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CARDIAC

Evaluation of fractional flow reserve in patients with stable angina: can CT compete with angiography?

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Abstract

Background We aimed to compare the performance of FFR_{CT} and FFR_{QCA} in assessing the functional significance of coronary artery stenosis in patients suffering from coronary artery disease with stable angina.

Method A total of 101 stable coronary heart disease (CAD) patients with 181 lesions were recruited. FFR_{CT} and FFR_{QCA} were compared using invasive fractional flow reserve (FFR) as a reference standard. Comparisons between FFR_{CT} and FFR_{QCA} were conducted based on strategies of the geometric reconstruction, boundary conditions, and geometric characteristics. The performance of FFR_{CT} and FFR_{QCA} in detecting hemodynamic significance was also investigated.

Results The performance of FFR_{CT} and FFR_{QCA} in discriminating hemodynamically significant lesions was compared. Good correlation and agreement with invasive FFR was found using FFR_{CT} and FFR_{QCA} ($r = 0.809$, $p < 0.001$ and $r = 0.755$, $p < 0.001$). A significant difference was observed in the complex coronary artery tree, in which relatively better prediction was observed using FFR_{CT} than FFR_{QCA} when analyzing the stenosis distributed in the middle segment of a stenotic branch ($p = 0.036$). Moreover, FFR_{CT} was found to be better at predicting hemodynamically insignificant stenosis than FFR_{QCA} ($p = 0.007$), while the performance of the two parameters was similar in discriminating functional significant lesions using an FFR threshold of ≤ 0.8 as a reference standard.

Conclusion FFR_{CT} and FFR_{QCA} could both accurately rule out functional insignificant lesions in stable CAD patients. FFR_{CT} was found to be better for the noninvasive screening of CAD patients with stable angina than FFR_{QCA}.

Key Points

- *FFR_{CT} and FFR_{QCA} were both in good correlation and agreement with invasive FFR measurements.*
- *FFR_{CT} is superior in accuracy and consistency compared to FFR_{QCA} in patients with stenoses distributed in left coronary artery.*
- *The noninvasive nature of FFR_{CT} could provide potential benefit for stable CAD patients on disease management.*

Xin Liu and Yabin Wang contributed equally to this work.

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Keywords Myocardial fractional flow reserve · Computed tomography angiography · Coronary artery disease · Hemodynamics · Myocardial ischemia

Abbreviations

ANOVA	Analysis of variance
AUC	Area under the receiver operating characteristic curve
BFN	Bifurcation number
CAD	Coronary artery disease
CCTA	Coronary CT angiography
DB	Diagonal artery
FAME	The fractional flow reserve versus angiography for guiding PCI in patients with multivessel coronary artery disease
FFR	Fractional flow reserve
FFR_{CT}	Computed tomography–derived FFR
FFR_{QCA}	Quantitative coronary angiography-derived FFR
GZ	Gray zone
IC	Ischemia confirmed
ICA	Invasive coronary angiography
LAD	Left anterior descending branches
LCA	Left coronary artery
LCX	Left circumflex branches
LR	Stenosis distribution in LCA and RCA
NPV	Negative predictive value
OM	Obtuse marginal artery
PCI	Percutaneous coronary intervention
PPV	Positive predictive value
QCA	Quantitative coronary angiography
RCA	Right coronary artery
S	Stratification according to FFR
SD	Standard deviation
StO	Number of lesions in a single branch

Introduction

Invasive pressure wire-derived fractional flow reserve (FFR) is a promising tool for functional assessment in coronary artery disease (CAD) [1]. Clinical trials have demonstrated that FFR ≤ 0.8 is an index for identifying significant lesions [2, 3]. FFR-guided revascularization also reduces the cost of CAD management and the rate of major adverse cardiac events (MACEs, including death, nonfatal myocardial infarction, and revascularization) compared to traditional procedure [4–7]. Despite improved clinical outcome [8], the requirement of adenosine-induced hyperemia [9], of additional catheterization with radiation exposure, and the cost of the pressure wire used for FFR measurement have hampered clinical usage of FFR [10]. Alternative methods for the calculation of FFR have emerged, such as computed tomography–derived FFR (FFR_{CT}) and quantitative coronary angiography–derived FFR (FFR_{QCA}) [11–15]. Several studies have demonstrated that FFR_{CT} improved the classification of ischemia compared to degree of CT stenosis along [16–19], and the recent NXT study showed an accuracy over 80% for FFR_{CT} to identify functional significant in 30~70% degree of stenosis, as determined by coronary CT angiography (CCTA) [20]. FFR_{QCA} provides rapid FFR calculation during angiography with high accuracy compared to invasive FFR [12, 21, 22]. However, a comparison between FFR_{CT} and FFR_{QCA} for CAD management in patients with stable angina has not been performed. Different CT-based stenotic severities in previous studies (30~70% in the Heartflow NXT study vs. 40~70% in the FFR_{QCA} study) resulted in different classification into ischemic or non-ischemic subjects, which could introduce bias in the comparison between FFR_{CT} and FFR_{QCA} [23, 24]. Furthermore, FFR_{CT} and FFR_{QCA} are seldom applied together in clinical practice for the diagnosis of ischemia [12, 25, 26].

The goal of this study was to compare FFR_{CT} and FFR_{QCA} in detecting functional significant stenosis. A quantitative comparison of FFR_{CT} with FFR_{QCA} was performed to evaluate the effect of different approaches on the accuracy of the calculated FFR.

Population

Images data were collected from routine clinical examinations initially acquired with informed patient consent. Retrospective analysis was performed for calculation of FFR_{CT} and FFR_{QCA} blinded to FFR. Present study was approved by the local ethics committee. Data were collected from the Chinese PLA General Hospital from May 14, 2016, to April 12, 2017.

Methods

Subjects suspected of having CAD with stable angina who underwent CCTA and were scheduled to undergo invasive coronary angiography (ICA) were recruited. The inclusion criteria were as follows: adult ≥ 18 years of age, CCTA with 30–90% stenosis in a major coronary artery ≥ 2.0 mm in diameter (determined by clinical site) and undergoing ICA and FFR within 7 days to avoid anatomic variations through time. The exclusion criteria were as follows: prior coronary artery bypass graft surgery; prior PCI; contraindication to adenosine; recent prior myocardial infarction within 40 days of ICA; prior pacemaker or initial defibrillator lead implantation; severe calcification; diffusive lesions and left main lesion; chronic total occlusion (CTO); and poor image quality.

Data acquisition

CCTA images were recorded with tube voltage of 120/100 kV for subjects who weight > 70 kg/< 70 kg to capture the whole heart data (Somatom Definition Flash, Siemens Healthineers) [27]. Selective ICA (Axiom Artis; Siemens Healthineers) was performed in five routine projection angle for the left coronary artery (LCA) and three for the right coronary artery (RCA) following the guidelines [28], and blinded quantitative coronary angiography (QCA) (QuantCor QCA, Siemens Healthineers) analysis of the stenotic artery were performed. FFR (PressureWire, RADI Medical Systems Inc.) assessment was performed by following the clinical practice guidelines [29] for clinically indicated lesions, and hyperemia was induced using an intravenous infusion of adenosine (140 μg kg^{-1} min^{-1}). Pressure pullback data were recorded from the segment immediately downstream of the stenosis distal to the ostium of the coronary artery. An FFR value ≤ 0.8 was used as an index for the discrimination of functional significant lesions as described in a previous study [30].

Computation of fluid dynamics

The in-house algorithms of calculating FFR developed as industrial preliminary prototype were descripted previously in [31–33]. The geometry of the coronary artery tree was reconstructed using CCTA and ICA by applying algorithms described in previous studies [12, 33, 34] (details in Appendix A). For FFR_{CT}, the computational fluid dynamics (CFD) analysis method was applied to calculate the blood pressure in the three-dimensional coronary artery reconstructed from CCTA images [35] (details in Appendix B). For FFR_{QCA}, volumetric flow rate estimated from Thrombolysis in Myocardial Infarction (TIMI) frame counts was employed in the CFD analysis in QCA-derived geometry [12] (details are provided in Appendix C). A threshold of FFR ≤ 0.8 was considered as an index to diagnose the functional significant lesions using FFR_{CT} and FFR_{QCA}. A commercial CFD software suit (COMSOL Multiphysics 5.2a trail edition, COMSOL) was adopted to conduct all calculations [36].

Anatomic characteristics for comparison between FFR_{CT} and FFR_{QCA}

To quantify the effect of different approaches on calculation accuracy, we compared the diagnostic performances of FFR_{CT} and FFR_{QCA} under different anatomic characteristics, including upstream bifurcation number (BFN), stenosis distribution in LCA and RCA (LR), number of lesions in a single branch (StO) and stratification according to FFR (S). The definitions of these parameters are as follows: BFN indicates the number of bifurcations upstream of the target stenosis to the ostium of the coronary artery, representing the effect of side branches on flow distribution. LR represents the effect of physiological variations on the accuracy of FFR_{CT} and FFR_{QCA}. StO represents the effect of tandem stenoses. Stratification (S) according to FFR aims to test the performance of methods for diagnosing functional significant lesions and their accuracy in medical decision making. There are three levels of ischemia: functional insignificant (FI) (FFR > 0.8), gray zone (GZ) (0.75 ≤ FFR ≤ 0.8) [37], and ischemia confirmed (IC) (FFR < 0.75). In particular, comparisons were performed based on the FFR downstream of the most distal stenosis when tandem stenoses were observed in a single branch.

Statistical analysis

The diagnostic performances of FFR_{CT} and FFR_{QCA} were evaluated by the area under the receiver operating characteristic curve (AUC). The accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were evaluated using FFR as a reference standard. Continuous variables are presented as the mean ± standard deviation (SD) or median (interquartile range, IQR), as appropriate. Categorical variables are presented as numbers and percentages. Pearson correlation analysis and the Bland–Altman plot with corresponding 95% confidence interval (CI) were used to analyze the correlation and consistency between FFR_{CT}\$FFR_{QCA}$ and FFR. Tests of normality showed that the FFR_{CT} and FFR_{QCA} were not normally distributed, and these data were compared with the Mann–Whitney U test. The differences in FFR_{CT} to FFR ($d_{CT} = FFR_{CT} - FFR$) and FFR_{QCA} to FFR ($d_{QCA} = FFR_{QCA} - FFR$) were normally distributed in groups stratified by BFN, lesion distribution, and tandem stenoses and were compared by Student's t test or one-way analysis of variance (ANOVA), as appropriate. Two-sided p-values < 0.05 were considered statistically significant. Data analysis was performed using SPSS 24.0 (SPSS Inc).

Results

Physiological and lesion characteristics

Baseline and lesion characteristics are summarized in Table 1. A total of 111 patients were enrolled, and the mean age was 59.5 yrs. However, after the data were reviewed, four patients were excluded for previous myocardial infarction, and six patients for previous PCI. Therefore, 101 patients with 181 lesions were identified. Due to cases of tandem stenosis, a comparison between FFR_{CT} and FFR_{QCA} was conducted based on 127 stenotic branches in which the FFR was measured at distal segments.

Table 1 Baseline and lesion characteristics

Baseline characteristics ($n = 101$)			CCTA	ICA
Age (years)	59.5 ± 8.5	Patients with maximum stenosis > 50%	73 (72.3)	44 (43.6)
Male sex *n* (%)	54 (51.3%)	Patients with maximum stenosis 30–50%	28 (27.7)	57 (56.4)
BMI	25.4 ± 3.5	Patients with single artery lesion	46 (46)	
LEVF	61.3 ± 5.0	Patients with multiple artery lesion	55 (55)	
Cardiovascular risk factors		Ischemic stenosis determined by FFR	48 (26.5)	
Hypertension	59 (59)			
Hyperlipidemia	22 (21.7)	Lesion characteristics. Which FFR_{CT} and FFR_{QCA} were performed ($n = 127$)		
Diabetes	18 (17.8)	LAD	54 (42.5)	
Family history of CAD	11 (10.9)	LCX	15 (11.8)	
Co-morbidity		DB	17 (13.4)	
Previous myocardial infarction	4 (3.6%)	OM	8 (6.3)	
Previous PCI	6 (5.4%)	RCA	33 (26.0)	

BMI body mass index (kg/m^2), *LEVF* left ventricular ejection fraction, %, *CAD* coronary artery disease, *PCI* percutaneous coronary intervention, *LAD* left anterior descending, *LCX* left circumflex artery, *DB* diagonal branches, *OM* obtuse marginal branches, *RCA* right coronary artery

All data were presented in number (percentage, %), except for age, BMI, and LEVF were presented in mean ± standard deviation

Reconstruction variations between modalities

Examples of reconstructed geometries of FFR_{CT} and FFR_{QCA} are illustrated in Fig. 1. Geometric details such as the number of outflow boundaries and bifurcations were different: the average numbers (range) were 15 ([12 to 16]) and 8.8 ([6 to 8]) for CCTA and 4 ([1 to 8]) and 2.6 ([1, 4]) for QCA, respectively.

Diagnostic performance of FFR_{CT} and FFR_{QCA}

Difference was observed in the degree of stenosis (65.9%, 95% CI [40%, 92%] vs. 49%, 95% CI [26,72]) between the reconstructions performed using CCTA and those using QCA (15.9 ± 11.8%, $p = 0.048$). Good correlation was found in FFR_{CT} ($r = 0.809$, $p < 0.001$) and FFR_{QCA} ($r = 0.755$, $p < 0.001$) compared with FFR (Fig. 2a). However, FFR_{CT} was relatively better in consistency of predicting the functional significant lesions compared to FFR_{QCA} (d_{CT} −0.004 ± 0.016 vs. d_{QCA} 0.047 ± 0.052 for FFR_{CT} and FFR_{QCA}, respectively) (Fig. 2c and d).

Considering FFR ≤ 0.8 as the threshold for hemodynamically significant findings, the per lesion accuracy, sensitivity, specificity, PPV, and NPV were found to be 90.6%, 87.5%, 91.3%, 70%, and 96.9% for FFR_{CT} and 90.6%, 75%, 94.2%, 75%, and 94.2% for FFR_{QCA}, respectively. The per patient accuracy, sensitivity, specificity, PPV, and NPV were 92.1%, 95.0%, 91.4%, 73.1%, and 98.7% for FFR_{CT} and 88.1%, 70%, 92.6%, 70%, and 92.6% for FFR_{QCA}, respectively. Improvement of diagnostic performance was observed compared to anatomy-based assessments (≥ 50% degree of stenosis). The accuracy, sensitivity, specificity, PPV, and NPV of CCTA were 62.2%, 83.0%, 53.5%, 43.0%, and 88.4%, respectively, while those of QCA were 68.9%, 88.2%, 61.3%, 47.0% and 93.1%, respectively. The diagnostic performance of the two modalities was evaluated using receiver operating characteristic (ROC) curve analysis. ROC curve analysis for FFR_{CT} and FFR_{QCA} showed AUCs of 0.966 and 0.921 while the AUCs evaluated CCTA and QCA were 0.742 and 0.765, respectively. (Fig. 2b).

Evaluation of bifurcations via FFR_{CT} and FFR_{QCA}

Bifurcations play an important role in blood flow distribution from the proximal artery to distal circulations [37, 38]. The categories were grouped according to the bifurcation number (BFN) upstream of the stenotic segment and per BFN to investigate the effect of different BFNs on the accuracy of FFR_{CT} and FFR_{QCA}. As shown in Fig. 3a, 4 categories of BFNs (*n*) were identified: 2 (38), 3 (56), 4 (20) and 5 (13). Similar findings were observed in FFR_{CT} and FFR_{QCA} for evaluating the functional significant lesions distributed in the proximal segment (BFN: 2, $p = 0.318$) and distal segment (BFN: 5, $p = 0.258$) of the stenotic branch. However, a different trend was observed in the middle segment (BFN: 3, $p = 0.036$ and BFN: 4, $p = 0.016$). Moreover, comparisons were performed in an artery with a single stenosis to adjust for the effect of tandem stenosis, and a similar result was observed. Detailed data are provided in Supplementary Table 1.

A comparison between FFR_{CT} and FFR_{QCA} showed difference in determining the functional significant lesions in the left coronary artery and right coronary artery (92.5% vs. 89.3% in LCA and 84.9% vs. 93.9% in RCA). The accuracy of FFR_{QCA} was similar in assessing the functional significant

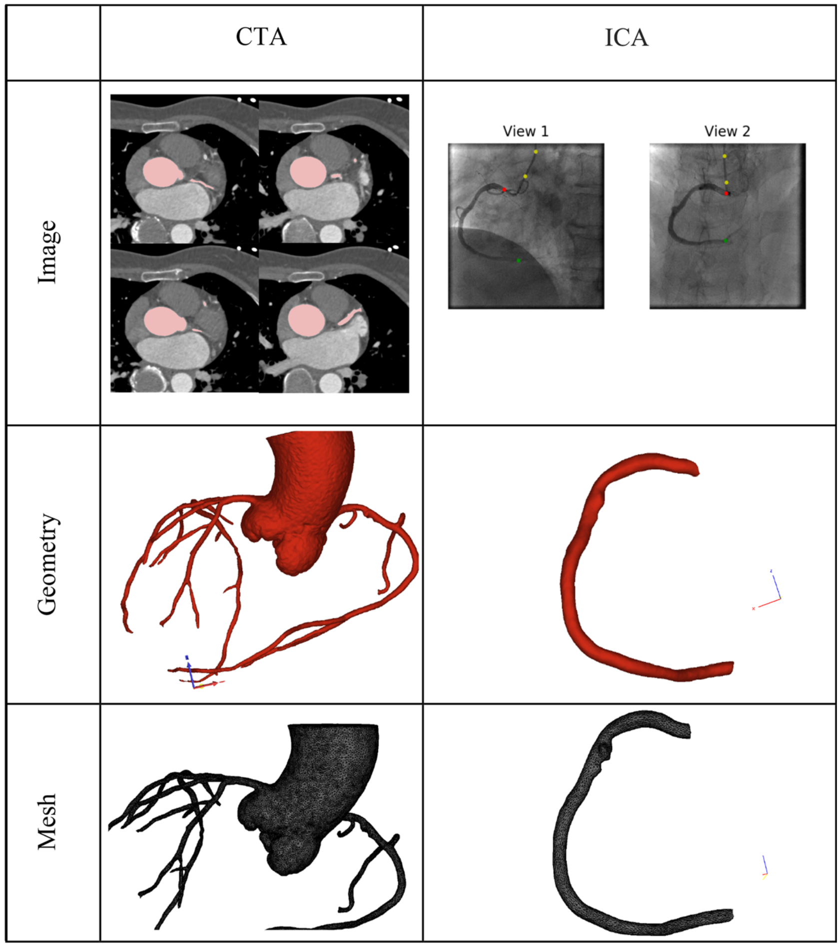

Fig. 1 Comparison between FFR_{CT} and FFR_{QCA} in geometric reconstructions. The view of interest was identified from CCTA and ICA images. Geometries were then established, and meshes were generated regarding the same density of elements

lesions distributed in both the LCA and RCA ($p = 0.848$), while FFR_{CT} showed higher accuracy in the LCA than in the RCA ($p = 0.007$). Moreover, FFR_{CT} was relatively better in predicting ischemia than FFR_{QCA} in the LCA ($p = 0.081$) (Fig. 3b). Detailed data are provided in Supplementary Table 2. In addition, the accuracy of FFR_{CT} was better than that of FFR_{QCA} in determining hemodynamically significant lesions at left anterior descending branches (LAD) (92.6% vs. 85.2%), and reversed in left circumflex branches (LCX) (93.3% vs 100%).

FFR_{CT} and FFR_{QCA} for analyzing tandem stenoses

Coronary tandem stenosis is an additional factor impacting the FFR value of the distal stenosis [39]. Thirty-eight stenotic branches (29.9%) were identified as having more than one stenosis with at least one stenosis ≥ 50% in a single branch. We categorized the cases into 3 groups (*n* vessels): (1) isolated stenosis in a single branch (89), (2) two separate stenoses (22), and (3) more than two separate stenoses (16). Comparison of consistency in predicting FFR showed no statistical differences in group 2 ($p = 0.945$) by using either FFR_{CT} or FFR_{QCA} (Fig. 3c). Different trend was observed between FFR_{CT} and FFR_{QCA} in group 1($p = 0.001$), and FFR_{CT} was found relatively better than FFR_{QCA} in group 3 ($p = 0.22$). Detailed data are provided in Supplementary Table 3.

Accuracy and consistency of FFR_{CT} and FFR_{QCA} for decision making

The ischemic extent was classified as (i) IC (for FFR < 0.75), (ii) GZ (for FFR ranging from 0.75 to 0.8), and (iii) FI) (FFR > 0.8). Significant differences between FFR_{CT} and FFR_{QCA} were observed in the IC group ($p = 0.043$) and FI group ($p = 0.007$). FFR_{CT} slightly overestimated the functional significant lesions in the GZ group, while FFR_{QCA} underestimated that risk (Fig. 3d). Detailed data are provided in Supplementary Table 4.

Discussion

In patients with stable angina, both FFR_{CT} and FFR_{QCA} improved the diagnostic performance of CCTA and QCA. Similar overall accuracy of discriminating functional

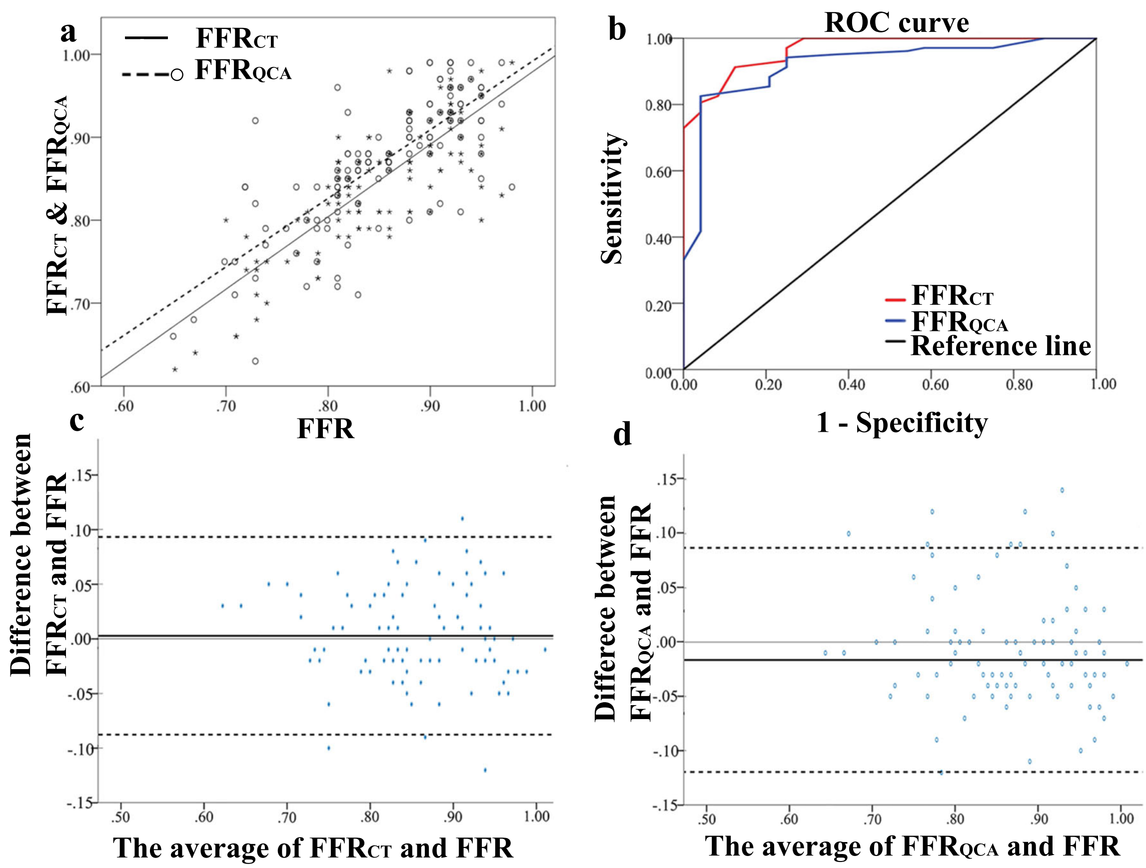

Fig. 2 Performance of FFR_{CT} and FFR_{QCA} compared with FFR. **a** Similar correlations were found for FFR_{CT} ($r = 0.809$, $p < 0.001$) and FFR_{QCA} ($r = 0.755$, $p < 0.001$). **b** ROC curves were developed to compare FFR_{CT} and FFR_{QCA} with an FFR cutoff value of 0.8 for the discrimination of hemodynamically significant lesions. The AUCs of FFR_{CT} and FFR_{QCA} are 0.966 and 0.921, respectively. **c** and **d** The Bland–Altman plot showed differences between FFR_{CT} and FFR_{QCA}. The consistency of FFR_{CT} (95% of CI [− 0.088 to 0.093]) was relatively better than that of FFR_{QCA} (95% CI [− 0.12 to 0.086])

significant lesions was observed between FFR_{CT} and FFR_{QCA} compared to invasive FFR.

Although ICA has been considered the standard reference for the anatomic assessment of coronary artery stenosis and CCTA was found to overestimate the degree of stenosis (lower specificity compared to ICA) [40], this study demonstrated similar accuracy in functional assessment by using CCTA or ICA-derived QCA, with an accuracy ranging from 69 to 71% [41]. Our results showed similar performance, with an accuracy ranging from 62.2 to 68.9%. However, the coronary artery tree reconstructed by CCTA preserved more details than that reconstructed by QCA. Branch reconstruction with QCA was limited by vessel overlap in 2D projection images from routine ICA [42], which led to variations in the calculation of FFR. The RCA dominated the volumetric flow compared to the other epicardial branches. Higher accuracy in discriminating the functional significant lesions distributed in the RCA was achieved by FFR_{QCA} than by FFR_{CT}. The LCA consisted of two major branches (LAD and LCX), while side branches were commonly found (diagonal artery (DB) and obtuse marginal artery (OM)), which contributed to the complex redistribution of flow in the LCA tree. A previous study suggested that 20% of side branches in the LCA supported a significant fractional myocardial mass, and the blood flow volume through these side branches was therefore important for analyzing the hemodynamics in the main branches [43]. Prediction of the functional significant lesions was more accurate with FFR_{CT} than with FFR_{QCA} in the LCA. Moreover, the accuracy was higher using FFR_{CT} than FFR_{QCA} in the LAD due to the involvement of the DB in the coronary artery tree derived from CCTA images, which is generally missing in the coronary artery tree derived from QCA images. The overestimation of flow through the stenotic vessel could be the cause of the overestimation of the ischemia in the LCA predicted by FFR_{QCA}, which was in accordance with a previous study [44].

Tandem stenosis could affect the true FFR indication of an individual stenosis. A previous study indicated that the true FFR value was masked by the apparent hemodynamic significance of tandem stenoses, especially for a proximal stenosis [45]. A post hoc analysis of FFR_{CT} based on the NXT trial showed promising results in calculating the apparent FFR, and

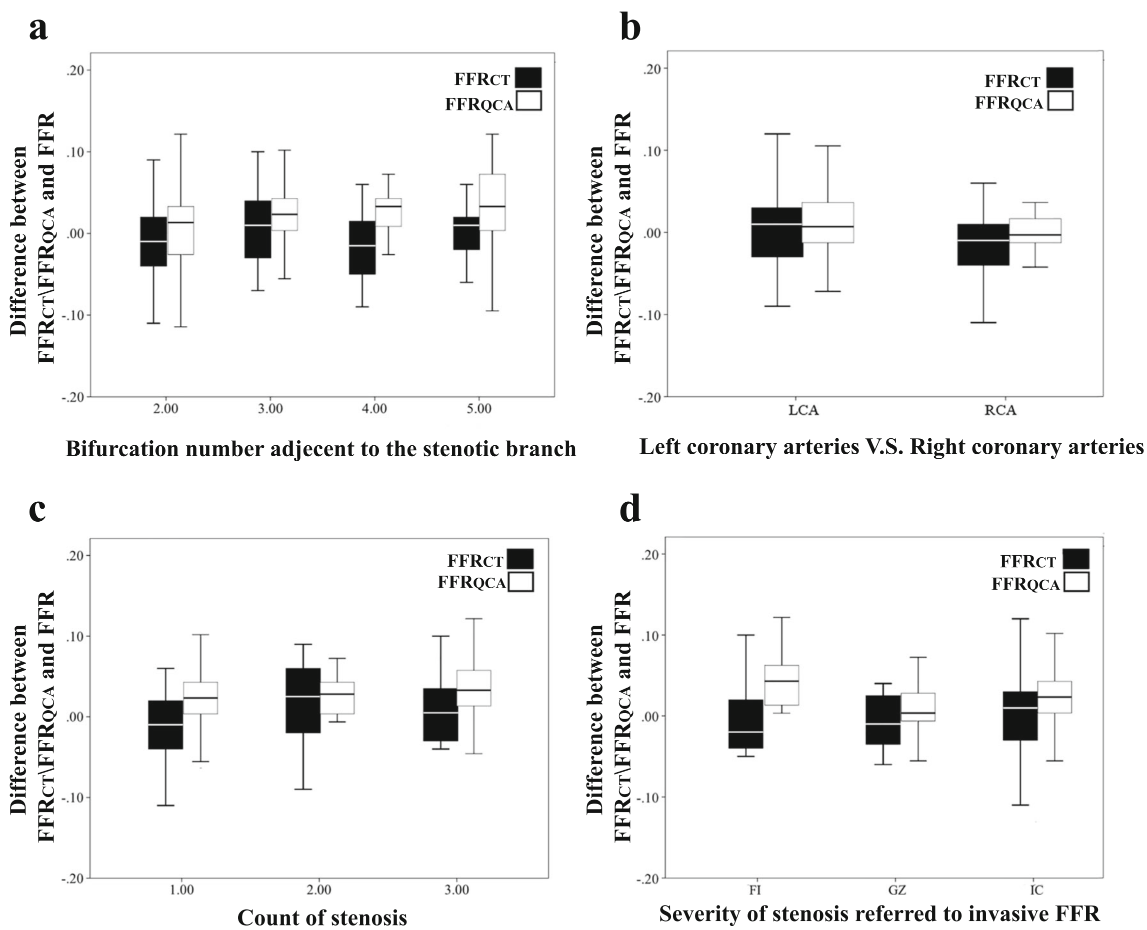

Fig. 3 Differences between FFR_{CT} and FFR_{QCA} compared to FFR. **a** Effect of the upstream bifurcation: there was no significant difference between FFR_{CT} and FFR_{QCA} in cases of proximal and distal stenoses (BFN of 2 and 5). However, a difference was observed in stenoses distributed in the middle segment of a stenotic artery (BFN of 3 and 4). **b** Difference in the left and right coronary artery: different levels of consistency were found in both the left and right coronary arteries when comparing FFR_{CT} to FFR_{QCA}. Meanwhile, the consistency of FFR_{QCA} between the LCA and RCA was better than that of FFR_{CT}. **c** Effect of tandem stenoses: the three categories are an isolated stenosis, 2 separate stenoses and multiple separate stenoses in a single branch (groups 1, 2, and 3 respectively). FFR_{CT} was found to be better at predicting the ischemia of single stenosis than FFR_{QCA}. The performance of FFR_{CT} and FFR_{QCA} was similar in cases of 2 separate stenoses, and a mild difference was found in cases of multiple stenoses. **d** Comparison of diagnostic performance between FFR_{CT} and FFR_{QCA} stratified by FFR: FFR_{CT} and FFR_{QCA} were found to be similar in the GZ, while differences were observed in the FI and IC groups

a translesional pressure gradient enabled the assessment of the role of individual stenoses [39], while the use of FFR_{QCA} for the assessment of tandem stenoses has not been reported. Regardless of the severity of the stenosis, our results showed that FFR_{CT} was more correlated to FFR compared to FFR_{QCA} in predicting the ischemia of an artery with an isolated stenosis, which may be due to the effect of side branches, as mentioned previously. Tanak et al reported that the interaction between tandem stenoses led to a reduction of the translesional pressure gradient at the distal stenosis compared to the proximal stenosis [39]. Moreover, foreshortening in the coronary artery tree reconstructed from QCA images could lead to overestimation of flow through multiple lesions. Combined with the missing side branches, the accumulation error could be the reason for the reduced consistency in FFR_{QCA}.

Medical decision making guided by FFR relies on a specific threshold. Differences in the consistency between FFR_{CT} or FFR_{QCA} and FFR were observed in the FI group and IC group. A similar distribution was found in the GZ group (FFR ranging from 0.75 to 0.8). FFR_{QCA} slightly underestimated the ischemia compared with invasive FFR, whereas FFR_{CT} overestimated. Koyuru et al reported that 0.72 could be the optimal cutoff of FFR_{CT} for the indication of revascularization, instead of 0.8 [46], which could be above 0.75 for FFR_{QCA} according to the present study. Therefore, further investigation is required to refine the threshold for the clinical indication of revascularization using FFR_{CT} and FFR_{QCA}.

The present study has several limitations. Firstly, present study contained only CAD patients with stable angina, which may hinder the comprehensive comparison of diagnostic performance in patients with complex lesions (CTO and LM stenosis).

However, with a focus on improving disease management among CAD patients, the characteristics of the present cohort could represent the early stage of CAD [47]. Secondly, this is a single-center study with small patient number. Further study with large sample size is needed. Thirdly, the comparison of diagnostic performance in tandem stenosis between FFR_{CT} and FFR_{QCA} was limited in assessing most distal segment. Therefore, the accuracy of FFR_{CT} and FFR_{QCA} for evaluating true FFR in individual stenosis of tandem stenosis required further studies.

In conclusion, FFR_{CT} and FFR_{QCA} facilitated the clinical screening of CAD patients with stable angina. Patients could benefit from medical decision making based on either FFR_{CT} or FFR_{QCA}, but FFR_{CT} was found to be superior to FFR_{QCA} in discriminating patients with lesions in the LCA. Moreover, the noninvasive nature of FFR_{CT} has facilitated its application in clinical practice, which improved CCTA for screening ischemia in CAD patients with stable angina. However, the optimal cutoff value for FFR_{CT} and FFR_{QCA} required further investigations.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Feng Cao.

Conflict of interest The authors report no relationships that could be construed as a conflict of interest.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was obtained.

Ethical approval Institutional Review Board approved the present study.

Methodology
• retrospective
• observational
• performed at one institution

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