Role of Quantitative Flow Ratio in Guiding PCI

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Disclosure

• I, (Bo Xu) DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
Background

• Wire-based physiological assessments are recommended in the Guidelines (IA, IIA)

• Physiological modalities should be appropriately selected in the entire revascularization processes to obtain optimal results, including choices of strategies (PCI or CABG), identification of treated vessels, and optimization during the procedure

• Computed coronary physiology indexes (e.g. quantitative flow ratio [QFR]) were currently well-validated against wire-based FFR as the reference standard; moreover, its simplicity, shorter assessment times, fewer complications, and lower costs may further promote the use of physiology-guided decisions in the catheterization laboratory

**Fractional flow reserve in clinical practice: from wire-based invasive measurement to image-based computation**

Shengxian Tu, Jelmer Westra, Julien Adjedj, Daixin Ding, Fuyou Liang, Bo Xu, Niels Ramsing Holm, Johan H.C. Reiber, and William Wijns

Quantitative Flow Ratio (QFR)

Standard Angiogram

Data Transmission System

Two image runs with angle difference $\geq 25^\circ$

AngioPlus System

3D Reconstruction

Modified Frame Count

QFR

Without Inducing Hyperemia

## Diagnostic Performance

### FAVOR II China

#### Agreement between QFR and FFR (Online Analysis)

![Mean difference: -0.01, SD: 0.063, p = 0.006](image)

#### Diagnostic Performance of QFR and QCA (Online Analysis)

<table>
<thead>
<tr>
<th></th>
<th>QFR ≤ 0.80</th>
<th>Diameter Stenosis by QCA ≥ 50%</th>
<th>Difference (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy, %</td>
<td>92.7 (89.3, 95.3)</td>
<td>59.6 (54.1, 65.0)</td>
<td>34.9 (28.3, 41.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>94.6 (88.7, 98.0)</td>
<td>62.5 (52.9, 71.5)</td>
<td>32.0 (21.0, 43.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>91.7 (87.1, 95.0)</td>
<td>58.1 (51.2, 64.8)</td>
<td>36.1 (27.9, 44.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PPV, %</td>
<td>85.5 (78.0, 91.2)</td>
<td>43.8 (35.9, 51.8)</td>
<td>42.0 (31.4, 52.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NPV, %</td>
<td>97.1 (93.7, 98.9)</td>
<td>74.9 (67.6, 81.2)</td>
<td>24.4 (15.6, 33.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>+ LR</td>
<td>11.4 (7.1, 17.0)</td>
<td>1.49 (1.21, 1.85)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- LR</td>
<td>0.06 (0.03, 0.13)</td>
<td>0.65 (0.50, 0.84)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Pre-PCI Assessment
QFR-based Functional SYNTAX Score ($\text{FSS}_{\text{QFR}}$)

- $\text{FSS}_{\text{QFR}}$ was calculated by summing the individual scores only in vessels with low vessel QFR ($\text{QFR} \leq 0.80$) and ignoring lesions with vessel QFR $>0.80$

- $\text{FSS}_{\text{QFR}}$-based Risk Stratification

- $\text{FSS}_{\text{QFR}}$-based Strategy Selection

Asano T, et al. *JACC Cardiovasc Interv* 2019
FSS\textsubscript{QFR}-based Risk Stratification

• After calculating the FSS\textsubscript{QFR}, 16% of study patients moved from higher-risk group (by SS) to lower-risk group

• FSS\textsubscript{QFR} appropriately reclassified patients from higher-risk groups to lower-risk groups, while better discriminating risk for MACE than SS

FSS_{QFR}-based Strategy Selection

- 6% of patients, for whom CABG would be recommended by SS converted to a lower-risk group and therefore another treatment option may be preferred.

- Compared with SS, FSS_{QFR} increased the risk of adverse events in “Favor CABG” group but not in “Favor PCI” group.

Procedural Guidance
QFR-based Precise PCI

- **QFR-based precise-treatment (PT):** patients in whom all physiologically significant ischemic vessels were treated by PCI and in whom all vessels with QFR >0.80 were deferred; otherwise, they were termed to have had **QFR-based imprecise-treatment (IPT)**

- The imprecise-treatment (IPT) group was further stratified into 3 subgroups: 1) **under-treatment (UT);** 2) **over-treatment (OT);** and 3) **over- and under-treatment (OUT)**

814 (58.5%) patients had QFR-based precise-treatment
577 (41.5%) patients had QFR-based imprecise-treatment

PANDA III trial (N=2,348)
An “all-comers”, angiography-based PCI cohort

1,391 patients achieved patient-level QFR assessment

814 (58.5%) patients had QFR-based precise-treatment
577 (41.5%) patients had QFR-based imprecise-treatment

Zhang R, et al. Submitted
QFR-based Precise PCI

- The achievement of QFR-based precise PCI was associated with improved 2-year clinical outcomes, both in unadjusted and IPTW analysis.

Zhang R, et al. Submitted
QFR-based Precise PCI

PT vs. UT Propensity 1:1 Matching (N=482)

- **PT** vs. **UT**
  - 2-year cumulative incidence:
    - MACE: 9.2% vs. 16.4%
    - All-cause death: 2.1% vs. 2.6%
    - All MI: 5.0% vs. 5.8%
    - ID Rev: 3.8% vs. 10.5%

  - **P** values:
    - MACE: **p = 0.02**
    - All-cause death: **p = 0.77**
    - All MI: **p = 0.68**
    - ID Rev: **p = 0.006**

  - Rationale between Treated and Untreated Vessels
    - Vessels with QFR ≤0.80 (N_v=1,932)
      - Treated (N_v=1,471): 8.59 ± 5.82, 51.0%, 2.65 ± 0.46, 75.4%
      - Untreated (N_v=461): 6.94 ± 5.55, 38.8%, 2.40 ± 0.51, 69.1%
      - **P** value: treatment, QFR, RVD, DS%
    - Vessels with QFR >0.80 (N_v=611)
      - Treated (N_v=246): 4.61 ± 3.37, 34.6%, 2.67 ± 0.53, 50.6%
      - Untreated (N_v=365): 3.37 ± 2.42, 24.1%, 2.37 ± 0.58, 51.5%
      - **P** value: treatment, QFR, RVD, DS%

PT vs. OT Propensity 1:1 Matching (N=286)

- **PT** vs. **OT**
  - 2-year cumulative incidence:
    - MACE: 6.3% vs. 9.8%
    - All-cause death: 0.7% vs. 3.5%
    - All MI: 3.5% vs. 2.8%
    - ID Rev: 2.1% vs. 5.6%

  - **P** values:
    - MACE: **p = 0.29**
    - All-cause death: **p = 0.14**
    - All MI: **p = 0.75**
    - ID Rev: **p = 0.14**

- Uses of Interventional Devices (PT vs. OT)
  - **Unweighted Sample**
    - PT (N=814): 1.18 ± 0.44, 1.57 ± 0.85, 2.05 ± 1.34
    - OT (N=205): 1.36 ± 0.54, 1.63 ± 0.91, 2.11 ± 1.52
    - **P** value: treatment, QFR, RVD, DS%
  - **Propensity 1:1 Matching**
    - PT (N=143): 1.12 ± 0.35, 1.52 ± 0.72, 2.02 ± 1.13
    - OT (N=143): 1.45 ± 0.58, 1.75 ± 0.99, 2.37 ± 1.47
    - **P** value: treatment, QFR, RVD, DS%
Procedural Guidance
Intermediate Coronary Lesion

- Retrospective QFR assessment was available in 820 patients (996 intermediate de novo coronary vessels)

- It appears **safe to defer** treatment of vessels with **functional insignificant intermediate lesion** at baseline angiography (baseline QFR>0.80) during long-term follow-up

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### Intermediated lesions

<table>
<thead>
<tr>
<th>QFR</th>
<th>Baseline QFR &gt;0.80</th>
<th>Baseline QFR ≤0.80</th>
</tr>
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<tbody>
<tr>
<td>0.5</td>
<td>1.0</td>
<td>0.5</td>
</tr>
<tr>
<td>0.6</td>
<td>0.8</td>
<td>0.6</td>
</tr>
<tr>
<td>0.7</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>0.8</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>0.9</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

- **Deferred and routine angiographic follow-up highly recommended**
- **PCI treatment recommended**

### Log-rank p < 0.0001

- Baseline QFR >0.80
- Baseline QFR ≤0.80

<table>
<thead>
<tr>
<th>Time since Index Procedure (Years)</th>
<th>VOCE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
</tr>
<tr>
<td>5</td>
<td>50</td>
</tr>
</tbody>
</table>

- 28.3%
- 17.0%

Guan C, et al. Submitted
Procedural Guidance
Intermediate Coronary Lesion

✓ ΔQFR, [baseline QFR – follow-up QFR] / years

- A useful tool to annually evaluate dynamic functional change of deferred intermediate lesions, which demonstrated having good prognostic value
Post-PCI Assessment
Prognostic Value of Post-PCI QFR

✓ Post-PCI QFR value was strongly associated with long-term prognosis

- **HAWKEYE study**: vessels with post-PCI QFR $\leq 0.89$ were associated with a higher risk of VOCE
- **SYNTAX II substudy**: vessels with post-PCI QFR $< 0.91$ were more likely to suffer VOCE

Prognostic Value of Post-PCI QFR

✓ Our data further confirmed this finding

• A total of **1,503 vessels** in the PANDA III trial were retrospectively analyzed for post-PCI QFR

• The AUC was **0.70 (p<0.001)** for post-PCI QFR to predict 2-year VOCE, and the best cutoff value was **0.92 (≤0.92)**

![ROC curve and sensitivity/specificity plots](image)

Zhang R, et al. Submitted
Pre-PCI Simulation
Simulated Residual QFR

- **Simulated residual QFR**: corresponds to the QFR value if a specified segment of the assessed vessel is successfully dilated, which is essentially predictive of actually post-PCI QFR.

- By advancing the time point of post-procedural functional assessment, this would help physicians to **develop the best strategies while planning the procedure**.

Zhang R, et al. Submitted

Residual QFR: obtained by simulating stenting in this zone

- Residual QFR = 0.95

Post-PCI QFR: actually measured after procedure

- Post-PCI QFR = 0.95
Concordance between QFRs

- **1,033 vessels** with paired simulated residual QFR and post-PCI QFR
- Good correlation and agreement were observed

**A**
Mean difference: 0.003, SD: 0.02

**B**
r = 0.945, p<0.001

**C**
Post-PCI QFR (0.959 ± 0.071)
Simulated residual QFR (0.962 ± 0.071)
Two-sample Kolmogorov-Smirnov test p=0.20

Zhang R, et al. Submitted
Prognostic Value of Simulated Residual QFR

- A total of **1,782 vessels** with available simulated residual QFR were included.
- Vessels with suboptimal residual QFR (≤0.92) suffered worse 2-year VOCE (**16.2%** vs. **4.3%**; HR 3.87 [95% CI: 2.67-5.62], p<0.001)

Zhang R, et al. Submitted

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![Graph showing ROC curve and cumulative incidence](image)

- **AUC (95% CI)**: 0.68 (0.62, 0.74)  
  **P-value**: <0.001

- **Cumulative Incidence**:
  - VOCE: 16.2%
  - Vessel-related cardiac death: 4.3%
  - Vessel-related MI: 9.5%
  - ID-TVR: 6.8%
  - **All P value <0.05**
FAVOR III China

Investigator-initiated, Multicenter, Subjects and Clinical Assessors Blinded, Randomized, Superiority Trial

Patients with CAD scheduled for coronary angiography

Meet all general inclusion and exclusion criteria
Inclusions: age ≥ 18 years; stable, unstable angina, or post-AMI (≥72 hours). Exclusions: cardiogenic shock or severe heart failure (NYHA ≥ III).

Written informed consent

Coronary angiography

Meet all angiographic inclusion and exclusion criteria
Inclusions: patients must have at least one lesion with DS% of 50%-90% in an artery with visually estimated RVD ≥ 2.5 mm and be eligible for PCI as determined by investigators. Exclusions: patients had only one lesion with DS%>90% and TIMI grade <3; interrogated lesions are related with AMI.

Identify the vessels intended to treat

1:1 Randomization

QFR-guided strategy
N=1,915

- QFR ≤0.80: PCI
- QFR >0.80: deferral
- All measured vessel QFR >0.8: OMT alone

Angiography-guided strategy
N=1,915

PCI is performed on all the vessels intended to treat identified prior to randomization, based on visual assessment of the angiogram

Randomization Stratifications
- Center
- Diabetes
- SVD vs. MVD
- DS% > 90% and TIMI Flow <3

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

ClinicalTrial.gov Identifier: NCT03656848

Primary endpoint: 1-year MACE, defined as the composite of all-cause death, MI, or any ischemia-driven revascularization

Major Secondary Endpoint: 1-year MACE excluding peri-procedural MI; Other Important Outcome: Cost-effectiveness

N=1,915

Imaging core lab analysis; Clinical follow-up at 1 month, 6 months,1 year, 2 years, and 3 years; EQ-5D questionnaires collected at 1, 6, and 12 months
FAVOR III China in Perspective

- As the world's largest randomized controlled clinical trial of coronary physiological guidance for revascularization, FAVOR III China aims to effectively identify the ischemic lesions that have real intervention value and can improve the long-term prognosis of patients, so as to formulate reasonable treatment strategies.

- The study aims to answer the following questions:

  1. In the era of contemporary DES, is a QFR-guided strategy better than a conservative angiography-guided PCI strategy and, if so, to what extent and why? QFR guidance may avoid unnecessary stent implantation, reducing procedural related complications and long-term adverse events. Conversely, QFR assessment may also identify angiographic borderline lesions that are functionally significant and require treatment.

  2. Will the 3D-QCA measurement be useful to achieve more appropriate device sizing than standard angiography?

  3. Will the QFR-guided strategy prove cost-effective?

Song L, et al. *Am Heart J* 2020