Cost-effectiveness of angiographic quantitative flow ratio-guided coronary intervention: A multicenter, randomized, sham-controlled trial

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Abstract

Background: The FAVOR (Comparison of Quantitative Flow Ratio Guided and Angiography Guided Percutaneous Intervention in Patients with Coronary Artery Disease) III China trial demonstrated that percutaneous coronary intervention (PCI) lesion selection using quantitative flow ratio (QFR) measurement, a novel angiography-based approach for estimating fractional flow reserve, improved two-year clinical outcomes compared with standard angiography guidance. This study aimed to assess the cost-effectiveness of QFR-guided PCI from the perspective of the current Chinese healthcare system.

Methods: This study is a pre-specified analysis of the FAVOR III China trial, which included 3825 patients randomized between December 25, 2018, and January 19, 2020, from 26 centers in China. Patients with stable or unstable angina pectoris or those ≥72 hours post-myocardial infarction who had at least one lesion with a diameter stenosis between 50% and 90% in a coronary artery with a ≥2.5 mm reference vessel diameter by visual assessment were randomized to a QFR-guided strategy or an angiography-guided strategy with 1:1 ratio. During the two-year follow-up, data were collected on clinical outcomes, quality-adjusted life-years (QALYs), estimated costs of index procedure hospitalization, outpatient cardiovascular medication use, and rehospitalization due to major adverse cardiac and cerebrovascular events (MACCE). The primary analysis calculated the incremental cost-effectiveness ratio (ICER) as the cost per MACCE avoided. An ICER of ¥10,000/MACCE event avoided was considered economically attractive in China.

Results: At two years, the QFR-guided group demonstrated a reduced rate of MACCE compared to the angiography-guided group (10.8% *vs.* 14.7%, P <0.01). Total two-year costs were similar between the groups (¥50,803 ± 21,121 *vs.* ¥50,685 ± 23,495, P = 0.87). The ICER for the QFR-guided strategy was ¥3055 per MACCE avoided, and the probability of QFR being economically attractive was 64% at a willingness-to-pay threshold of ¥10,000/MACCE avoided. Sensitivity analysis showed that QFR-guided

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PCI would become cost-saving if the cost of QFR were below ¥3682 (current cost: ¥3800). Cost-utility analysis yielded an ICER of ¥56,163 per QALY gained, with a 53% probability of being cost-effective at a willingness-to-pay threshold of ¥85,000 per QALY gained.
Conclusion: In patients undergoing PCI, a QFR-guided strategy appears economically attractive compared to angiographic guidance from the perspective of the Chinese healthcare system.
Trial Registration: ClinicalTrials.gov, NCT03656848.
Keywords: Quantitative flow ratio; Coronary artery disease; Percutaneous coronary intervention; Major adverse cardiac and cerebrovascular events; Quality-adjusted life-years; Incremental cost-effectiveness ratio; European Quality of Life-5 Dimensions

Introduction

Ischemic heart disease remains a significant global healthcare burden and is currently one of the leading causes of death.[1] Despite the established benefits of pressure wire-based physiology-guided percutaneous coronary intervention (PCI) over angiographic guidance,[2–7] the use of fractional flow reserve (FFR) or instantaneous wave-free ratio in the catheterization laboratory remains lower than expected. This is largely due to the additional procedural time and effort required, as well as economic considerations.[8–10] Quantitative flow ratio (QFR), a novel angiography-based diagnostic technique, has been shown to correlate with pressure wire-based FFR measurements. As a simple-to-implement technique with several advantages over wire-based physiology (including no risk of coronary injury, less discomfort from coronary vasodilators, and shorter procedure time), the application of QFR may increase the routine use of physiological assessment in clinical practice.[11–13]

The clinical benefits of using QFR to guide PCI were demonstrated in the FAVOR (Comparison of Quantitative Flow Ratio Guided and Angiography Guided Percutaneous Intervention in Patients with Coronary Artery Disease) III China trial, an investigator-initiated, prospective, multicenter, randomized, sham-controlled study comparing a QFR-guided strategy with the standard angiography-guided strategy in patients undergoing PCI.[14] At one year, the QFR-guided vessel and lesion selection strategy was found to be superior to the angiography-guided strategy in terms of the primary endpoint of major adverse cardiac events,[15] and the benefits of QFR-guided PCI were sustained up to two years.[16] The present study aims to investigate the economic and health-related quality-of-life outcomes of the FAVOR III China trial from the perspective of the reformed Chinese healthcare system, providing additional evidence to inform both disease management and economic policy. To enhance the generalizability of the results to other countries, we also performed a sensitivity analysis using cost data from a European healthcare system.

Methods

Ethical approval

The FAVOR III China trial was conducted in accordance with the *Declaration of Helsinki* and the Good Clinical Practice guidelines of the China National Medical Products Administration. The study protocol was approved by the ethics committee at each participating site which is provided in Supplementary Materials, http://links.lww.com/CM9/C400, and all enrolled patients provided written informed consent.

Patient population and study design

The design of the FAVOR III China trial has been described previously and is registered at ClinicalTrials.gov (NCT03656848).[14–16] Patients with stable or unstable angina, or acute myocardial infarction (MI) occurring at least 72 hours before screening, and who had at least one lesion with a diameter stenosis of 50–90% in a coronary artery with a reference vessel of at least 2.5 mm diameter by visual assessment, were randomly assigned to either a QFR-guided strategy or an angiography-guided strategy. Patients were randomly assigned with 1:1 ratio. The randomization process was performed by using Internet Web Response System. The full study dataset, including baseline clinical, angiographic, and procedural characteristics, was prospectively collected into a web-based electronic data capture system. Furthermore, the target vessels intended for PCI, based on angiographic guidance alone, were declared by the operator and recorded prior to randomization. This allowed for the adjudication of patients with or without strategy changes post-procedure. Patients randomized to the QFR-guided strategy underwent QFR measurement in all eligible vessels, and PCI treatment was performed in lesions with QFR ≤0.80, while lesions with QFR >0.80 were deferred. In the angiography-guided group, PCI was performed based on visual angiographic assessment according to local standard practices. The inclusion and exclusion criteria, as well as management strategies, are detailed in Supplementary Table 1, http://links.lww.com/CM9/C311.

Economic analysis plan

The economic analysis of the FAVOR III China trial was pre-specified and conducted based on the intention-to-treat population. The analysis aimed to compare the costs of each strategy group over a two-year follow-up period and to perform an incremental cost-effectiveness analysis if the more effective strategy was also more costly. Costs were not discounted due to the limited follow-up period. All costs were assessed from the perspective of the Chinese healthcare system.

Costs

Direct costs for each strategy included those of (1) the index procedure and associated hospitalization, (2) two-year outpatient cardiovascular medication use, and (3) rehospitalization(s) due to adverse cardiovascular event(s) within the two-year follow-up period. All costs were assessed in 2023 Chinese Yuan (CNY). According to the original study protocol, detailed costs during the index

procedure were prospectively recorded. However, shortly after the completion of study enrollment, the cost of coronary stents was markedly reduced due to the reform of the healthcare purchasing system in China, which took effect in 2021. To focus this analysis on current and future practice, the costs of the index hospitalization were re-estimated based on contemporary acquisition costs in China. The average costs of the procedure and devices are listed in Supplementary Table 2, http://links.lww.com/CM9/C311. These costs included total payments from both insurance and patients. The QFR measurements were free of charge during the sham-controlled trial; for the economic evaluation, an examination fee of ¥3800 was added to the individual patient's costs for the index procedure in the QFR-guided arm, based on the current price of QFR measurements in China. This value was varied in sensitivity analyses.

Rehospitalization costs for adverse events were calculated based on the average hospitalization costs for each type of adverse event, including non-procedural MI, any revascularization, stent thrombosis, cerebrovascular events, and major bleeding. These costs included payments from both insurance and patients, as estimated by each participating site during the same period. Given the variation in these costs across different centers, the costs were assigned to each event based on their cost at the original treating center [Supplementary Table 3, http://links.lww.com/CM9/C311]. The estimation of medication costs was calculated by multiplying the duration (in weeks) of drug use by the price weights in China for 2020, which have not changed substantially since then [Supplementary Table 4, http://links.lww.com/CM9/C311].

Clinical outcomes

The primary endpoint of the economic analysis of the FAVOR III China trial was major adverse cardiac and cerebrovascular events (MACCE), which included any revascularization, all MI, stent thrombosis (according to the Academic Research Consortium [ARC] definition), cerebrovascular events,[17] and major bleeding (defined as Bleeding Academic Research Consortium type ≥3 bleeding).[18]

Quality-adjusted life years (QALYs)

The European Quality of Life-5 Dimensions (EQ-5D) health survey was administered at baseline, hospital discharge, 1 month, 6 months, 1 year, and 2 years to assess the health status of each patient. The EQ-5D results are reported for both the visual analog scale (range 0–100) and utilities (range 0–1, where 0 represents death and 1 represents perfect health). For the utility measure, individual item responses were converted into health utility weights using the Japanese population time trade-off conversion formula.[19] A sensitivity analysis was performed to explore the impact of variation in the cost of the QFR examination and to re-estimate QALYs using the utility algorithms developed for the British and American populations.

For each patient, QALYs were calculated as the time-weighted average of the individual utility weights assigned during the index hospitalization and follow-up. Missing utility data were imputed using a linear regression model that included baseline characteristics and time-dependent MACCE. The baseline variables included age, sex, diabetes, acute coronary syndrome, postoperative residual stenosis, the anatomic Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score, and left ventricular ejection fraction.

Cost-effectiveness/utility

To align with the clinical protocol, the pre-specified primary endpoint for the cost-effectiveness analysis was the incremental cost-effectiveness ratio (ICER), calculated as the cost per MACCE event avoided. Additionally, we performed a cost-utility analysis in which the ICER was assessed in terms of cost per QALY gained. Beyond calculating the point estimate for these quantities, we also computed the confidence intervals (CIs) for differences in costs, event rates, and QALYs, along with the distribution of the resulting ICERs, using bootstrap resampling of the trial data (1000 replicates).

In the US, a "disease-specific" ICER of $10,000 per event avoided is generally considered reasonably cost-effective,[20–23] which is roughly equivalent to ¥17,000 per event avoided in China after adjusting for per capita gross domestic product (GDP). Therefore, we made the conservative assumption that an ICER of ¥10,000 per MACCE event avoided would be economically attractive in China. When cost-effectiveness was assessed in terms of cost per QALY gained, a threshold of ¥85,000 per QALY, approximately equivalent to the per capita GDP in China in 2022, was considered to represent high economic value, based on current World Health Organization (WHO) guidelines.[24]

Sensitivity and subgroup analyses

In order to provide in-depth analyses, we performed a sensitivity analysis using costs associated with rehospitalization due to major adverse cardiac events (MACE, a composite of death, MI, or ischemia-driven revascularization), the primary endpoint of the FAVOR III China trial. We also performed analyses in the following pre-specified subgroups: age (<65 years *vs.* ≥65 years), sex, diabetic status, acute coronary syndrome presentation, single vessel *vs.* multi-vessel disease, severe disease (one or more lesions with diameter stenosis >90% and thrombolysis in myocardial infarction [TIMI] flow <3), SYNTAX score (≤8 *vs.* >8), diameter stenosis (<70% *vs.* ≥70%), bifurcation, lesion location, and lesion length (<20 mm *vs.* ≥20 mm). Finally, to provide mechanistic insight into our findings, we examined economic outcomes in patients with or without strategy changes after QFR guidance.

Statistical analysis

The sample size calculation was based on the primary FAVOR III China study.[14,15] Categorical data are presented as counts and percentages, while continuous data are

presented as means ± standard deviation. Categorical data were compared between the two groups using the likelihood ratio chi-squared test or Fisher's exact test, as appropriate. Continuous variables with a normal distribution were compared using two-sample *t*-tests, while non-normally distributed continuous data were analyzed using the Wilcoxon rank-sum test. Consistent with current recommendations for economic evaluation, cost data are reported as means ± standard deviation and were compared using normal approximation. Clinical event rates and between-group differences were calculated using the Kaplan–Meier survival method. All statistical analyses were performed at a two-sided significance level of 0.05 using SAS software, version 9.4 (SAS Institute, Cary, NC, USA).

Results

A total of 3847 patients were randomized to either the QFR-guided or angiography-guided group between December 25, 2018, and January 19, 2020. Among them, 22 patients withdrew consent and refused to allow the use of any data. The remaining 3825 patients in the intention-to-treat population were included in this analysis [Figure 1]. Baseline characteristics were balanced between the two study groups [Table 1]. Compared with angiographic guidance, QFR guidance led to the use of fewer stents (1.45 ± 1.02 *vs*. 1.58 ± 0.97, P <0.01), less contrast (163.0 ± 75.6 mL *vs*. 169.7 ± 74.2 mL, P <0.01), and shorter procedural times (53.7 ± 30.4 min *vs*. 59.4 ± 30.4 min, P <0.01) [Supplementary Table 5, http://links.lww.com/CM9/C311].

At two years, MACCE occurred in 205 (10.8%) patients in the QFR-guided group and in 278 (14.7%) in the angiography-guided group (P <0.01), driven mainly by differences in non-procedural MI and revascularization procedures. There were no significant differences between the groups in terms of stent thrombosis, cerebrovascular events, or major bleeding events [Table 2].

Costs for the initial procedure and hospitalization are summarized in Supplementary Table 6, http://links.lww.com/CM9/C311. Mean procedural costs excluding QFR, were significantly lower in the QFR-guided group (¥17,836 ± 6715 *vs*. ¥19,113 ± 6051, P <0.01), primarily driven by fewer PCI procedures performed and lower utilization of guidewires, guiding catheters, and other consumables. After including the cost of the QFR examination (¥3800), procedural costs were significantly higher in the QFR-guided group (¥21,636 ± 6715 *vs*. ¥19,113 ± 6051, P <0.01). On the other hand, costs for the hospital stay were lower in the QFR-guided group (¥11,085 ± 12,965 *vs*. ¥11,952 ± 12,764, P = 0.04), driven mainly by a lower rate of peri-procedural MI in the QFR-guided group. When combined with procedural costs, total index hospitalization costs were significantly higher in the QFR-guided group compared with the angiography-guided group (¥32,721 ± 15,363 *vs*. ¥31,065 ± 14,919, P <0.01).

Costs over the two-year follow-up period are summarized in Table 3. Costs for rehospitalization due to MACCE were significantly lower in the QFR-guided group (¥3306 ± 13,055 *vs*. ¥4668 ± 16,272, P <0.01), driven mainly by lower costs related to non-procedural MI and ischemia-driven revascularization. Costs for outpatient medications were similar between the two groups (¥14,777 ± 4799 *vs*. ¥14,952 ± 4650, P = 0.25), the details of medication costs are provided in Supplementary Table 7, http://links.lww.com/CM9/C311. As a result, total two-year costs were similar between the groups (¥50,803 ± 21,121 *vs*. ¥50,685 ± 23,495, P = 0.87) [Figure 2]. The median costs were ¥46,117 (Q1: ¥38,554; Q3: ¥56,275) for the QFR-guided group and ¥44,456 (Q1: ¥36,484; Q3: ¥55,907) for the angiography-guided group. When performing sensitivity analysis using two-year MACE, total costs remained similar (¥49,600 ± 19,536 *vs*. ¥49,535 ± 22,303, P = 0.92).

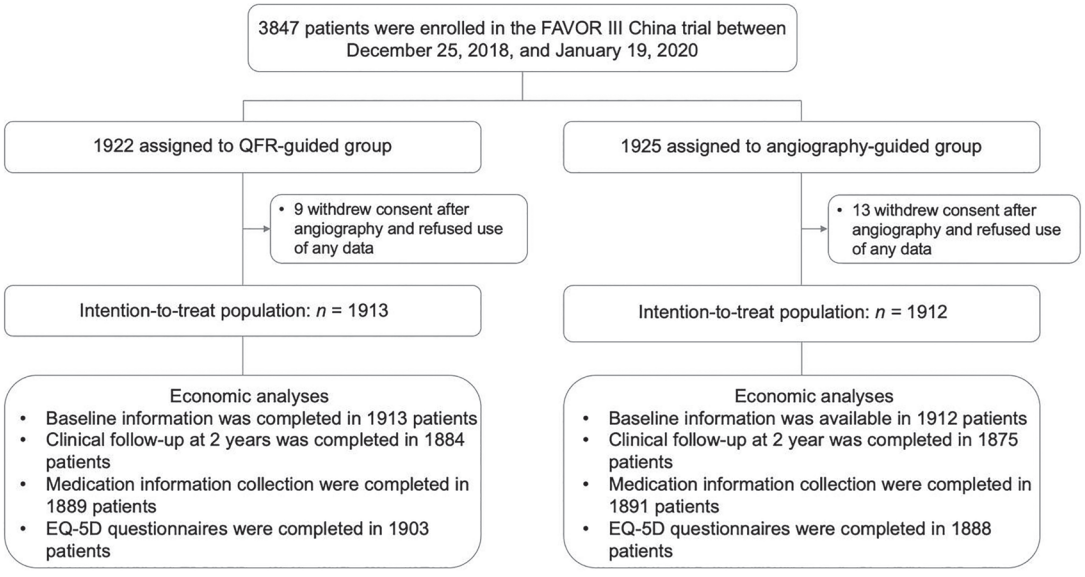

Figure 1: Study profile of economic analyses in the FAVOR III China trial. EQ-5D: European Quality of Life-5 Dimensions; FAVOR: Comparison of Quantitative Flow Ratio Guided and Angiography Guided Percutaneous Intervention in Patients with Coronary Artery Disease; QFR: Quantitative flow ratio.

Table 1: Baseline characteristics of the participants in the FAVOR III China trial.

Variables	QFR-guided group ($n = 1913$)	Angiography-guided group ($n = 1912$)	Statistical values	*P*-value
Age (years)	62.7 ± 10.1	62.7 ± 10.2	0.25*	0.81
Male	1349 (70.5)	1350 (70.6)	<0.01†	0.95
Diabetes mellitus	648 (33.9)	647 (33.8)	<0.01†	0.98
Hypertension	1270 (66.4)	1252 (65.5)	0.35†	0.55
Hypercholesterolemia	729 (38.1)	728 (38.1)	<0.01†	0.98
Tobacco use	574 (30.0)	568 (29.7)	0.04†	0.84
Previous MI	179 (9.4)	179 (9.4)	<0.01†	1.00
Previous PCI	485 (25.4)	466 (24.4)	0.49†	0.48
Unstable angina	1111 (58.1)	1110 (58.1)	<0.01†	0.99
Post MI (within 30 days)	102 (5.3)	105 (5.5)	0.05†	0.83
Left ventricular ejection fraction (%)	63.1 ± 6.6	62.8 ± 6.9	1.38*	0.17
Angiographic characteristics				
Multivessel disease (%)	1032 (53.9)	1043 (54.6)	0.44†	0.71
Anatomic SYNTAX score	9.3 ± 6.0	9.6 ± 6.3	–1.19*	0.23
Functional SYNTAX score	8.1 ± 6.3	8.0 ± 6.6	0.22*	0.83
Any vessel with one or more lesions with diameter stenosis >90% and TIMI flow <3	170 (8.9)	182 (9.5)	0.46†	0.50
Offline QFR value	0.72 ± 0.15	0.72 ± 0.15	–0.13*	0.90

Data are shown as *n* (%) or mean ± SD. *t values in student's t test; †χ^2 values in chi-squared test. FAVOR: Comparison of Quantitative Flow Ratio Guided and Angiography Guided Percutaneous Intervention in Patients with Coronary Artery Disease; MI: Myocardial infarction; PCI: Percutaneous coronary intervention; QFR: Quantitative flow ratio; SD: Standard deviation; SYNTAX: Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery; TIMI: Thrombolysis in myocardial infarction.

Table 2: Cumulative events during two-year follow-up of two groups in the FAVOR III China trial.

Variables	QFR-guided group ($n = 1913$)	Angiography-guided group ($n = 1912$)	Difference (95% CI)	χ^2 values	*P*-value
MACCE*	205 (10.8)	278 (14.7)	–3.9 (–6.0 to –1.7)	12.75	<0.01
MI	76 (4.0)	130 (6.8)	–2.9 (–4.3 to –1.4)	14.88	<0.01
Any revascularization	108 (5.7)	138 (7.3)	–1.6 (–3.2 to –0.02)	4.06	0.05
Definite or probable stent thrombosis	6 (0.3)	10 (0.5)	–0.2 (–0.6 to 0.2)	1.01	0.32
Cerebrovascular events	22 (1.2)	16 (0.9)	0.3 (–0.3 to 1.0)	0.95	0.33
Major bleeding	27 (1.4)	23 (1.2)	0.2 (–0.5 to 0.9)	0.32	0.57

Data are shown as *n* (Kaplan–Meier estimated %) and compared by log-rank test. ARC: Academic Research Consortium; BARC: Bleeding Academic Research Consortium; CI: Confidence interval; FAVOR: Comparison of Quantitative Flow Ratio Guided and Angiography Guided Percutaneous Intervention in Patients with Coronary Artery Disease; MI: Myocardial infarction; QFR: Quantitative flow ratio. *MACCE defined as the composite of any revascularization, all MI, stent thrombosis according to ARC definition, cerebrovascular events, and major bleeding (BARC type ≥3 bleeding).

At two years, EQ-5D questionnaires were completed in 1903 (99.5%) patients in the QFR-guided group and 1888 (98.7%) patients in the angiography-guided group [Figure 1]. Utility weights, as assessed based on the EQ-5D, are summarized in Table 4. In both groups, utilities improved after the catheterization procedure and remained stable through the two-year follow-up. There were no significant differences in utilities at any time point. As a result, mean QALYs at the two-year follow-up were also similar between groups (1.93 *vs.* 1.93 QALYs, $P = 0.70$). Results were similar when using British (1.94 *vs.* 1.94, $P = 0.69$) or American (1.92 *vs.* 1.92, $P = 0.67$) utility weights.

The point estimate for the ICER of the QFR-guided PCI strategy was ¥3055 per MACCE avoided. The probability that the QFR-guided PCI strategy would provide high economic value (defined as ICER <¥10,000 per MACCE avoided) was 63.7% [Supplementary Figure 1, http://links.lww.com/CM9/C311]. In our secondary cost-utility analysis, the ICER for QFR was 56,163 per QALY gained, and the probability that QFR would be cost-effective at a threshold of ¥85,000 per QALY was 53.3% [Supplementary Figure 2, http://links.lww.com/CM9/C311].

Additionally, the sensitivity analysis showed a more conservative estimate, with an ICER of ¥1606 per MACE avoided. Sensitivity analysis according to various QFR costs demonstrated that the ICER remained reasonably favorable (at a willingness-to-pay threshold of ¥10,000/MACCE avoided) as long as the QFR cost was less than ¥4072 (a 7% increase from the current cost), but would be unfavorable if the cost was the same as for wire-based FFR (¥9400). QFR guidance was projected to be cost-saving if the cost of QFR was lower than ¥3682 [Supplementary Figure 3, http://links.lww.com/CM9/C311].

Table 3: Costs during two-year follow-up of two groups in the FAVOR III China trial (¥).

Variables	QFR-guided group (n = 1913)	Angiography-guided group (n = 1912)	Difference (95% CI)	Statistic values	P-value
Costs during follow-up					
Medications	14,777 ± 4799	14,952 ± 4650	–175 (–475 to 124)	–1.15	0.25
MACCE-related costs	3306 ± 13,055	4668 ± 16,272	–1362 (–2298 to –427.1)	–2.86	<0.01
Non-procedural MI	252 ± 3108	737 ± 5590	–485 (–772 to –199)	–3.32	<0.01
Ischemia-driven revascularization	2000 ± 10,217	3155 ± 14,201	–1154 (–1939 to –370)	–2.89	<0.01
Non-ischemia-driven revascularization	817 ± 6505	793 ± 6549	24 (–390 to 438)	0.12	0.91
Cerebrovascular events	259 ± 2604	238 ± 2763	21 (–149 to 191)	0.24	0.81
Major bleeding	234 ± 2157	216 ± 2151	18 (–119 to 154)	0.26	0.80
Total two-year costs including index hospitalization, QFR examination, medication used, and management for MACCE during follow-up	50,803 ± 21,121	50,685 ± 23,495	118 (–1298 to 1534)	0.16	0.87
Total two-year costs including index hospitalization, QFR examination, medication used, and management for MACE during follow-up	49,600 ± 19,536	49,535 ± 22,303	64.5 (–1265 to 1394)	0.10	0.92

All costs are stated per person, in Chinese Yuan. CI: Confidence interval; FAVOR: Comparison of Quantitative Flow Ratio Guided and Angiography Guided Percutaneous Intervention in Patients with Coronary Artery Disease; MACCE: Major adverse cardiac and cerebrovascular events; MI: Myocardial infarction; QFR: Quantitative flow ratio.

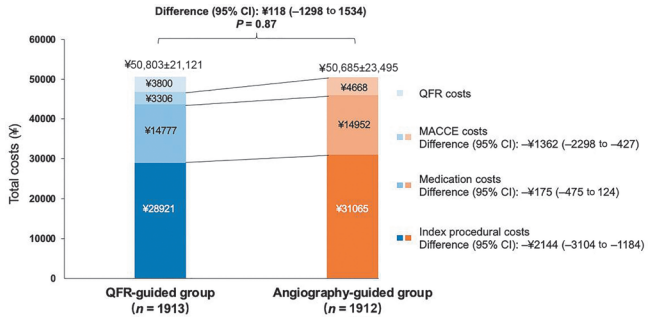

Figure 2: Total costs of FAVOR III China trial between two groups in the FAVOR III China Trial. Total costs for each strategy included those of the index hospitalization, costs for medication, and rehospitalization costs due to adverse events during two-year follow-up. MACCE defined as the composite of any revascularization, all MI, stent thrombosis according to ARC definition, cerebrovascular events, and major bleeding (BARC type ≥3 bleeding). ARC: Academic Research Consortium; BARC: Bleeding Academic Research Consortium; CI: Confidence interval; FAVOR: Comparison of Quantitative Flow Ratio Guided and Angiography Guided Percutaneous Intervention in Patients with Coronary Artery Disease; MACCE: Major adverse cardiac and cerebrovascular events; MI: Myocardial infarction; QFR: Quantitative flow ratio.

In the subgroup analysis, patients who were younger, female, with mild symptoms (asymptomatic ischemia or stable angina), and patients with less lesion complexity (i.e., no lesion with diameter stenosis >90% and TIMI flow <3, SYNTAX score ≤8, lesion length <20 mm, diameter stenosis <70%, non-bifurcation lesion, lesion located in the left circumflex or right coronary artery) had lower costs with QFR guidance, making QFR guidance an economically dominant strategy [Supplementary Table 8, http://links.lww.com/CM9/C311]. Nonetheless, QFR guidance was associated with improved clinical outcomes in the complementary subgroups such that the ICER remained acceptable (<¥10,000/MACCE avoided). Mechanistic analysis demonstrated that the two-year cost savings with QFR guidance were largely explained by large cost offsets in patients in whom PCI was deferred [Supplementary Table 9, http://links.lww.com/CM9/C311].

Discussion

This pre-specified analysis of the randomized FAVOR III China trial is a study to examine the economic and health-related quality-of-life outcomes associated with QFR guidance during PCI, compared with standard angiographic guidance, from the perspective of the Chinese healthcare system. As China is one of the largest middle-income countries, according to the World Bank's income classification, these findings may have important implications for similar countries globally.

The main findings of our study can be summarized as follows. First, while the QFR-guided PCI strategy resulted in a marginal increase in total two-year costs compared with standard angiographic guidance, this increase was not statistically significant. However, QFR guidance was associated with significantly lower rates of adverse events at two years, resulting in an ICER of ¥3055 per MACCE avoided—a value that likely represents high economic value based on a combination of previous studies from other healthcare systems and expert opinion. Second, despite the reduced use of PCI in the QFR group, there was no evidence of worse health outcomes at any follow-up time point, and total two-year QALYs were virtually identical between the two groups. These findings provide critical evidence supporting the greater adoption of angiography-based physiological assessment into routine clinical practice, given its superior clinical outcomes and minimal increase in cost compared with angiographic guidance alone.

During the index procedure, QFR guidance led to 8.6 fewer PCI procedures per 100 patients compared with angiography alone (90.5 *vs*. 99.1). This reduction in PCI procedures resulted in lower procedure-related resource utilization and costs in the QFR group. After discharge, the economic benefit of QFR was primarily driven by lower rates of non-procedural MI and ischemia-driven

Table 4: EQ-5D health scores and utility values through 2 years of the participants in the FAVOR III China trial.

Variables	Baseline	Discharge	Follow up times			
			1 month	6 months	1 year	2 years‡
EQ-5D health scores*						
QFR-guided group (n = 1913)	74.5 ± 12.9	84.4 ± 10.7	83.8 ± 10.2	85.5 ± 10.3	87.4 ± 11.7	86.4 ± 11.5
Angiography-guided group (n = 1912)	74.1 ± 13.3	84.5 ± 10.7	83.6 ± 10.0	85.4 ± 10.6	87.1 ± 11.5	86.1 ± 11.9
Difference (95% CI)	0.4 (–0.5 to 1.1)	–0.1 (–0.8 to 0.6)	0.2 (–0.4 to 0.8)	0.1 (–0.6 to 0.8)	0.2 (–0.5 to 1.0)	0.3 (–0.5 to 1.0)
P–value	0.47	0.77	0.53	0.78	0.52	0.44
EQ-5D utility values†						
QFR-guided group (n = 1913)	0.81 ± 0.15	0.96 ± 0.10	0.95 ± 0.11	0.97 ± 0.10	0.96 ± 0.12	0.98 ± 0.11
Angiography-guided group (n = 1912)	0.81 ± 0.16	0.96 ± 0.10	0.96 ± 0.11	0.96 ± 0.11	0.96 ± 0.11	0.98 ± 0.11
Difference (95% CI)	0 (–0.01 to 0.01)	0 (–0.01 to 0.01)	0 (–0.01 to 0.01)	0 (0, 0.01)	0 (–0.01 to 0.01)	0 (–0.01 to 0.01)
P-value	0.69	0.81	0.94	0.33	0.89	0.94

Data are shown as mean ± standard deviation. The analyses were based on the intention-to-treat population with missing data imputed. CI: Confidence interval; EQ-5D: European Quality of Life-5 Dimensions; QFR: Quantitative flow ratio. *Based on a visual analog scale scores. †According to the Japanese population time balance conversion formula. ‡EQ-5D questionnaires were completed in 1,903 patients in the QFR-guided group and 1,888 patients in the angiography-guided group.

revascularization events. Although the cost-effectiveness of QFR guidance was acceptable (<¥85,000/MACCE avoided) in nearly all pre-specified subgroups, QFR guidance was particularly attractive in patients for whom the value of PCI was uncertain, such as those with stable CAD, less severe lesions, and a SYNTAX score <8. These findings align with the results of a previous economic analysis of wire-based physiological assessment in the Fractional Flow Reserve versus Angiography in Guiding Management to Optimize Outcomes in Non-ST Elevation Myocardial Infarction (FAMOUS-NSTEMI) trial.[25]

Previous studies have shown that much of the economic benefit of functional assessment with FFR occurs during the index procedure.[10,26,27] For example, the Fractional Flow Reserve versus Angiography for Multivessel Evaluation (FAME) trial,[10] which included only patients with multivessel CAD undergoing planned PCI, found that only 63% of lesions were functionally significant (FFR ≤0.80) and required stenting. This led to substantial cost savings with FFR guidance during the index procedure compared to angiographic guidance. In contrast, the FAVOR III China trial, which enrolled an all-comer population, demonstrated similar procedural and follow-up cost savings. Given the lower procedural costs associated with QFR and the absence of complications linked to pressure wire instrumentation, QFR might be more suitable for clinical practice.

Despite fewer PCI procedures being performed in the QFR group, there were no significant differences in health outcomes, as assessed by the EQ-5D health survey, between the QFR-guided and angiography-guided strategies. These results are consistent with findings from the FAME I trial[10] and the DEFER trial,[28] suggesting that deferral of PCI based on angiography-derived physiological lesion assessment does not lead to major clinical disadvantages.

Our study has several limitations. First, procedural resource use costs were simulated using data from Beijing, rather than from all study centers. However, this approach is justifiable, as nearly half of the patients (1811/3825, 47.3%) were enrolled in Beijing. Second, there was a small amount of missing utility data, which were imputed based on baseline characteristics of similar patients. Third, while the study population was limited to Chinese adults, the generalizability of these results to other populations requires further investigation. Additionally, we did not examine the impact of varying insurance systems across different regions on the results. Fourth, the willingness-to-pay threshold of ¥10,000 per MACCE event avoided was based on expert opinion, rather than a broader societal or political consensus. Nevertheless, after adjusting for per capita GDP, this threshold represents only 60% of the accepted U.S. threshold of $10,000 per event avoided,[20,22], suggesting that the threshold applied in this study is relatively conservative. Fifth, although average rehospitalization costs were used for the final analysis, discrepancies in these costs among participating centers led to wide confidence intervals. Finally, the FAVOR III China trial excluded patients with moderate or severe chronic kidney disease, acute ST-segment elevation MI, and certain complex lesions, meaning the effects of QFR guidance on costs, cost-effectiveness, and quality of life in these populations remain unknown.

In conclusion, based on the data from the FAVOR III China randomized trial, a QFR-guided strategy appears to be economically attractive from the perspective of the Chinese healthcare system when compared to angiographic guidance in patients undergoing PCI. These findings not only provide valuable evidence for China but may also have important implications for healthcare policy in other low- and middle-income countries.

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Conflicts of interest

None.

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