FAVOR II China

Diagnostic Accuracy of the Angiographic Quantitative Flow Ratio in Patients With Coronary Artery Disease

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On behalf of the FAVOR II China Investigators

Disclosure Statement of Financial Interest

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- I, (Bo Xu) have no relevant conflicts of interest to disclose

Quantitative Flow Ratio (QFR)

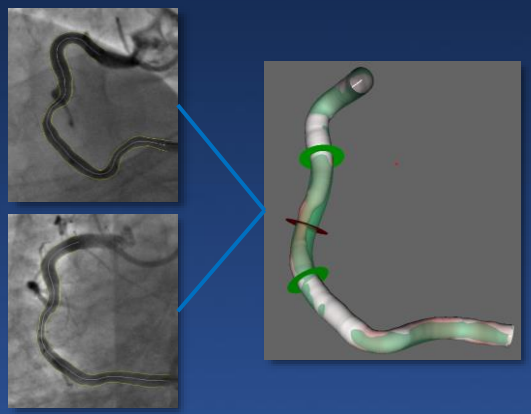
Standard Angiogram

Data Transmission System

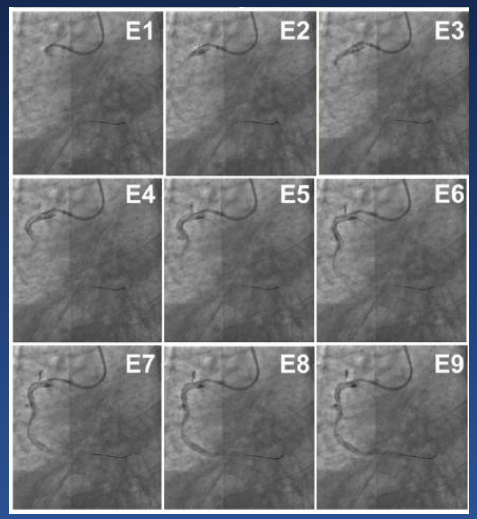
Two image runs with angle difference ≥25°

AngioPlus System

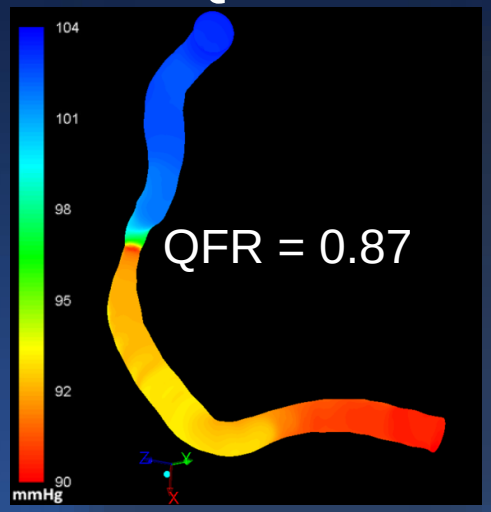
3D Reconstruction



Modified Frame Count



QFR



Without Inducing Hyperemia

Tu S et al. *JACC Cardiovasc Interv*. 2014;7:768-77; Tu S et al. *JACC Cardiovasc Interv*. 2016;9:2024-35

QFR Validation: FAVOR Pilot Study

	fQFR ≤ 0.8	cQFR ≤ 0.8	aQFR ≤ 0.8	DS% ≥ 50%
Accuracy	80 (71-89)	86 (78-93)	87 (80-94)	65 (55-76)
Sensitivity	67 (46-84)	74 (54-89)	78 (58-91)	44 (26-65)
Specificity	86 (74-94)	91 (81-97)	91 (81-97)	79 (66-89)
PPV	69 (48-86)	80 (59-93)	81 (61-93)	50 (29-71)
NPV	85 (73-93)	88 (77-95)	90 (79-96)	75 (62-85)
LR+	4.8 (2.4-9.5)	8.4 (3.6-20.1)	8.9 (3.7-21.0)	2.1(1.1-4.1)
LR-	0.4 (0.2-0.7)	0.3 (0.1-0.5)	0.2 (0.1-0.5)	0.7 (0.5-1.0)
AUC	0.88 (0.79-0.94)	0.92 (0.85-0.97)	0.91 (0.83-0.96)	0.72 (0.62-0.82)

- Good diagnostic accuracy for contrast-flow QFR (without inducing hyperemia);
- However, QFR analysis was performed in the core lab; QFR accuracy when performed **online** in the cath lab had not been properly examined to date.

Tu S et al. *JACC Cardiovasc Interv*. 2016;9:2024-35

FAVOR II China (N=308)

Prospective, multicenter clinical study (in a blinded fashion)

Major Inclusion: Age ≥ 18 years; stable, unstable angina; diameter stenosis between 30% and 90% in a vessel ≥ 2 mm by visual estimation

Major Exclusion: Myocardial infarction within 72 hours; severe heart failure (NYHA ≥ III); ostial lesions, or main vessels with stenotic side branches downstream the interrogated lesion

↓

Online QFR and QCA assessment
(blinded to the investigators who measured FFR)

↓

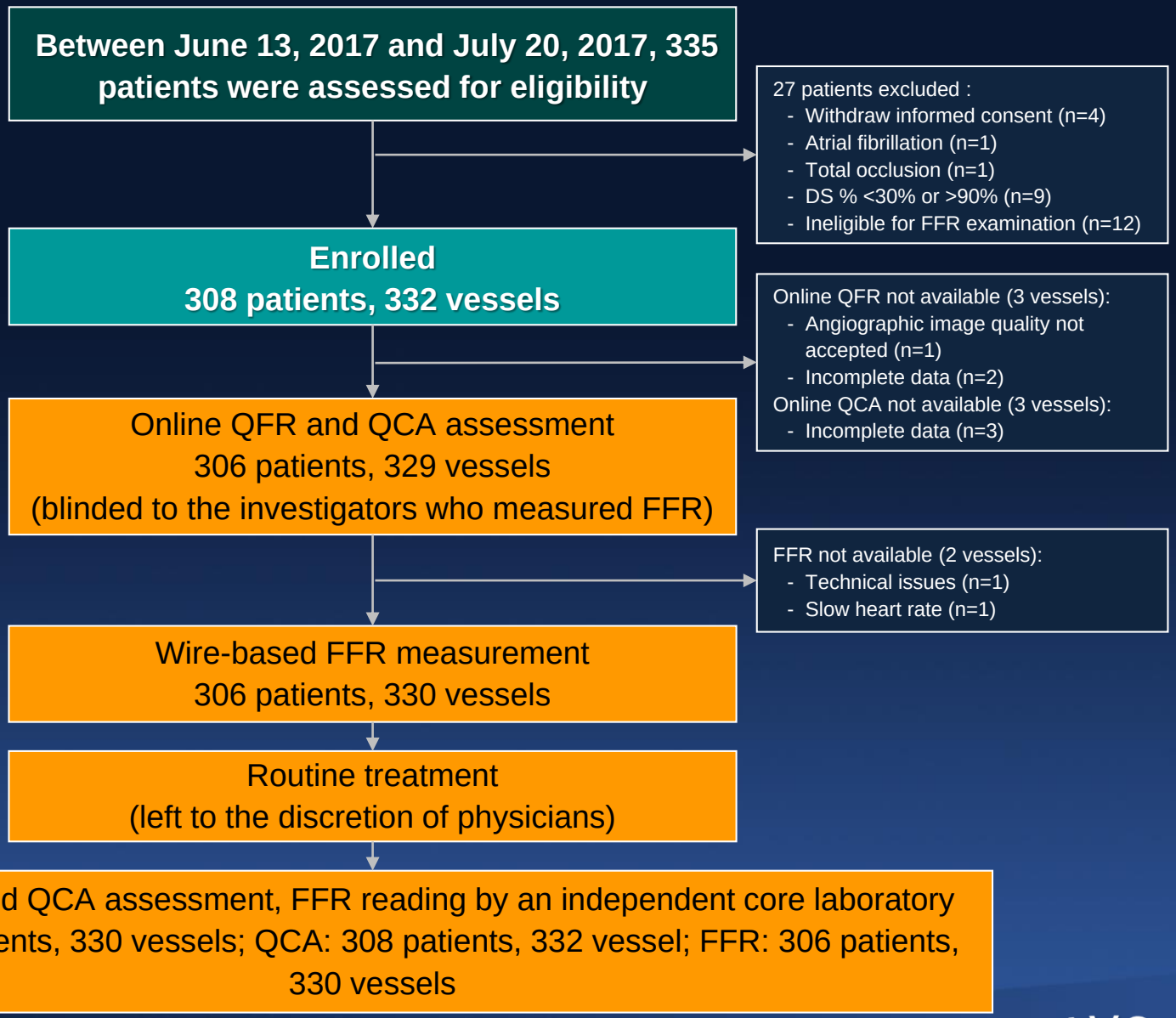
Wire-based FFR measurement

Primary Endpoint: Diagnostic accuracy* of online QFR as compared with FFR.

Major Secondary Endpoint: Sensitivity^ and specificity‖ of online QFR as compared with online QCA, when using FFR as a reference standard.

*Diagnostic accuracy: defined as consistency ratio of QFR evaluated outcomes (≤0.8 or >0.8) with the reference standard FFR evaluated outcomes (≤0.8 or >0.8); ^Sensitivity: proportion of QFR≤0.8 or QCA≥50% in vessels with hemodynamically-significant stenosis as measured by FFR (FFR≤0.8); ‖Specificity: proportion of QFR>0.8 or QCA<50% in vessels without hemodynamically-significant stenosis as measured by FFR (FFR≤0.8).

Study Flow Chart



Baseline Patient Demographics

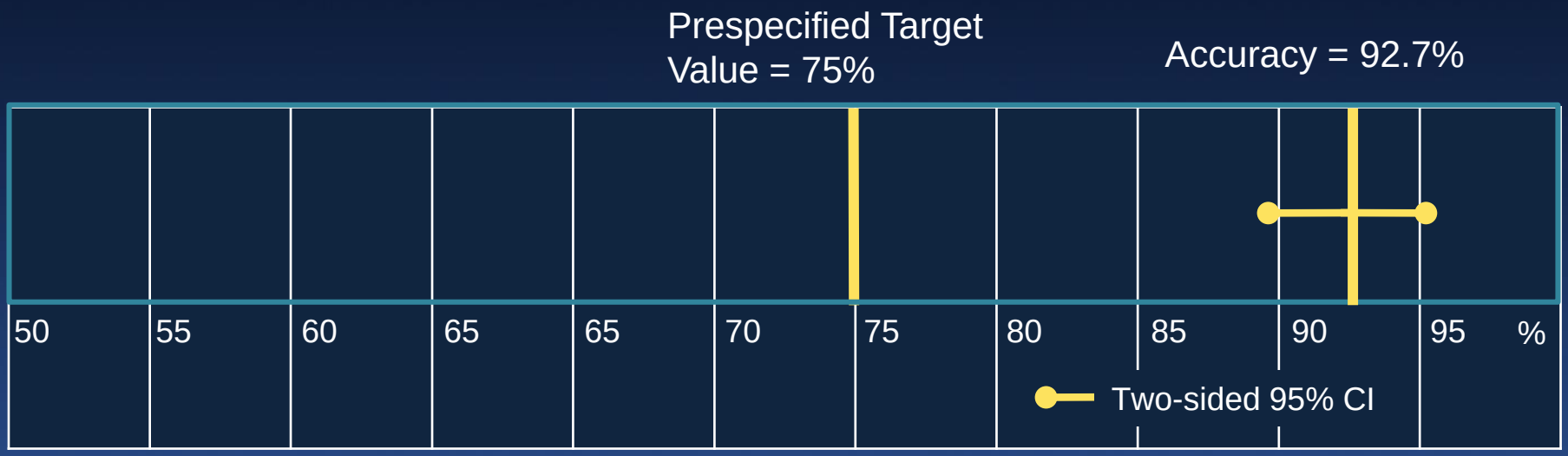
	Patients (N=308)
Age, years	61.3 ± 10.4
Women	26.3%
Diabetes Mellitus	27.9%
Hypertension	60.1%
Hyperlipidemia	45.1%
Current Smoker	28.2%
Family History of CAD	16.6%
Previous MI	15.6%
Previous PCI	21.1%
AMI within 1 Month	4.5%
Stable Angina	23.4%
Unstable Angina	61.0%
Left Ventricular Ejection Fraction, %	63.4 ± 6.3

Lesion/Procedural Characteristics

	Patients (N=308) Vessels (N=332)
Bifurcation Lesions	24.7%
Tortuous Vessels	14.2%
Moderate or Severe Calcified Lesions	18.4%
Thrombotic Lesions	0.3%
Tandem Lesions	46.3%
Online FFR Analysis	
FFR (Per Vessel)	0.82 ± 0.12
Vessels with FFR ≤ 0.80	34.2%
Vessels with 0.75 ≤ FFR ≤ 0.85	32.4%
Patients with FFR Measurement in > 1 Vessel	7.2%
Mean Time for QFR Assessment, mins	4.36 ± 2.55

Primary Endpoint: Online Per-Vessel QFR Diagnostic Accuracy

Accuracy	Target Value	p Value
Point Estimate: 92.7% (304/328) 95% Confidence Interval: 89.3% to 95.3%	75%	< 0.0001



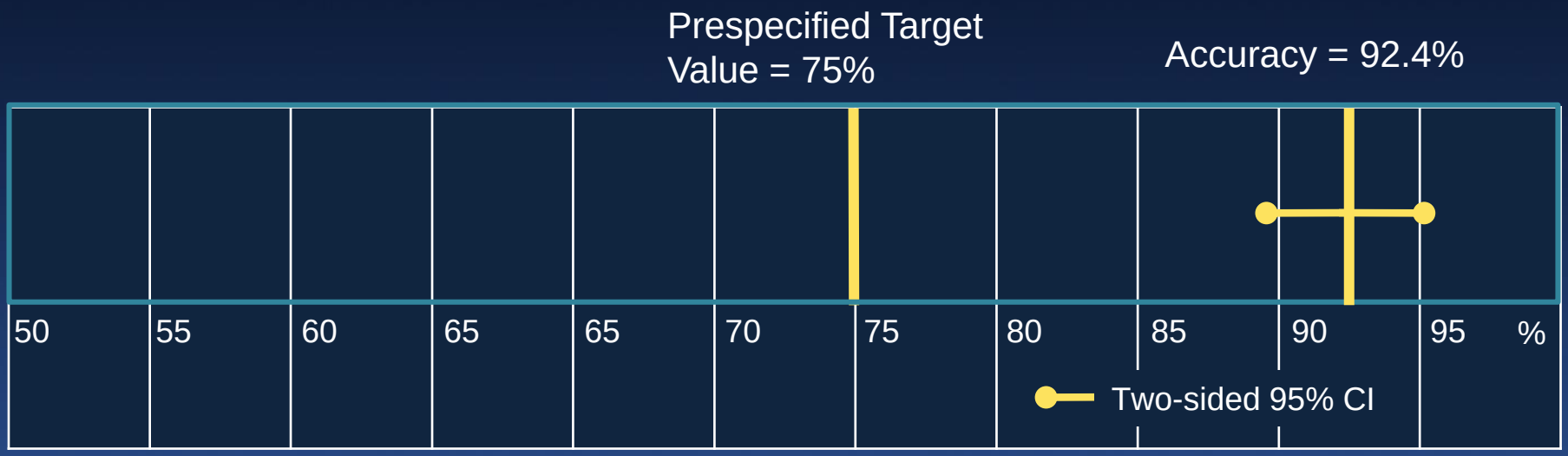
Prespecified Performance Goal Met

Diagnostic Accuracy of QFR in Different Interrogated Vessels

Interrogated Vessels	Accuracy	
	Estimate, % (95% CI)	No. of Patients in Group
LAD	92.4 (87.6, 95.8)	184
LCX	96.4 (87.5, 99.6)	55
RCA	91.0 (83.1, 96.0)	89
	Difference, % (95% CI)	p Value
LAD vs. LCX	-4.0 (-9.9, 2.3)	0.30
LAD vs. RCA	1.4 (-5.5, 8.8)	0.70
LCX vs. RCA	5.4 (-2.3, 13.7)	0.22

Online Per-Patient Diagnostic Accuracy of QFR

Accuracy	Target Value	p Value
Point Estimate: 92.4% (281/304) 95% Confidence Interval: 88.9% to 95.1%	75%	< 0.0001



Prespecified Performance Goal Met

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)	-	-

PPV = positive predictive value; NPV = negative predictive value; +LR = positive likelihood ratio; -LR = negative likelihood ratio

Diagnostic Performance of QFR and QCA (Offline Analysis)

	QFR ≤ 0.8	Diameter Stenosis by QCA ≥ 50%	Difference 95% (CI)	p Value
Accuracy, %	93.3 (90.0, 95.7)	64.0 (58.6, 69.2)	29.9 (23.2, 36.7)	<0.001
Sensitivity, %	94.1 (88.3, 97.6)	49.6 (41.1, 59.7)	44.4 (33.0, 55.7)	<0.001
Specificity, %	92.8 (88.4, 95.9)	72.2 (65.7, 78.2)	21.3 (13.2, 29.4)	<0.001
PPV, %	88.2 (81.3, 93.2)	50.4 (41.0, 59.8)	37.0 (25.4, 48.6)	<0.001
NPV, %	96.5 (93.0, 98.6)	71.6 (65.0, 77.5)	26.8 (18.5, 35.0)	<0.001
+ LR	13.1 (8.04, 21.0)	1.81 (1.36, 2.40)	-	-
- LR	0.06 (0.03, 0.13)	0.69 (0.57, 0.84)	-	-

PPV = positive predictive value; NPV = negative predictive value; +LR = positive likelihood ratio; -LR = negative likelihood ratio

Limitations

- Not all the vessels were interrogated for the enrolled patients: the vessels with diameter stenosis below 30% or above 90% were not assessed as performing physiological assessment in such lesions was left unnecessary. Side branches of bifurcation lesions with medina type 1,1,1 or 1,0,1 were not assessed. Generalizability of QFR to the side branches of coronary bifurcation lesions still requires further investigation.
- Although the accuracy of QFR was high in the present study, there was still numerical difference between QFR and FFR. Nevertheless, for the subgroup with FFR between 0.75 and 0.85 where a small numerical difference between QFR and FFR can lead to clinical discordance, QFR still had high diagnostic accuracy.
- Additionally, there were 15.6% patients with previous myocardial infarction, which might have increased the possibility of inaccurate physiology measurements but also reflects a standard clinical population.
- As clinical decisions in the study population were based on FFR measurements, it was not possible to directly evaluate clinical outcome by a QFR based diagnostic strategy. Randomized trials comparing clinical outcomes after QFR based diagnostic strategies and standard diagnostic strategies are warranted.

Conclusions

- The FAVOR II China study met its prespecified primary performance goal for the level of diagnostic accuracy of QFR in identifying hemodynamically-significant coronary stenosis.
- It demonstrates clinical utility of QFR for use in diagnostic catheterization laboratories and QFR bears the potential of improving angiography-based identification of functionally-significant stenosis during coronary angiography.