Supplementary data

Supplementary Appendix 1. Computation methods of Murray law-based quantitative flow ratio (μQFR).

Vessel μQFR was analysed from the ostium of the main vessels (right coronary artery [RCA] or left main coronary artery) until the distal point, defined as an anatomical landmark (i.e., side branch) in the segment in which its diameter became <2.0 mm. If a vessel had ≥2 daughter branches in the distal segment (e.g., right posterior descending artery or posterolateral branch from RCA, left posterolateral or posterior descending artery in left circumflex artery), the vessel with the greater diameter was analysed as the main vessel. The software automatically delineated the lumen contour of the main analysis vessel and all its side branches with diameters of ≥1.0 mm. The lumen contour was corrected manually if needed.

Supplementary Appendix 2. Echogenicity quantification of plaque component observed by IVUS.

The automated quantitative echogenicity of plaque components in target lesions observed by pre-percutaneous coronary intervention (PCI) intravascular ultrasound (IVUS) and in non-stented segments observed by post-PCI IVUS was performed using dedicated software (QCU-CMS, Leiden University Medical Center).[18] Following echogenicity-based tissue components were defined using the reference grey-level intensity of the adventitia: hypo- and hyper-echogenic tissue, calcification, and upper and lower tissue. The calcifications were identified through a combination of highly echogenic tissue accompanied by radial acoustic shadowing.

Supplementary Table 1. Baseline clinical, angiographic and procedural characteristics.

Patient characteristics (n=206 patients)	
Age, years (SD)	69.0 (9.8)
Male, % (n)	81.6 (168)
BMI, kg/m^2 (SD)	24.6 (3.9)
Hypertension, % (n)	80.1 (165)
Diabetes mellitus, % (n)	35.9 (74)
Insulin-dependent, % (n)	7.3 (15)
Dyslipidemia, % (n)	85.4 (176)
Current smoking, % (n)	17.5 (36)
Previous myocardial infarction, % (n)	13.1 (27)
Previous PCI, % (n)	24.8 (51)
Previous CABG, % (n)	1.9 (4)
Left ventricular ejection fraction, % (SD)	60.5 (10.0)
Renal insufficiency [a], % (n)	34.4 (71)
Anatomical SYNTAX score (SD)	8.0 (4.6)
Vessels treated per patient, % (n)	
1 vessel	94.7 (195)
2 vessels	5.3 (11)
Vessel characteristics (n=217 vessels)	
Target vessel, % (n)	
Left main-LAD	1.8 (4)
LAD territory	63.1 (137)
LCX	15.7 (34)
RCA	19.4 (42)
Intravascular imaging device use for stent optimization, % (n)	
No use for imaging modality (angiography alone)	0.5 (1)
IVUS	67.7 (147)
OCT or OFDI	31.8 (69)
Number of stents used per vessel, % (n)	
1 stent	96.8 (210)
2 stents	3.2 (7)
Lesion characteristics (n=224 lesions [b])	

Pre-PCI QCA	
Reference vessel diameter, mm (SD)	2.78 (0.69)
Minimum lumen diameter, mm (SD)	1.12 (0.50)
Diameter stenosis, % (SD)	59 (14)
Lesion length, mm (SD)	14.4 (8.0)
Post-PCI QCA	
Reference vessel diameter, mm (SD)	2.87 (0.66)
Minimum lumen diameter, mm (SD)	2.46 (0.64)
Diameter stenosis, % (SD)	14 (9)
Stent characteristics (n=235 stents)	
SYNERGY stent used, % (n)	100.0 (235)
Stent length, mm (SD)	25.0 (8.7)
Stent nominal diameter, mm (SD)	3.0 (0.5)

[a] Renal insufficiency was defined as an estimated glomerular filtration rate of creatinine clearance <60 ml/min/1.73 m^2. **[b]** Due to the incompatibility of software, out of 225 treated lesions, QCA was not assessed in one lesion (0.4%). BMI = body mass index; CABG = coronary artery bypass graft; IVUS = intravascular ultrasound; QCA = quantitative coronary angiography; LAD = left anterior descending; LCX = left circumflex; OCT = optical coherence tomography; OFDI = optical frequency domain imaging; PCI = percutaneous coronary intervention.

Supplementary Table 2. Differences in non-stented segments observed by intracoronary imaging.

	Vessels with diffuse disease	Vessels with focal disease	Mean difference (95% CI) [a]
Post-PCI Intracoronary Imaging	**(n=140)**	**(n=53)**	
Reference lumen area, mm^2 (SD)	6.95 (3.08)	8.32 (3.39)	**1.371 (0.537 to 2.231)†**
IVUS derived (n=134)	7.01 (3.17)	8.35 (3.68)	**1.355 (0.282 to 2.412)†**
OCT derived (n=59)	6.83 (2.90)	8.24 (2.55)	**1.369 (0.083 to 2.647)†**
Proximal Segment			
Analysable length, mm (SD)	11.24 (14.80)	12.03 (16.27)	0.754 (-3.214 to 5.157)
Analysable proximal segment	n=81	n=27	
MLA, mm^2 (SD)	5.86 (3.51)	6.59 (2.80)	0.751 (-0.322 to 1.851)
IVUS derived (n=66)	5.86 (3.65)	6.28 (2.34)	0.463 (-0.802 to 1.685)
OCT derived (n=42)	5.85 (3.35)	7.12 (3.52)	1.273 (-0.700 to 3.234)
Average plaque burden, %	49.4 (10.4)	46.3 (8.3)	**-3.120 (-6.298 to -0.051)†**
Distal Segment			
Analysable length, mm (SD)	9.30 (6.43)	8.51 (6.37)	-0.811 (-2.473 to 0.906)
Analysable proximal segment	n=102	n=39	
MLA, mm^2 (SD)	4.00 (2.65)	4.64 (2.48)	0.650 (-0.071 to 1.486)
IVUS derived (n=93)	3.91 (2.63)	4.95 (2.75)	**1.046 (0.098 to 2.054)†**
OCT derived (n=48)	4.15 (2.71)	3.76 (1.16)	-0.396 (-1.296 to 0.465)
Average plaque burden, %	41.5 (11.8)	38.0 (11.4)	-3.433 (-6.840 to 0.109)

Diffuse disease and focal disease were defined according to a µQFR-PPG index <0.78 or ≥0.78, respectively. Continuous variables are presented as mean and standard deviation (SD). [a] Confidence intervals (CI) for differences in the mean value were estimated by bootstrapping using 2000 replications. **The cross (†) after 95% CI shows a significant difference.**

IVUS = intravascular ultrasound; MLA = minimal lumen area; OCT = optical coherence tomography; PCI = percutaneous coronary intervention; PPG = pullback pressure gradient; µQFR = Murray law-based quantitative flow ratio.

Supplementary Table 3. Comparison of automated quantitative echogenicity of plaque components in the target lesion between vessels with diffuse disease and those with focal disease.

	Vessels with diffuse disease	Vessels with focal disease	p value
Target lesion observed in pre-PCI IVUS	**(n=69)**	**(n=23)**	
% Total hypo-echogenic tissue	66.0 (11.8)	69.9 (7.7)	0.146
% Total hyper-echogenic tissue	9.7 (4.9)	7.2 (3.7)	0.027
% Total upper-echogenic tissue	2.0 (1.2)	1.9 (1.1)	0.850
% Total lower-echogenic tissue	13.0 (8.9)	11.9 (5.5)	0.610
Presence of calcification, %	46.4%	60.9%	0.336

Diffuse disease and focal disease were defined according to a μQFR-PPG index <0.78 or ≥0.78, respectively. Continuous variables are presented as mean and standard deviation (SD). Abbreviations as **Supplementary Table 2.**

Supplementary Table 4. Comparison of automated quantitative echogenicity of plaque components in non-stented segments between vessels with diffuse disease and those with focal disease.

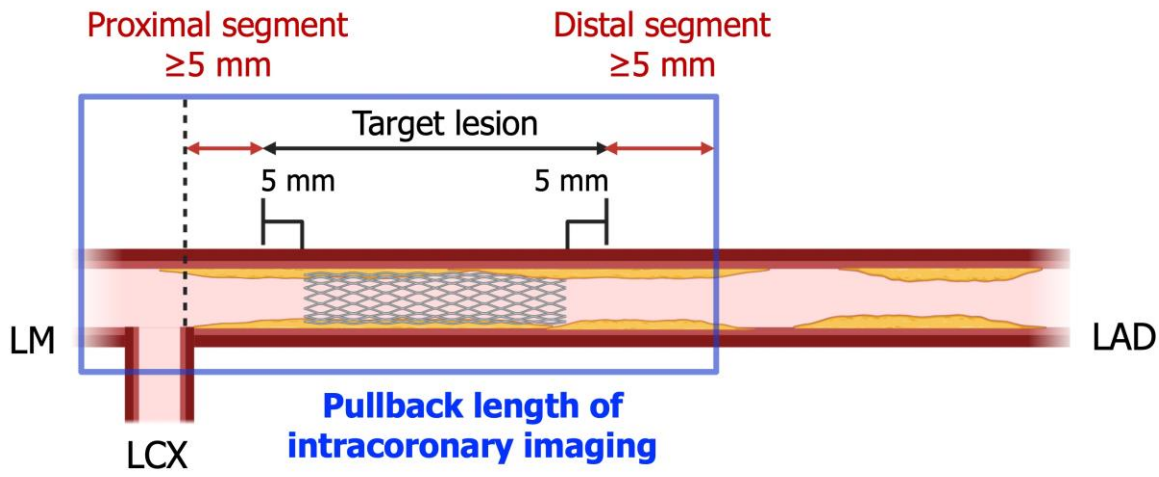
	Vessels with diffuse disease	Vessels with focal disease	p value
Non-stented segment in post-PCI IVUS			
Proximal Segment	**n=49**	**n=17**	
% Total hypo-echogenic tissue	68.8 (15.9)	71.3 (15.8)	0.572
% Total hyper-echogenic tissue	7.6 (5.8)	6.1 (3.9)	0.327
% Total upper-echogenic tissue	1.4 (0.9)	1.5 (1.1)	0.588
% Total lower-echogenic tissue	11.1 (7.9)	11.9 (8.4)	0.720
Presence of calcification, %	40.8%	41.2%	1.000
Distal Segment	**n=64**	**n=29**	
% Total hypo-echogenic tissue	80.7 (11.4)	80.6 (9.7)	0.960
% Total hyper-echogenic tissue	5.1 (4.8)	4.8 (5.2)	0.796
% Total upper-echogenic tissue	2.1 (1.4)	2.9 (3.4)	0.095
% Total lower-echogenic tissue	4.8 (7.1)	4.6 (6.1)	0.914
Presence of calcification, %	18.5%	7.7%	0.333

Diffuse disease and focal disease were defined according to a μQFR-PPG index <0.78 or ≥0.78, respectively. Continuous variables are presented as mean and standard deviation (SD). Abbreviations as **Supplementary Table 2.**

Supplementary Table 5. Comparison of MLA in non-stented segments and MSA between vessels with a post-PCI μQFR <0.91 and those with a post-PCI μQFR ≥0.91.

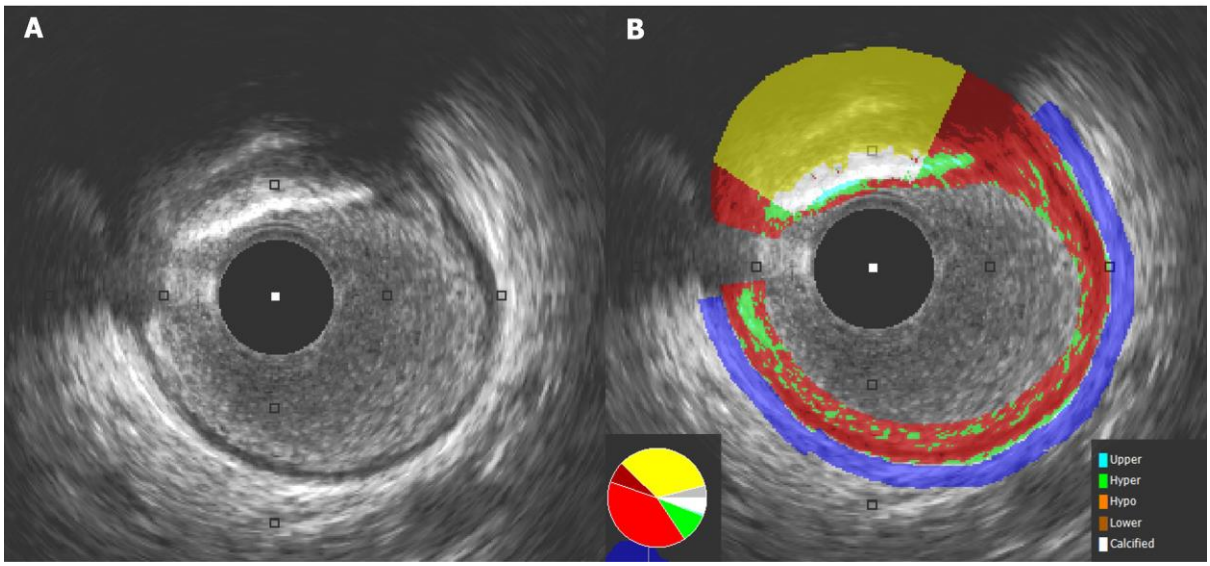
	Vessels with post-PCI μQFR<0.91	Vessels with post-PCI μQFR≥0.91	p value
MLA in proximal segment, mm^2 (SD)	4.89 (3.10)	6.39 (3.36)	0.049
MSA, mm^2 (SD)	5.37 (2.02)	6.02 (2.53)	0.124
MLA in distal segment, mm^2 (SD)	3.30 (2.03)	4.43 (2.71)	0.033

Continuous variables are presented as mean and standard deviation (SD). MSA = minimal stent area. Other abbreviations as **Supplementary Table 2.**



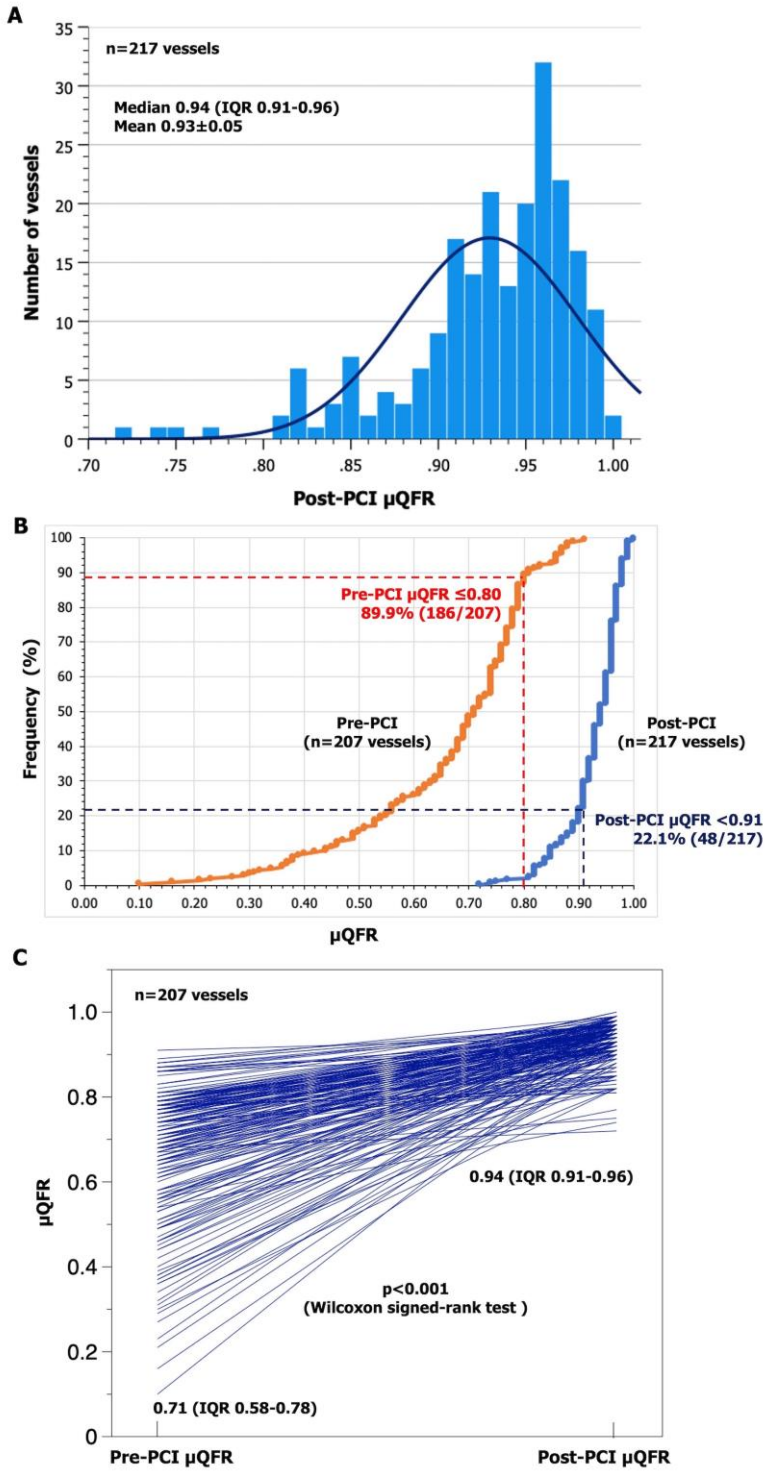
Supplementary Figure 1. Case example of intracoronary imaging analysis in non-stented segments.

Non-stented segment length had to be ≥ 5 mm in order to be included in the analysis. When the target lesion was in the left anterior descending artery or the circumflex artery, the non-stented proximal segment was analysed up to its ostium. LAD = left anterior descending artery; LCX = left circumflex artery; LM = left main coronary artery.



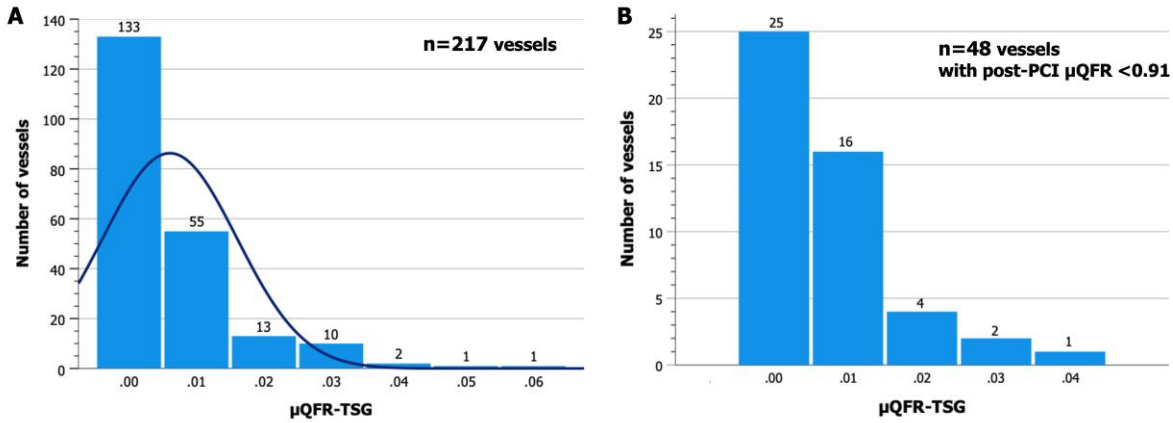
Supplementary Figure 2. Example of automated quantitative echogenicity of plaque component observed by IVUS.

According to echogenicity, tissue components — hypo- and hyper-echogenic tissue, calcification, and upper and lower tissue — were defined using the reference grey-level intensity of the adventitia (purple area). The calcifications were identified through a combination of highly echogenic tissue (white area) accompanied by radial acoustic shadowing (yellow area). IVUS = intravascular ultrasound.



Supplementary Figure 3. Assessment of pre- and post-PCI μQFR.

Histogram showing the distribution of post-PCI μQFR (A), cumulative curves of pre- and post-PCI μQFR (B), and improvement of μQFR by PCI (C). In 207 vessels with paired pre- and post-PCI μQFR, μQFR significantly improved from 0.71 (IQR: 0.58-0.78) to 0.94 (IQR: 0.91-0.96) (p<0.001, Wilcoxon signed-rank test)(C). IQR = interquartile range; PCI = percutaneous coronary intervention; μQFR = Murray law-based quantitative flow ratio.



Supplementary Figure 4. Histogram showing the distribution of post-PCI μQFR-TSG.

Panel A shows the distribution of post-PCI μQFR-based trans-stent gradient (TSG) in all 217 vessels, and the median value of μQFR-TSG was 0.00 (IQR: 0.00-0.01). Panel B shows the distribution of μQFR-TSG in 48 vessels with post-PCI μQFR <0.91. Abbreviations as **Supplementary Figure 3**.