Online supplementals

Figure Legend

Online Figure 1. Clinical outcomes at two years in patients with and without complex PCI.

Kaplan-Meier curves show a cumulative incidence of POCE (A), all-cause mortality (B), any stroke (C), any myocardial infarction (D), any revascularization (E), and BARC type 3 or 5 bleeding (F) in patients with complex PCI (red) and non-complex PCI (blue).

BARC: Bleeding Academic Research Consortium; CI: confidence interval; HR: hazard ratio; PCI: percutaneous coronary intervention; POCE: patient-oriented composite endpoint.

Online Table 1. Prevalence of complex PCI components according to allocated antiplatelet regimens*

	Experimental strategy (n= 2,283)	Reference strategy (n= 2,287)	Within complex PCI cohort (n= 4,570)	Within overall cohort (n= 15,450)
Multivessel PCI	74.2 (1,694)	73.2 (1,675)	73.7 (3,369)	21.8 (3,369)
≥3 stents implanted	60.8 (1,388)	60.3 (1,380)	60.6 (2,768)	17.9 (2,768)
≥3 lesions treated	27.8 (635)	29.1 (666)	28.5 (1,301)	8.4 (1,301)
Bifurcation PCI with two stents	10.1 (231)	10.6 (242)	10.4 (473)	3.1 (473)
Total stent length> 60mm	44.5 (1,015)	46.4 (1,062)	45.4 (2,077)	13.4 (2,077)

Data are presented as percentage (number).

* Not mutually exclusive.

PCI; percutaneous coronary intervention.

Online Table 2. Baseline characteristics according to complex PCI

	Complex PCI (n= 4,570)	Non-complex PCI (n= 10,880)	p-value
Age (year)	65.2± 10.2	64.2± 10.3	<0.001
BMI (kg/m^2)	28.1± 4.5	28.2± 4.6	0.037
Gender			<0.001
Male	78.7 (3595/ 4570)	75.8 (8248/ 10880)	
Female	21.3 (975/ 4570)	24.2 (2632/ 10880)	
Diabetes	26.3 (1200/ 4566)	24.6 (2680/ 10873)	0.033
Insulin-dependent diabetes mellitus	8.2 (373/ 4559)	7.4 (799/ 10845)	0.082
Hypertension	73.8 (3362/ 4556)	73.5 (7962/ 10840)	0.660
Hypercholesterolemia	70.5 (3128/ 4439)	69.4 (7300/ 10523)	0.183
Current smoker	26.7 (1218/ 4570)	25.9 (2818/ 10880)	0.332
PVD	6.9 (311/ 4536)	6.0 (651/ 10771)	0.059
COPD	5.5 (251/ 4553)	4.9 (533/ 10830)	0.128
Previous major bleeding	0.6 (29/ 4562)	0.6 (67/ 10867)	0.890
Impaired renal failure*	14.1 (641/ 4554)	13.5 (1463/ 10813)	0.369
Previous stroke	2.8 (127/ 4560)	2.5 (275/ 10867)	0.365
Previous MI	21.4 (973/ 4554)	23.8 (2581/ 10851)	0.001
Previous PCI	29.4 (1341/ 4565)	33.7 (3667/ 10871)	<0.001
Previous CABG	6.0 (276/ 4565)	5.8 (628/ 10873)	0.514
Clinical presentation			0.009
Stable CAD	51.4 (2349/ 4570)	53.7 (5841/ 10880)	
ACS	48.6 (2221/ 4570)	46.3 (5039/ 10880)	
Overall			<0.001
UA	11.6 (530/ 4570)	13.2 (1433/ 10880)	
NSTEMI	23.1 (1057/ 4570)	20.4 (2222/ 10880)	
STEMI	13.9 (634/ 4570)	12.7 (1384/ 10880)	

Vascular access site			
Femoral	31.3 (1415/ 4517)	25.2 (2712/ 10743)	<0.001
Brachial	0.8 (36/ 4517)	0.6 (68/ 10743)	0.261
Radial	74.7 (3376/ 4517)	74.9 (8046/ 10743)	0.840
Lesion treated per patient			<0.001
1 lesion	17.2 (785/ 4570)	91.0 (9896/ 10880)	
2 lesions	54.4 (2484/ 4570)	9.0 (984/ 10880)	
≥3 lesions	28.5 (1301/ 4570)	0 (0/ 10880)	
Treated lesions			<0.001
LM	4.1 (410/ 10056)	0 (0/ 11864)	
LAD	37.3 (3749/ 10056)	44.3 (5256/ 11864)	
LCX	26.2 (2634/ 10056)	23.0 (2732/ 11864)	
RCA	31.9 (3205/ 10056)	31.3 (3717/ 11864)	
Bypass graft	0.6 (58/ 10056)	1.3 (159/ 11864)	
Stented lesions			
Mean stents per lesion	1.35± 0.67	1.11± 0.31	<0.001
Biomatrix stent	91.4 (9189/ 10056)	95.5 (11325/ 11864)	<0.001
Other stent	10.3 (1038/ 10056)	5.2 (616/ 11864)	<0.001
Mean total stent length per lesion	28.2± 17.5	22.2± 9.6	<0.001
Mean total stent diameter per lesion	2.95± 0.46	3.01± 0.47	<0.001
Direct stenting	29.2 (2932/ 10056)	35.8 (4247/ 11864)	<0.001
Bifurcation	15.0 (1506/ 10056)	9.7 (1152/ 11864)	<0.001
Thrombus aspiration	3.4 (337/ 10056)	5.7 (674/ 11864)	<0.001
TIMI flow			
Pre-procedure			<0.001
0 or 1	13.0 (1025/ 7859)	12.8 (1443/ 11242)	
2	10.7 (839/ 7859)	12.9 (1448/ 11242)	
3	76.3 (5995/ 7859)	74.3 (8351/ 11242)	

Post-procedure			0.090
0 or 1	0.1 (10/ 8104)	0.1 (8/ 11468)	
2	0.5 (43/ 8104)	0.4 (41/ 11468)	
3	99.3 (8051/ 8104)	99.6 (11419/ 11468)	

Data are presented as mean ± standard deviation or percentage (number).

* Based on creatinine-estimated GFR (eGFR) clearance of <60 ml/min/1.73 m^2, using the Modification of Diet in Renal Disease (MDRD) formula.

ACS: acute coronary syndrome; BMI: body mass index; CABG: coronary artery bypass graft; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; LAD: left anterior descending coronary artery; LCX: left circumflex coronary artery; LM: left main; NSTEMI: non-ST-elevation myocardial infarction; PCI: percutaneous coronary intervention; PVD: peripheral vascular disease; RCA: right coronary artery; STEMI: ST-elevation myocardial infarction; TIMI: thrombolysis in myocardial infarction; UA: unstable angina.

Online Table 3. Efficacy and safety outcomes in patients with and without complex PCI

	Complex PCI (n= 4,570)	Non-complex PCI (n= 10,880)	HR (95% CI)	p-value
At one year				
Primary endpoint	2.52 (115/ 4570)	2.07 (225/ 10880)	1.22 (0.98-1.53)	0.082
All-cause mortality	1.71 (78/ 4570)	1.41 (153/ 10880)	1.22 (0.93-1.60)	0.159
New Q-wave MI	0.86 (39/ 4570)	0.68 (73/ 10880)	1.28 (0.86-1.88)	0.219
POCE	10.64 (483/ 4570)	7.81 (843/ 10880)	1.39 (1.24-1.55)	<0.001
NACE	11.99 (544/ 4570)	8.84 (954/ 10880)	1.39 (1.25-1.54)	<0.001
Any stroke	0.53 (24/ 4570)	0.68 (73/ 10880)	0.78 (0.49-1.24)	0.300
Any MI	2.66 (120/ 4570)	1.78 (191/ 10880)	1.51 (1.20-1.89)	<0.001
Any revascularization	8.12 (365/ 4570)	5.59 (599/ 10880)	1.48 (1.30-1.68)	<0.001
Target vessel revascularization	4.58 (206/ 4570)	2.67 (288/ 10880)	1.72 (1.44-2.06)	<0.001
Definite ST	0.71 (32/ 4570)	0.54 (58/ 10880)	1.32 (0.85-2.03)	0.212
BARC type 3 or 5 bleeding	1.90 (86/ 4570)	1.47 (158/ 10880)	1.30 (1.001-1.69)	0.0495
BARC type 5	0.24 (11/ 4570)	0.17 (18/ 10880)	1.46 (0.69-3.09)	0.324
BARC type 3	1.73 (78/ 4570)	1.39 (149/ 10880)	1.25 (0.95-1.65)	0.108
Between one year and two years				
Primary endpoint	2.00 (89/ 4450)	1.91 (203/ 10652)	1.05 (0.82-1.35)	0.702
All-cause mortality	1.58 (71/ 4487)	1.49 (160/ 10724)	1.06 (0.80-1.40)	0.681
New Q-wave MI	0.48 (21/ 4450)	0.44 (46/ 10652)	1.09 (0.65-1.83)	0.732
POCE	5.56 (224/ 4037)	5.00 (494/ 9912)	1.12 (0.95-1.31)	0.174
NACE	5.75 (228/ 3976)	5.24 (512/ 9801)	1.10 (0.94-1.29)	0.229
Any stroke	0.27 (12/ 4420)	0.50 (48/ 10530)	0.59 (0.32-1.12)	0.107
Any MI	1.03 (44/ 4326)	1.06 (109/ 10422)	0.97 (0.68-1.38)	0.872
Any revascularization	3.71 (150/ 4083)	3.04 (302/ 10015)	1.22 (1.004-1.49)	0.045
Target vessel revascularization	2.40 (101/ 4242)	1.42 (145/ 10318)	1.70 (1.32-2.19)	<0.001
Definite ST	0.30 (13/ 4410)	0.19 (20/ 10541)	1.55 (0.77-3.12)	0.217

BARC type 3 or 5 bleeding	0.60 (26/ 4366)	0.49 (51/ 10460)	1.22 (0.76-1.96)	0.407
BARC type 5	0.09 (4/ 4438)	0.11 (12/ 10590)	0.79 (0.26-2.46)	0.690
BARC type 3	0.58 (25/ 4366)	0.45 (47/ 10461)	1.27 (0.78-2.07)	0.328
At two years				
Primary endpoint	4.47 (204/ 4570)	3.94 (428/ 10880)	1.14 (0.96-1.35)	0.124
All-cause mortality	3.26 (149/ 4570)	2.88 (313/ 10880)	1.14 (0.94-1.38)	0.198
New Q-wave MI	1.34 (60/ 4570)	1.11 (119/ 10880)	1.21 (0.88-1.64)	0.237
POCE	15.62 (707/ 4570)	12.41 (1337/ 10880)	1.29 (1.18-1.41)	<0.001
NACE	17.05 (772/ 4570)	13.61 (1466/ 10880)	1.29 (1.18-1.40)	<0.001
Any stroke	0.80 (36/ 4570)	1.14 (121/ 10880)	0.71 (0.49-1.03)	0.070
Any MI	3.66 (164/ 4570)	2.81 (300/ 10880)	1.31 (1.08-1.59)	0.005
Any revascularization	11.52 (515/ 4570)	8.46 (901/ 10880)	1.39 (1.25-1.55)	<0.001
Target vessel revascularization	6.87 (307/ 4570)	4.07 (433/ 10880)	1.72 (1.48-1.99)	<0.001
Definite ST	1.00 (45/ 4570)	0.73 (78/ 10880)	1.38 (0.95-1.99)	0.088
BARC type 3 or 5 bleeding	2.49 (112/ 4570)	1.96 (209/ 10880)	1.28 (1.02-1.61)	0.034
BARC type 5	0.33 (15/ 4570)	0.28 (30/ 10880)	1.19 (0.64-2.22)	0.579
BARC type 3	2.30 (103/ 4570)	1.83 (196/ 10880)	1.26 (0.99-1.60)	0.060

1 Data are presented as mean ± standard deviation or percentage (number).

2 BARC: Bleeding Academic Research Consortium; CI: confidence interval; HR: hazard ratio;

3 MI: myocardial infarction; NACE: net adverse clinical events; PCI: percutaneous coronary

4 intervention; POCE: patient-oriented composite endpoint; ST: stent thrombosis.

Online Table 4. Clinical outcomes and treatment effect of the experimental strategy vs. the reference regimen in patients with complex PCI vs. non-complex PCI.

	Complex PCI (n= 4,570)				Non-complex PCI (n= 10,880)				
	Experimental strategy (n= 2,283)	Reference strategy (n= 2,287)	Hazard ratio (95% CI)	p-value	Experimental strategy (n= 5,434)	Reference strategy (n= 5,446)	Hazard ratio (95% CI)	p-value	p-value for interaction
At one year									
Primary endpoint	1.80 (41/ 2283)	3.24 (74/ 2287)	0.55 (0.38-0.81)	0.002	1.97 (107/ 5434)	2.17 (118/ 5446)	0.91 (0.70-1.18)	0.472	0.034
All-cause mortality	1.18 (27/ 2283)	2.23 (51/ 2287)	0.53 (0.33-0.84)	0.007	1.40 (76/ 5434)	1.41 (77/ 5446)	0.99 (0.72-1.36)	0.950	0.029
New Q-wave MI	0.62 (14/ 2283)	1.10 (25/ 2287)	0.56 (0.29-1.07)	0.080	0.57 (31/ 5434)	0.78 (42/ 5446)	0.74 (0.46-1.18)	0.202	0.491
POCE	9.42 (213/ 2283)	11.86 (270/ 2287)	0.78 (0.65-0.93)	0.007	7.97 (429/ 5434)	7.65 (414/ 5446)	1.04 (0.91-1.19)	0.539	0.011
NACE	10.52 (238/ 2283)	13.44 (306/ 2287)	0.77 (0.65-0.91)	0.002	8.93 (481/ 5434)	8.74 (473/ 5446)	1.02 (0.90-1.16)	0.720	0.008
Any stroke	0.71 (16/ 2283)	0.35 (8/ 2287)	2.00 (0.86-4.68)	0.109	0.62 (33/ 5434)	0.74 (40/ 5446)	0.83 (0.52-1.32)	0.427	0.074
Any MI	2.44 (55/ 2283)	2.88 (65/ 2287)	0.85 (0.59-1.21)	0.360	2.01 (108/ 5434)	1.54 (83/ 5446)	1.31 (0.98-1.75)	0.064	0.061
Any revascularization	7.22 (162/ 2283)	9.01 (203/ 2287)	0.79 (0.64-0.97)	0.026	5.77 (308/ 5434)	5.41 (291/ 5446)	1.07 (0.91-1.25)	0.434	0.025
Target vessel revascularization	3.47 (78/ 2283)	5.68 (128/ 2287)	0.60 (0.46-0.80)	<0.001	2.84 (152/ 5434)	2.53 (136/ 5446)	1.13 (0.89-1.42)	0.314	0.001
Definite ST	0.84 (19/ 2283)	0.57 (13/ 2287)	1.47 (0.72-2.97)	0.289	0.58 (31/ 5434)	0.50 (27/ 5446)	1.15 (0.69-1.93)	0.588	0.591
BARC type 3 or 5 bleeding	1.77 (40/ 2283)	2.04 (46/ 2287)	0.87 (0.57-1.33)	0.525	1.38 (74/ 5434)	1.56 (84/ 5446)	0.89 (0.65-1.21)	0.445	0.953

BARC type 5	0.22 (5/ 2283)	0.26 (6/ 2287)	0.83 (0.25-2.73)	0.763	0.15 (8/ 5434)	0.19 (10/ 5446)	0.80 (0.32-2.03)	0.641	0.963
BARC type 3	1.55 (35/ 2283)	1.91 (43/ 2287)	0.82 (0.52-1.27)	0.371	1.31 (70/ 5434)	1.47 (79/ 5446)	0.89 (0.65-1.23)	0.480	0.754
Between one and two years									
Primary endpoint	1.75 (39/ 2238)	2.26 (50/ 2212)	0.77 (0.51-1.17)	0.222	1.96 (104/ 5325)	1.86 (99/ 5327)	1.05 (0.80-1.38)	0.726	0.225
All-cause mortality	1.47 (33/ 2252)	1.70 (38/ 2235)	0.86 (0.54-1.37)	0.533	1.49 (80/ 5356)	1.49 (80/ 5368)	1.00 (0.73-1.37)	0.992	0.600
New Q-wave MI	0.32 (7/ 2238)	0.64 (14/ 2212)	0.49 (0.20-1.22)	0.128	0.50 (26/ 5325)	0.38 (20/ 5327)	1.30 (0.73-2.33)	0.374	0.078
POCE	5.08 (103/ 2037)	6.06 (121/ 2000)	0.83 (0.64-1.09)	0.178	4.80 (236/ 4935)	5.19 (258/ 4977)	0.92 (0.77-1.10)	0.360	0.544
NACE	5.34 (107/ 2012)	6.17 (121/ 1964)	0.86 (0.67-1.12)	0.268	5.12 (249/ 4882)	5.36 (263/ 4919)	0.95 (0.80-1.13)	0.586	0.535
Any stroke	0.32 (7/ 2210)	0.23 (5/ 2210)	1.40 (0.45-4.42)	0.562	0.38 (20/ 5254)	0.54 (28/ 5276)	0.72 (0.40-1.27)	0.256	0.305
Any MI	0.75 (16/ 2170)	1.31 (28/ 2156)	0.57 (0.31-1.05)	0.071	0.93 (48/ 5187)	1.18 (61/ 5235)	0.79 (0.54-1.16)	0.232	0.363
Any revascularization	3.33 (68/ 2062)	4.08 (82/ 2021)	0.81 (0.59-1.12)	0.203	2.96 (146/ 4985)	3.13 (156/ 5030)	0.94 (0.75-1.18)	0.613	0.452
Target vessel revascularization	2.26 (48/ 2146)	2.54 (53/ 2096)	0.89 (0.60-1.31)	0.542	1.32 (67/ 5137)	1.52 (78/ 5181)	0.87 (0.62-1.20)	0.386	0.929
Definite ST	0.23 (5/ 2203)	0.37 (8/ 2207)	0.63 (0.21-1.92)	0.415	0.12 (6/ 5254)	0.27 (14/ 5287)	0.43 (0.17-1.12)	0.085	0.616
BARC type 3 or 5 bleeding	0.69 (15/ 2188)	0.51 (11/ 2178)	1.36 (0.63-2.97)	0.436	0.60 (31/ 5219)	0.38 (20/ 5241)	1.56 (0.89-2.74)	0.122	0.784
BARC type 5	0.14 (3/ 2221)	0.05 (1/ 2217)	3.00 (0.31-28.87)	0.341	0.10 (5/ 5282)	0.13 (7/ 5308)	0.72 (0.23-2.26)	0.573	0.269
BARC type 3	0.65 (14/ 2188)	0.51 (11/ 2178)	1.27 (0.58-2.80)	0.551	0.56 (29/ 5219)	0.35 (18/ 5242)	1.62 (0.90-2.92)	0.108	0.630
At two years									

Primary endpoint	3.51 (80/ 2283)	5.43 (124/ 2287)	0.64 (0.48-0.85)	0.002	3.89 (211/ 5434)	3.99 (217/ 5446)	0.97 (0.81-1.18)	0.779	0.015
All-cause mortality	2.63 (60/ 2283)	3.89 (89/ 2287)	0.67 (0.48-0.93)	0.017	2.88 (156/ 5434)	2.88 (157/ 5446)	1.00 (0.80-1.24)	0.971	0.0503
New Q-wave MI	0.94 (21/ 2283)	1.74 (39/ 2287)	0.53 (0.31-0.91)	0.021	1.07 (57/ 5434)	1.15 (62/ 5446)	0.92 (0.64-1.32)	0.654	0.096
POCE	14.02 (316/ 2283)	17.20 (391/ 2287)	0.80 (0.69-0.93)	0.003	12.38 (665/ 5434)	12.45 (672/ 5446)	1.00 (0.89-1.11)	0.945	0.017
NACE	15.30 (345/ 2283)	18.78 (427/ 2287)	0.80 (0.69-0.92)	0.002	13.59 (730/ 5434)	13.63 (736/ 5446)	1.00 (0.90-1.11)	0.973	0.011
Any stroke	1.03 (23/ 2283)	0.58 (13/ 2287)	1.77 (0.90-3.50)	0.099	1.00 (53/ 5434)	1.27 (68/ 5446)	0.78 (0.55-1.12)	0.182	0.037
Any MI	3.17 (71/ 2283)	4.15 (93/ 2287)	0.76 (0.56-1.04)	0.085	2.93 (156/ 5434)	2.70 (144/ 5446)	1.09 (0.87-1.37)	0.446	0.065
Any revascularization	10.31 (230/ 2283)	12.73 (285/ 2287)	0.80 (0.67-0.95)	0.010	8.56 (454/ 5434)	8.37 (447/ 5446)	1.02 (0.90-1.17)	0.730	0.024
Target vessel revascularization	5.65 (126/ 2283)	8.08 (181/ 2287)	0.69 (0.55-0.86)	0.001	4.12 (219/ 5434)	4.01 (214/ 5446)	1.03 (0.85-1.25)	0.749	0.007
Definite ST	1.07 (24/ 2283)	0.94 (21/ 2287)	1.15 (0.64-2.06)	0.647	0.69 (37/ 5434)	0.76 (41/ 5446)	0.91 (0.58-1.41)	0.666	0.532
BARC type 3 or 5	2.45 (55/ 2283)	2.54 (57/ 2287)	0.97 (0.67-1.40)	0.856	1.97 (105/ 5434)	1.94 (104/ 5446)	1.01 (0.77-1.33)	0.915	0.834
BARC type 5	0.36 (8/ 2283)	0.31 (7/ 2287)	1.14 (0.42-3.16)	0.794	0.24 (13/ 5434)	0.32 (17/ 5446)	0.77 (0.37-1.58)	0.476	0.531
BARC type 3	2.19 (49/ 2283)	2.41 (54/ 2287)	0.91 (0.62-1.34)	0.628	1.86 (99/ 5434)	1.81 (97/ 5446)	1.03 (0.78-1.36)	0.858	0.618

1 Data are presented as percentage (number of events).

2 Abbreviations as in **Online Table 3.**

Online Table 5. Clinical outcomes and treatment effect of the experimental strategy vs. the reference regimen in patients with stable CAD

	Complex PCI (n= 2,349)				Non-complex PCI (n= 5,841)				
	Experimental strategy (n=1,174)	Reference strategy (n=1,175)	Hazard ratio (95% CI)	p-value	Experimental strategy (n=2,910)	Reference strategy (n=2,931)	Hazard ratio (95% CI)	p-value	p-value for interaction
At two years									
Primary endpoint	3.93 (46/ 1174)	5.03 (59/ 1175)	0.78 (0.53-1.14)	0.197	3.51 (102/ 2910)	4.03 (118/ 2931)	0.87 (0.67-1.13)	0.299	0.634
All-cause mortality	2.90 (34/ 1174)	3.41 (40/ 1175)	0.85 (0.54-1.34)	0.483	2.37 (69/ 2910)	2.70 (79/ 2931)	0.88 (0.64-1.21)	0.435	0.902
New Q-wave MI	1.13 (13/ 1174)	1.81 (21/ 1175)	0.62 (0.31-1.23)	0.171	1.15 (33/ 2910)	1.38 (40/ 2931)	0.83 (0.52-1.32)	0.429	0.483
POCE	15.06 (174/ 1174)	17.78 (208/ 1175)	0.83 (0.68-1.02)	0.073	11.79 (339/ 2910)	12.44 (361/ 2931)	0.95 (0.82-1.10)	0.483	0.301
NACE	16.36 (189/ 1174)	18.72 (219/ 1175)	0.86 (0.71-1.05)	0.132	13.21 (380/ 2910)	13.58 (394/ 2931)	0.98 (0.85-1.12)	0.737	0.305
Any stroke	0.96 (11/ 1174)	0.52 (6/ 1175)	1.85 (0.69-5.01)	0.224	0.77 (22/ 2910)	1.15 (33/ 2931)	0.67 (0.39-1.15)	0.150	0.079
Any MI	3.21 (37/ 1174)	3.98 (46/ 1175)	0.81 (0.52-1.25)	0.337	2.34 (67/ 2910)	2.23 (64/ 2931)	1.06 (0.75-1.49)	0.743	0.340
Any revascularization	10.67 (122/ 1174)	13.58 (157/ 1175)	0.77 (0.61-0.98)	0.031	8.64 (246/ 2910)	8.62 (248/ 2931)	1.00 (0.84-1.20)	0.967	0.079
Target vessel revascularization	6.30 (72/ 1174)	8.64 (100/ 1175)	0.71 (0.53-0.97)	0.030	4.28 (122/ 2910)	3.79 (109/ 2931)	1.13 (0.88-1.47)	0.338	0.023
Definite ST	1.04 (12/ 1174)	0.86 (10/ 1175)	1.21 (0.52-2.80)	0.654	0.66 (19/ 2910)	0.59 (17/ 2931)	1.13 (0.59-2.17)	0.716	0.896
BARC type 3 or 5 bleeding	2.61 (30/ 1174)	1.64 (19/ 1175)	1.60 (0.90-2.84)	0.109	2.03 (58/ 2910)	1.63 (47/ 2931)	1.25 (0.85-1.83)	0.258	0.481
BARC type 5	0.17 (2/ 1174)	0.26 (3/ 1175)	0.67 (0.11-4.00)	0.660	0.17 (5/ 2910)	0.28 (8/ 2931)	0.63 (0.21-1.93)	0.420	0.953

BARC type 3	2.44 (28/ 1174)	1.47 (17/ 1175)	1.67 (0.91-3.05)	0.096	1.93 (55/ 2910)	1.46 (42/ 2931)	1.33 (0.89-1.98)	0.169	0.531

1 Data are presented as mean ± standard deviation or percentage (number).

2 Abbreviations as in Online Table 3.

3

Online Table 6. Clinical outcomes and treatment effect of the experimental strategy vs. the reference regimen in patients with ACS

	Complex PCI (n= 2,221)				Non-complex PCI (n= 5,039)				
	Experimental strategy (n=1,109)	Reference strategy (n=1,112)	Hazard ratio (95% CI)	p-value	Experimental strategy (n=2,524)	Reference strategy (n=2,515)	Hazard ratio (95% CI)	p-value	p-value for interaction
At two years									
Primary endpoint	3.07 (34/ 1109)	5.85 (65/ 1112)	0.52 (0.34-0.78)	0.002	4.32 (109/ 2524)	3.94 (99/ 2515)	1.10 (0.84-1.44)	0.508	0.003
All-cause mortality	2.35 (26/ 1109)	4.41 (49/ 1112)	0.53 (0.33-0.85)	0.008	3.45 (87/ 2524)	3.10 (78/ 2515)	1.11 (0.82-1.51)	0.495	0.009
New Q-wave MI	0.73 (8/ 1109)	1.66 (18/ 1112)	0.44 (0.19-1.01)	0.053	0.98 (24/ 2524)	0.89 (22/ 2515)	1.09 (0.61-1.94)	0.778	0.081
POCE	12.92 (142/ 1109)	16.58 (183/ 1112)	0.76 (0.61-0.95)	0.014	13.07 (326/ 2524)	12.46 (311/ 2515)	1.05 (0.90-1.23)	0.528	0.018
NACE	14.19 (156/ 1109)	18.84 (208/ 1112)	0.73 (0.59-0.90)	0.003	14.03 (350/ 2524)	13.69 (342/ 2515)	1.02 (0.88-1.19)	0.763	0.010
Any stroke	1.10 (12/ 1109)	0.64 (7/ 1112)	1.71 (0.67-4.33)	0.262	1.26 (31/ 2524)	1.42 (35/ 2515)	0.89 (0.55-1.44)	0.621	0.222
Any MI	3.12 (34/ 1109)	4.33 (47/ 1112)	0.72 (0.46-1.11)	0.137	3.60 (89/ 2524)	3.25 (80/ 2515)	1.12 (0.83-1.51)	0.473	0.102
Any revascularization	9.93 (108/ 1109)	11.81 (128/ 1112)	0.83 (0.64-1.07)	0.150	8.46 (208/ 2524)	8.08 (199/ 2515)	1.05 (0.86-1.27)	0.639	0.152
Target vessel revascularization	4.97 (54/ 1109)	7.48 (81/ 1112)	0.65 (0.46-0.92)	0.015	3.94 (97/ 2524)	4.27 (105/ 2515)	0.92 (0.70-1.22)	0.578	0.123
Definite ST	1.10 (12/ 1109)	1.01 (11/ 1112)	1.09 (0.48-2.46)	0.840	0.72 (18/ 2524)	0.97 (24/ 2515)	0.75 (0.41-1.38)	0.354	0.474
BARC type 3 or 5 bleeding	2.28 (25/ 1109)	3.49 (38/ 1112)	0.65 (0.39-1.08)	0.098	1.90 (47/ 2524)	2.30 (57/ 2515)	0.82 (0.56-1.21)	0.321	0.474
BARC type 5	0.55 (6/ 1109)	0.37 (4/ 1112)	1.50 (0.42-5.30)	0.533	0.32 (8/ 2524)	0.37 (9/ 2515)	0.89 (0.34-2.30)	0.809	0.521

BARC type 3	1.92 (21/ 1109)	3.40 (37/ 1112)	0.56 (0.33-0.96)	0.035	1.78 (44/ 2524)	2.22 (55/ 2515)	0.80 (0.54-1.19)	0.264	0.303

1 Data are presented as mean ± standard deviation or percentage (number).

2 Abbreviations as in **Online Table 3**.

Online Table 7. Definition of complex PCI in previous studies

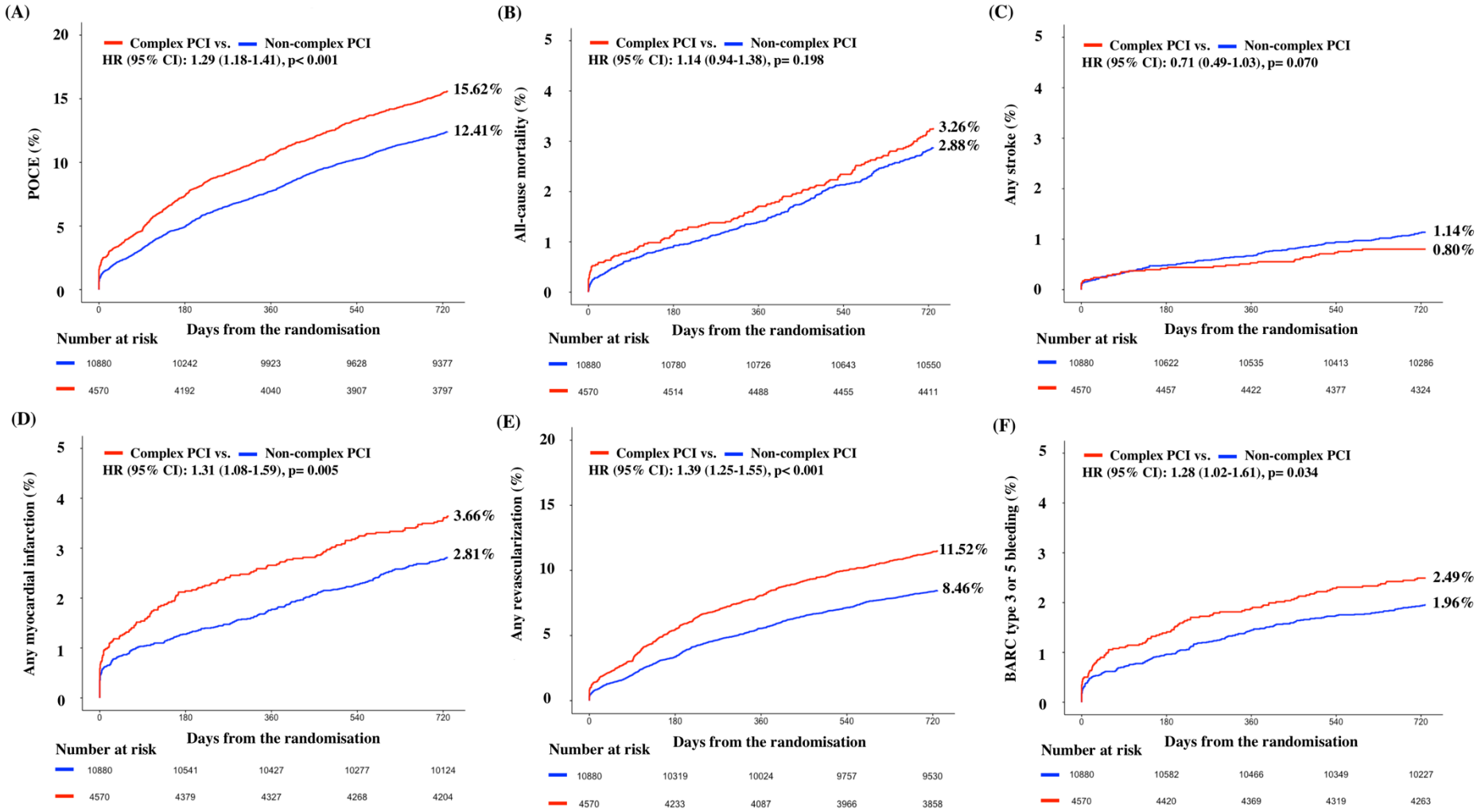
Study	Journal	Publication	Definition of complex PCI
Chieffo et al [1]	Am Heart J	2013	At least one of the following: 1. Bifurcation 2. Chronic total occlusion 3. Long lesion 4. Small vessel
Kirtane et al [2]	Circulation	2016	At least one of the following: 5. Multivessel disease 6. Left main stenosis/bifurcation 7. Calcific disease 8. Stent underexpansion or in-stent restenosis 9. Chronic total occlusion 10. Poor hemodynamic status or left ventricular function
Giustino et al [3]	J Am Coll Cardiol	2016	At least one of the following: 1. 3 vessels treated 2. ≥ 3 stents implanted 3. ≥ 3 lesions treated 4. Bifurcation with 2 stents 5. Total stent length > 60 mm 6. Chronic total occlusion
Giustino et al [4]	JACC Cardiovasc Interv	2016	At least one of the following: 1. ≥ 2 stents implanted 2. ≥ 2 lesions treated 3. Bifurcation lesion as target vessel 4. Total stent length > 30 mm
Yeh et al [5]	J Am Coll Cardiol	2017	At least one of the following: 1. > 2 lesions per vessel 2. Bifurcation with side branch ≥ 2.5 mm 3. Unprotected left main 4. Total stent length ≥ 30mm 5. Thrombus containing lesion
Genereux et al [6]	Int J Cardiol	2018	At least one of the following: 1. ≥ 3 stents implanted 2. Bifurcation PCI with 2 stents 3. PCI of left main 4. Rotational atherectomy use for severely calcified lesions 5. PCI of saphenous vein graft
Chandrasekhar et al [7]	Can J Cardiol	2018	At least one of the following: 1. Bifurcation lesion treated with any technique 2. PCI of Left main 3. Total stent length ≥ 30mm 4. Moderate or severely target calcified lesion
Lipiecki et al [8]	EuroIntervention	2018	At least one of the following: 1. 3 vessels treated 2. ≥ 3 stents implanted 3. ≥ 3 lesions treated 4. Bifurcation with 2 stents 5. Total stent length ≥ 60 mm 6. Chronic total occlusion 11. Restenotic or saphenous vein graft lesion
Costa et al [9]	J Am Coll Cardiol	2019	At least one of the following: 1. 3 vessels treated

			2. ≥ 3 stents implanted 3. ≥ 3 lesions treated 4. Bifurcation with 2 stents 5. Total stent length > 60 mm 6. Chronic total occlusion
Choi et al [10]	JACC Cardiovasc Interv	2019	At least one of the following: 1. Multivessel PCI 2. Multiple stent implantation (≥ 3 stents per patient) 3. Bifurcation with side branch ≥ 2.5mm size 4. Unprotected left main disease 5. Chronic total occlusion (≥ 3 months) 6. Heavy calcified lesion (requiring a rotablator system) 7. In-stent restenosis 8. Long lesion (implanted stent length ≥ 38mm)

1 PCI; percutaneous coronary intervention.

2

Online Figure 1.



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