FAVOR
Series of QFR Studies

Less-invasive QFR, It's Next Revolution

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

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Grant/Research Support	Beijing Municipal Science and Technology Commission
Grant/Research Support	Chinese Academy of Medical Sciences
Grant/Research Support	National Clinical Research Center for Cardiovascular Diseases, Fuwai Hospital

Quantitative Flow Ratio (QFR)

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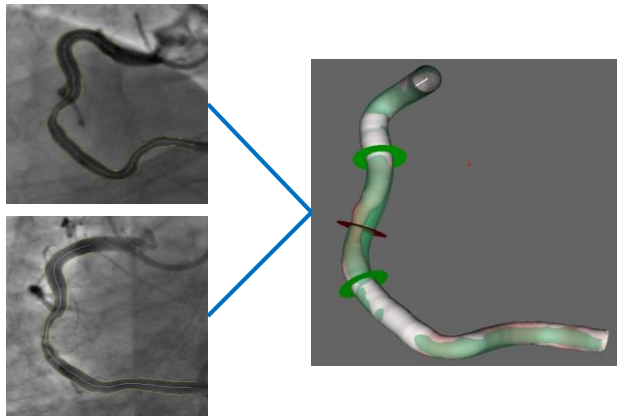
Standard Angiogram

Data Transmission System

Two image runs with angle difference ≥25°

AngioPlus System

3D Reconstruction



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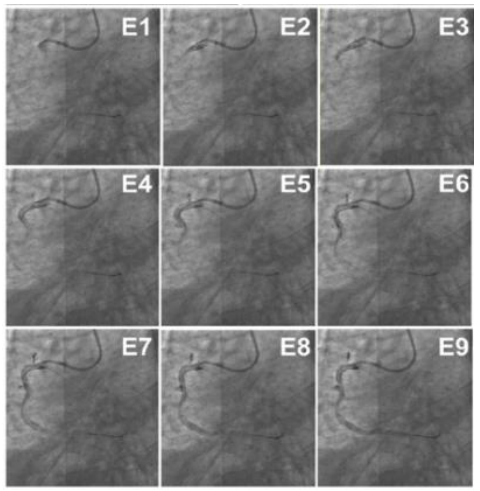
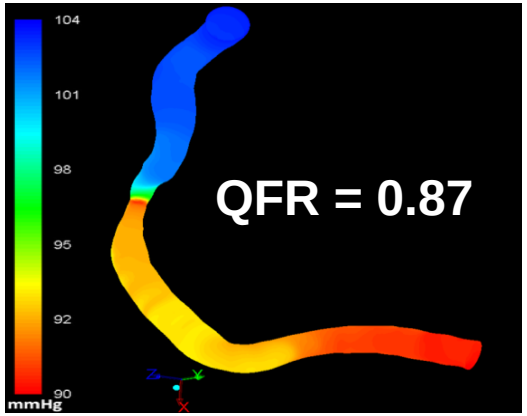


QFR

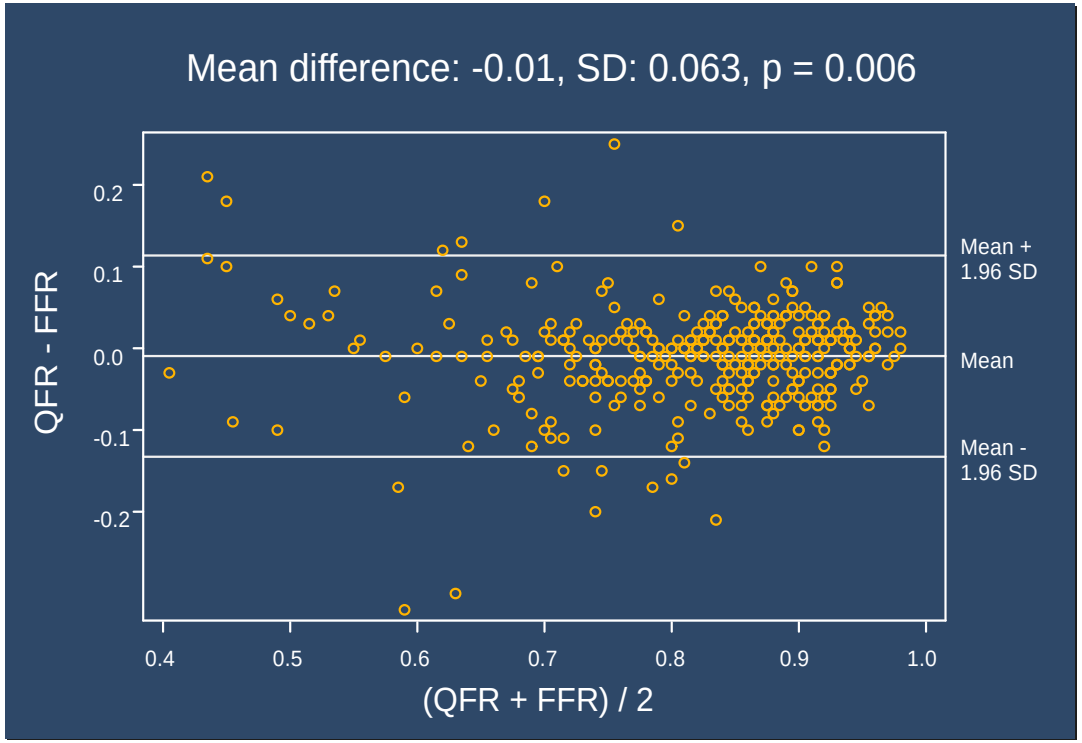


Without Inducing Hyperemia

Tu S, et al. *JACC Cardiovasc Interv* 2016; Xu B, et al. *J Am Coll Cardiol* 2017

Diagnostic Performance
FAVOR II China

Agreement of QFR and FFR (Online Analysis)

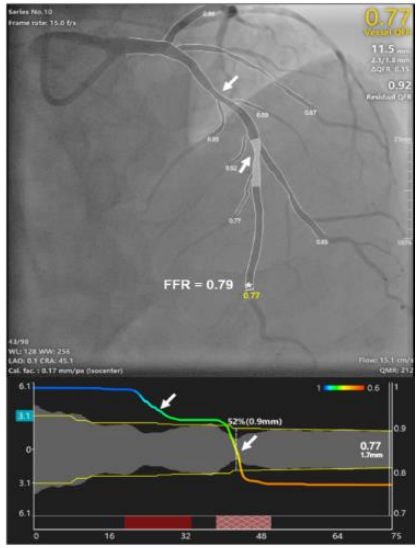


Diagnostic Performance of QFR and QCA (Online Analysis)

	QFR ≤ 0.8	Diameter Stenosis by QCA ≥ 50%	Difference (95% CI)	p Value
Accuracy, %	**92.7 (89.3, 95.3)**	59.6 (54.1, 65.0)	34.9 (28.3, 41.5)	<0.001
Sensitivity, %	**94.6 (88.7, 98.0)**	62.5 (52.9, 71.5)	32.0 (21.0, 43.1)	<0.001
Specificity, %	**91.7 (87.1, 95.0)**	58.1 (51.2, 64.8)	36.1 (27.9, 44.3)	<0.001
PPV, %	85.5 (78.0, 91.2)	43.8 (35.9, 51.8)	42.0 (31.4, 52.7)	<0.001
NPV, %	97.1 (93.7, 98.9)	74.9 (67.6, 81.2)	24.4 (15.6, 33.2)	<0.001
+ LR	11.4 (7.1, 17.0)	1.49 (1.21, 1.85)	-	-
- LR	0.06 (0.03, 0.13)	0.65 (0.50, 0.84)	-	-

Xu B, et al. *J Am Coll Cardiol* 2017

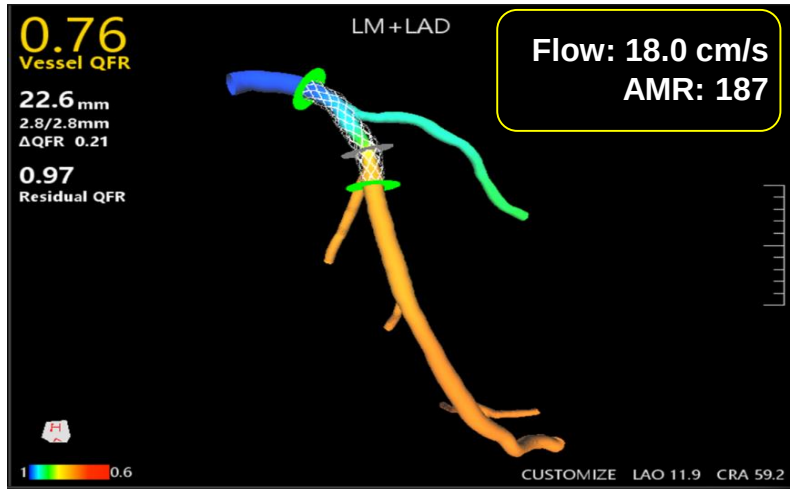
μQFR and Angio-based Microvascular Resistance



Diagnostic Performance of μQFR

	μQFR ≤0.80	DS% ≥50%
Accuracy, % (95% CI)	93.0 (90.2, 95.8)	76.1 (71.4, 80.7)
Sensitivity, % (95% CI)	87.5 (80.2, 92.8)	57.5 (48.1, 66.5)
Specificity, % (95% CI)	96.2 (92.6, 98.3)	86.7 (81.3, 91.0)
PPV, % (95% CI)	92.9 (86.5, 96.9)	71.1 (61.0, 79.9)
NPV, % (95% CI)	93.1 (88.9, 96.1)	78.1 (72.2, 83.2)
+LR (95% CI)	23.0 (11.6, 45.5)	4.3 (3.0, 6.3)
-LR (95% CI)	0.13 (0.08, 0.20)	0.49 (0.40, 0.60)

Angio-based Microvascular Resistance



Key features of μQFR

(Powered by AI)

- Support single angiographic view computation
- Support analysis of bifurcation lesions
- Support analysis of all side branches
- AI-powered automation, analysis time ≈ 1 min
- Support analysis of patients with myocardial bridge
- Support analysis of plaque vulnerability: strain

Diagnostic Performance of AMR*

(with IMR < 25U as reference)

Sensitivity %	91.7 (84.9-96.2)
Specificity %	83.4 (76.5-89.0)
+LR	5.54
-LR	0.099

Tu S, et al. *Catheter Cardiovasc Interv* 2021; *AMR Unpublished data

FAVOR III China - Study Design

Investigator-Initiated, Multicenter, Sham-Controlled Blinded Randomized Trial

Patients with coronary artery disease scheduled for coronary angiography

Meet all general inclusion and not meet any exclusion criteria

Inclusions: age ≥ 18 years; stable, unstable angina, or post-AMI (≥72 hours). Exclusions: moderate or severe chronic kidney disease (defined as creatinine >150 μmol/L or estimated glomerular filtration rate (GFR) <45 ml/kg/1.73 m^2).

Informed consent

Coronary angiography

Meet all angiographic inclusion and not meet any exclusion criteria

Inclusions: patients must have at least one lesion with a percent diameter stenosis between **50% and 90%** in a coronary artery with a **≥2.5 mm** reference vessel diameter by visual assessment. Exclusions: patients had only one lesion with DS%>90% and TIMI flow <3; interrogated lesions are related with AMI.

Identify target vessels intended to be treated with standard angiography guidance

N=3830 (1:1 randomization)

Randomization Stratifications
- Diabetes Mellitus
- Multivessel Disease
- Presence of any vessel with DS% >90% and TIMI flow <3
- Center

QFR-guided strategy N=1915	Angiography-guided strategy N=1915
QFR was measured in all coronary arteries containing any lesion with visually-assessed DS% ≥50% and ≤90% and RVD ≥2.5 mm • QFR ≤0.80: PCI • QFR >0.80: deferral • All measured vessel QFR >0.80: OMT alone	PCI was performed based on visual angiographic assessment per local standard of practice

Independent Organizations
- Core Lab
- CEC
- DSMB
- Data Management
- Statistical Analysis

Imaging core lab analysis; clinical follow-up at 1 month, 6 months,1, 2, 3, 4, and 5 years; EQ-5D questionnaires collected at 1, 6, and 12 months

ClinicalTrial.gov Identifier: NCT03656848

Song L, et al. *Am Heart J* 2020; Xu B, et al. *Lancet* 2021

How QFR Guidance Changed the Strategy

Vessels intended to be treated pre randomization	QFR-guided group N=2503	Angiography-guided group N=2559
LM, p=0.46	1.3%	1.6%
LAD, p=0.069	52.6%	50.1%
LCX, p=0.084	20.9%	22.9%
RCA, p=0.80	25.2%	25.5%

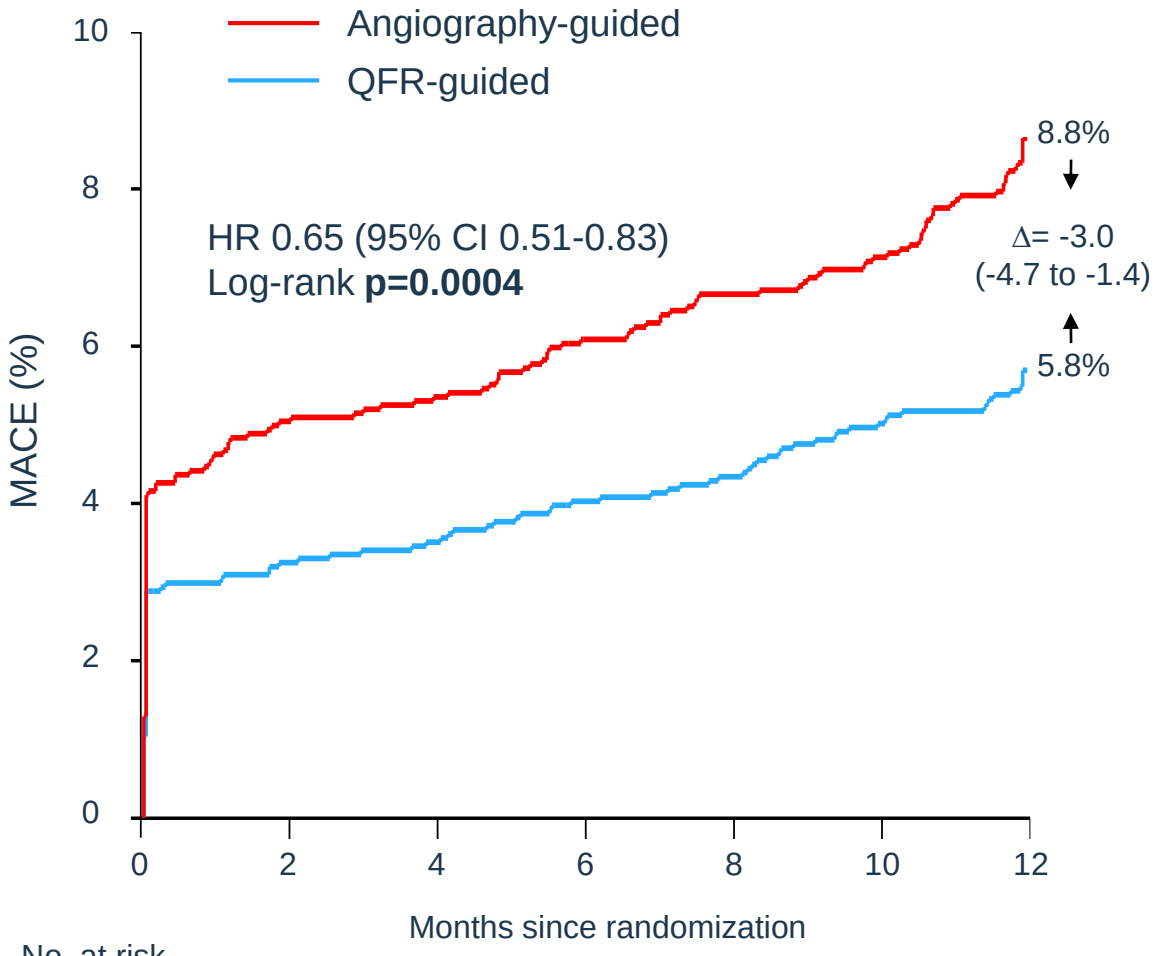
Vessels actually treated of those originally intended	QFR-guided group N=2112	Angiography-guided group N=2449
LM, p=0.62	1.4%	1.6%
LAD, **p=0.0007**	55.6%	50.6%
LCX, **p=0.015**	19.8%	22.7%
RCA, p=0.14	23.2%	25.1%

	QFR-guided group	Angiography-guided group	p value
Vessels actually treated of those originally intended	84.4% (2112/2503)	95.7% (2449/2559)	**<0.0001**
Patients with intended vessel deferral or unintended vessel treatment	23.3% (445/1913)	6.2% (119/1912)	**<0.0001**
Deferral (non-treatment) of at least one vessel originally intended for PCI	19.6% (375/1913)	5.2% (100/1912)	**<0.0001**
Treatment of at least one vessel not originally intended for PCI	4.4% (85/1913)	1.5% (28/1912)	**<0.0001**

Key Procedural Results

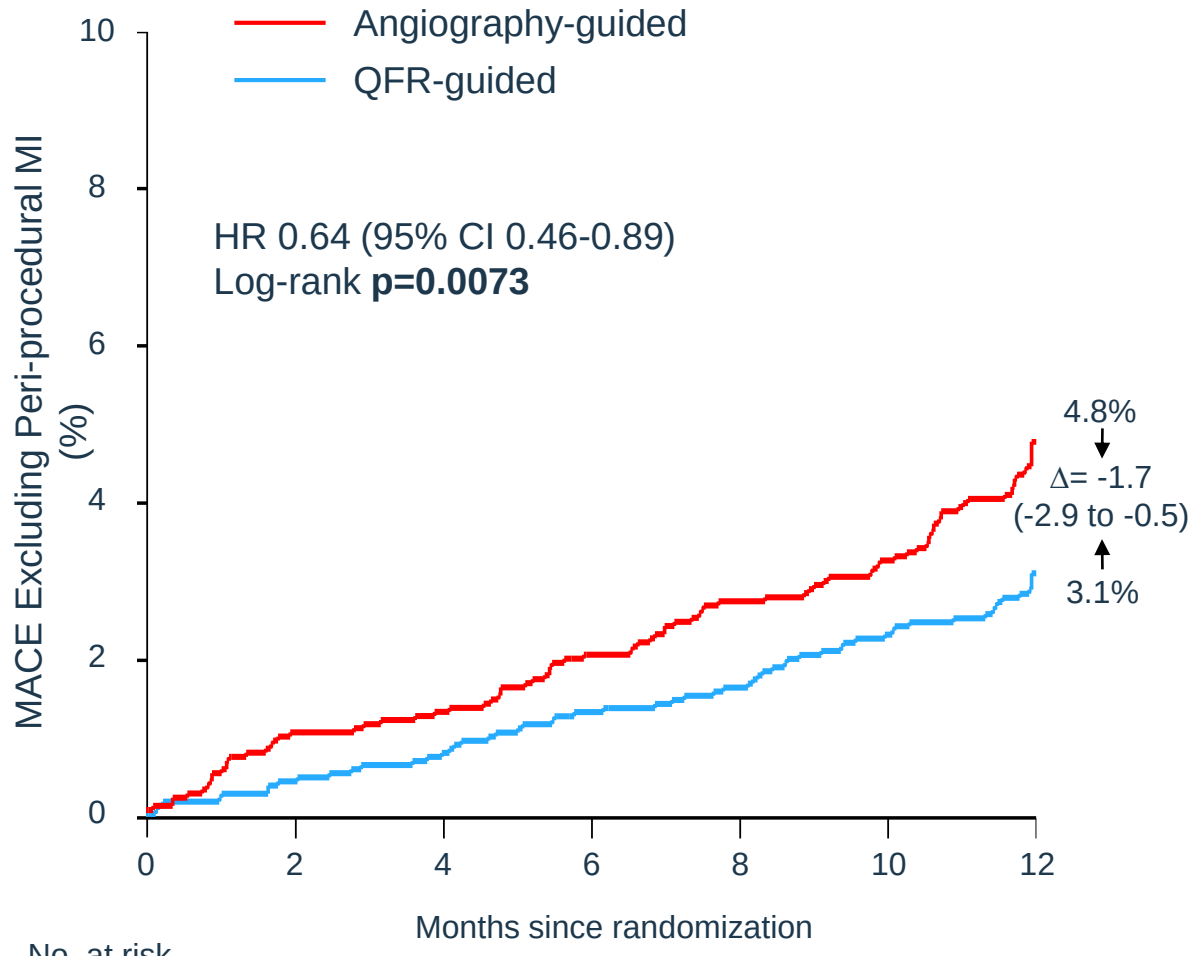
	QFR-guided group (N=1913)	Angiography-guided group (N=1912)	p value
PCI performed	90.5%	99.1%	**<0.0001**
Number of stents placed per patient	1.45 ± 1.02	1.58 ± 0.97	**<0.0001**
Use of intravascular imaging	6.2%	6.3%	0.89
Contrast medium used per patient, ml	163.0 ± 75.6	169.7 ± 74.2	**0.0060**
Fluoroscopy time, min	14.1 ± 8.0	14.9 ± 7.4	**0.0013**
Procedure time, min	53.7 ± 30.4	59.4 ± 30.4	**<0.0001**
Adjusted procedure time, min	44.6 ± 28.8	49.5 ± 30.2	**<0.0001**
PCI lesion success	99.0%	99.3%	0.38
Residual anatomic SYNTAX score	2.4 ± 3.6	2.4 ± 4.0	0.49
Residual functional SYNTAX score	0.7 ± 2.3	1.0 ± 2.8	**<0.0001**
Residual functional SYNTAX score=0	88.1%	82.2%	**<0.0001**

Primary and Major Secondary Endpoints



No. at risk

QFR-guided	1913	1845	1840	1828	1821	1809	1795
Angiography-guided	1912	1804	1798	1783	1770	1762	1732



No. at risk

QFR-guided	1913	1900	1894	1881	1874	1862	1846
Angiography-guided	1912	1883	1877	1862	1847	1839	1808

One-Year Clinical Outcomes

	QFR-guided group (N=1913)	Angiography-guided group (N=1912)	Hazard ratio (95% CI)	p value
Primary endpoint	5.8%	8.8%	**0.65 (0.51-0.83)**	**0.0004**
Death from any cause	0.7%	0.5%	1.44 (0.62-3.37)	0.40
Myocardial infarction	3.4%	5.7%	**0.59 (0.44-0.81)**	**0.0008**
Ischemia-driven revascularization	2.0%	3.1%	**0.64 (0.43-0.96)**	**0.031**
Major secondary endpoint	3.1%	4.8%	**0.64 (0.46-0.89)**	**0.0078**
Other secondary endpoints				
Cardiovascular death	0.5%	0.4%	1.28 (0.48-3.44)	0.62
Peri-procedural myocardial infarction	2.9%	4.2%	**0.69 (0.49-0.97)**	**0.033**
Non-procedural myocardial infarction	0.5%	1.6%	**0.33 (0.16-0.68)**	**0.0025**
Any revascularization	2.6%	3.5%	0.73 (0.50-1.05)	0.089
Target vessel revascularization	1.2%	1.3%	0.88 (0.50-1.56)	0.66
Stent thrombosis, definite or probable	0.2%	0.3%	0.50 (0.12-1.99)	0.33

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How to Use QFR to Guide PCI in the Cath Lab?

A Case Illustration

A Patient with Three Vessel Disease

- Which revascularization strategy (PCI or CABG)?
- If PCI, which vessel/lesion to treat?
- How to treat?

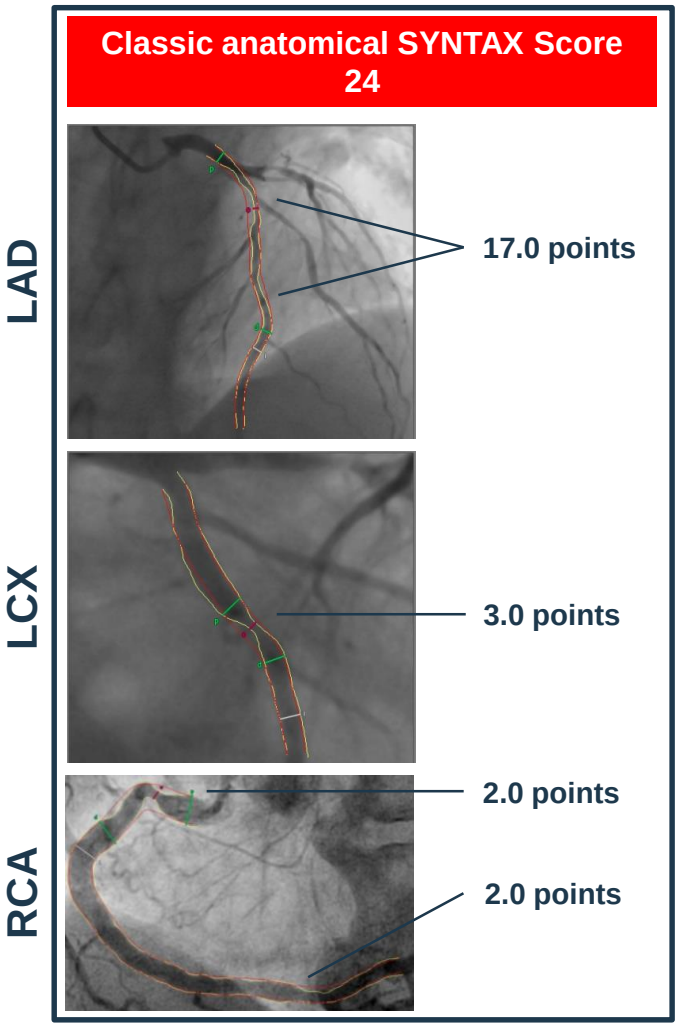
LAD

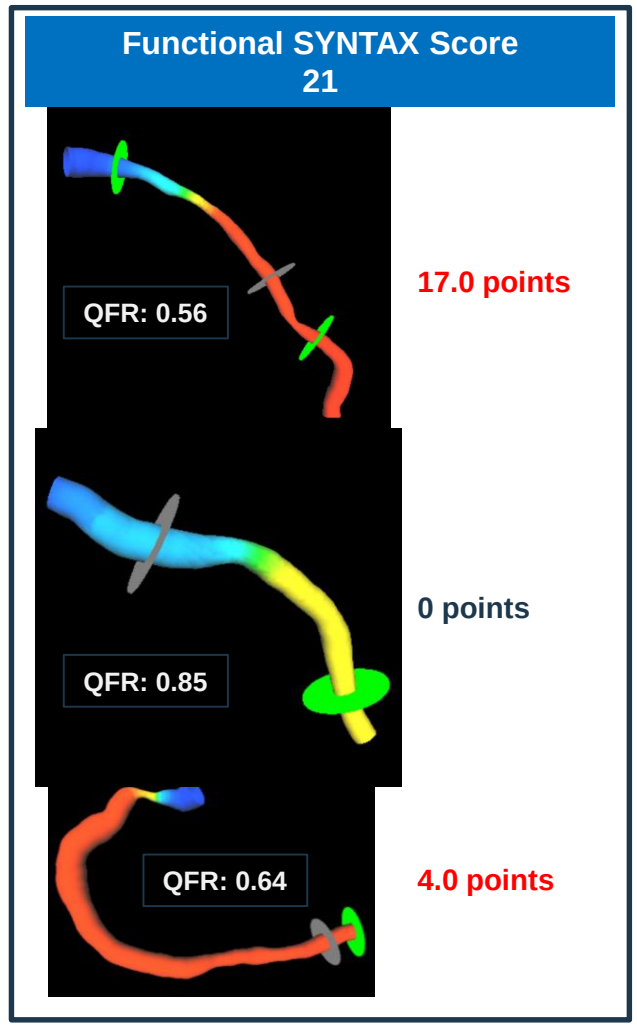
LCX

RCA

Step 1: Which Revascularization Strategy

- **Functional SYNTAX score (FSS_{QFR}):** sum the individual scores only in vessels with functional ischemia (QFR ≤0.80) and ignoring lesions with vessel QFR >0.80
- **SS 24 points → favor CABG**
- **FSS 21 points → favor PCI**
- After calculating the FSS_{QFR}, PCI strategy would be preferred
- Therefore, this patient underwent multivessel PCI





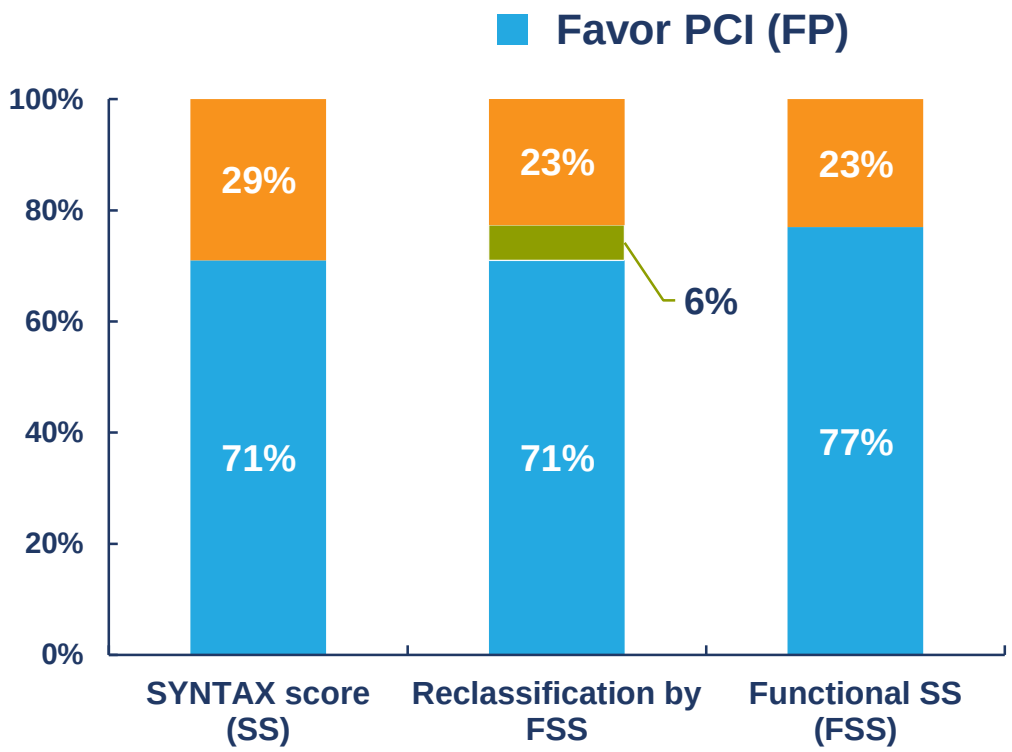
Strategy recommendation by guideline:
Favor CABG

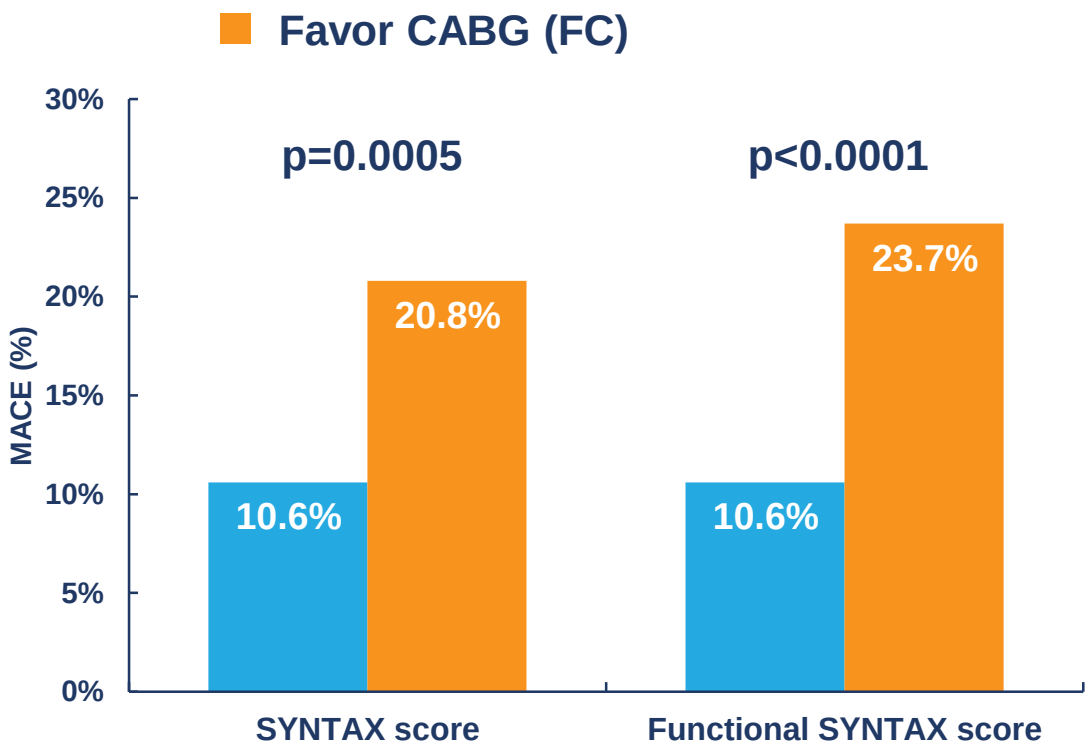
Strategy recommendation by guideline:
Favor PCI

1) Favor CABG, >22 (multivessel) or >32 (LM); **2) Favor PCI**, ≤22 (multivessel) or ≤32 (LM)

QFR-based Strategy Selection

- 6% of patients, for whom CABG would be recommended according to SS converted to a lower-risk group and therefore another treatment option may be preferred
- FSS_{QFR} can effectively identify the PCI beneficiaries among high-risk patients. Compared with SS, FSS_{QFR} increased the risk of adverse events in FC group but not in FP group

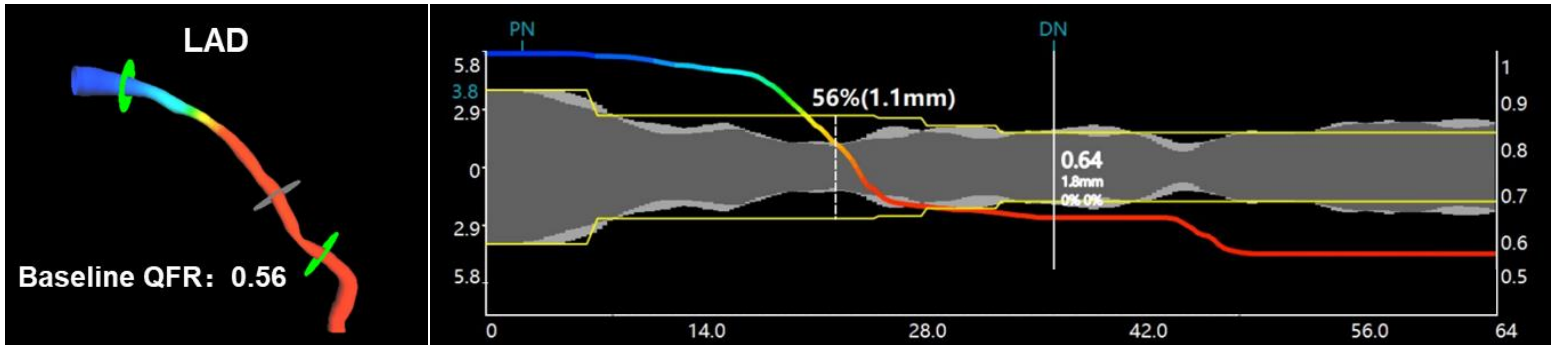


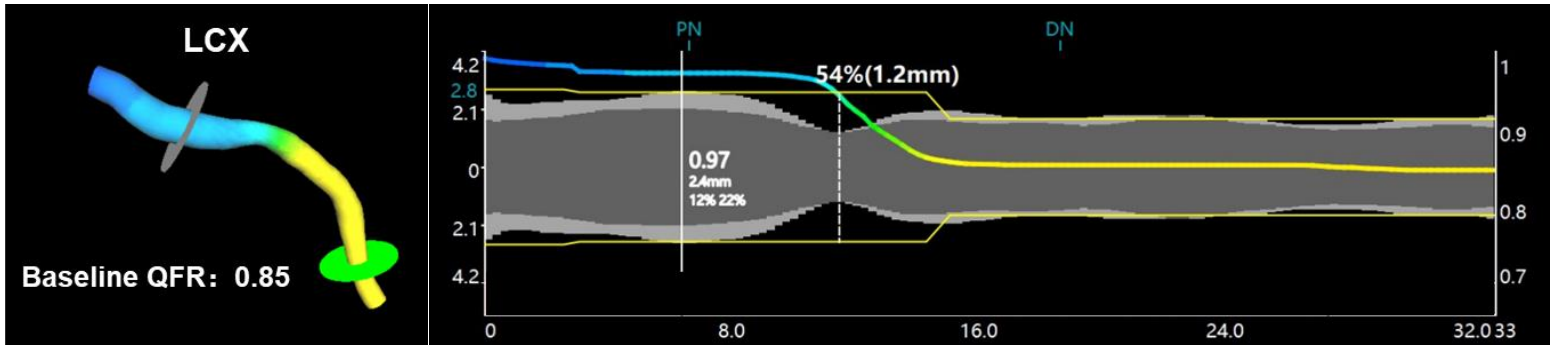


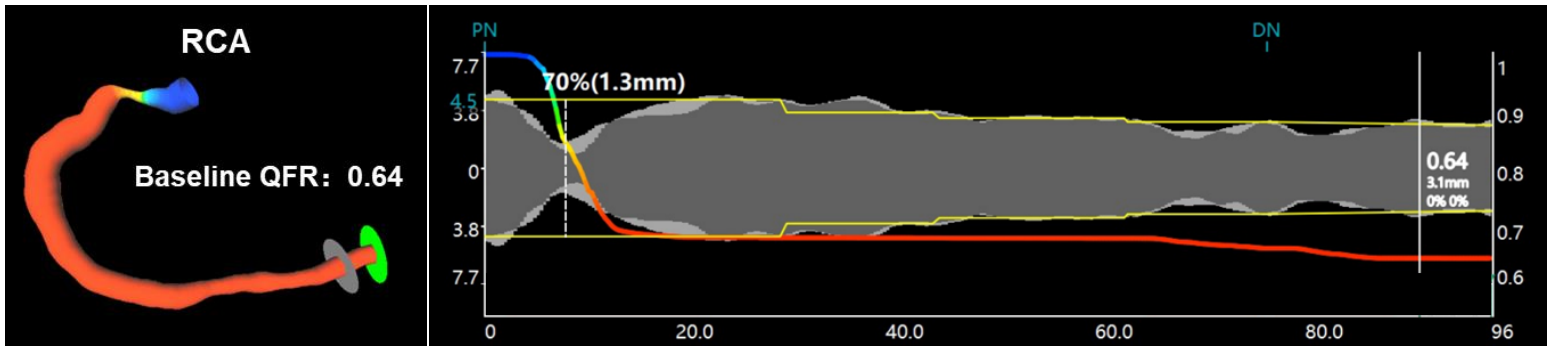
Zhang R, et al. *Circ Cardiovasc Interv* 2020

Step 2: Which Vessel/Lesion to Treat

- **QFR-consistent PCI:** all functionally significant vessels were treated and vessels with QFR >0.80 were deferred
- QFR-consistent PCI was **associated with improved long-term prognosis**
- **Baseline QFR assessment**
  - ✓ **LAD**: QFR **0.56** → treatment
  - ✓ **LCX**: QFR **0.85** → deferral
  - ✓ **RCA**: QFR **0.64** → treatment
- For this patient, PCI treatment was performed in LAD and RCA, while LCX was deferred

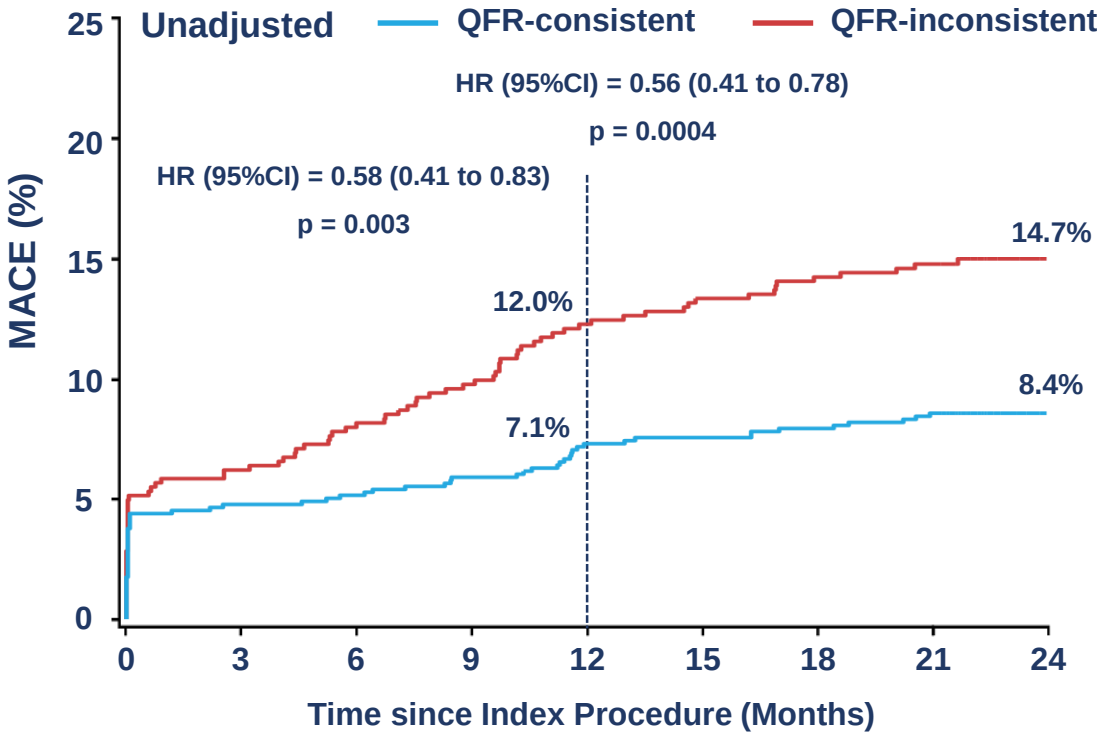


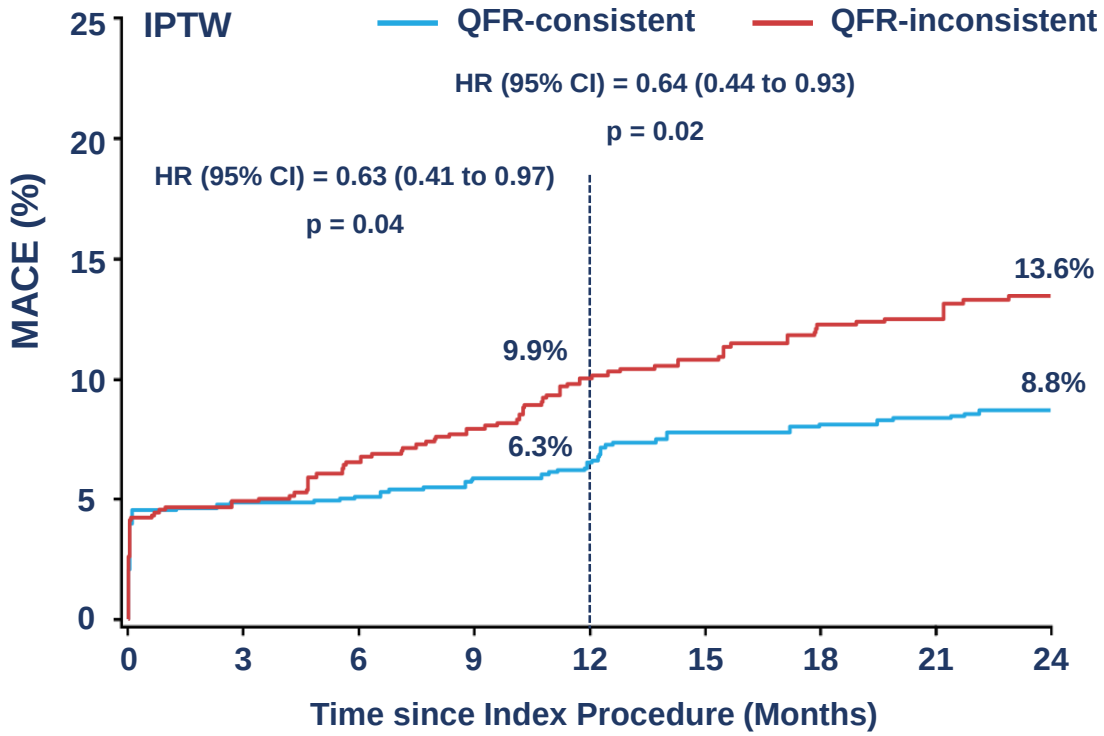




QFR-consistent PCI

- **QFR-consistent treatment was significantly associated with improved 2-year outcomes**
  - ✓ Unadjusted analysis: 8.4% vs 14.7%; HR 0.56 (95% CI 0.41-0.78), p=0.0004
  - ✓ IPTW anlysis: 8.8% vs 13.6%; HR 0.64 (95% CI 0.44-0.93), p=0.02





Number at Risk:

QFR-consistent	814	776	774	770	759	747	745	742	740
QFR-inconsistent	577	541	532	521	507	501	497	492	489

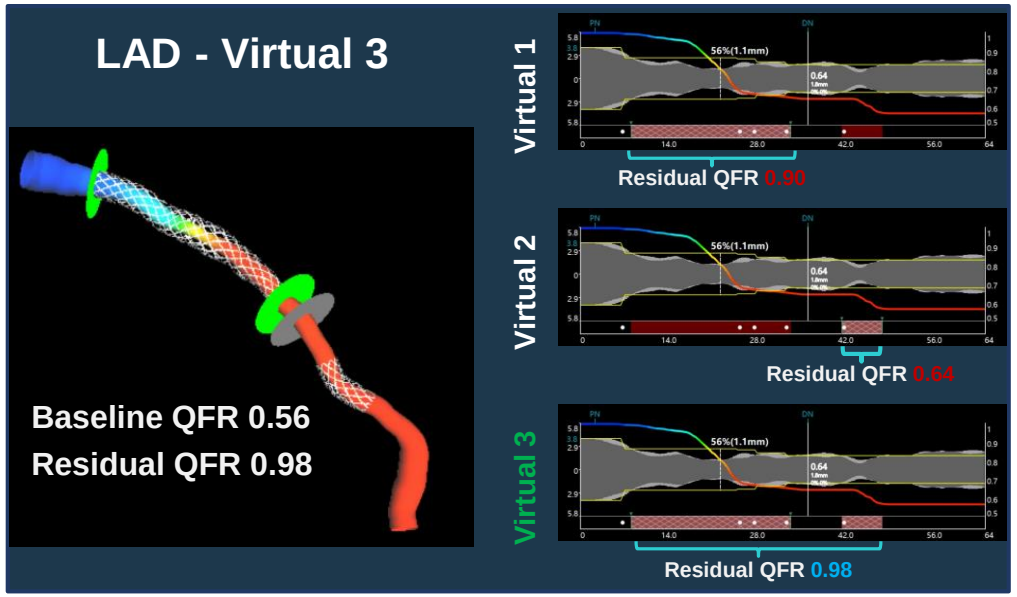
Number at Risk:

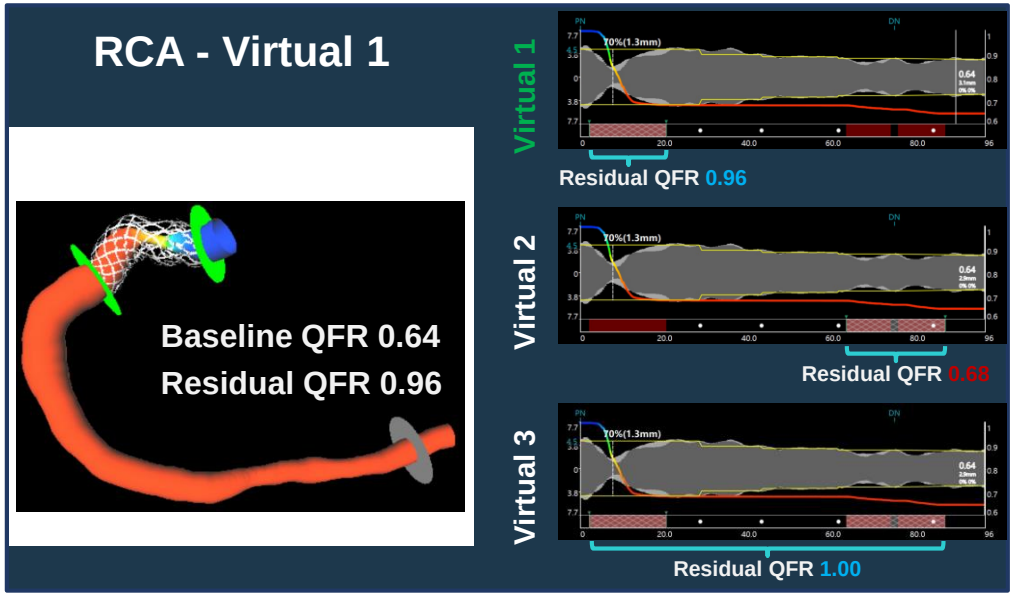
QFR-consistent	859	817	815	811	799	783	781	778	777
QFR-inconsistent	507	481	473	465	454	449	444	440	436

Zhang R, et al. *EuroIntervention* 2022

Step 3: How to Treat?

- Patients with **optimal post-PCI functional results (QFR>0.92)** were associated with improved prognosis
- **Virtual stenting / residual QFR** is a **prediction of actually post-PCI QFR**, and could be a promising approach to PCI optimization
- **By current virtual stenting assessment**
  - ✓ **Principal:** Optimal virtual results + less stenting
  - ✓ **LAD**: virtual 3 - residual QFR **0.98**
  - ✓ **RCA**: virtual 1 - residual QFR **0.96**
- **3D QCA data** (e.g., reference vessel diameter, lesion length), could help with stent size selections

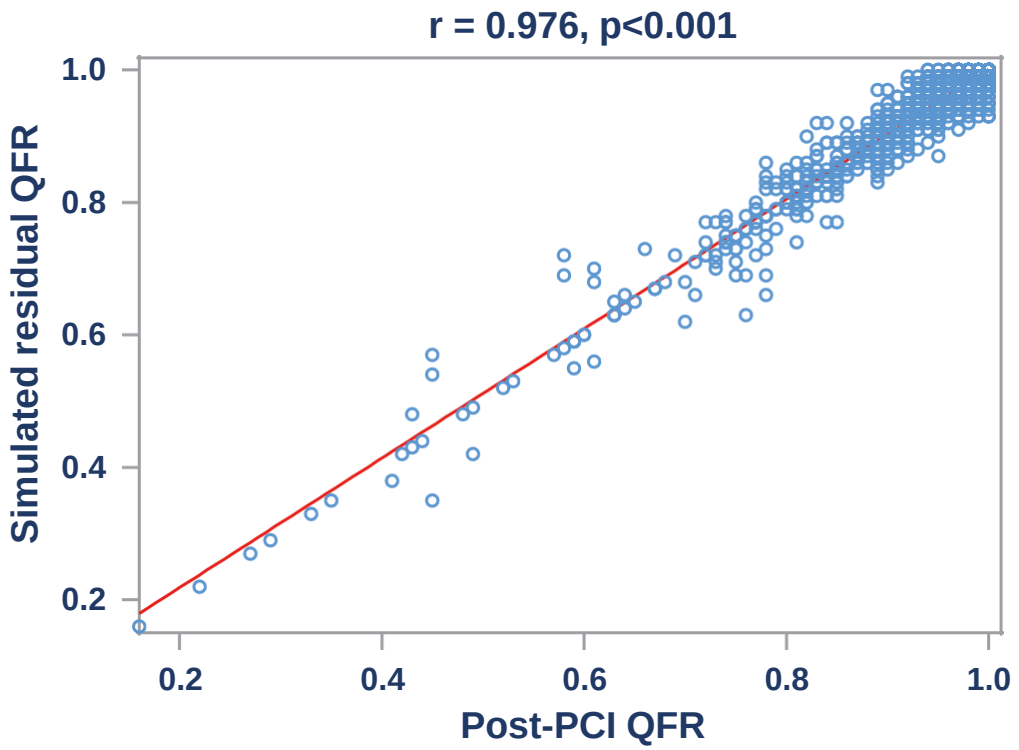




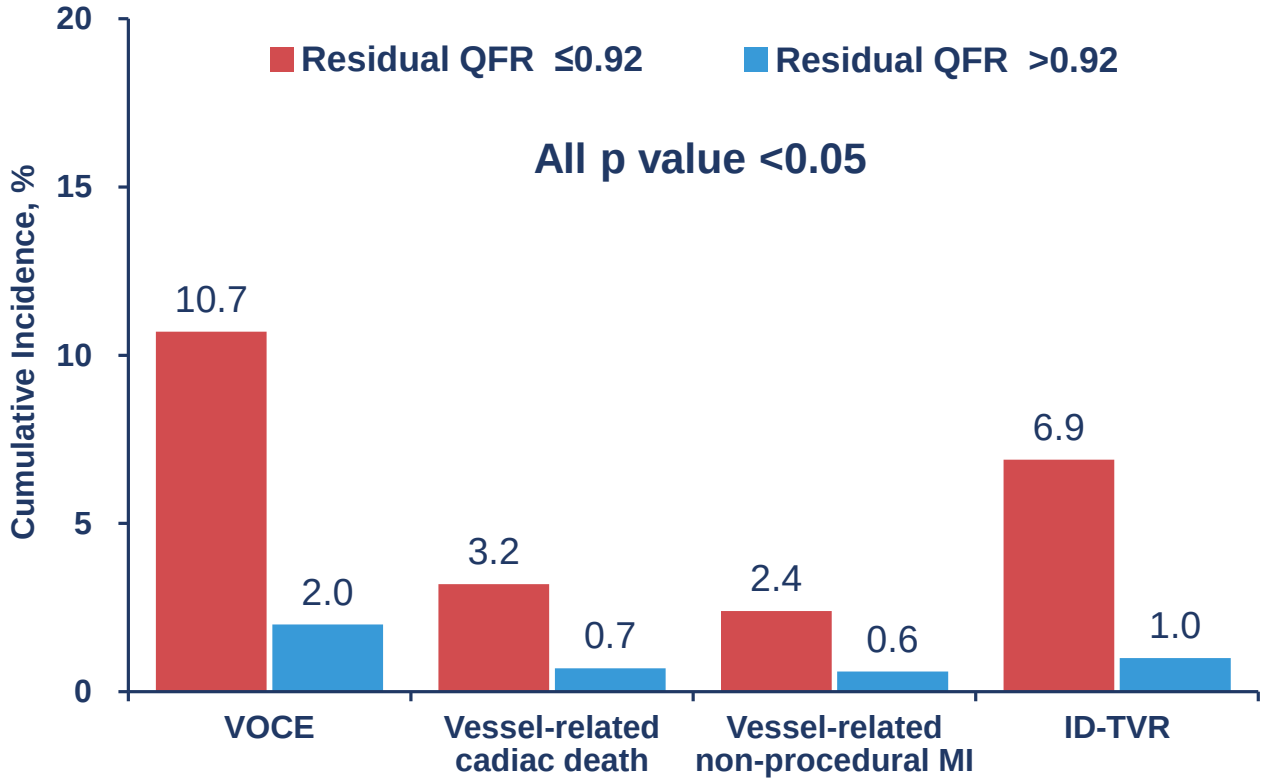
Virtual Stenting / Residual QFR

- **Good correlation and agreement** between residual QFR and post-PCI QFR were observed
- **Virtual suboptimal PCI result** (residual QFR ≤0.92) was associated with **worse prognosis** (including VOCE and its individual components)

A. Correlation Between QFRs



B. Two-year Clinical Outcomes



Zhang R, et al. *Int J Cardiol* 2022

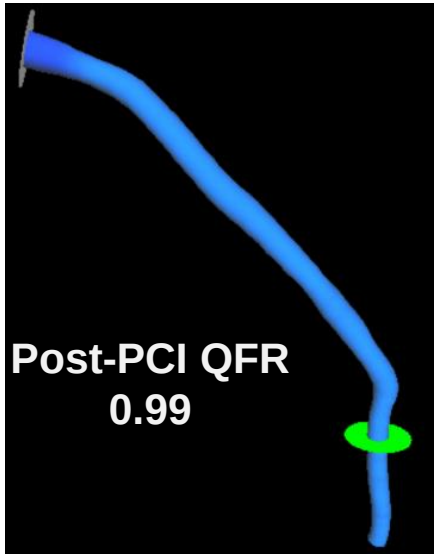
Final Results

- Actual post-PCI QFR assessment

LAD

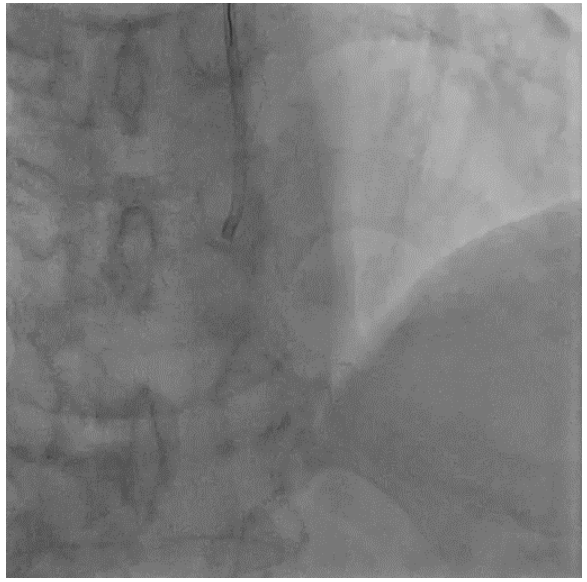
Anatomy

Physiology

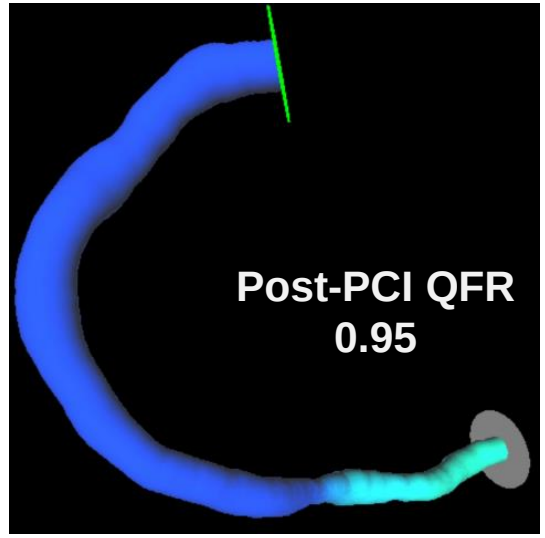


RCA

Anatomy



Physiology



- Long-term prognosis
  - ✓ 2-year follow-up: no adverse events and good quality of life

Summary

- In patients undergoing PCI, a QFR-guided strategy improved 1-year clinical outcomes compared with standard angiography guidance while reducing resource consumption
- The simplicity and safety of QFR compared with wire-based physiological measurements should facilitate the adoption of physiologic lesion assessment into routine clinical practice
- New-generation QFR system will require only a single projection and incorporates more automated processes that could further reduce analysis variability and time