Angiographic Quantitative Flow Ratio-Guided Coronary Intervention: Two-Year Outcomes of the FAVOR III China Trial

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FAVOR III China Study Group

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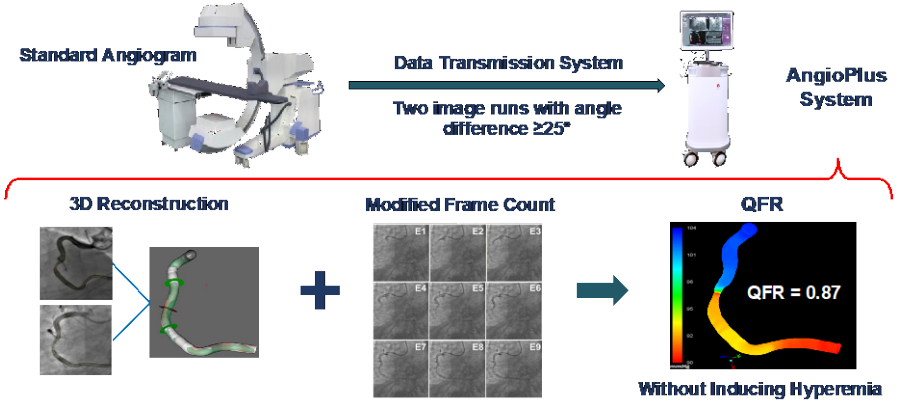
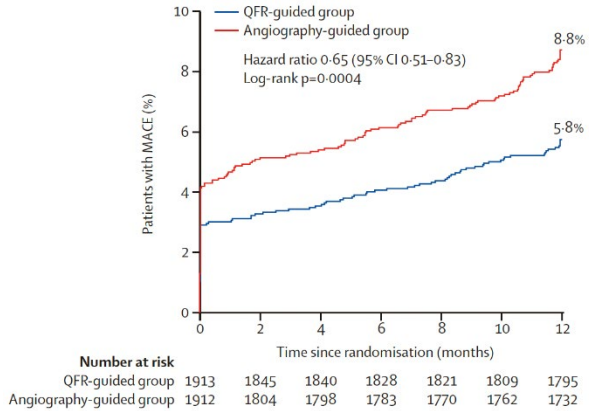
- I, [Lei Song] report no competing interests.

Faculty disclosure information can be found on the app

Background

- In the multicenter, randomized, sham-controlled FAVOR III China trial, quantitative flow ratio (QFR)-based lesion selection improved 1-year clinical outcomes compared with conventional angiographic guidance for percutaneous coronary intervention (PCI).





- Whether these early gains would be preserved, increase or diminish over time is uncertain, an issue of particular interest among those patients in whom the pre-planned revascularization strategy was altered by QFR. We herein report the 2-year results from the FAVOR III China trial.

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 year, 2 years, 3 years, 4 years, and 5 years; EQ-5D questionnaires collected at 1, 6, and 12 months

CRF TCT

ClinicalTrial.gov Identifier: NCT03656848

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

FAVOR Series of QFR Studies

Endpoints

Primary Endpoint:

1-year rate of major adverse cardiac events (MACE), defined as the composite of death from any cause, MI, or ischemia-driven revascularization

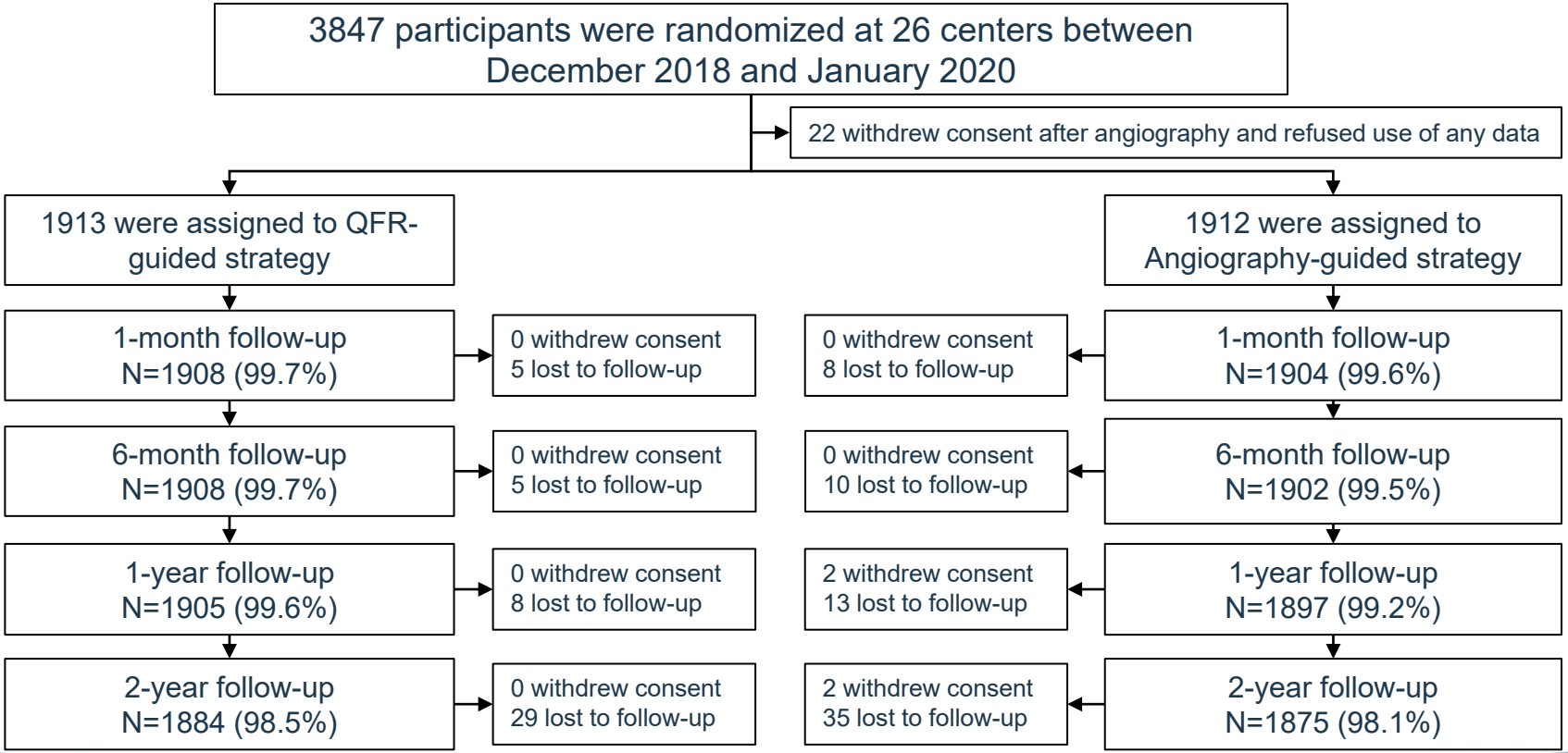
Major Secondary End Point:

1-year rate of MACE excluding peri-procedural MI arising from the index or planned staged procedures

Other Secondary End Points:

- MACE at 1 month, 6 months, 2 years, 3 years, 4 years, and 5 years
- Death (cardiovascular, non-cardiovascular, and undetermined) at 1 month, 6 months, 1 year, 2 years, 3 years, 4 years, and 5 years
- MI (peri-procedural and non-procedural) at 1 month, 6 months, 1 year, 2 years, 3 years, 4 years, and 5 years
- Repeat revascularization (ischemia driven and non-ischemia driven) at 1 month, 6 months,1 year, 2 years, 3 years, 4 years, and 5 years
- Target vessel revascularization (ischemia driven and non-ischemia driven) at 1 month, 6 months,1 year, 2 years, 3 years, 4 years, and 5 years
- Definite/probable stent thrombosis (acute, subacute, late, and very late according to ARC-2 definition)
- Cost-effectiveness and quality of life outcomes at 1 month, 6 months, and 1 year

Patient Flow Chart



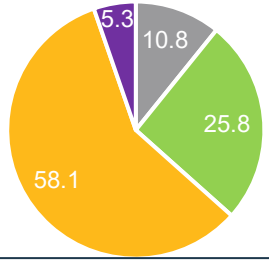
Key Baseline Characteristics

	QFR-guided group (N=1913)	Angiography-guided group (N=1912)
Age, years	62.7 ± 10.1	62.7 ± 10.2
Male sex	70.5%	70.6%
Diabetes mellitus	33.9%	33.8%
Multivessel disease	53.5%	54.6%
Any vessel with one or more lesions with diameter stenosis >90% and TIMI flow <3	8.9%	9.5%

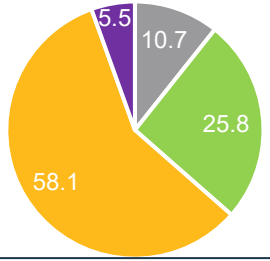
Clinical presentation

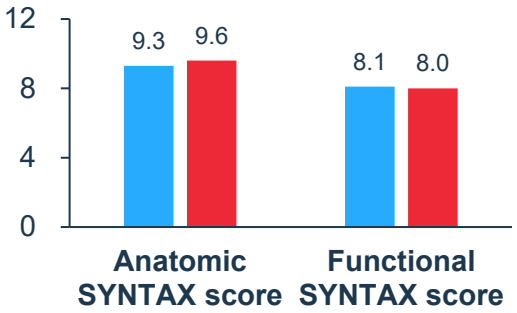
- Asymptomatic ischemia
- Stable angina
- Unstable angina
- Post myocardial infarction (within 30 days)

QFR-guided group

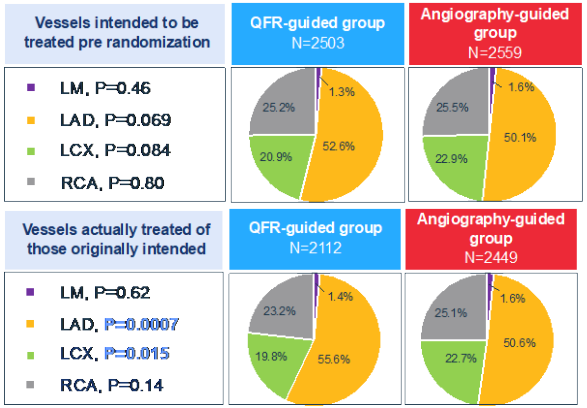


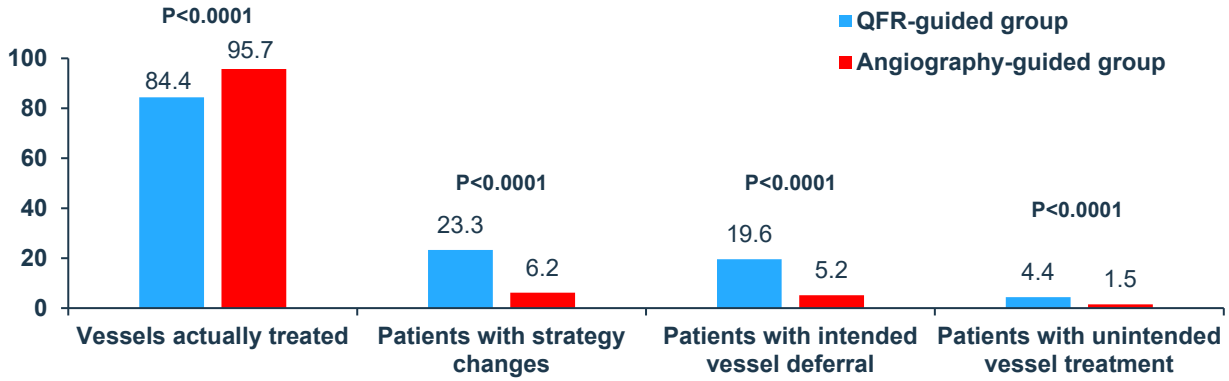
Angiography-guided group





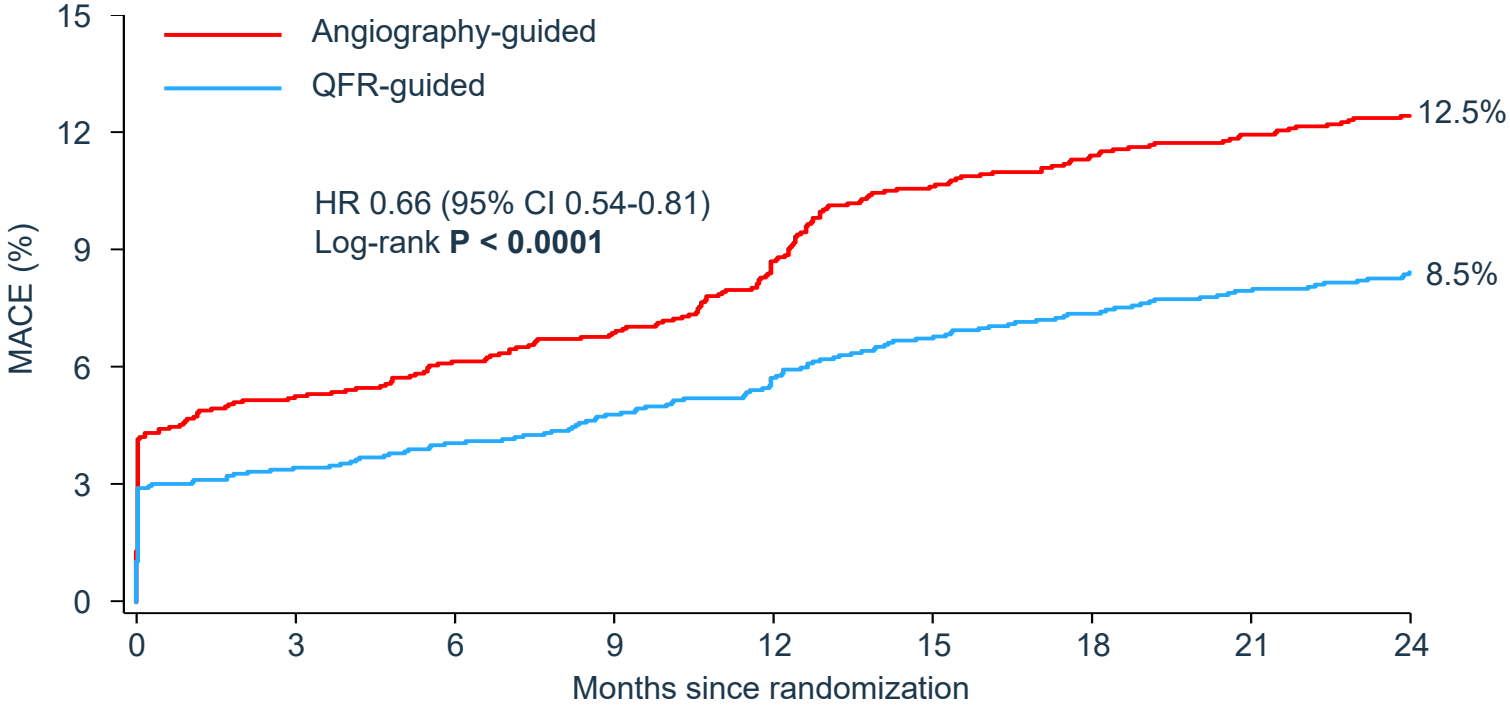
Changes of Pre-Planned Revascularization Strategy and Key Procedural Results





	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**
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**
PCI lesion success	99.0%	99.3%	0.38
Residual functional SYNTAX score=0	88.1%	82.2%	**<0.0001**

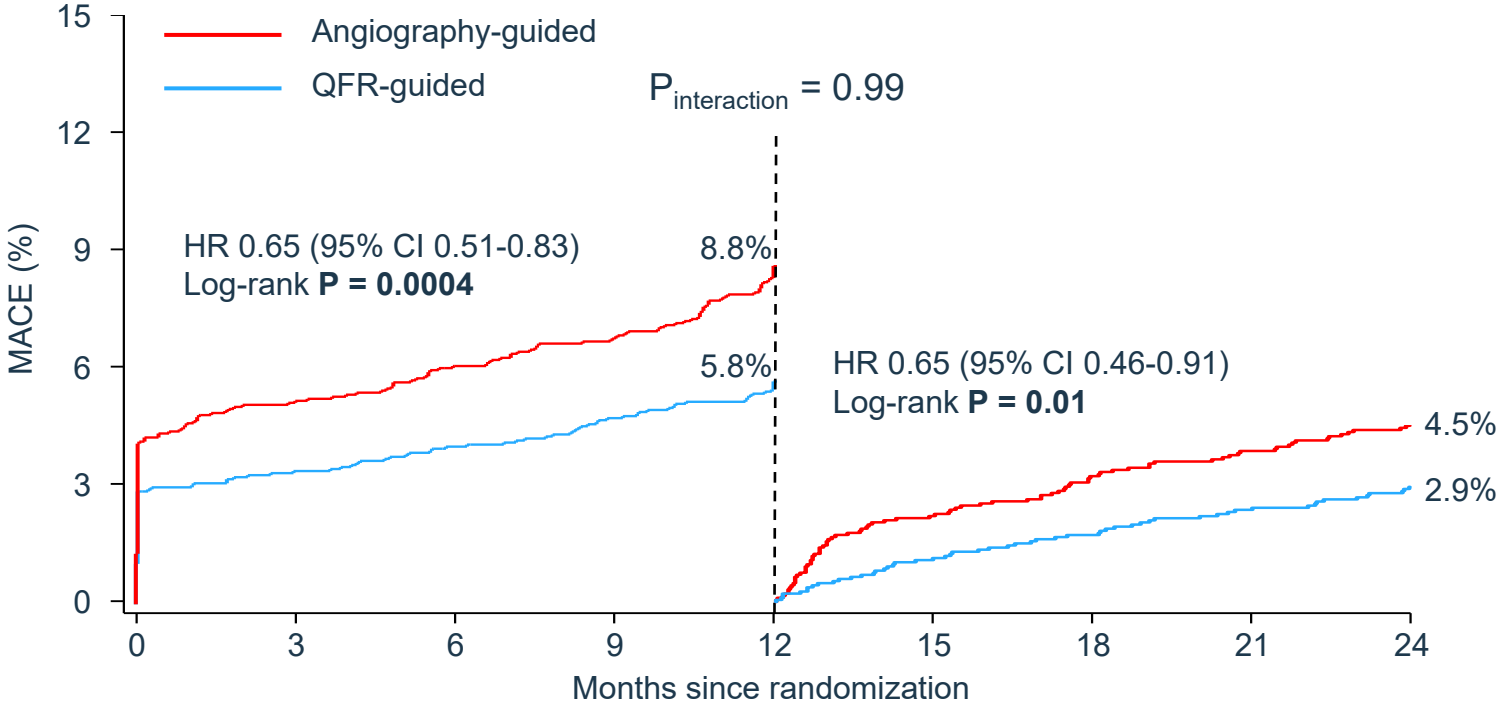
Kaplan-Meier Curves of 2-Year MACE



No. at risk

QFR-guided	1913	1845	1833	1819	1806	1755	1743	1732	1723
Angiography-guided	1912	1810	1793	1778	1749	1674	1660	1650	1641

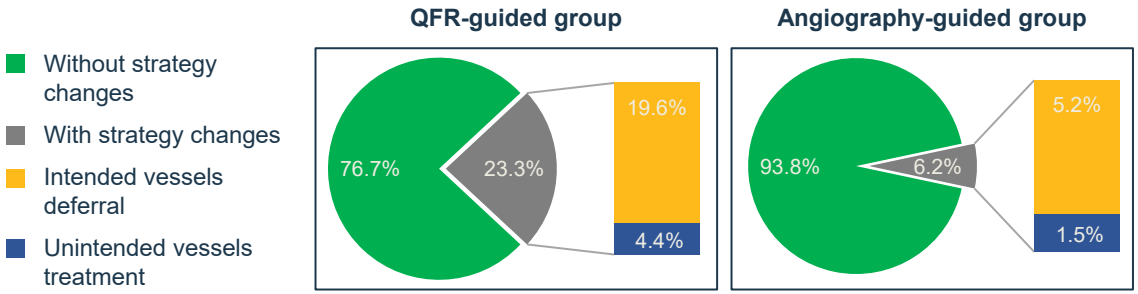
Landmark Analysis of 2-Year MACE

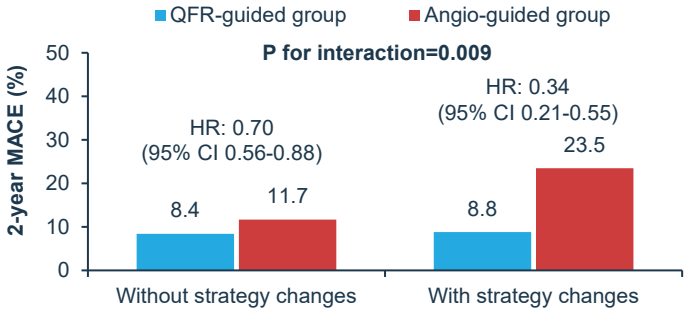


Two-Year Clinical Outcomes

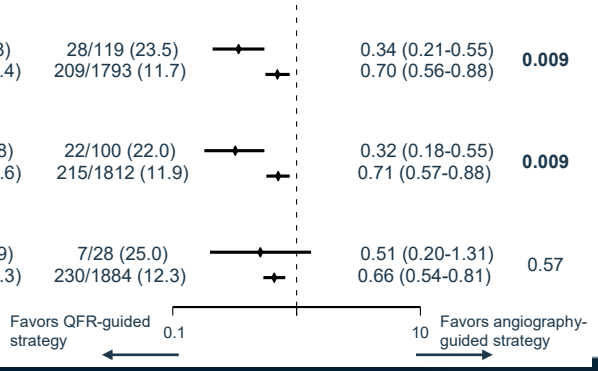
	QFR-guided group (N=1913)	Angiography-guided group (N=1912)	Hazard Ratio (95% CI)	P value
MACE	8.5%	12.5%	0.66 (0.54-0.81)	**<0.0001**
Death from any cause	1.1%	1.1%	0.95 (0.52-1.75)	0.87
Myocardial infarction	4.0%	6.8%	0.58 (0.44-0.77)	**0.0002**
Ischemia-driven revascularization	4.2%	5.8%	0.71 (0.53-0.95)	**0.02**
MACE excluding peri-procedural MI	5.8%	8.8%	0.65 (0.51-0.83)	**0.0004**
Other secondary endpoints				
Cardiovascular death	0.6%	0.6%	0.92 (0.40-2.07)	0.83
Peri-procedural myocardial infarction	2.9%	4.2%	0.69 (0.49-0.97)	**0.03**
Non-procedural myocardial infarction	1.1%	2.8%	0.40 (0.24-0.66)	**0.0004**
Any revascularization	5.7%	7.3%	0.77 (0.60-0.99)	**0.045**
Target vessel revascularization	2.4%	3.5%	0.70 (0.48-1.03)	0.07
Stent thrombosis, definite or probable	0.3%	0.5%	0.60 (0.22-1.65)	0.32

Results in Patients With and Without Changes in the Pre-PCI Declared Revascularization Plan

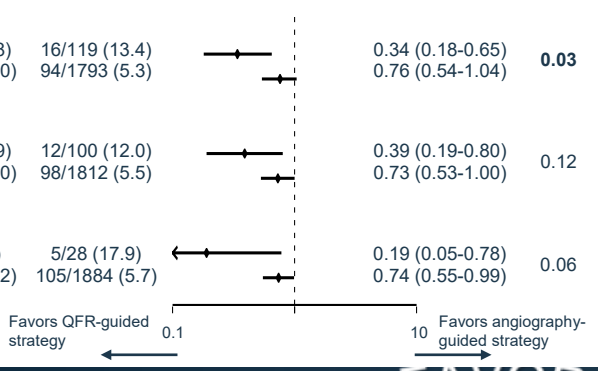




Subgroup	QFR-guided group (No. of events/total no. (%))	Angiography-guided group (No. of events/total no. (%))	Hazard ratio (95% CI)	P_{int}
MACE				
Strategy Change				
Yes	39/445 (8.8)	28/119 (23.5)	0.34 (0.21-0.55)	**0.009**
No	122/1468 (8.4)	209/1793 (11.7)	0.70 (0.56-0.88)	
Deferral of vessels intended for treatment				
Yes	29/375 (7.8)	22/100 (22.0)	0.32 (0.18-0.55)	**0.009**
No	132/1538 (8.6)	215/1812 (11.9)	0.71 (0.57-0.88)	
Treatment of vessels intended for deferral				
Yes	11/85 (12.9)	7/28 (25.0)	0.51 (0.20-1.31)	0.57
No	150/1828 (8.3)	230/1884 (12.3)	0.66 (0.54-0.81)	



Subgroup	QFR-guided group (No. of events/total no. (%))	Angiography-guided group (No. of events/total no. (%))	Hazard ratio (95% CI)	P_{int}
Ischemia-driven revascularization				
Strategy Change				
Yes	21/445 (4.8)	16/119 (13.4)	0.34 (0.18-0.65)	**0.03**
No	58/1468 (4.0)	94/1793 (5.3)	0.76 (0.54-1.04)	
Deferral of vessels intended for treatment				
Yes	18/375 (4.9)	12/100 (12.0)	0.39 (0.19-0.80)	0.12
No	61/1538 (4.0)	98/1812 (5.5)	0.73 (0.53-1.00)	
Treatment of vessels intended for deferral				
Yes	3/85 (3.6)	5/28 (17.9)	0.19 (0.05-0.78)	0.06
No	76/1828 (4.2)	105/1884 (5.7)	0.74 (0.55-0.99)	

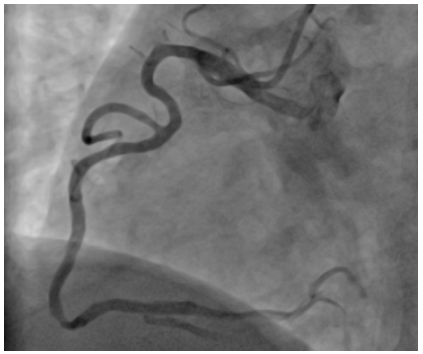


Two-Year Ischemia-Driven Revascularization

Ischemia-driven revascularization (IDR) was performed in 215 vessels in 189 patients within 2 years. In 38 (17.7%) of these vessels in 38 (20.1%) patients, the IDR was required for rapid progression (%DS <50% at baseline) in lesion severity.

Baseline Deferred Vessel

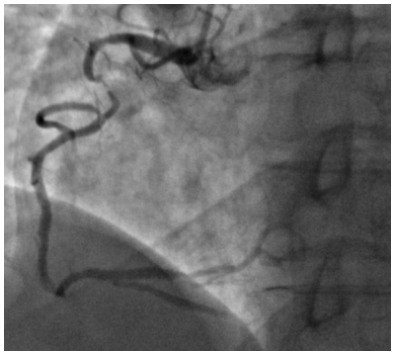
- Location: RCA
- %DS: <20% (visual estimated)

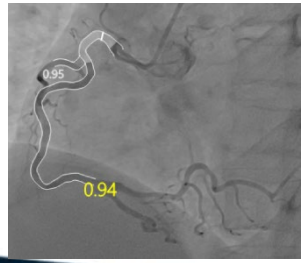


IDR

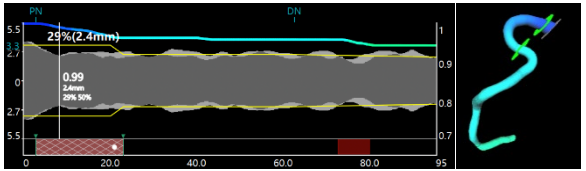
(15 months after index procedure)

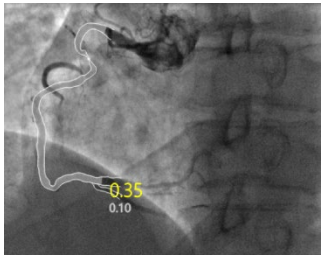
- Patient underwent repeat angiography due to aggravating angina within 2 months



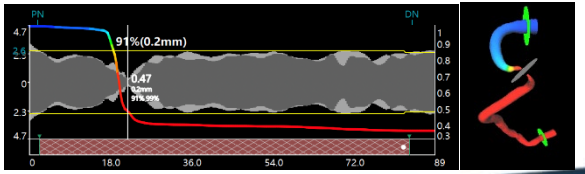


Baseline QFR: 0.94

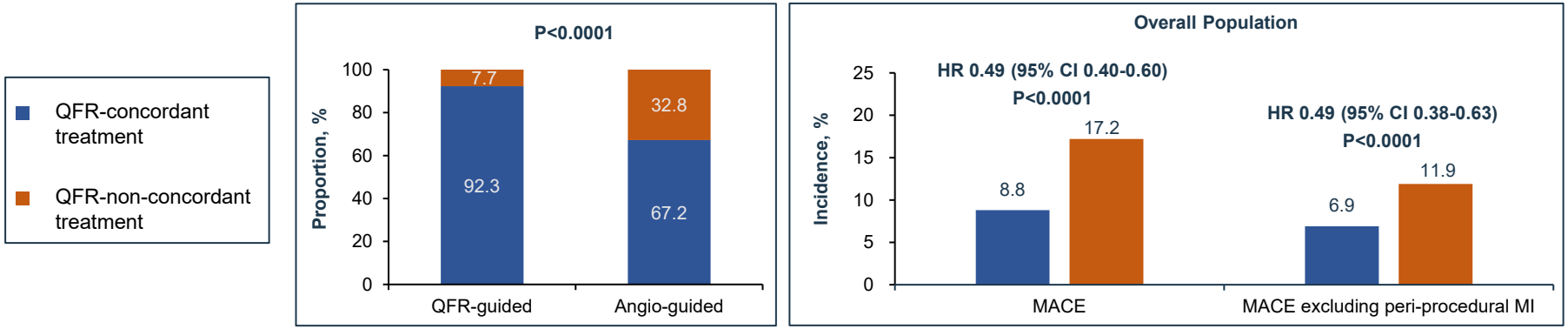




Follow-up QFR: 0.35



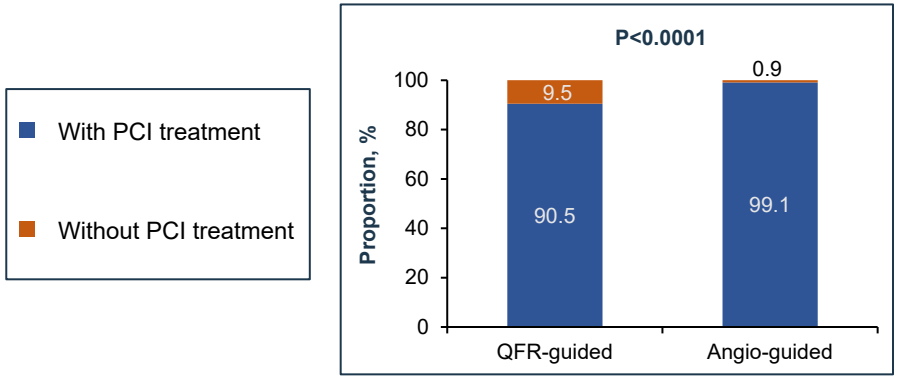
Results in Patients With QFR-concordant and QFR-non-concordant Target Vessel Selection

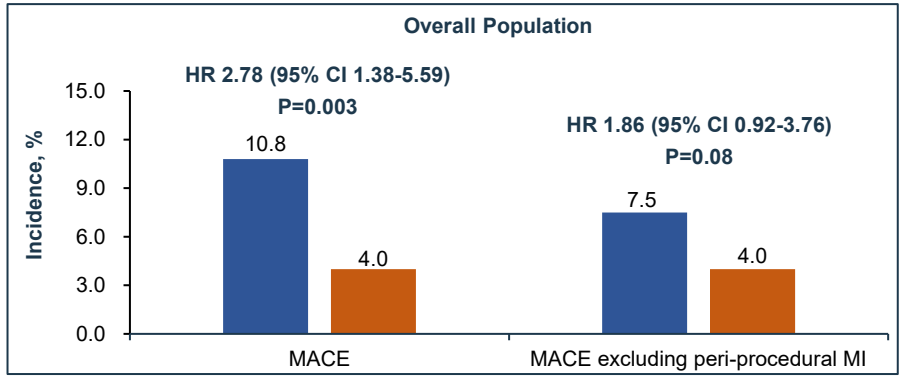


	QFR-Guided Group (N=1891)	Angiography-Guided Group (N=1877)	Hazard Ratio (95% CI)	P for interaction
MACE				
QFR-concordant selection†	8.1%	9.8%	0.82 (0.65-1.05)	0.52
QFR-non-concordant selection‡	13.0%	18.1%	0.69 (0.43-1.13)	
MACE excluding peri-procedural MI				
QFR-concordant selection†	5.4%	7.1%	0.75 (0.56-1.002)	0.56
QFR-non-concordant selection‡	11.0%	12.1%	0.90 (0.53-1.55)	

†Pre-PCI QFR-concordant vessel selection, defined as treatment of all vessels with QFR ≤0.80 and deferral of all vessels with QFR >0.80; ‡Pre-PCI QFR-non-concordant vessel selection included QFR-based over-treatment (treatment of vessels with QFR >0.80) and under-treatment (deferral of vessels with QFR ≤0.80). Note: Some patients had both QFR-based over-treatment and under-treatment (in different vessels)

Results in Patients With and Without PCI Treatment





	QFR-Guided Group (N=1913)	Angiography-Guided Group (N=1912)	Hazard Ratio (95% CI)	P for interaction
MACE				
With PCI treatment	8.9%	12.5%	0.70 (0.57-0.86)	0.94
Without PCI treatment	3.9%	5.9%	0.63 (0.08-5.14)	
MACE excluding peri-procedural MI				
With PCI treatment	6.0%	8.8%	0.70 (0.57-0.88)	0.96
Without PCI treatment	3.9%	5.9%	0.63 (0.08-5.14)	

Limitations

1. The PCI operators were aware of study-group assignments and thus some degree of intra-procedural bias cannot be excluded.
2. Although study enrollment concluded before the COVID-19 pandemic became widespread in China, follow-up procedures and event ascertainment might have been affected.
3. Current follow-up is complete through only two years. Whether the event curves continue to diverge, remain parallel or converge over time will be addressed during the 5-year follow-up from this study.
4. Patients enrolled in the present study had mostly stable chronic coronary syndromes or biomarker-negative unstable angina and relatively low SYNTAX scores.
5. Although routine angiographic follow-up was not a protocol procedure, per local practice in China a low threshold was present for repeat angiography after the 1-year follow-up visit in patients who had recurrent angina or other atypical symptoms, which might have increased the rate of repeat revascularizations after 1 year.

Conclusions

- Two-year follow-up of the multicenter, sham-controlled FAVOR III China trial demonstrated that:
  - ✓ A QFR-guided strategy of lesion selection for PCI improved 2-year clinical outcomes compared with standard angiography guidance, with incrementally increasing benefits over time
  - ✓ The reductions in MACE were most pronounced in patients in whom QFR assessment directed changes in the pre-PCI revascularization plan and in whom a QFR-concordant PCI strategy was performed
- Longer-term follow-up is needed to determine whether the 2-year benefits of QFR guidance for PCI lesion selection are sustained or further increase

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For more information about the 2-year outcomes of the FAVOR III China trial,

please see today's **Just Accepted** on the Journal of the American College of Cardiology