

Supplementary Material

Supplementary Table 1. Baseline characteristics of VH-IVUS cohort

	VH-IVUS cohort
<i>Clinical and demographic characteristics</i>	
Patient No.	40
Age, years	63.8 ± 10.1
Male	23 (57.5)
Body mass index, kg/m ²	24.8 ± 4.8
Hypertension	29 (72.5)
Diabetes mellitus	10 (25.0)
Dyslipidemia	11 (27.5)
Smoking	7 (17.5)
Previous MI	1 (2.5)
Previous PCI	3 (7.5)
LVEF, %	68.3 (65.3–74.8)
Triglyceride, mmol/L	1.3 (1.0–2.1)
Total cholesterol, mmol/L	4.3 (3.4–4.9)
LDL cholesterol, mmol/L	2.4 (1.9–3.1)
HDL cholesterol, mmol/L	1.2 (1.0–1.4)
Symptoms	
Stable angina	19 (47.5)
Unstable angina	20 (50.0)
NSTEMI	1 (2.5)
Medications	
Aspirin	9 (22.5)
Statins	8 (20.0)
β-blockers	4 (10.0)
ACEI/ARB	14 (35.0)
Calcium channel blockers	13 (32.5)
<i>Interrogated vessel characteristics</i>	
Lesion No.	40
Lesion location	
LAD	32 (80.0)
LCX	3 (7.5)
RCA	5 (12.5)
3D-QCA	
Diameter stenosis, %	45.3 (36.8–48.5)
Lesion length, mm	19.8 (11.9–25.8)
MLD, mm	1.6 (1.5–1.9)
QFR	0.88 (0.83–0.93)

Values are expressed as n (%) or mean ± standard deviation or median (interquartile range).

ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor inhibitor; HDL, high-density lipoprotein; LAD, left anterior descending artery; LCX, left circumflex artery; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MLD, minimal lumen diameter; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; QCA, quantitative coronary angiography; QFR, quantitative flow ratio; RCA, right coronary artery; VH-IVUS, virtual histology intravascular ultrasound.

Supplementary Table 2. Lesion characteristics according to the presence or absence of OCT-TCFA

	OCT-TCFA		p-value
	Yes (n = 23)	No (n = 60)	
Lesion location			0.210
LAD	16 (69.6)	46 (76.7)	
LCX	5 (21.7)	5 (8.3)	
RCA	2 (8.7)	9 (15.0)	
3D-QCA			
Diameter stenosis, %	49.1 (39.2–73.8)	38.1 (33.0–44.1)	0.001
Lesion length, mm	19.6 (12.3–28.6)	15.6 (11.0–20.8)	0.037
MLD, mm	1.3 (0.8–1.9)	1.6 (1.4–1.9)	0.038
QFR	0.83 (0.73–0.88)	0.92 (0.86–0.96)	0.002
OCT findings			
MLA, mm ²	2.35 (1.64–3.13)	2.89 (2.07–3.81)	0.092
Area stenosis, %	65.9 ± 13.3	59.1 ± 12.6	0.035
Lipid-rich plaque	23 (100.0)	51 (85.0)	0.057
Maximum lipid arc, °	330 (220–360)	220 (180–310)	0.023
Lipid length, mm	20.0 (14.0–22.0)	12.0 (8.0–21.0)	0.037
Lipid index, ° × mm	2720 (1970–3895)	1901 (880–3032)	0.045
Thinnest FCT, μm	50 (30–60)	150 (100–190)	<0.001
Plaque rupture	5 (21.7)	0 (0.0)	0.001
Plaque erosion	8 (34.8)	2 (3.3)	<0.001
Thrombus	12 (52.2)	3 (5.0)	<0.001
Calcification	13 (56.5)	24 (40.0)	0.175
Calcified nodule	0 (0.0)	5 (8.3)	0.316
Microchannel	10 (43.5)	19 (31.7)	0.312
Macrophage accumulation	12 (52.2)	22 (36.7)	0.199
Cholesterol crystal	10 (43.5)	19 (31.7)	0.312

Values are expressed as n (%) or mean ± standard deviation or median (interquartile range).

FCT, fibrous cap thickness; MLA, minimal lumen area; OCT, optical coherence tomography; TCFA, thin-capped fibroatheroma; other abbreviations as Supplementary Table 1.

Supplementary Table 3. Lesion characteristics according to the presence or absence of VH-TCFA

	VH-TCFA		p-value
	Yes (n = 6)	No (n = 34)	
Lesion location			1.000
LAD	5 (83.3)	27 (79.4)	
LCX	0 (0.0)	3 (8.8)	
RCA	1 (16.7)	4 (11.8)	
3D-QCA			
Diameter stenosis, %	46.5 (35.5–48.8)	43.7 (36.8–48.6)	0.733
Lesion length, mm	13.6 (11.4–24.9)	20.2 (12.0–26.1)	0.495
MLD, mm	1.6 (1.5–1.9)	1.7 (1.5–1.9)	0.804
QFR	0.89 (0.84–0.94)	0.88 (0.82–0.94)	0.732
Grayscale IVUS findings			
EEM CSA, mm ²	13.1 (11.1–16.4)	12.3 (10.5–15.4)	0.596
Plaque + media, mm ²	9.1 (7.5–9.4)	8.6 (7.0–11.1)	0.820
Plaque burden, %	67.7 (58.4–71.5)	69.9 (64.5–77.1)	0.248
MLA, mm ²	4.1 (3.3–6.9)	3.8 (3.2–4.5)	0.343
Reference EEM CSA, mm ²	13.7 (11.0–16.6)	13.3 (11.6–15.5)	0.895
Remodeling index	1.01 (0.90–1.07)	0.89 (0.80–1.08)	0.353
Positive remodeling	2 (33.3)	11 (32.4)	1.000
Negative remodeling	2 (33.3)	20 (58.8)	0.381
VH-IVUS findings			
Fibrous tissue, mm ²	2.7 (2.1–3.6)	2.7 (1.9–4.9)	0.940
Fibrous tissue, %	57.1 (48.8–63.0)	60.2 (45.8–66.8)	0.622
Fibrofatty tissue, mm ²	1.0 (0.3–2.0)	1.4 (0.6–2.1)	0.353
Fibrofatty tissue, %	15.2 (9.0–31.5)	22.5 (15.0–32.5)	0.256
Necrotic core, mm ²	1.0 (0.6–1.3)	0.5 (0.2–1.1)	0.217
Necrotic core, %	21.0 (11.2–25.2)	9.7 (5.1–19.1)	0.140
Dense calcium, mm ²	0.2 (0.0–0.4)	0.1 (0.0–0.4)	0.664
Dense calcium, %	4.2 (0.5–7.9)	1.9 (0.0–6.1)	0.358

Values are expressed as n (%) or median (interquartile range).

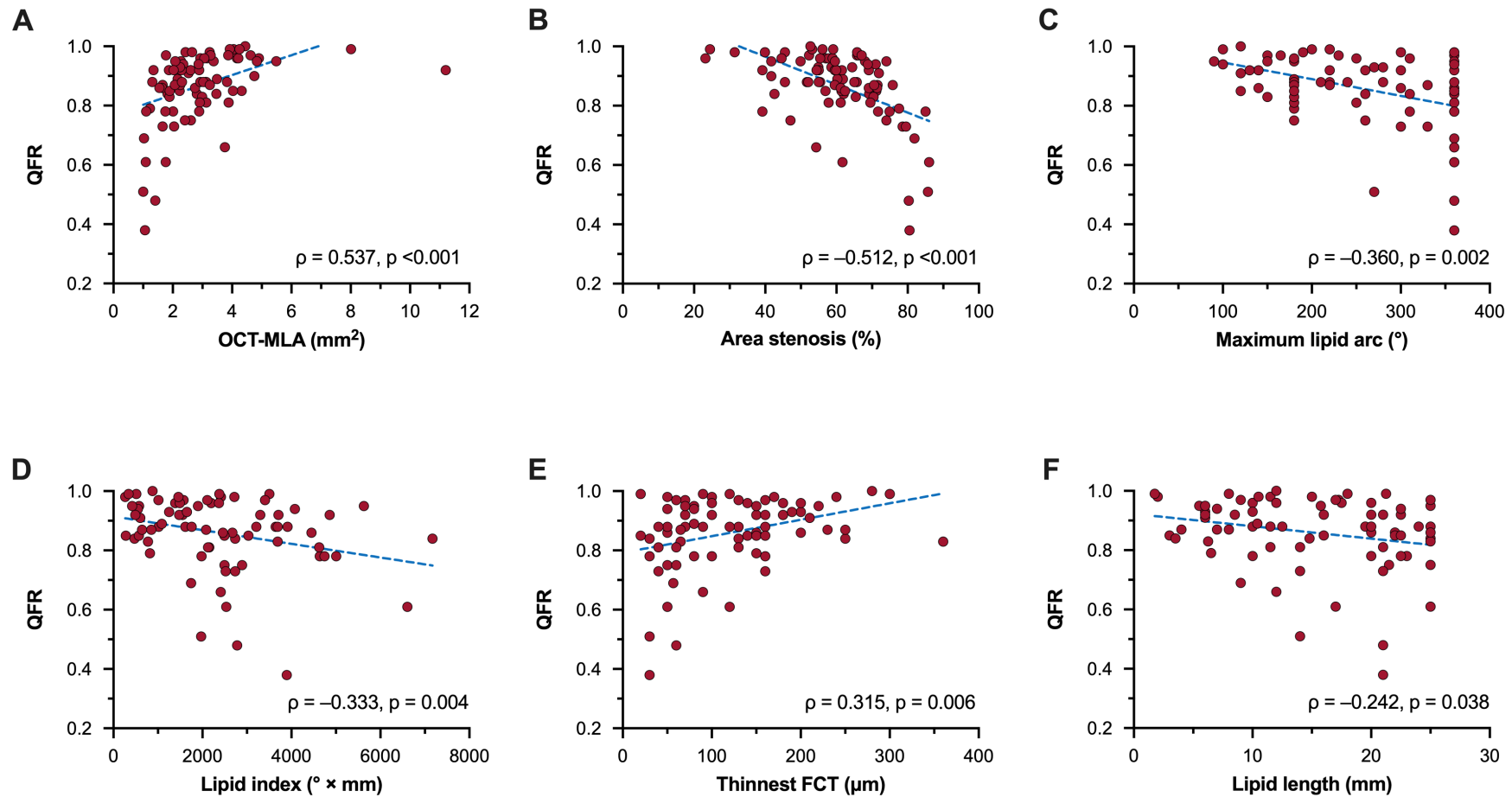
CSA, cross-sectional area; EEM, external elastic membrane; other abbreviations as Supplementary Tables 1 and 2.

Supplementary Table 4. Diagnostic performance of QFR for the evaluation of plaque morphology

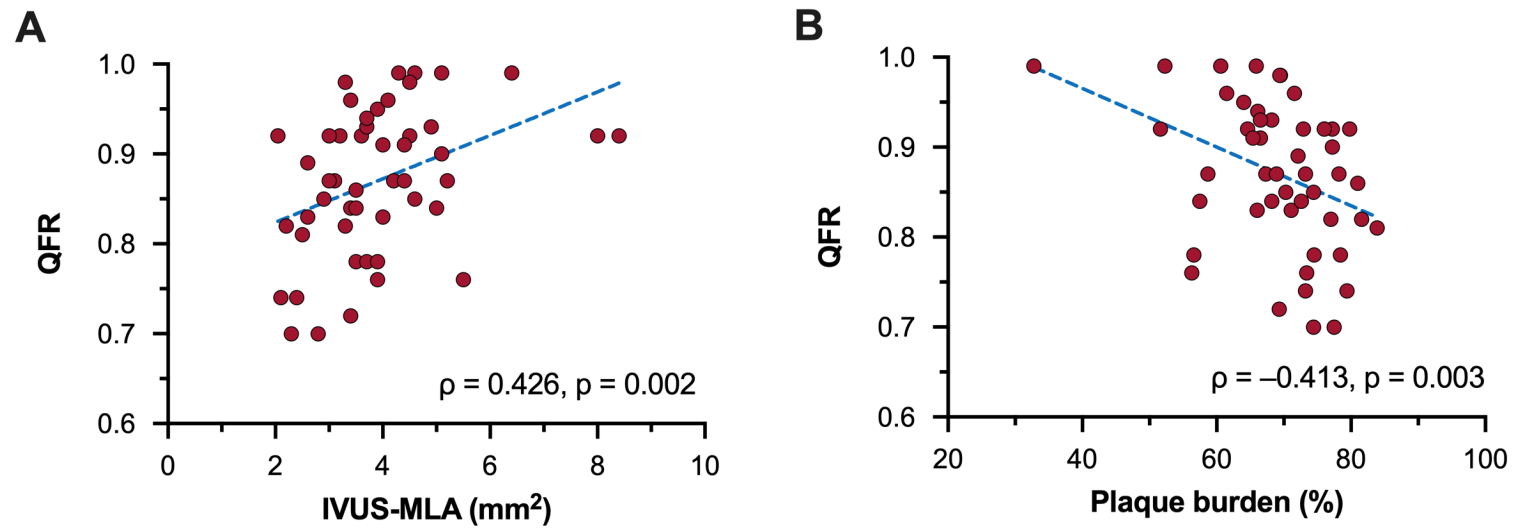
	Cutoff	Sensitivity, %	Specificity, %	+LR	-LR	PPV, %	NPV, %	Accuracy, %
OCT-TCFA	≤0.86	65.2 (42.7–83.6)	73.3 (60.3–83.9)	2.5 (1.5–4.1)	0.5 (0.3–0.8)	48.4 (35.9–61.1)	84.6 (75.5–90.8)	71.1 (60.1–80.5)
OCT-MLA <3.5 mm ²	≤0.94	82.5 (70.9–91.0)	65.0 (40.8–84.6)	2.4 (1.3–4.3)	0.3 (0.1–0.5)	88.1 (80.2–93.2)	54.2 (38.7–68.9)	78.3 (67.9–86.6)
Plaque burden ≥70%	≤0.92	96.0 (80.0–99.9)	45.8 (25.6–67.2)	1.8 (1.2–2.6)	0.1 (0.01–0.6)	64.9 (55.9–72.9)	91.7 (60.6–98.8)	71.4 (56.7–83.4)
IVUS-MLA <4 mm ²	≤0.86	58.6 (38.9–76.5)	80.0 (56.3–94.3)	2.9 (1.2–7.4)	0.5 (0.3–0.8)	81.0 (62.7–91.5)	57.1 (45.1–68.4)	67.4 (52.5–80.1)

Values are expressed as absolute numbers (95% CI).

CI, confidence interval; +LR, positive likelihood ratio; -LR, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; other abbreviations as Supplementary Tables 1 and 2.



Supplementary Figure 1. Relationship between QFR and OCT-derived parameters. The Spearman's correlation analysis indicated that QFR was strongly related to OCT-MLA (A) and % area stenosis (B); QFR was modestly related to maximum lipid arc (C), lipid index (D), and thinnest FCT (E); QFR was weakly related to lipid length (F). Abbreviations as Supplementary Tables 1 and 2.



Supplementary Figure 2. Relationship between QFR and IVUS-derived parameters. QFR was modestly related to IVUS-MLA (A) and plaque burden (B). Abbreviations as Supplementary Tables 1 and 2.