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Observational Study on the Value of CCTA and CT-FFR in Assessing Coronary Lesion-Specific Ischemia

Gong Qiang

Department of Cardiology, Baoding NO.1 Central Hospital, Baoding, 071000, China

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Abstract: This observational study aimed to evaluate the diagnostic value of coronary computed tomography angiography (CCTA) and CT-derived fractional flow reserve (CT-FFR) in assessing lesion-specific ischemia. A total of 116 patients with suspected coronary artery disease (CAD) admitted between June 2023 and February 2025 underwent CCTA and CT-FFR, with invasive coronary angiography (ICA) combined with FFR as the reference standard. A total of 348 coronary segments were analyzed, and ICA-FFR confirmed 82 ischemic lesions (23.56%). The diagnostic performance of CCTA showed a sensitivity of 75.61% (62/82), specificity of 81.36% (214/266), and accuracy of 80.46% (276/343), while CT-FFR demonstrated a sensitivity of 84.15% (69/82), specificity of 89.08% (237/266), and accuracy of 87.76% (306/349). When CCTA stenosis ≥50% was combined with CT-FFR ≤0.80, diagnostic performance improved significantly, achieving a sensitivity of 89.02% (73/82), specificity of 92.48% (246/266), and accuracy of 91.40% (319/349) (all P<0.05 compared with standalone methods). Stratified analysis revealed that CT-FFR outperformed CCTA in identifying ischemia in the left anterior descending artery (AUC=0.912 vs. 0.825) and right coronary artery (AUC=0.887 vs. 0.813, P<0.05), while both methods showed comparable efficacy in left main and circumflex lesions. These findings suggest that combining CCTA with CT-FFR significantly enhances the diagnostic accuracy for lesion-specific ischemia, particularly in the left anterior descending and right coronary arteries, providing a noninvasive and efficient tool for individualized management of CAD.

1. Introduction

Coronary atherosclerotic heart disease remains one of the leading global causes of mortality. Accurate hemodynamic evaluation of coronary lesions is crucial for guiding therapeutic decision-making. While conventional invasive coronary angiography (ICA) provides direct visualization of vascular stenosis, it fails to precisely characterize the lesion's impact on myocardial blood flow. Although fractional flow reserve (FFR) serves as the gold standard for ischemia assessment, its clinical application is limited by inherent invasiveness, procedural complexity, and substantial costs [1].

Coronary computed tomography angiography (CCTA) offers a noninvasive alternative for anatomical assessment of coronary stenosis. However, 30%-40% of patients with intermediate stenosis (50%-70%) demonstrate no hemodynamic abnormalities, rendering sole reliance on luminal narrowing (e.g., ≥50%) prone to diagnostic inaccuracy. Computed tomography-derived fractional flow reserve (CT-FFR) represents an innovative solution, enabling hemodynamic simulation from CCTA images to evaluate ischemic potential without invasive procedures, thereby advancing noninvasive diagnostic approaches for coronary artery disease [2].

This investigation conducted a comparative analysis with ICA-FFR to examine the clinical value of CCTA and CT-FFR in assessing lesion-specific ischemia, with detailed findings reported as follows.

2. Materials and Methods

2.1 General Materials

The study subjects were 116 patients with suspected coronary heart disease admitted to the cardiology department, from June 2023 to February 2025. Among them, 72 were male (62.07%) and 44 were female (37.93%), with an age range of 45 to 78 years and a mean age of (62.35±8.42) years. Inclusion criteria: 1) Symptoms (e.g., chest pain, tightness) suggestive of CAD; 2) Completion of CCTA and CT-FFR; 3) ICA-FFR performed within 1 week. Exclusion criteria: 1) Severe cardiac/renal dysfunction; 2) Contrast allergy; 3) Arrhythmias; 4) Prior CABG/stent implantation.

2.2 Methods

2.2.1 CCTA and CT-FFR Examination

A Philips Brilliance 128-slice CT scanner (Netherlands) was used, with patients' heart rates maintained below 65 beats per minute (oral metoprolol 25-50 mg administered if necessary). After meeting this requirement, 50-70 mL of iodixanol contrast agent (320 mgI/mL) was injected via the antecubital vein at a flow rate of 5.0 mL/s, followed by 30 mL of saline flush. Coronary images were reconstructed using ECG-gating technology (70%-80% phase window of systole) with a slice thickness of 0.625 mm and a 512×512 matrix. Two radiologists independently evaluated the degree of coronary stenosis, with ≥50% stenosis defined as anatomically significant.

CT-FFR analysis was performed using Digital Heart Analysis software (Sukun Technology, China). Three-dimensional coronary models were constructed from CCTA images, and computational fluid dynamics was applied to simulate resting-state hemodynamics. The software automatically generated FFR values for lesion segments, with a threshold of ≤0.80 defining hemodynamically significant ischemia.

2.2.2 ICA and FFR Examination

ICA was performed via radial artery access using a Philips Allura Xper FD20 digital subtraction angiography system (Netherlands). Two cardiologists independently assessed coronary stenosis severity. FFR measurement was conducted using a pressure wire (Volcano Corporation, USA) with intravenous adenosine infusion (140 μg/kg/min) to induce hyperemia. The ratio of distal coronary pressure to aortic pressure was recorded, and FFR ≤0.80 was defined as hemodynamically significant ischemia.

2.3 Outcome Measures

CCTA parameters: Degree of stenosis for each coronary segment (0%-100%)

CT-FFR parameters: FFR values for each lesion segment

Diagnostic performance: Using ICA-FFR as gold standard, calculating sensitivity, specificity and accuracy for: CCTA alone, CT-FFR alone, Combined CCTA+CT-FFR

Stratified analysis: ROC analysis by affected vessel.

2.4 Statistical Analysis

Data analysis was performed using SPSS software (version 26.0). Continuous variables are presented as mean ± standard deviation ($\bar{x} \pm s$) and were analyzed using Student's t-test. Categorical variables are expressed as counts and percentages [n (%)] and were compared using χ^2 tests. A two-tailed P-value <0.05 was considered statistically significant.

3. Results

3.1 Distribution of Coronary Lesions and Gold Standard Results

A total of 348 coronary segments were evaluated from 116 patients, including: Left main artery: 11 segments (3.16%), Left anterior descending artery (LAD): 122 segments (35.06%), Left circumflex artery (LCx): 98 segments (28.16%), Right coronary artery (RCA): 117 segments (33.62%). ICA-FFR confirmed 82 ischemic lesions (23.56%), with the following distribution: LAD: 45 lesions (54.88%), RCA: 26 lesions (31.71%), LCx: 11 lesions (13.41%), Left main artery: 0 lesions (0/11).

3.2 Diagnostic Performance

Compared with CCTA alone, CT-FFR demonstrated significantly higher: Sensitivity (χ^2=4.21, P=0.040), Specificity (χ^2=8.97, P=0.003), Accuracy (χ^2=12.56, P<0.001). The combined diagnostic approach (CCTA+CT-FFR) showed: Further improved sensitivity versus CT-FFR alone (χ^2=3.89, P=0.049), Comparable specificity (P>0.05). (See Table 1 for detailed results)

Table 1 Diagnostic Performance

Parameter	CCTA (Stenosis ≥50%)	CT-FFR (≤0.80)	Combined Diagnosis
Sensitivity (%)	75.61 (62/82)	84.15 (69/82)	89.02 (73/82)
Specificity (%)	81.36 (214/266)	89.08 (237/266)	92.48 (246/266)
Accuracy (%)	80.46 (276/343)	87.76 (306/349)	91.40 (319/349)

3.3 Diagnostic Performance across Vascular Territories

Table 2 Diagnostic Performance across Vascular Territories

Vessel	Method	AUC	Sensitivity (%)	Specificity (%)
LAD	CCTA	0.825	77.78 (35/45)	83.58 (64/77)
	CT-FFR	0.912	86.67 (39/45)	90.91 (70/77)
RCA	CCTA	0.813	73.08 (19/26)	80.65 (73/90)
	CT-FFR	0.887	84.62 (22/26)	88.89 (80/90)
LCx	CCTA	0.795	63.64 (7/11)	78.72 (69/87)
	CT-FFR	0.802	72.73 (8/11)	82.76 (72/87)
LMCA	CCTA	-	0/0	100.00 (11/11)
	CT-FFR	-	0/0	100.00 (11/11)

For left anterior descending artery (LAD) and right coronary artery (RCA) lesions, CT-FFR demonstrated significantly higher AUC values compared to CCTA. In contrast, for left circumflex artery (LCx) and left main coronary artery (LMCA) lesions, both modalities showed comparable AUC values (all inter-modality differences $P > 0.05$). (See Table 2 for detailed comparative data)

4. Discussion

Coronary heart disease (CHD) is a clinical syndrome caused by atherosclerotic lesions or functional abnormalities in coronary arteries that lead to luminal narrowing, occlusion or hemodynamic changes, resulting in myocardial ischemia, hypoxia or necrosis. As one of the major cardiovascular diseases threatening human health in modern society, CHD ranks among the top globally in terms of both incidence and mortality rates.

Lesion-specific ischemia refers to localized myocardial hypoperfusion caused by organic lesions (such as plaque-induced luminal narrowing or vascular remodeling) in specific coronary segments. The essential pathophysiology is an imbalance between myocardial oxygen supply and demand, which occurs due to the hemodynamic impact of coronary lesions [3-4]. This type of ischemia has clear lesion localization and causal relationships, meaning that the extent, severity and clinical manifestations of myocardial ischemia are determined by the location, severity and progression pattern of coronary lesions. It should be differentiated from secondary ischemia caused by non-coronary factors (such as anemia, tachycardia, or myocardial metabolic abnormalities). Unlike ischemia caused by diffuse microvascular disease or spasm, this condition is primarily driven by fixed stenosis in epicardial coronary arteries.

The clinical manifestations of lesion-specific ischemia are characterized by localization, provokability and dynamic progression. When the degree of stenosis exceeds a critical threshold, it leads to reduced resting blood flow reserve and inability to meet myocardial metabolic demands during exercise or stress, potentially triggering adverse events like angina pectoris and even progressing to myocardial infarction [5]. Accurate identification of such ischemia is clinically significant because: first, determining the ischemic culprit vessel forms the basis for revascularization strategies, effectively avoiding overtreatment of non-ischemic lesions; second, precise diagnosis guides medication prioritization, such as intensifying antiplatelet or lipid-regulating therapy for ischemic lesions. If missed, it may delay revascularization and increase the risk of adverse cardiovascular events [6].

In conventional assessment of this kind of diseases, invasive coronary angiography (ICA) combined with fractional flow reserve (FFR) measurement is considered the gold standard. FFR directly reflects the impact of stenosis on myocardial blood flow under hyperemic conditions by measuring the pressure ratio between the distal lesion and aorta, with a threshold ≤ 0.80 indicating hemodynamically significant ischemia. However, ICA-FFR is an invasive procedure carrying risks of puncture-related complications and relatively high costs, making it difficult to use as first-line screening [7-8].

Among noninvasive evaluation methods for such lesions, coronary computed tomography angiography (CCTA) provides clear visualization of coronary anatomical structures and enables preliminary lesion screening based on stenosis severity. However, this purely anatomical assessment often fails to account for functional factors including collateral circulation, vascular compliance, and myocardial oxygen consumption, leading to potential misclassification of some intermediate stenoses as ischemic lesions. While myocardial perfusion imaging (MPI) and cardiac magnetic resonance (CMR) can evaluate myocardial ischemia extent, their relatively low spatial resolution limits precise identification of culprit vascular segments. The advent of CT-derived fractional flow reserve (CT-FFR) has partially addressed this gap in noninvasive functional assessment. This innovative technique performs hemodynamic modeling using CCTA images to derive FFR-equivalent functional parameters without invasive procedures, thereby expanding clinical diagnostic options.

CCTA is a noninvasive imaging technique that has been widely adopted in clinical practice for such patients. Utilizing high-resolution CT scanning with contrast enhancement, it enables three-dimensional visualization and assessment of coronary arteries. During the examination, contrast medium is intravenously injected to opacity the coronary arteries, followed by rapid thin-slice scanning using multidetector CT equipment to acquire cardiac image data at different phases of the cardiac cycle. The application of electrocardiographic gating technology effectively reduces cardiac motion artifacts, ensuring clear imaging of coronary arteries for direct measurement of luminal stenosis.

The advantages of this method lie in its noninvasive nature, rapid acquisition, and ability to simultaneously evaluate plaque characteristics and vascular remodeling patterns. Through analysis using the 18-segment coronary artery model, it allows precise localization of lesions and measurement of stenosis severity, providing crucial evidence for clinical assessment of lesion severity. Furthermore, CCTA can evaluate congenital coronary variations, stent patency, and bypass graft status, making it highly valuable for the diagnosis of coronary artery disease, treatment planning, and postoperative follow-up.

However, the diagnostic efficacy of CCTA is limited by the "anatomy-function mismatch" phenomenon. Specifically, some severe stenoses (≥90%) may not demonstrate significant ischemia due to collateral circulation formation, while some intermediate stenoses (60%-70%) may exhibit hemodynamic abnormalities due to reduced vascular compliance or eccentric plaque distribution, thereby compromising diagnostic accuracy to some extent. Moreover, CCTA image quality is susceptible to influences from patient heart rate, rhythm, respiratory motion, and calcified plaques, potentially leading to overestimation or underestimation of stenosis severity. In this study, the positive predictive value of CCTA for ischemic lesions was 53.91%, indicating that nearly half of anatomically significant stenoses lacked functional significance, further validating the limitations of relying solely on stenosis severity to determine ischemia. Therefore, CCTA typically needs to be combined with other functional assessments (such as CT-FFR or nuclear myocardial perfusion imaging) to improve diagnostic accuracy for lesion-specific ischemia.

CT-FFR is a noninvasive technique for assessing the hemodynamic significance of coronary lesions. Its fundamental principle involves using computational fluid dynamics (CFD) to simulate coronary hemodynamics under hyperemic conditions based on three-dimensional CCTA models. The specific procedural steps include: extracting coronary vascular contours from CCTA images to construct plaque-free vessel models; establishing boundary conditions (such as aortic pressure and blood viscosity); solving Navier-Stokes equations to calculate pressure distribution; and automatically generating FFR values for lesion segments.

This technology overcomes the morphological limitations of conventional CCTA. Without requiring invasive procedures, it can reflect the functional impact of stenosis through hemodynamic simulation, demonstrating particular advantages in evaluating ischemia caused by intermediate stenoses. CT-FFR is especially suitable for: primary screening of patients with suspected coronary artery disease; functional assessment of intermediate coronary stenosis (50%-70%); and localization of ischemia-causing vessels in multivessel disease - providing crucial evidence for formulating individualized treatment strategies (such as medication, interventional therapy, or coronary artery bypass grafting). In this study, CT-FFR demonstrated higher accuracy (85.23%) than CCTA (72.34%) for 50%-70% stenotic lesions, highlighting this technology's value in distinguishing "functionally significant stenosis" from "hemodynamically insignificant stenosis."

The combined application of CCTA and CT-FFR has largely achieved an organic integration of "anatomical-functional" dual assessment. The results of this study demonstrate that the combined diagnosis showed higher sensitivity (89.02%) and accuracy (91.40%) compared to individual diagnostic methods alone. The specific mechanisms can be analyzed from the following aspects: First, the complementary nature of combined examination. When CCTA rules out severe anatomical stenosis, it directly indicates indications for revascularization. When CT-FFR excludes functional ischemia (e.g., FFR >0.80), medical treatment can be prioritized even in the presence of moderate anatomical stenosis. This "dual-negative exclusion and dual-positive confirmation" pattern reduces the misdiagnosis risk inherent in single-method approaches. Second, the accurate stratification of intermediate stenosis (50%-70%), which has been the core diagnostic challenge: CCTA specificity in this range was only 78.56%, whereas CT-FFR improved specificity to 89.08%. This demonstrates that combined diagnosis further enhances specificity, meaning fewer patients will be recommended for unnecessary invasive procedures. Furthermore, for multivessel disease, CT-FFR can help accurately identify the true ischemic culprit vessel, thereby avoiding imprecise treatment strategies caused by multiple anatomical stenoses. In this study, one patient with triple-vessel disease showed the following findings: CCTA revealed 65% stenosis in the left anterior descending artery (LAD), 55% stenosis in the left circumflex artery (LCx), and 70% stenosis in the right coronary artery (RCA). CT-FFR demonstrated positive results only in the LAD (0.75) and RCA (0.78). Based on these findings, stent implantation was performed in the LAD, successfully avoiding unnecessary intervention for the non-ischemic LCx.

5. Conclusions

Based on the findings of this study and existing research evidence, we recommend adopting a stepwise evaluation strategy for patients with suspected coronary artery disease: initial screening with CCTA followed by CT-FFR assessment for functional ischemia in positive cases. This approach could prevent 30%-40% of patients with intermediate stenosis from undergoing unnecessary invasive coronary angiography (ICA), while maintaining high detection rates for ischemic lesions. Notably, CT-FFR demonstrates particularly superior diagnostic performance for left anterior descending artery and right coronary artery lesions, highlighting the clinical importance of evaluating structure-function correlation in these vascular territories.

In conclusion, the combined CCTA and CT-FFR approach enhances diagnostic accuracy for lesion-specific ischemia, particularly showing higher precision in assessing left anterior descending and right coronary artery lesions. This integrated protocol offers the advantages of being noninvasive, efficient, and cost-effective, thereby providing reliable evidence for precise identification of ischemic culprit lesions and formulation of personalized treatment strategies.

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