Evaluation of the Advantages of Myocardial Blood Flow Index in the Diagnosis of Chronic Obstructive Coronary Artery Disease Versus Coronary Computed Tomography Angiography: A Feasibility Study

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Abstract

Background: There is a hidden relationship between the degree of coronary artery stenosis and downstream myocardial remodeling. The mutual influence in myocardial ischemia and myocardial remodeling provides an index for quantifying the myocardial blood flow based on the principles of physics.

Objectives: This study aimed to evaluate the advantages of myocardial blood flow index (MBFI) in the diagnosis of chronic obstructive coronary artery disease (CAD).

Patients and Methods: The data of 68 patients (39 males; mean age: 57.0 ± 10.20 years) with suspected CAD were analyzed retrospectively, including the imaging findings of coronary computed tomography angiography (CCTA) and invasive coronary angiography (ICA) within one week. The MBFI was also calculated for the patients. After determining the optimal cut-off value based on ICA (stenosis ≥ 70%) as the gold standard test, the diagnostic performance of MBFI and CCTA was compared. The diagnostic accuracy was examined by the receiver operating characteristic (ROC) curve. For statistical analysis, chi-square test was performed to analyze influence data, and a P-value less than 0.05 was considered statistically significant.

Results: In 68 cases evaluated in this study, the average scan dose of CCTA was 3.02 ± 1.15 mSv. There were 28 cases with stenosis ≥ 70%. The optimal cutoff value of MBFI and CCTA was 0.111 and 70%, respectively. Also, the area under the curve (AUC) for MBFI and CCTA was 0.857 and 0.621 (Z = 2.091, P = 0.0365), respectively. The sensitivity, specificity, positive predictive value, and negative predictive value were 92.31%, 92.86%, 88.89%, and 95.12% for MBFI and 61.54%, 78.57%, 64.00%, and 76.74% for CCTA, respectively. The diagnostic accuracy was also estimated at 92.65% for MBFI and 72.06% for CCTA (χ² = 9.844, P = 0.0017).

Conclusion: In this study, MBFI performed better than CCTA in identifying lesions with stenosis ≥ 70%. A lower MBFI indicated the need for an upcoming active intervention, while a higher MBFI suggested avoiding unnecessary invasive testing.

Keywords: Coronary Artery Disease, Invasive Coronary Angiography, Myocardial Blood Flow Index, Functional Assessment, Diagnostic Test

1. Background

Recently, there has been a renewed interest in the functional evaluation of coronary lesions. Multiple studies have described the value of functional indicators in the accurate diagnosis of coronary artery disease (CAD). Some research has been conducted on the fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI) (1), myocardial microcirculation resistance index (2), and myocardial blood flow (3). The results of these studies suggested a hidden relationship between the degree of coronary artery stenosis and downstream myocardial remodeling (4, 5). In CAD, myocardial ischemia is the primary indication for PCI and also a prominent factor in myocardial remodeling (6, 7). On the other hand, myocardial remodeling aggravates myocardial ischemia (8). Therefore, there is a mutual increase in myocardial ischemia and myocardial remodeling, which may aid in quantifying the myocardial blood flow (9).
2. Objectives

The present study aimed to evaluate the advantages of myocardial blood flow index (MBFI) in the diagnosis of chronic obstructive CAD compared to coronary computed tomography angiography (CCTA).

3. Patients and Methods

3.1. Clinical Protocols

3.1.1. Consecutive Collection of Medical Records

The clinical medical follow-up data of 920 patients suspected of CAD were collected continuously, including the imaging data of CCTA and invasive coronary angiography (ICA) from February 2018 to September 2018. Finally, 68 cases were selected for this study. This research was approved by the ethics committee (No. 2022-B009) and implemented according to the tenets of the Declaration of Helsinki (www.wma.net/e/policy/). All patients signed a written informed consent form. The exclusion criteria are listed in Figure 1.

3.2. Coronary Computed Tomography Angiography Protocol

3.2.1. Scanning Parameters

Using CCTA (Dual-Source CT Somatom Definition, Siemens, Germany) with prospective ECG triggering (Adaptive Sequential, Siemens Healthcare, Germany), the scanning parameters were as follows using a CareDose 4D automatic exposure control system: 2 × 64 × 0.6 mm collimation with a Z-flying focal spot; gantry rotation time, 330 ms; pitch, 0.2 - 0.43; and voltage/tube product, 100 - 120 kV. The tube current was set automatically according to the weight of each patient.

Image acquisition was triggered at 35 - 75% of R-R interval. The Hounsfield unit (HU) of the descending aorta was dynamically detected 10 seconds after the contrast agent injection with the tracer technique. If the threshold was 120 HU, the triggering started four seconds later. The total dosage was 50 - 70 mL (contrast agent: 370 mgI/mL of iopromide, Ultravist, Bayer, Germany) followed by 30 mL of saline. The injection rate (3.8 - 4.2 mL/s) was adjusted according to the patient’s heart rate, body mass index (BMI), and cardiac function. Reconstruction was also performed with a medium smooth convolution kernel (B26f) at a slice thickness of 0.75 mm in 0.3-mm increments.

3.2.2. Computed Tomography Image Reconstruction

An offline commercial Siemens Syngo platform (Siemens Medical Solutions, Erlangen, Germany) was used for computed tomography (CT) image reconstruction. The severest lesion was selected for analysis using the semi-automatic software. It was calculated according to the minimal lumen diameter and the corresponding reference diameter. The stenosis degree was categorized as: Normal (0%), mild (1% - 49%), moderate (50% - 69%), severe (70% - 99%) and total occlusion.

3.2.3. Image Quality Assessment

The image quality was evaluated by two prominent experts with 10 years of experience in CCTA, who reached consensus through consultation. The fine images were selected for this study (10).

3.3. Myocardial Blood Flow Index

3.3.1. Myocardial Blood Flow Model

As current is equal to the ratio of voltage to resistance, myocardial blood flow is equal to the ratio of myocardial perfusion pressure to myocardial resistance. Based on the lumped parameter network (LPN) (11), as a parallel characteristic impedance model (12), the myocardial blood flow is primarily equal to the ratio of myocardial perfusion pressure to the myocardial mass (13). Blood circulation in the myocardium was completed within five cardiac cycles (14); in other words, after five cardiac cycles, the blood flow volume can distribute throughout the myocardium. Additionally, the right atrial pressure is about 0 mmHg at rest (15); consequently, the patient’s diastolic blood pressure (DP) can be regarded as the myocardial perfusion pressure. Therefore, the ratio of DP multiplied by five cardiac cycles to the mass represents the myocardial blood flow. As the BMI (16), sex (17), and age (18) are all associated with the myocardial blood flow, the myocardium blood flow model (Figure 2) should integrate these factors, which differs from the hyperemic myocardial blood flow index (19).

3.3.2. Calculation of Myocardial Blood Flow Index

The MBFI was calculated and adjusted according to the literature (9, 12, 14, 20). The MBFI formula is as follows:

\[
MBFI = \frac{5 \times 60}{HR} \times \frac{DP}{M \times MBI} - 0.015 \times n
\]

where \(n\) represents the age interval.

3.4. Invasive Coronary Angiography Protocol

Basic ICA was performed within one week after the CCTA protocol. The coronary arteries were divided into 15 segments according to the standards of the American Heart Association. The results were reported by two experts with 20 years of experience in cardiac intervention, who was unaware of the results of CCTA. They reached consensus through consultation. The stenosis degree was categorized as normal (no stenosis), mild (< 50% stenosis),
Enrolled subjects (n = 920)

Exclusions

Screened subjects of CC'TA (n = 625)

Exclusions

Screened subjects (n = 273)

Exclusions

Screened subjects of ICA (n = 76)

Exclusions

Study population (n = 68)

image artifacts: n = 352

Denied informed consent: n = 197

ICA datasets could not be fully read: n = 8

Notes: STEMI is ST segment elevation myocardial infarction, LVEF is left ventricular ejection fraction, BMI is body mass index, eGFR is estimated glomerular filtration rate, BP is blood pressure, CCTA is coronary computed tomography angiography, and ICA is invasive coronary angiography.

Figure 1. The flowchart of patient enrollment; STEMI, ST segment elevation myocardial infarction; LVEF, left ventricular ejection fraction; BMI, body mass index; eGFR, estimated glomerular filtration rate; BP, blood pressure; CCTA, coronary computed tomography angiography; and ICA, invasive coronary angiography.

Figure 2. The myocardial blood flow model.
moderate (50 - 69% stenosis), severe (≥ 70% stenosis), and total occlusion. The stenosis degree was categorized as:
normal (0%), mild (1% - 49%), moderate (50% - 69%), severe (70% - 99%) and total occlusion.

3.5. Diagnostic Analysis
By using ICA as the gold standard (≥ 70% stenosis), the diagnostic performance of MBFI and CCTA was investigated. If the value of MBFI was less than or equal to the optimal cutoff value, the more obvious lesion was considered as severe. Similarly, if the result of CCTA was more than or equal to 70% (diameter narrowing), the lesion was considered severe.

3.6. Statistical Analysis
Continuous variables are expressed as mean ± standard deviation (SD), while categorical variables are presented as frequency or percentage. The diagnostic power of MBFI and CCTA was evaluated using the receiver operating characteristic (ROC) curve. The area under the curve (AUC) of MBFI was compared with that of CCTA by DeLong’s test. Chi-square test was also used for enumeration data, and P < 0.05 was considered statistically significant.

4. Results
The baseline data of the enrolled patients are summarized in Table 1. In 68 cases, the average scan dose of CCTA was 3.02 ± 1.15 mSv. There were 28 cases with ≥ 70% stenosis. The optimal cutoff values for MBFI and CCTA were 0.111 and 70%, respectively. The AUC was 0.857 for MBFI and 0.621 for CCTA, showing a significant difference (Z = 2.091, P = 0.0365) (Figure 3). The sensitivity, specificity, positive predictive value, and negative predictive value were 92.31%, 92.86%, 88.89%, and 95.12% for MBFI versus 61.54%, 78.57%, 64.00%, and 76.74% for CCTA, respectively. The diagnostic accuracy was also estimated at 92.65% for MBFI and 72.06% for CCTA (χ² = 9.844, P = 0.0017) (Table 2 and Figures 4 and 5).

5. Discussion
Due to its high temporal and spatial resolution, CCTA can provide the anatomical information of lesions, including the features, extent, and severity of stenosis. This method enjoys a reputation as an accurate noninvasive first-line method in the guidelines to evaluate patients with a low-to-intermediate risk of CAD due to its high sensitivity, specificity, and negative predictive value (21). However, its diagnostic accuracy may reduce because of respiratory artifacts and calcified plaques; besides, it cannot show whether coronary artery lesions have any hemodynamic significance (22). Nevertheless, it has the potential to screen patients with ischemic heart disease (IHD) (23).

Noninvasive methods, such as stress echocardiography, cardiovascular magnetic resonance, CCTA combined with myocardial perfusion imaging, and FFR derived from CCTA, can play an important role in evaluating IHD (24, 25). Radionuclide myocardial perfusion, echocardiography, and cardiac magnetic resonance imaging are accurate methods for evaluating myocardial ischemia and are also suitable for the follow-up of IHD cases. Nevertheless, it is difficult to diagnose IHD using these techniques, as they cannot clearly show the coronary arteries. Computed tomography-derived FFR (CT-FFR) has been employed to evaluate functional lesions, resulting in improved prognosis (19), although this method is limited by massive calcifications and image quality (25).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total (n = 68)</th>
</tr>
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<tbody>
<tr>
<td>Gender</td>
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<tr>
<td>Male</td>
<td>39</td>
</tr>
<tr>
<td>Female</td>
<td>29</td>
</tr>
<tr>
<td>Age (y)</td>
<td>57 ± 10.2</td>
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<tr>
<td>History of risk factors</td>
<td></td>
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<tr>
<td>Hypertension b</td>
<td>21</td>
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<tr>
<td>Diabetes mellitus c</td>
<td>24</td>
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<tr>
<td>Dyslipidemia d</td>
<td>38</td>
</tr>
<tr>
<td>Smoking (n)</td>
<td>17</td>
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<tr>
<td>Family history of CAD</td>
<td>5</td>
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<tr>
<td>Average heart rate (time/min)</td>
<td>71 ± 11.7</td>
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<td>Average diastolic blood pressure (mmHg)</td>
<td>81 ± 11.9</td>
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<td>Average serum creatinine (µmol/L)</td>
<td>82</td>
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<tr>
<td>Average body mass index (kg/m²)</td>
<td>23 ± 3.5</td>
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<tr>
<td>Results of ICA</td>
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<tr>
<td>One-vessel stenosis</td>
<td>33</td>
</tr>
<tr>
<td>Two-vessel stenosis</td>
<td>21</td>
</tr>
<tr>
<td>Multi-vessel stenosis</td>
<td>14</td>
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<tr>
<td>A left main lesion with three-vessel stenosis e</td>
<td>1</td>
</tr>
<tr>
<td>Average radiation dose (mSv)</td>
<td>3.02 ± 1.15</td>
</tr>
</tbody>
</table>

Abbreviations: CAD, coronary artery disease; ICA, invasive coronary angiography
a Values are presented as mean ± SD or frequency (percentage).
≥ Blood pressure ≥ 140/90 mmHg or treatment for hypertension
b Fasting blood glucose is above 7.0 mmol/L, or the glucose tolerance test is above 11.1 mmol/L two hours after a meal.
c Total cholesterol > 180 mg/dL or treatment for hypercholesterolaemia
e There were only 2 patients with left main coronary artery disease combined with two-vessel stenosis.
In the present study, MBFI demonstrated a larger AUC than CCTA in the diagnosis of chronic obstructive CAD, with a significant difference ($Z = 2.091, P < 0.05$). By considering ICA stenosis $\geq 70\%$ as the gold standard for the diagnosis of severe lesions, the sensitivity, specificity, positive predictive value, and negative predictive value of MBFI were estimated at 92.31%, 92.86%, 88.89%, and 95.12%, respectively, which exceeded those of CCTA (61.54%, 78.57%, 64.00%, and 76.74%, respectively). Besides, the diagnostic accuracy of MBFI was significantly higher than that of CCTA ($\chi^2 = 9.844, P < 0.01$). Similar to other functional parameters (26), this model, which was composed of cardiac physiological parameters, yielded better diagnostic results compared to the conventional diagnostic method of CCTA and made the diagnosis more accurate.

Although previous studies, using stenosis $\geq 50\%$ as the gold standard, have reported that CCTA has high sensitivity and specificity in the diagnosis of CAD (27, 28), there is little information in the literature to confirm the ability of CCTA in diagnosing CAD, with stenosis $\geq 70\%$ as the gold standard. If stenosis was $\geq 70\%$, it commonly suggested the possibility of ischemic myocardium. To confirm this possi-
Figure 4. A 68-year-old male patient with unstable angina. The imaging findings of the left anterior descending (LAD) artery. A, The computed coronary tomography angiography (CCTA) image shows suspected stenosis in the LAD (arrow). The myocardial blood flow index (MBFI) is 0.082, which indicates a suspected lesion with severe stenosis; B, The invasive coronary angiography (ICA) image shows the severe lesion with 95% stenosis (arrow).

Figure 5. The imaging findings of the left anterior descending (LAD) artery in a 71-year-old male patient with unstable angina. A, Computed coronary tomography angiography (CCTA) image shows a suspected severe stenosis (arrow) in the LAD (arrow); B, The invasive coronary angiography images show a gentle lesion (arrow) with 10% stenosis. Myocardial blood flow index is 0.128, which suggests a lesion with no severe stenosis.
bility, CCTA should be preferably combined with other indices (19, 29). Accordingly, the use of functional parameters is becoming more common to improve diagnostic accuracy, and MBFI may have potential applications in the diagnosis or screening of CAD.

The current study had some limitations. This was a retrospective study, while a prospective study with a larger sample size is suggested to demonstrate the MBFI advantages. Besides, further experimental information is needed to determine whether diabetes plays a role in the model.

In conclusion, the diagnostic ability of MBFI was superior to that of CCTA in identifying lesions with stenosis ≥ 70%. A lower MBFI indicated the need for an upcoming active intervention, while a higher MBFI suggested avoiding unnecessary invasive testing.

Footnotes

Authors’ Contributions: Study concept and design: Q. X.; analysis and interpretation of data: Q. X. and X. M.; drafting of the manuscript: X. F. and D. Z.; critical revision of the manuscript for important intellectual content: Q. X., X. F., and X. M.; and statistical analysis: Q. X. and S. G.

Clinical Trial Registration Code: The clinical trial code of this study is chictr180018376 (link: www.chictr.org.cn/historyversionpub.aspx?regno = ChiCTR180018376).

Conflict of Interests: The authors declare that there is no conflict of interests regarding the publication of this paper.

Data Reproducibility: The dataset presented in this study is available on request from the corresponding author during submission or after publication.

Ethical Approval: This study was approved under the ethical approval code, 2022-B009 (link: wjw.wuhan.gov.cn/gsgg/202001/t20200114_802118.shtml).

Informed Consent: All patients signed a written consent form.

References


