SUPPLEMENTARY DATA

Table 1 of the supplementary data. Study inclusion and exclusion criteria

| Inclusion criteria | Exclusion criteria |
|---|---|
| Clinical | |
| Age > 18 y | Age < 18 y |
| Diagnosis of ischemic heart disease | Inability to give informed consent |
| | Female with child-bearing potential |
| | Life expectancy < 12 mo |
| | Factors making clinical follow-up difficult (such as no fixed address) |
| | Poor cardiac function as defined by global left ventricular ejection fraction $\leq 30\%$ |
| | Recent (< 7 d) ST-segment elevation myocardial infarction |
| | Recent (< 48 h) non–ST-segment elevation myocardial infarction |
| | Prior ST-segment elevation myocardial infarction in the territory supplied by the vessel with the intermediate lesion under investigation |
| | Severe myocardial hypertrophy (interventricular septum thickness > 15 mm, ECG Sokolow's criteria fulfilled) |
| | Severe valvular heart disease |
| | Significant platelet count alteration (< 100 000 cells/mm³ or > 700 000 cells/mm³) |
| | Gastrointestinal bleeding requiring surgery or blood transfusions within the previous 4 wk |
| | History of clotting pathology |
| | Known hypersensitivity to aspirin, heparin, or contrast dye |
| | Advanced renal failure with a glomerular filtration rate < 30 mL/min |
| Angiographic | |
| Single-vessel disease with angiographically intermediate coronary lesion OR | Multivessel disease with one or more untreated angiographically critical stenosis or coronary occlusion |
| Multivessel disease with only angiographically intermediate coronary lesion OR | Lesions in coronary artery bypass grafts |
| Multivessel disease with a least 1 angiographically intermediate coronary lesion and already treated angiographically critical stenosis | Multivessel disease requiring coronary aortic bypass graft intervention |

 $\textbf{Table 2 of the supplementary data.} \ \textbf{Baseline patient characteristics according to lesion complexity and} \\$

treatment arm

| | Complex | | | Noncomplex | | | |
|------------------------|------------|------------|------|------------|------------|------|--|
| | (n = 199) | | | (n = 151) | | | |
| | OCT FFR P | | OCT | FFR | Р | | |
| | (n = 99) | (n = 100) | | (n = 75) | (n = 76) | | |
| Age, y | 70 [64-76] | 69 [62-75] | .579 | 69 [62-76] | 68 [62-75] | .984 | |
| Male sex | 77 (77.8) | 78 (78.0) | .970 | 56 (74.7) | 50 (65.8) | .233 | |
| BMI, kg/m ² | 26 [23-29] | 26 [24-28] | .675 | 28 [24-29] | 27 [24-29] | .173 | |
| Diabetes mellitus | 37 (37.4) | 33 (33.0) | .519 | 18 (24.0) | 20 (26.3) | .743 | |
| Hypertension | 86 (86.9) | 81 (81.0) | .260 | 65 (86.7) | 67 (88.2) | .782 | |
| Dyslipidemia | 77 (77.8) | 67 (67.0) | .089 | 53 (70.7) | 53 (69.7) | .901 | |
| Smoking | 38 (38.4) | 42 (42.0) | .603 | 28 (37.3) | 27 (35.5) | .818 | |
| Family history of | 37 (37.4) | 26 (26.0) | .085 | 22 (29.3) | 26 (34.2) | .520 | |
| CAD | | | | | | | |
| Chronic kidney | 19 (19.2) | 21 (21.0) | .750 | 12 (16.0) | 11 (14.5) | .794 | |
| disease | | | | | | | |
| Previous PCI | 40 (40.4) | 35 (35.0) | .432 | 36 (48.0) | 37 (48.7) | .933 | |
| Previous CABG | 5 (5.1) | 1 (1.0) | .095 | 0 (0.0) | 3 (3.9) | .082 | |
| Previous MI | 27 (27.3) | 17 (17.0) | .081 | 25 (33.3) | 16 (21.1) | .090 | |
| Clinical presentation | | | .502 | | | .704 | |
| ACS | 18 (18.2) | 22 (22.0) | | 13 (17.3) | 15 (19.7) | | |
| CCS | 81 (81.8) | 78 (78.0) | | 62 (82.7) | 61 (80.3) | | |
| LVEF, % | 60 [54-64] | 60 [55-61] | .277 | 60 [53-65] | 60 [55-61] | .134 | |
| Management | | | | | | | |
| Patient treated | 57 (57.6) | 41 (41.0) | .019 | 34 (45.3) | 18 (23.7) | .005 | |
| with PCI | | | | | | | |
| Contrast media, | 300 ± 134 | 266 ± 152 | .098 | 251 ± 118 | 205 ± 105 | .014 | |
| mL | | | | | | | |
| CI-AKI | 10 (10.1) | 2 (2.0) | .016 | 5 (6.7) | 1 (1.3) | .092 | |
| Dialysis | 0 (0.0) | 0 (0.0) | .999 | 0 (0.0) | 0 (0.0) | .999 | |

ACS, acute coronary syndrome; BMI, body mass index; CABG, coronary artery bypass grafting; CCS, chronic coronary syndrome; FFR, fractional flow reserve; MI, myocardial infarction; LVEF, left ventricular ejection fraction; OCT, optical coherence tomography; PCI, percutaneous coronary intervention.

The data are expressed as No. (%), mean ± standard deviation, or median [25th-75th percentile]. *Defined according to the Acute Kidney Injury Network definition.

Table 3 of the supplementary data. Prevalence and overlap of the individual components of the complex lesion definition

| | Long lesion (n = 55) | Severely | Bifurcation | | |
|---------------------------|----------------------|------------------|-------------|--|--|
| | | calcified lesion | lesion | | |
| | | (n = 53) | (n = 169) | | |
| Long lesion | 17 (30.9) | 4 (7.5) | 25 (14.8) | | |
| Severely calcified lesion | 4 (7.2) | 22 (41.5) | 18 (10.7) | | |
| Bifurcation lesion | 25 (45.5) | 18 (34.0) | 117 (69.2) | | |
| All criteria | 9 (16.4) | 9 (17.0) | 9 (5.3) | | |

The data are presented as No. (%).

Table 4 of the supplementary data. Vessel characteristics according to lesion complexity and treatment arm

| | Complex | | | Noncomplex | | | |
|--|-------------------------|----------------------|-------|-------------------------|----------------------|-------|--|
| | (n = 212) | | | (n = 208) | | | |
| | OCT | FFR | Р | ОСТ | FFR | Р | |
| | (n = 102) | (n = 110) | | (n = 98) | (n = 110) | | |
| FFR value | , | , | | , | , | | |
| FFR baseline | - | 0.83 [0.79- 0.88] | - | - | 0.86 [0.82- 0.91] | - | |
| FFR baseline ≤0.80 | - | 42 (38.2) | - | - | 22 (20.0) | - | |
| OCT parameters | | | | | | | |
| MLA, mm ² | 2.39 [1.80- 3.20] | - | - | 2.88 [2.32- 3.55] | - | - | |
| AS, % | 65 [59- 73] | - | - | 65 [57-70] | - | - | |
| AS ≥75% | 19 (18.8) | - | - | 12 (12.5) | - | - | |
| AS 50%-75% and MLA < 2.5 mm ² | 35 (34.7) | - | - | 28 (29.2) | - | - | |
| AS 50%-75% and plaque rupture | 5 (5.0) | - | - | 3 (3.1) | - | - | |
| Failure in crossing the lesion with the tool | 1 (1.0) | 0 (0.0) | .298 | 1 (1.0) | 0 (0.0) | .288 | |
| Investigated lesion | | | .555 | | | .117 | |
| location | | | | | | | |
| LAD | 76 (74.5) | 85 (77.3) | | 52 (53.1) | 64 (58.2) | | |
| LCx | 11 (10.8) | 14 (12.7) | | 13 (13.3) | 22 (20.0) | | |
| RCA | 15 (14.7) | 11 (10.0) | | 33 (33.7) | 24 (21.8) | | |
| Lesions treated with PCI | 60 (58.8) | 42 (38.2) | .003 | 39 (39.8) | 22 (20.0) | .002 | |
| Number of stent(s) | 1.0 [1.0- 2.0] | 1.0 [1.0-2.0] | .969 | 1.0 [1.0- 1.0] | 1.0 [1.0-1.0] | .418 | |
| Stent length, mm | 34 [26- 46] | 36 [22-49] | .764 | 22 [18-28] | 26 [18-30] | .163 | |
| Balloon predilatation | 57 (95.0) | 34 (82.9) | .046 | 20 (52.6) | 16 (72.7) | .126 | |
| Balloon postdilatation | 54 (90.0) | 36 (87.8) | .728 | 34 (89.5) | 15 (75.0) | .148 | |
| Calcium modification techniques* | 0 (0.0) | 0 (0.0) | 1.000 | 0 (0.0) | 0 (0.0) | 1.000 | |
| Long lesion | 27 (26.5) | 28 (25.5) | .866 | 0 (0.0) | 0 (0.0) | - | |
| Treated with PCI | n = 27, | n = 28, | .173 | - | - | - | |
| | 19 (70.4) | 18 (64.3) | | | | | |
| Severely calcified lesion | 24 (23.5) | 29 (26.4) | .634 | 0 (0.0) | 0 (0.0) | - | |
| Treated with PCI | n = 24, 13 (54.2) | n = 29, 7 (24.1) | .694 | - | - | - | |
| Bifurcation lesion | 81 (79.4) | 88 (80.0) | .915 | 0 (0.0) | 0 (0.0) | - | |
| Treated with PCI | n = 81, 48 (59.3) | n = 88, 37 (42.0) | .220 | - | - | - | |

| Treated with | n = 81, | n = 88, | .138 | - | - | - |
|----------------------|-----------|-----------|--------|------------|-----------|--------|
| double-stenting | 2 (2.5) | 0 (0.0) | | | | |
| technique | | | | | | |
| Acute side-branch | n = 48, | n = 37, | 1.000 | - | - | - |
| occlusion during PCI | 0 (0.0) | 0 (0.0) | | | | |
| Poststenting | n = 60, | n = 42, | .008 | n = 39, | n = 22, | .061 |
| assessment according | 51 (85.0) | 26 (61.9) | | 33 (84.6) | 14 (63.6) | |
| to protocol | | | | | | |
| Poststenting | n = 51, | n = 26, | .291 | n = 33, | n = 14, | .966 |
| optimal result | 30 (58.8) | 12 (46.2) | | 21 (63.6) | 9 (64.3) | |
| PCI optimization | n = 51, | n = 26, | .054 | n = 33, | n = 14, | .041 |
| | 21 (41.2) | 5 (19.2) | | 12 (36.4) | 1 (7.1) | |
| Further balloon | n = 51, | n = 26, | .106 | n = 33, | n = 14, | .060 |
| dilation | 19 (37.3) | 5 (19.2) | | 11 (33.3) | 1 (7.1) | |
| Additional stent | n = 51, | n = 26, | .356 | n = 33, | n = 14, | .827 |
| implantation | 5 (9.8) | 1 (3.8) | | 3 (9.1) | 1 (7.1) | |
| Final optimal result | n = 45, | n = 24, | < .001 | n = 32, | n = 14, | < .001 |
| | 45 | 14 (58.3) | | 32 (100.0) | 9 (64.3) | |
| | (100.0) | - • | | , | | |

FFR, fractional flow reserve; LAD, left anterior descending artery; LCx, left circumflex artery;

MI, myocardial infarction; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; RCA, right coronary artery.

The data are expressed as No. (%) or median [25th-75th percentile].

^{*}Rota-ablation, ShockWave, or cutting balloon.

Table 5 of the supplementary data. Clinical outcomes according to lesion complexity

| | | | Hazard ratio (95%CI) | P |
|-------------------------------|-----------|-----------|-------------------------|------|
| MACE | 44 (20.8) | 29 (13.9) | 1.52 (0.95-2.44) | .078 |
| Cardiac death or MI | 10 (4.7) | 7 (3.4) | 1.42 (0.54-3.73) | .476 |
| All-cause death | 27 (12.7) | 17 (8.2) | 1.57 (0.86-2.88) | .145 |
| Cardiac death | 6 (2.8) | 5 (2.4) | 1.19 (0.36-3.90) | .775 |
| MI | 5 (2.4) | 2 (1.0) | 2.48 (0.48-12.76) | .279 |
| TVR | 17 (8.0) | 12 (5.8) | 1.40 (0.67-2.94) | .368 |
| Due to side-branch restenosis | 1 (0.5) | 0 (0.0) | - | - |

MACE, major adverse cardiac events; MI, myocardial infarction; TVR, target vessel revascularization.

Unless otherwise indicated, the data are expressed as No. (%).

Table 6 of the supplementary data. Subgroup analysis for the primary outcome according to angiographic lesion complexity and PCI/deferral

| | Deferred | | | PCI | | | | P _{interaction} | |
|------------|----------------|-----------------|------------------|------|----------------|----------------|------------------|--------------------------|------|
| | OCT | FFR | HR (95%CI) | Р | OCT | FFR | HR (95%CI) | Р | |
| Complex | 7/42 (16.7) | 22/68 (32.4) | 0.47 (0.20-1.11) | .085 | 8/60 (13.3) | 7/42 (16.7) | 0.79 (0.29-2.18) | .651 | .451 |
| Noncomplex | 13/59 | 8/88 | 2.63 (1.09-6.34) | .032 | 6/39 | 2/22 | 1.65 (0.33-8.19) | .538 | .614 |
| | (22.0) | (9.1) | | | (15.4) | (9.1) | | | |

Unless otherwise indicated, the data are expressed as No. (%).