

## Supplementary data

**Supplementary Table 1. The individual components of VOCCO.**

	Number (%)
Cardiac death	6 (0.9)
Vessel-related myocardial infarction	5 (0.7)
Vessel-related ischemia-driven revascularisation	25 (3.6)
Acute coronary syndrome	2
Abnormal functional test	
Low FFR	14
Abnormal non-invasive functional test	5
Recurrent angina with definite lesion progression of a lesion	2
Target lesion failure of stented segment	2

FFR: fractional flow reserve; VOCCO: vessel-oriented composite outcome.

**Supplementary Table 2. Reclassification ability of individual and combination of quantitative and qualitative plaque characteristics in the medical treatment group.**

Model	NRI	P-value	IDI	P-value
qn-HRP (reference)	NA	NA	NA	NA
qn-HRP + ql-HRP	0.437	0.027	0.014	0.017
ql-HRP (reference)	NA	NA	NA	NA
ql-HRP + qn-HRP	0.487	0.019	0.018	0.018

qn-HRP:  $MLA < 3.3 \text{ mm}^2$  and plaque burden  $\geq 70.0\%$ , ql-HRP: low-attenuation plaque or positive remodelling.

FFR: fractional flow reserve; HRP: high-risk plaque; IDI: integrated discrimination improvement; MLA: minimum lumen area; NRI: net reclassification index; ql-HRP: qualitative HRP; qn-HRP: quantitative HRP

**Supplementary Table 3. The risk of VOCO in the PCI group relative to the medical treatment group according to FFR strata among lesions with qn-HRP and ql-HRP.**

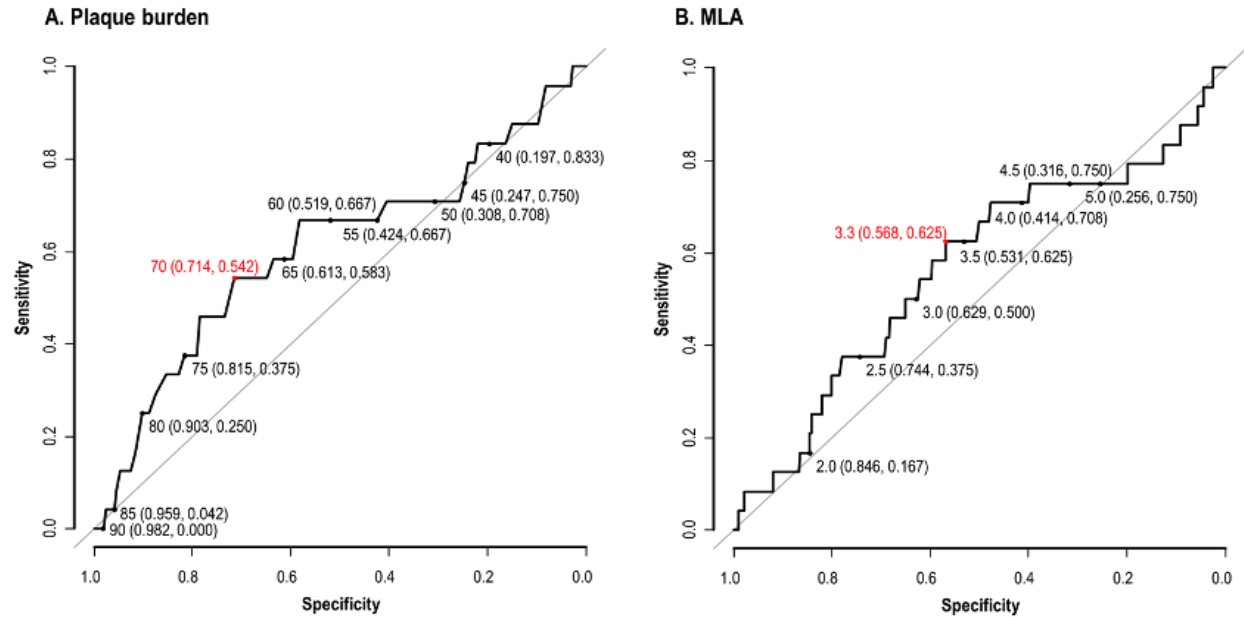
Adjusted variables	Lesions with qn-HRP and ql-HRP & FFR 0.81 – 0.90		Lesions with qn-HRP and ql-HRP & FFR >0.90	
	HR (95% CI) of PCI group (vs. medical treatment)	P-value	HR (95% CI) of PCI group (vs. medical treatment)	P-value
Male	0.17 (0.04 – 0.80)	0.025	0.68 (0.12 – 3.84)	0.665
Hyperlipidemia	0.17 (0.04 – 0.85)	0.030	0.51 (0.07 – 4.02)	0.525
Acute coronary syndrome	0.16 (0.02 – 1.02)	0.053	0.64 (0.11 – 3.64)	0.616
Use of aspirin	0.18 (0.04 – 0.86)	0.032	0.58 (0.10 – 3.29)	0.538
Use of P2Y <sub>12</sub> inhibitor	0.14 (0.03 – 0.70)	0.017	0.47 (0.03 – 6.63)	0.574
Use of statin	0.19 (0.04 – 0.99)	0.049	0.57 (0.10 – 3.28)	0.533
LAD	0.23 (0.04 – 1.18)	0.079	1.11 (0.20 – 6.17)	0.903
% diameter stenosis	0.13 (0.02 – 0.96)	0.045	0.37 (0.06 – 2.18)	0.270
FFR	0.18 (0.04 – 0.87)	0.033	0.68 (0.11 – 4.37)	0.683
LAP volume	0.21 (0.04 – 1.00)	0.050	0.62 (0.10 – 3.84)	0.606

Lesions with both qn-HRP and ql-HRP (n=138) were stratified into those with FFR of 0.81 – 0.90 (n=89) and FFR >0.90 (n=49).

qn-HRP: MLA<3.3 mm<sup>2</sup> and plaque burden ≥70.0%, ql-HRP: low-attenuation plaque or positive remodelling

CI: confidence interval; FFR: fractional flow reserve; HR: hazard ratio; HRP: high-risk plaque; LAD: left anterior descending artery; LAP: low-attenuation plaque; MLA: minimum lumen area; PCI: percutaneous coronary intervention; ql-HRP: qualitative HRP; qn-HRP: quantitative HRP; VOCO: vessel-oriented composite outcome.

**Supplementary Figure 1. ROC curve analysis for plaque burden and MLA in prediction of VOCO in the medical treatment group.**

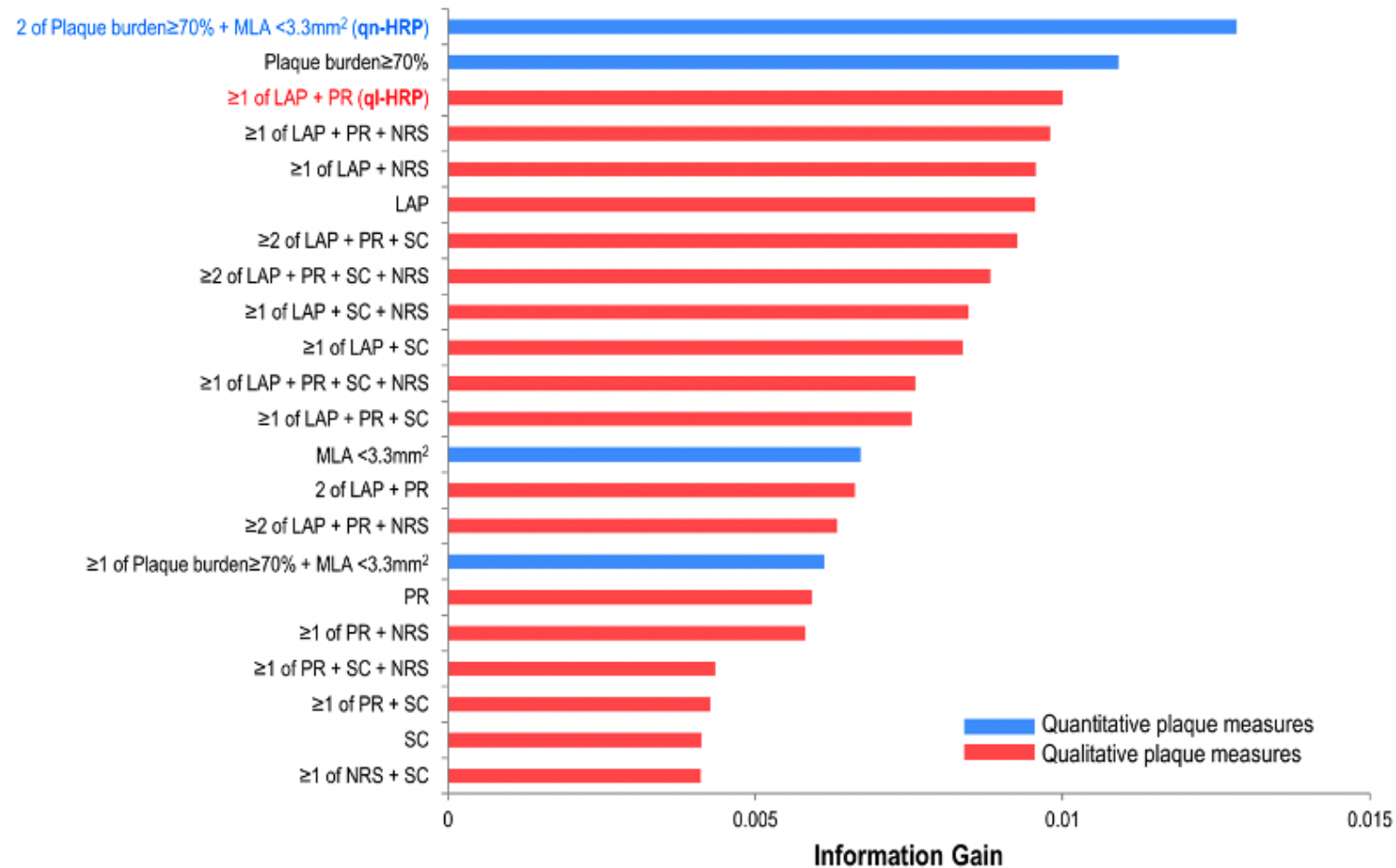


**Supplementary Figure 1. ROC curve analysis for plaque burden and MLA in prediction of VOCO in the medical treatment group**

In prediction of VOCO in the medical treatment group with FFR >0.80, the ROC curve analysis for plaque burden and MLA are presented. The optimal cut-off values derived from Youden's index for plaque burden and MLA were 70.0%, and 3.3 mm<sup>2</sup>, respectively.

MLA: minimum lumen area; ROC: receiver operating characteristic; VOCO: vessel-oriented composite outcomes.

**Supplementary Figure 2. Relative importance of quantitative and qualitative plaque measures for defining qn-HRP and ql-HRP in prediction of VOCO in the medical treatment group.**

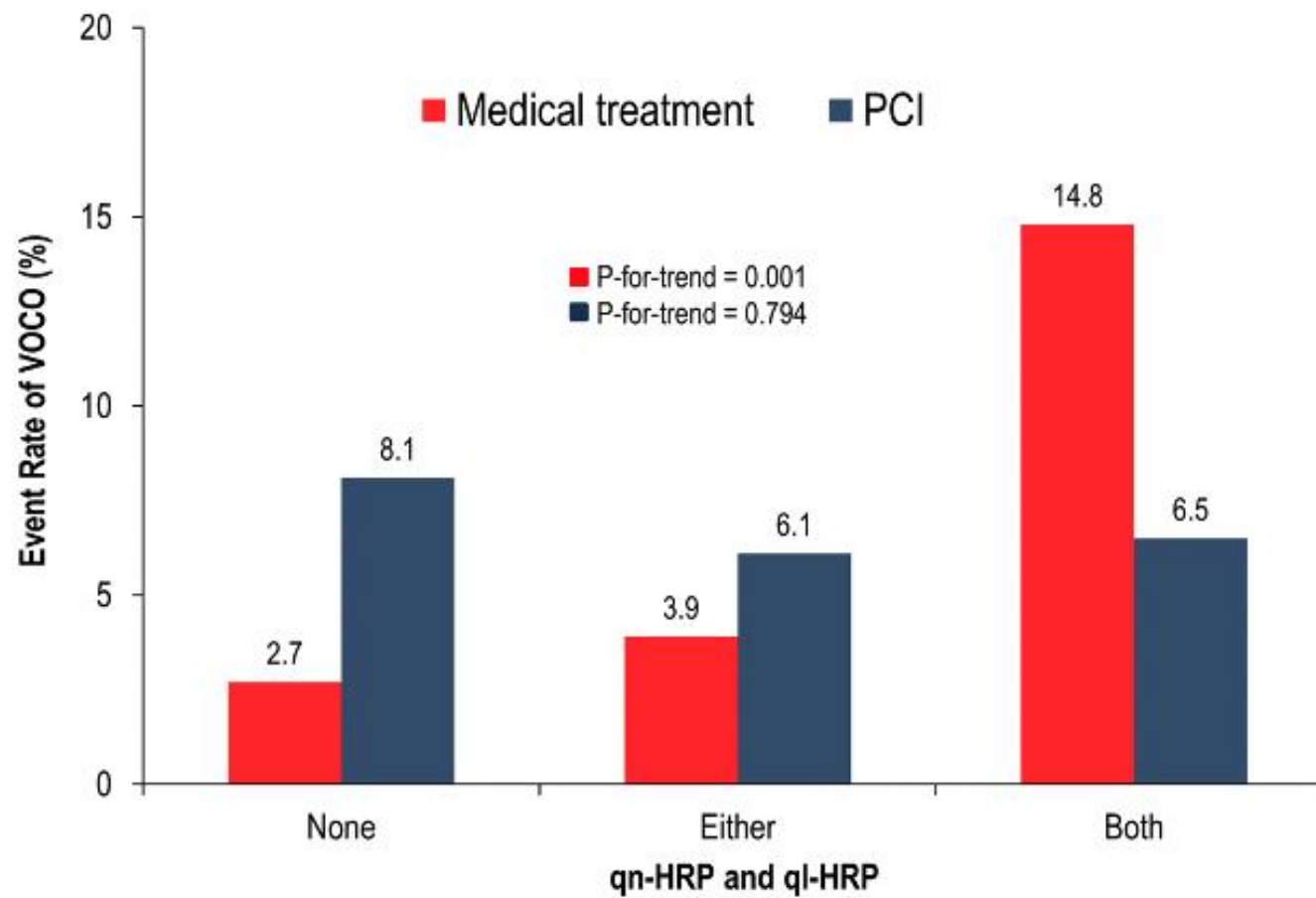


**Supplementary Figure 2.** Relative importance of quantitative and qualitative plaque measures for defining qn-HRP and ql-HRP in prediction of VOCCO in the medical treatment group.

The relative importance of possible combinations with quantitative plaque measure (i.e., plaque burden  $\geq 70\%$  and MLA  $< 3.3 \text{ mm}^2$ ) and qualitative plaque measure (i.e., LAP, PR, SC, and NRS) were compared according to the information criterion in the medical treatment group with FFR  $> 0.80$ . Among each category, 2 of plaque burden  $\geq 70\%$  + MLA  $< 3.3 \text{ mm}^2$  and  $\geq 1$  of LAP + PR showed the highest information gain and were defined as qn-HRP and ql-HRP, respectively. Of note, information gain was not available in the combinations of four of LAP + PR + SC + NRS,  $\geq 3$  of LAP + PR + SC + NRS, 3 of LAP + PR + SC, 3 of LAP + PR + NRS, 3 of LAP + SC + NRS,  $\geq 2$  of LAP + SC + NRS, 3 of PR + SC + NRS,  $\geq 2$  of PR + SC + NRS, 2 of LAP + NRS, 2 of LAP + SC, 2 of PR + NRS, 2 of PR + SC, 2 of SC + NRS, and NRS because of the small number of cases.

HRP: high-risk plaque; LAP: low-attenuation plaque; MLA: minimum lumen area; NRS: napkin-ring sign; ql-HRP: qualitative HRP; qn-HRP: quantitative HRP; PR: positive remodelling; SC: spotty calcification.

Supplementary Figure 3. Rates of VOCO according to HRP in the medical treatment group and the PCI group.



**Supplementary Figure 3.** Rates of VOCO according to HRP in the medical treatment group and the PCI group.

This analysis was done in the whole population (n=697). In the order of none, either, or both qn-HRP and ql-HRP, the event rate of VOCO increased in the medical treatment group, but there was no such trend in the PCI group.

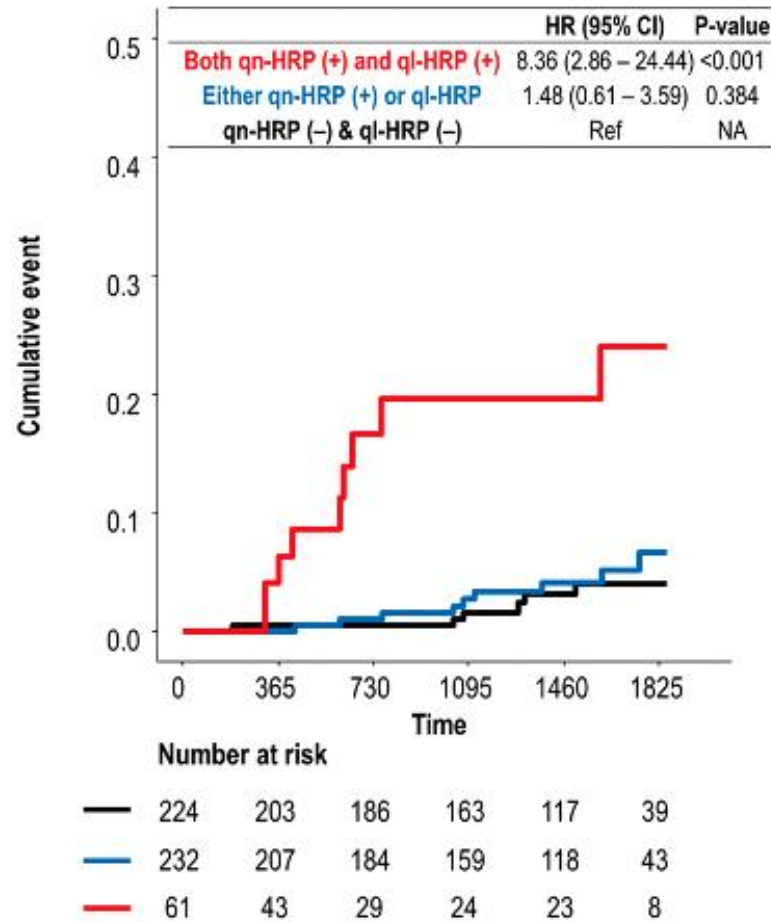
The definitions of qn-HRP and ql-HRP are shown in Supplementary Figure 2.

HRP: high-risk plaque; PCI: percutaneous coronary intervention; ql-HRP: qualitative HRP; qn-HRP: quantitative HRP; VOCO: vessel-oriented composite outcomes.

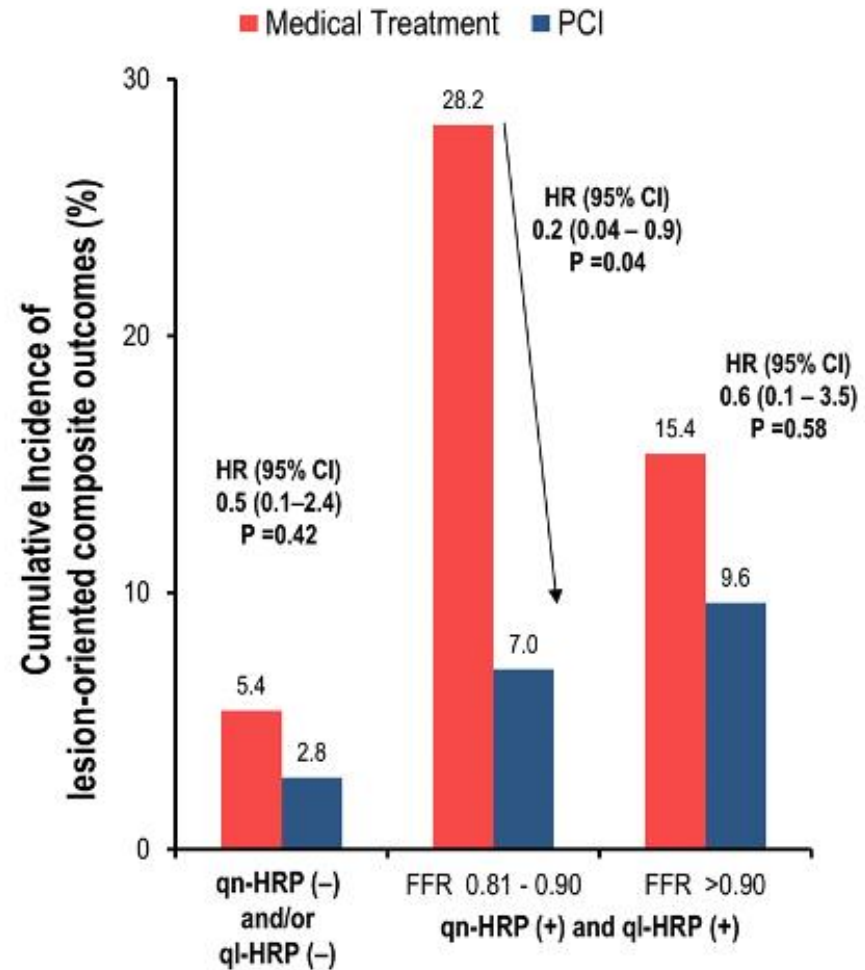


**Supplementary Figure 4. Prognostic implications of qn-HRP and ql-HRP for lesion-oriented composite outcomes**

**A. Prognostic implications in medical treatment group**



**B. Prognostic Interaction with treatment strategy and FFR**



**Supplementary Figure 4.** Prognostic implications of qn-HRP and ql-HRP for lesion-oriented composite outcomes.

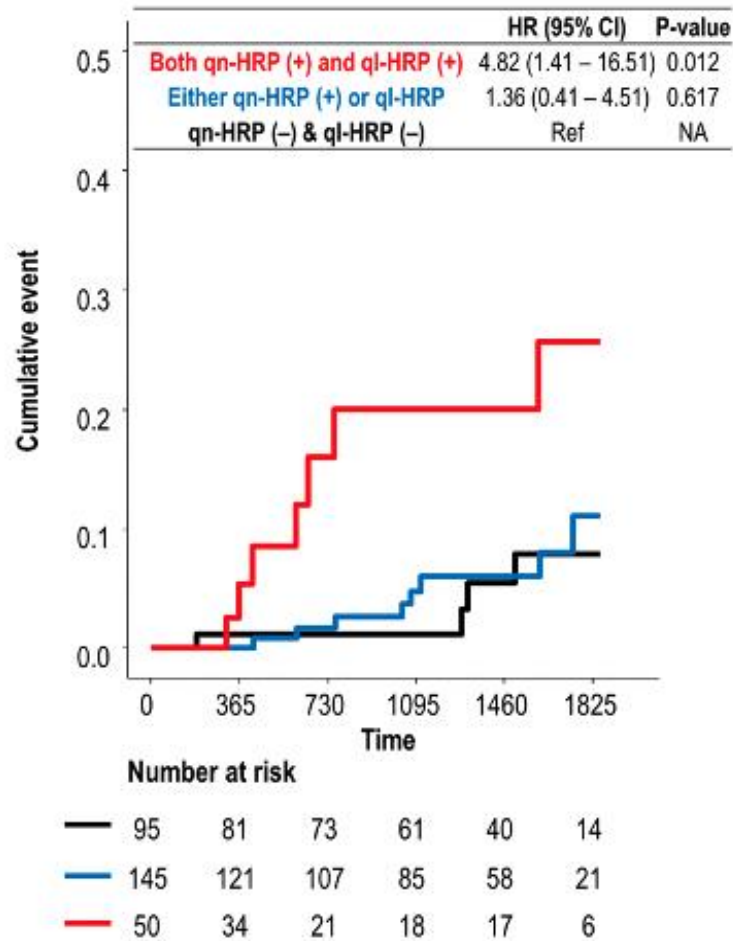
Prognostic implications of qn-HRP and ql-HRP were investigated for lesion-oriented composite outcomes (i.e., a composite of target lesion revascularisation, target vessel myocardial infarction, and cardiac death). (A) When lesions were divided according to qn-HRP and ql-HRP, the risk of lesion-oriented composite outcomes was the highest in lesions with both qn-HRP and ql-HRP in the medical treatment group. (B) When lesions were stratified by FFR strata, qn-HRP, and ql-HRP, the PCI group showed a lower risk for lesion-oriented composite outcomes than the medical treatment group in lesions with both qn-HRP and ql-HRP and FFR of 0.81–0.90.

The definitions of qn-HRP and ql-HRP are shown in Supplementary Figure 2.

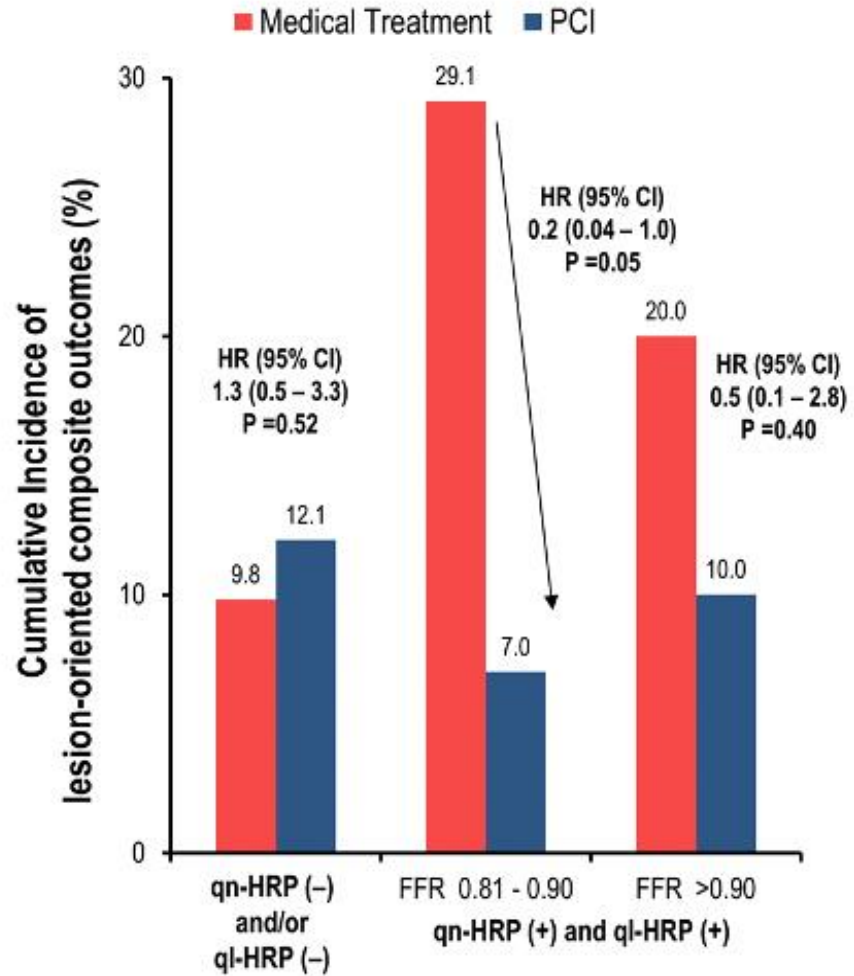
CI: confidence interval; FFR: fractional flow reserve; HR: hazard ratio; HRP: high-risk plaque; PCI: percutaneous coronary intervention; ql-HRP: qualitative HRP; qn-HRP: quantitative HRP.

## Supplementary Figure 5. Prognostic implications of qn-HRP and ql-HRP for patient-oriented composite outcomes

### A. Prognostic implications in medical treatment group



### B. Prognostic Interaction with treatment strategy and FFR



**Supplementary Figure 5.** Prognostic implications of qn-HRP and ql-HRP for patient-oriented composite outcomes.

This analysis was performed on a per-patient basis (n=458). In cases of multiple lesions in one patient, the representative lesion was designated following the hierarchy with the highest number of qn-HRP and ql-HRP, and low FFR. Prognostic implications of qn-HRP and ql-HRP were investigated for patient-oriented composite outcomes (i.e., a composite of target vessel revascularisation, target vessel myocardial infarction, and cardiac death). (A) When patients were divided according to qn-HRP and ql-HRP, the risk of patient-oriented composite outcomes was the highest in patients with both qn-HRP and ql-HRP in the medical treatment group. (B) As in the per-vessel analysis, the PCI group showed a lower risk for patient-oriented composite outcomes than the medical treatment group in patients with both qn-HRP and ql-HRP and FFR of 0.81–0.90.

The definitions of qn-HRP and ql-HRP are shown in Supplementary Figure 2.

CI: confidence interval; FFR: fractional flow reserve; HR: hazard ratio; HRP: high-risk plaque; PCI: percutaneous coronary intervention; ql-HRP: qualitative HRP; qn-HRP: quantitative HRP.