et al. *Eur Heart J* 2019;40:87-165

Objective

In patients with high-risk anatomical or clinical features who underwent PCI

- Evaluate whether routine stress testing results in changes in subsequent management and preventive strategies (such as preemptive coronary angiography or revascularization or more aggressive medical therapies)
- Determine the effect of a follow-up strategy that includes routine functional-testing on a reduction of ischemic cardiovascular events or mortality.

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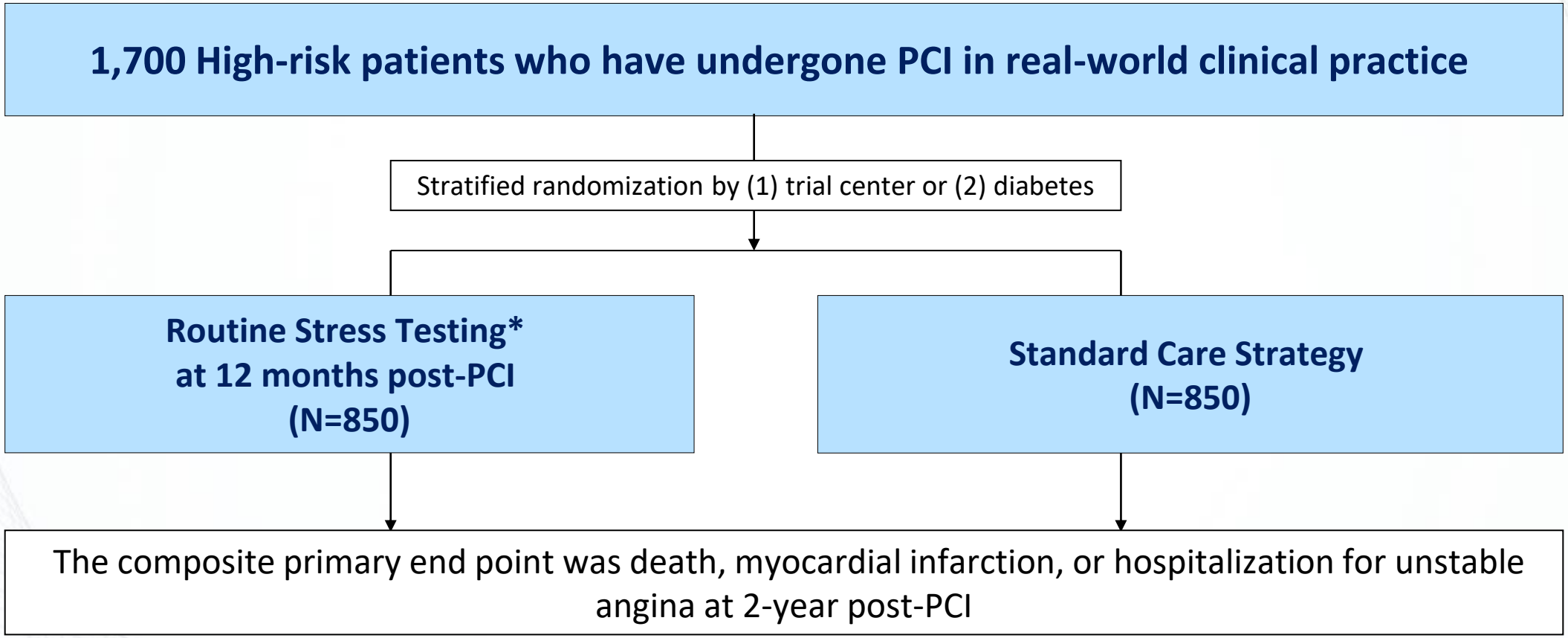
Trial Design

Pragmatic Trial Comparing Symptom-Oriented Versus Routine Stress Testing in High-Risk Patients Undergoing Percutaneous Coronary Intervention

POST-PCI Trial



*Cardiac stress tests include exercise ECG, nuclear stress imaging, or stress echocardiography

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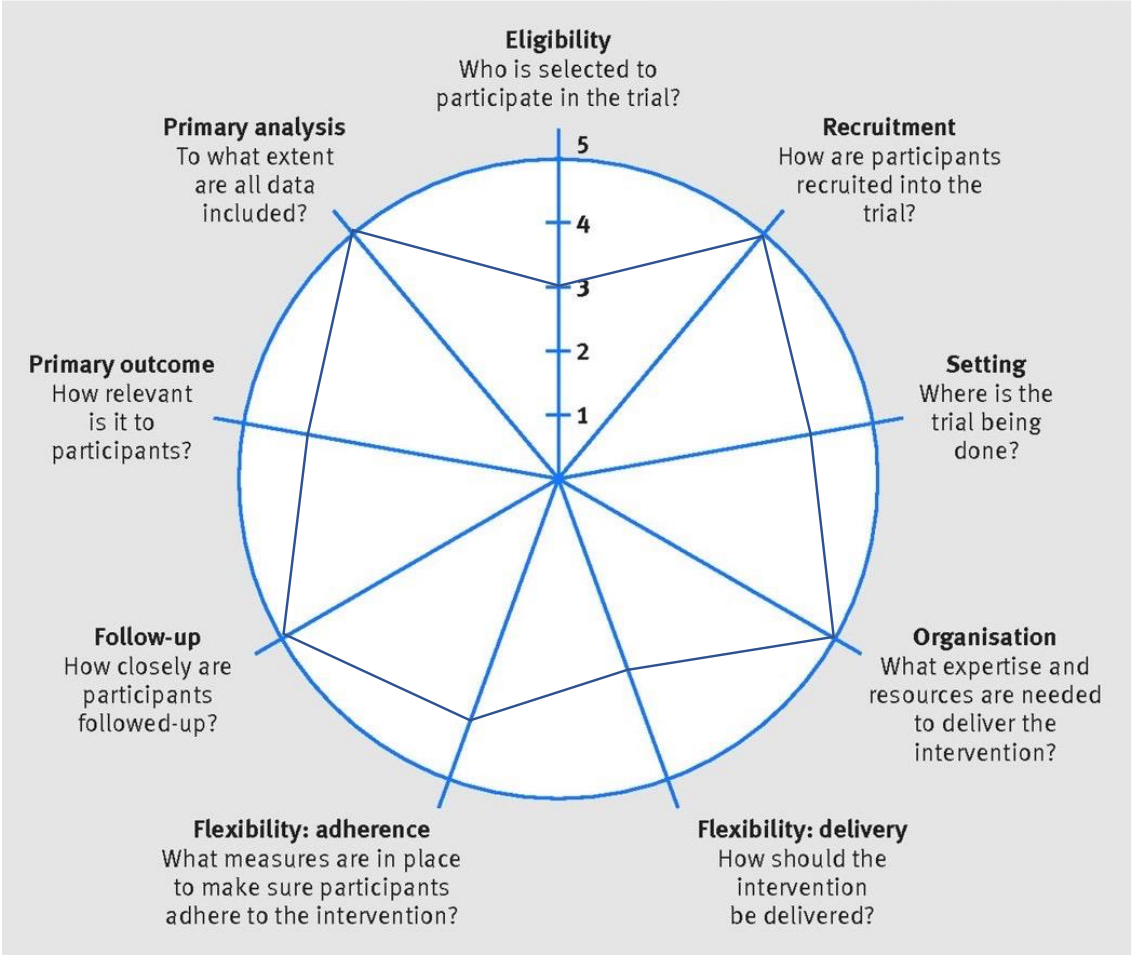
Pragmatic Trial Design of POST-PCI

- (1) Use of nationwide, real-world, prospective registries (IRIS-DES, IRIS-BVS, or IRIS-DEB registry) [1-3] as trial platforms for randomization, case-record forms, and follow-up clinical data,
- (2) The clinically relevant strategy of routine functional testing and usual clinical care,
- (3) A diverse study population reflecting real-world patients,
- (4) Heterogeneous post-PCI management practice settings, and
- (5) Clinically unmet issues in the routine clinical practice



[1]Park DW , et al. Circ Cardiovasc Interv 2012;5:365-71. [2]Lee PH, et al. *J Am Coll Cardiol* 2018;71:832-41. [3]Park H et al. *JACC Cardiovasc Interv* 2020;13:1403-13.

Yoon YH, Park DW et al. *Am Heart J* 2020;224:156-65

Inclusion and Exclusion Criteria

INCLUSION

1. Patients >19 years of age who underwent successful PCI with contemporary drug-eluting stents, bioresorbable scaffolds, or drug-coated balloons.

2. Have at least one of the following **high-risk anatomical or clinical characteristics** associated with an increased risk of ischemic or thrombotic events during follow-up [1-3]:
   - **Anatomical characteristics:** left main lesion, bifurcation lesion, ostial lesion, chronic total occlusion lesion, multivessel disease (≥ 2 vessels stented), restenotic lesion, diffuse long lesion (lesion length ≥30 mm or stent length ≥32 mm), or bypass graft disease.
   - **Clinical characteristics:** medically-treated diabetes, chronic renal failure (serum creatinine level ≥ 2.0mg/dL or long-term hemodialysis), and enzyme-positive ACS.

EXCLUSION

1. Cardiogenic shock at the index admission.
2. Patients treated only with bare-metal stents or balloon angioplasty only.
3. Pregnant and/or lactating women.
4. Concurrent medical condition with a life expectancy < 1 year.
5. Patients who were actively participating in another drug or device investigational study and had not completed the primary endpoint follow-up period.
6. Patients who were unable to provide written informed consent or participate in long-term follow-up.

[1]Mauri L et al. *N Engl J Med* 2014;371:2155-66 . [2]Yeh RW et al. *J Am Coll Cardiol* 2017;70:2213-23.
[3]Cuisset T et al. *Lancet* 2017;390:810-20.

Endpoints

Primary endpoint

- Composite of major cardiovascular events (death from any cause, MI, or hospitalization for unstable angina) at 2 years after randomization

Secondary endpoints

- Individual components of the primary composite outcome
- Composite of death or MI
- Hospitalization for any reason (for either cardiac causes or noncardiac causes)
- Invasive coronary angiography
- Repeat revascularization procedures (target-lesion or nontarget-lesion revascularization)

MI, myocardial infarction; PCI, percutaneous coronary intervention

Statistical Considerations

Power Calculation (N = 1,700)

- 90% power to detect 30% relative reduction in primary outcome assuming a 2-year cumulative rate of 15% in the standard-care group

Pre-Specified Statistical Analysis

- Intention-to-treat
- Kaplan-Meier estimates for calculating cumulative event rates
- Cox proportional hazard models
  - Estimate the relative risks if proportional hazards assumption is not violated
- Landmark analysis & sensitivity analysis
  - Evaluate the time-dependent risks with the use of cutoff at 1 year, which corresponded to the planned period of routine functional-testing — intervals during which proportional hazards were preserved.
  - The interaction term between randomized groups and key subgroups was evaluated for primary outcome.

Participating Investigators and Trial Organization

Participating Investigators (11 Sites in South Korea)

Duk-Woo Park, Do-Yoon Kang, Jung-Min Ahn, Sung-Cheol Yun, Seung-Jung Park (Asan Medical Centers); Yong-Hoon Yoon (Chungnam National University Sejong Hospital); Seung-Ho Hur, Cheol Hyun Lee (Keimyung University Dongsan Hospital); Won-Jang Kim, Se Hun Kang (CHA Bundang Medical Center); Chul Soo Park (Yeouido St. Mary's Hospital); Bong-Ki Lee (Kangwon National University Hospital); Jung-Won Suh (Seoul National University Bundang Hospital); Jung Han Yoon (Wonju Severance Christian Hospital); Jae Woong Choi (Eulji General Hospital); Kee-Sik Kim (Daegu Catholic University Medical Center); Si Wan Choi (Chungnam National University Hospital); Su Nam Lee (St. Vincent's Hospital).

Executive Committee

Duk-Woo Park (Trial PI) | Seung-Jung Park (Trial Co-PI) | Do-Yoon Kang

Additional Steering Committee

Jung-Min Ahn | Yong-Hoon Yoon | Seung-Ho Hur
Cheol Hyun Lee | Won-Jang Kim

Event Adjudication Committee

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Independent Data Monitoring Committee

Jang-Whan Bae | Bum-Jun Kim | Jong-Young Lee
Kyung-Min Park

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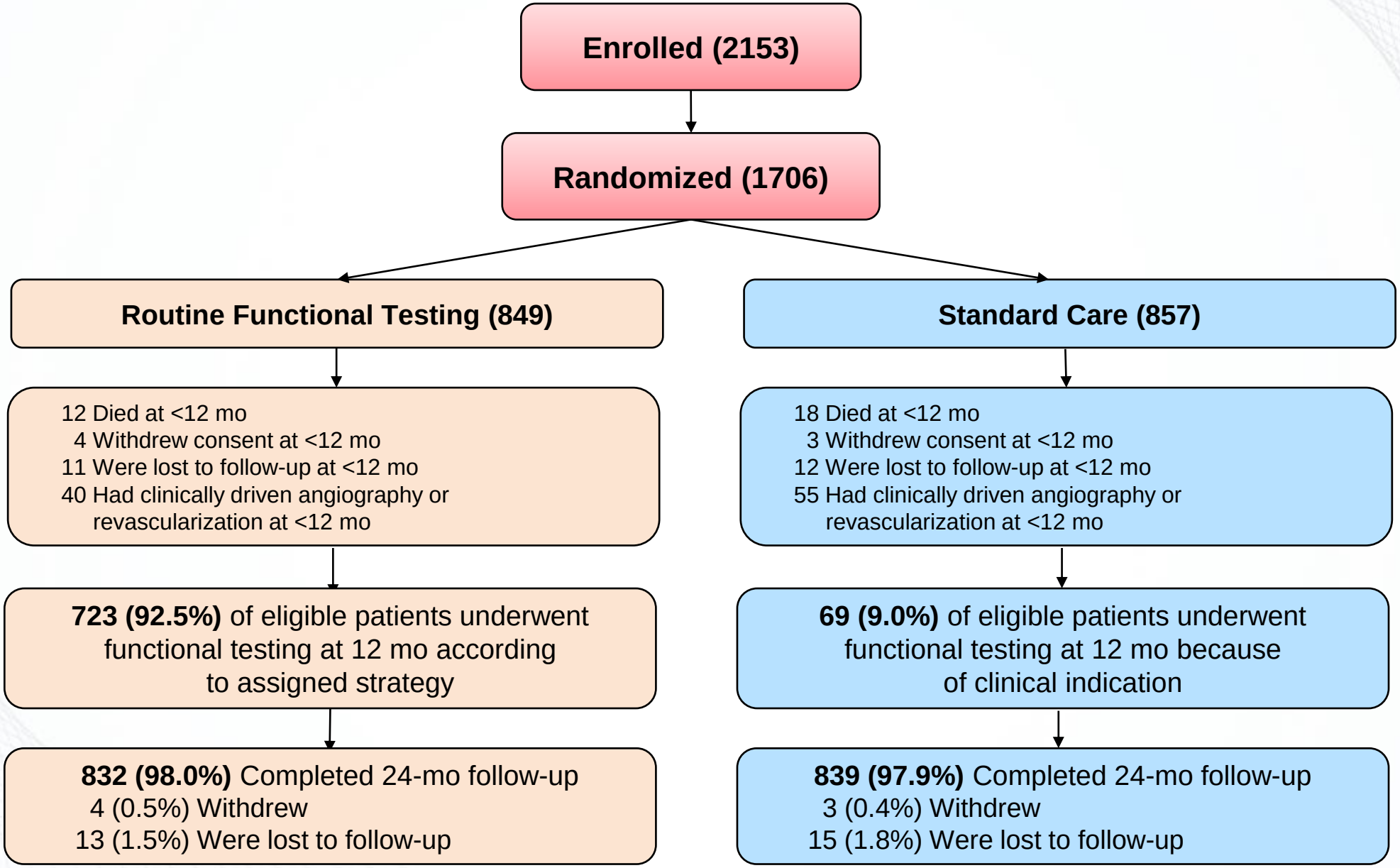
Patient Flow and Follow-Up



Key Baseline Characteristics

	Functional Testing (N = 849)	Standard Care (N = 857)
Age [yrs], mean (SD)	64.6 (10.3)	64.8 (10.3)
Male sex	666 (78.4)	690 (80.5)
Body-mass index	24.8 (3.0)	25.0 (3.2)
Criteria for high risk after PCI, n (%)		
High-risk anatomical characteristics		
Left main disease	181 (21.3)	178 (20.8)
Bifurcation disease	373 (43.9)	369 (43.1)
Ostial lesion	128 (15.1)	127 (14.8)
Chronic total occlusion	152 (17.9)	190 (22.2)
Multivessel disease (≥2 vessels stented)	376 (44.3)	389 (45.4)
Restenotic lesion	91 (10.7)	103 (12.0)
Diffuse long lesion	585 (68.9)	611 (71.3)
Bypass graft disease	4 (0.5)	7 (0.8)
High-risk clinical characteristics, n (%)		
Diabetes mellitus	321 (37.8)	339 (39.6)
Chronic renal failure	42 (4.9)	45 (5.3)
Enzyme-positive ACS	161 (19.0)	170 (19.8)
Clinical indication for index PCI, n (%)		
Stable angina or silent ischemia	598 (70.4)	582 (67.9)
Unstable angina	90 (10.6)	105 (12.3)
Non-STEMI	105 (12.4)	98 (11.4)
STEMI	56 (6.6)	72 (8.4)
Left ventricular ejection fraction [%], mean (SD)	58.8 (9.1)	58.3 (10.1)

Procedural Characteristics

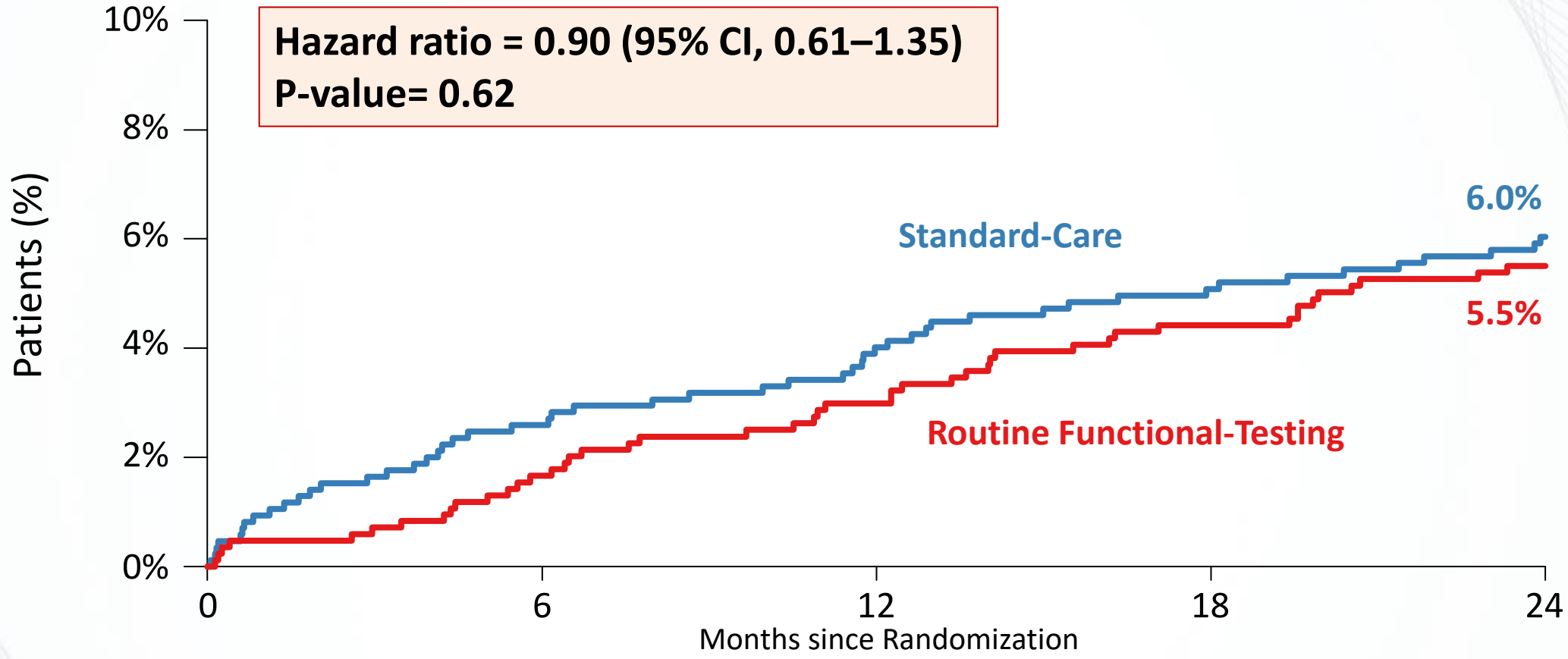
	Functional Testing (N = 849)	Standard Care (N = 857)
Total no. of diseased lesions per patient, mean (SD)	2.2 (1.2)	2.3 (1.1)
Total no. of treated lesions per patient, mean (SD)	1.4 (0.7)	1.5 (0.7)
Total no. of stents per patient, mean (SD)	1.9 (1.1)	2.0 (1.2)
Total stent length per patient [mm], mean (SD)	56.1 (33.5)	58.1 (34.2)
Use of drug-eluting stents, n (%)	824 (97.1)	821 (95.8)
Use of bioabsorbable scaffold	6 (0.7)	10 (1.2)
Use of drug-coated balloon	46 (5.4)	59 (6.9)
Intravascular ultrasound guidance	622 (73.3)	647 (75.5)
Fractional flow reserve assessed	305 (35.9)	304 (35.5)

Follow-Up Stress Testing: Types and Results*

	All Patients (n=1706)	Functional-Testing Strategy (N = 849)	Standard-Care Strategy (N = 857)
Any stress testing performed	792	723	69
Only 1 stress testing performed	415 (52.4%)	358 (49.5%)	57 (82.6%)
Two stress testing performed	377 (47.6%)	365 (50.5%)	12 (17.4%)
Results from functional stress testing available			
Positive on nuclear imaging test	195/616 (31.7%)	180/575 (31.3%)	15/41 (36.6%)
Positive on exercise ECG test	53/543 (9.8%)	46/505 (9.1%)	7/38 (18.4%)
Positive on stress echocardiography	0/10 (0%)	0/8 (0%)	0/2 (0%)
Results from both nuclear imaging test and exercise ECG test	375	363	12
Both tests positive	21 (5.6%)	20 (5.5%)	1 (8.3%)
Positive on nuclear imaging but negative/intermediate on exercise ECG	96 (25.6%)	93 (25.6%)	3 (25.0%)
Positive on exercise ECG but negative/intermediate on nuclear imaging	14 (3.7%)	12 (3.3%)	2 (16.7%)
Results from both exercise ECG and stress echocardiography	2	2	0
Both tests positive	0	0	0

*The results of all stress testing were site-reported and interpreted in real- time by qualified physicians at each participating site to ensure timely availability of results for patient treatment

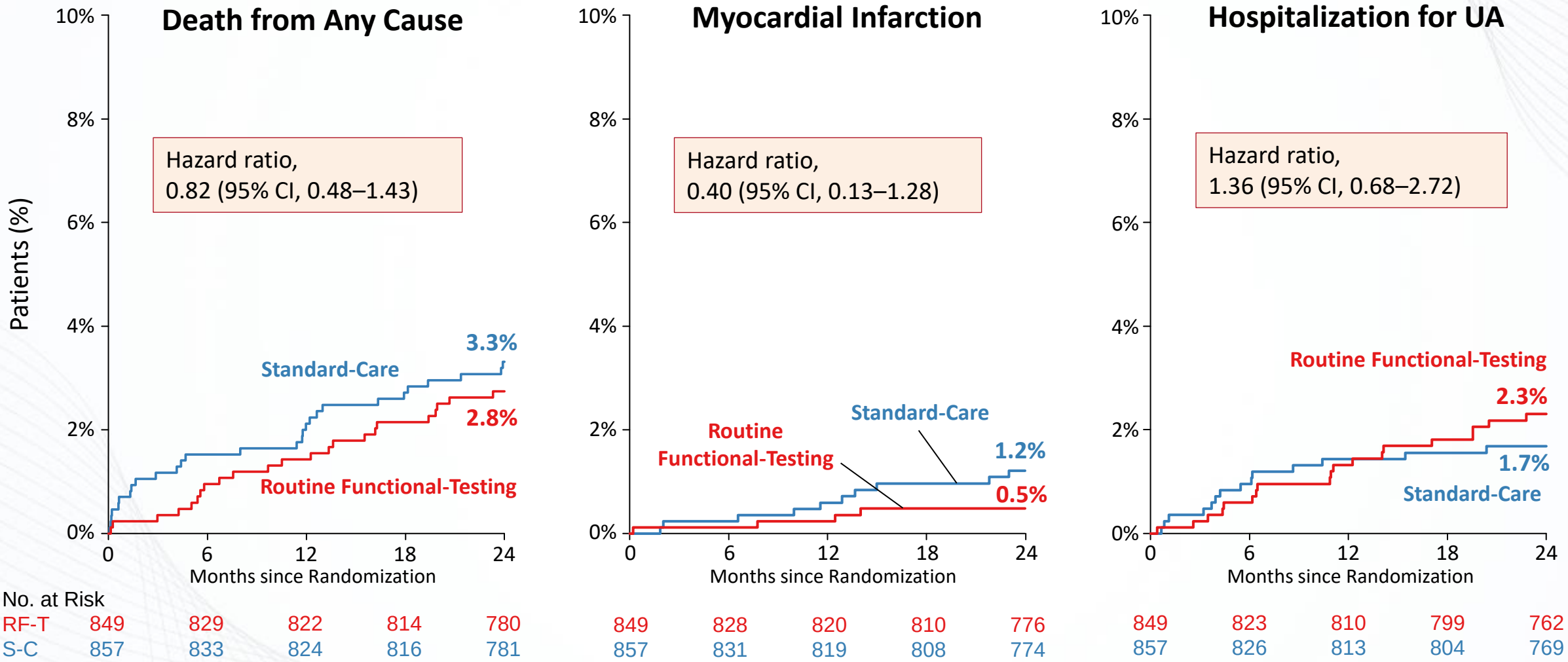
Primary Outcome: Death, MI, Hospitalization for UA



No. at Risk					
Routine Functional-Testing	849	821	807	795	758
Standard-Care	857	824	808	796	762

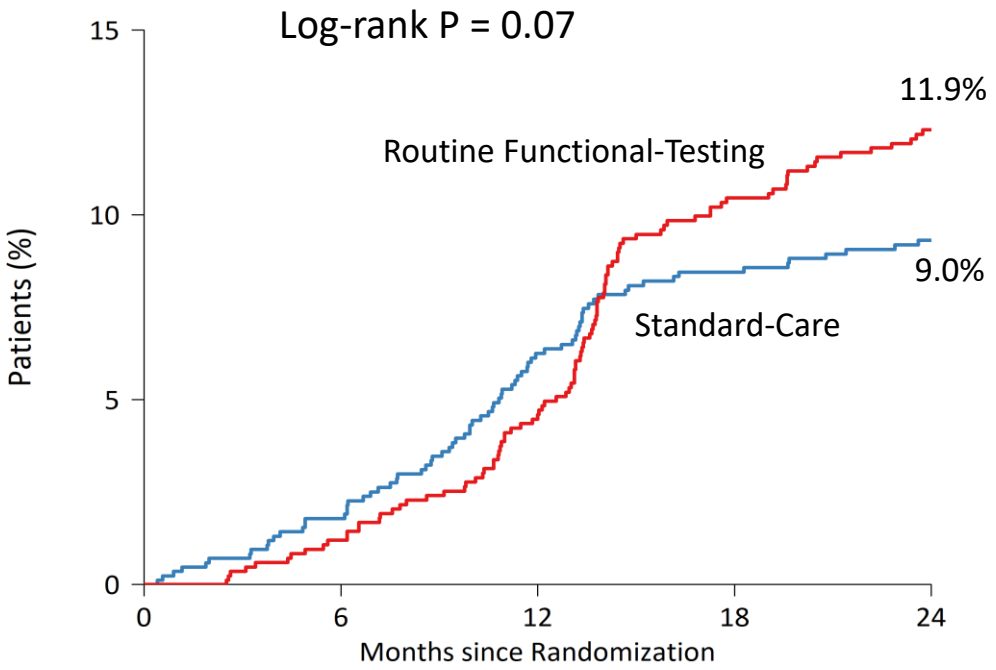
CI, confidence interval; UA, unstable angina

Components of the Primary Composite Outcome



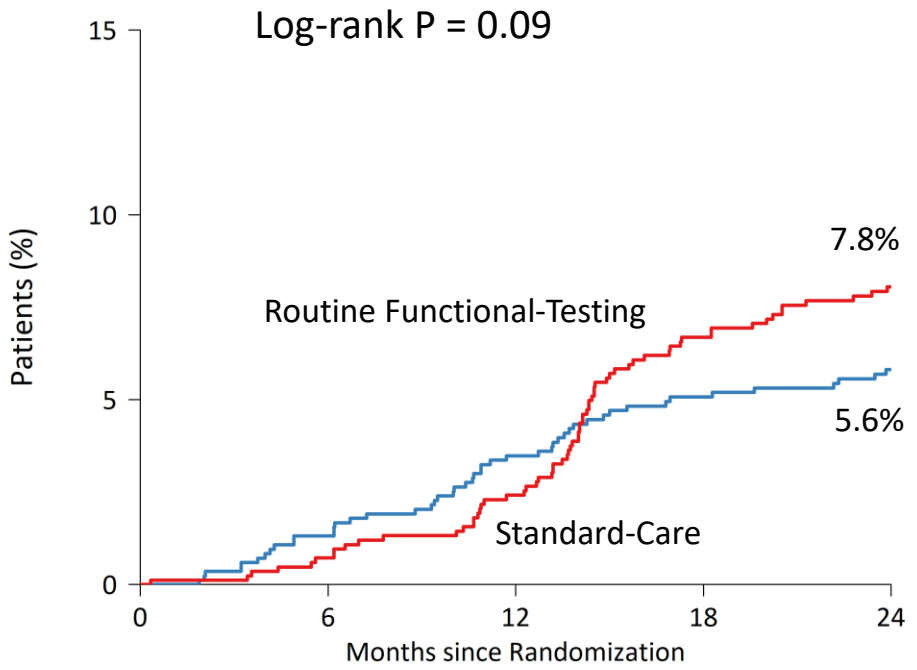
Key Secondary Endpoints

Invasive Cardiac Catheterization



No. at Risk					
Routine Functional-Testing	849	804	774	729	686
Standard-Care	857	815	771	746	716

Repeat Revascularization



No. at Risk					
Routine Functional-Testing	849	813	794	757	716
Standard-Care	857	820	795	774	741

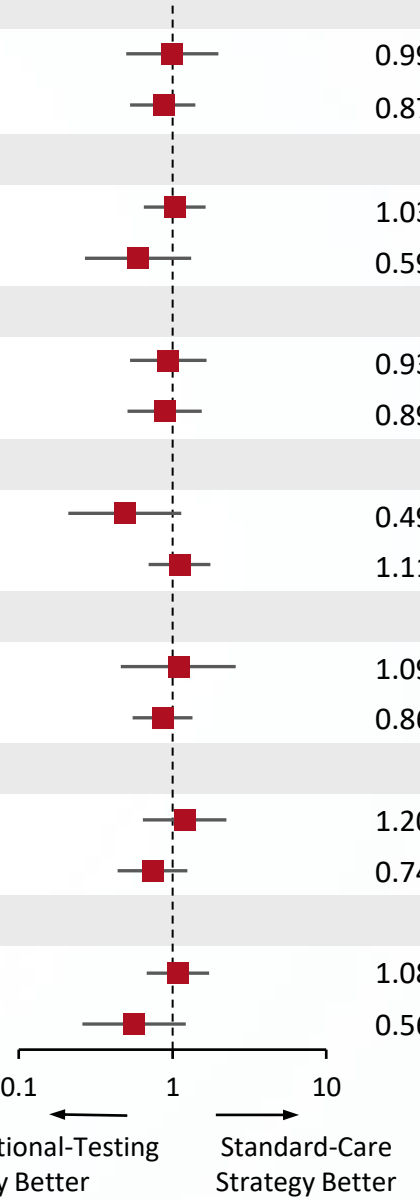
Types of CV Outcomes

Outcome*	Functional Testing (N = 849)	Standard Care (N = 857)	Difference in Event Rates (95% CI)	HR (95% CI)†
Primary composite outcome‡	46 (5.5%)	51 (6.0%)	−0.53 (−2.76 to 1.70)	0.90 (0.61 to 1.35)
Death from any cause	23 (2.8%)	28 (3.3%)	−0.57 (−2.21 to 1.07)	0.82 (0.48 to 1.43)
Myocardial infarction	4 (0.5%)	10 (1.2%)	−0.73 (−1.61 to 0.16)	0.40 (0.13 to 1.28)
Hospitalization for unstable angina	19 (2.3%)	14 (1.7%)	0.63 (−0.72 to 1.98)	1.36 (0.68 to 2.72)
Secondary outcomes				
Death or myocardial infarction	27 (3.2%)	38 (4.5%)	−1.28 (−3.12 to 0.56)	0.71 (0.43 to 1.17)
Hospitalization, any	211 (25.5%)	190 (22.8%)	2.64 (−1.48 to 6.76)	1.12 (0.92 to 1.36)
Cardiac reason	122 (14.8%)	110 (13.3%)	1.47 (−1.88 to 4.82)	1.10 (0.85 to 1.43)
Noncardiac reason	89 (10.8%)	77 (9.3%)	1.16 (−1.75 to 4.07)	1.13 (0.83 to 1.52)
Invasive coronary angiography	101 (12.3%)	77 (9.3%)	2.99 (−0.01 to 5.99)	Not calculated
Showing restenosis or obstructive CAD	69 (68.3%)	45 (58.4%)		
Showing no restenosis or obstructive CAD	32 (31.7%)	32 (41.6%)		
Repeat revascularization	66 (8.1%)	48 (5.8%)	2.23 (−0.22 to 4.68)	Not calculated
Target-lesion revascularization	34 (4.2%)	26 (3.2%)	1.00 (−0.81 to 2.81)	Not calculated
Non-target lesion revascularization	32 (3.9%)	22 (2.7%)	1.24 (−0.48 to 2.96)	Not calculated

*The percentages were estimated by the Kaplan–Meier estimates.
†Hazard ratios are for the routine functional-testing strategy as compared with the standard-care strategy by use of Cox proportional hazard models.
‡The primary composite outcome was death from any cause, myocardial infarction, or hospitalization for unstable angina.
CAD, coronary artery disease; CI, confidence interval; HR, hazard ratio;

Prespecified Key Subgroups Analysis

Subgroup	Percent of Patients	Estimated 2-Yr Event Rate (%)		Hazard Ratios (95% CI)
		Routine Functional-Testing Strategy	Standard-Care Strategy	
Age				
< 65	48.9	3.9	3.9	0.99 (0.50 to 1.99)
≥ 65	51.1	7.1	8.1	0.87 (0.53 to 1.41)
Sex				
Male	79.5	5.5	5.3	1.03 (0.65 to 1.64)
Female	20.5	5.6	9.1	0.59 (0.27 to 1.32)
Diabetes mellitus				
Yes	38.7	7.1	7.5	0.93 (0.53 to 1.66)
No	61.3	4.6	5.1	0.89 (0.51 to 1.55)
Acute coronary syndrome				
Yes	19.4	5.1	10.1	0.49 (0.21 to 1.14)
No	80.6	5.6	5.0	1.11 (0.70 to 1.76)
Left main disease				
Yes	21.0	6.2	5.7	1.09 (0.46 to 2.57)
No	79.0	5.3	6.1	0.86 (0.55 to 1.35)
Bifurcation disease				
Yes	43.5	6.0	5.0	1.20 (0.64 to 2.24)
No	56.5	5.1	6.9	0.74 (0.44 to 1.25)
Multivessel disease				
Yes	69.8	6.2	5.7	1.08 (0.68 to 1.73)
No	30.2	3.9	6.8	0.56 (0.26 to 1.22)



Study Limitations

- It was not possible to mask the follow-up strategy from the patients and investigators (the possibility of ascertainment bias)
- The observed number of primary-outcome events was lower than expected (several explanations would be possible)
- Some nonadherence of stress testing in the functional-testing group was observed owing to several medical reasons
- Routine stress testing included three different types of methods with diagnostic accuracy varying across the tests
- Our trial did not address quality of life, cost-effectiveness, or radiation exposure, which could be crucial components of decision-making

Summary for the POST-PCI Key Findings

- In this pragmatic RCT comparing routine functional testing and standard care in patients with high-risk anatomical or clinical characteristics who underwent PCI, we found no significant between-group difference in the primary composite of death, MI, or UA hospitalization at 2 year.
- The incidence of such events was lower than expected in the two investigational groups, possibly due to improvements in the methods/techniques to perform complex PCI and general improvements in cardiovascular care during the past few years.
- The routine stress testing appeared to be associated with more frequent CAG and repeat revascularization after 1 year, which did not result in a significant reduction in major cardiovascular events or mortality.

Conclusions

In this trial involving high-risk patients who had undergone PCI,

1. **Routine functional testing, as compared with standard care, did not result in a lower risk of ischemic cardiovascular events or death from any cause at 2 years.**
2. **Our trial do not support active surveillance with routine functional testing for follow-up strategy in high-risk patients who undergo PCI.**

Further Details

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Routine Functional Testing or Standard Care in High-Risk Patients after PCI

Duk-Woo Park, M.D.,* Do-Yoon Kang, M.D.,* Jung-Min Ahn, M.D., Sung-Cheol Yun, Ph.D., Yong-Hoon Yoon, M.D., Seung-Ho Hur, M.D., Cheol Hyun Lee, M.D., Won-Jang Kim, M.D., Se Hun Kang, M.D., Chul Soo Park, M.D., Bong-Ki Lee, M.D., Jung-Won Suh, M.D., Jung Han Yoon, M.D., Jae Woong Choi, M.D., Kee-Sik Kim, M.D., Si Wan Choi, M.D., Su Nam Lee, M.D., and Seung-Jung Park, M.D., for the POST-PCI Investigators*

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