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Research article

The coronary angiography-derived index of microcirculatory resistance predicts perioperative myocardial injury in stable coronary artery disease patients undergoing PCI

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ABSTRACT

Background: Coronary microvascular dysfunction (CMD) assessed by the index of microcirculatory resistance (IMR) is associated with perioperative myocardial injury (PMI).The angiographically derived index of microcirculatory resistance (caIMR) represents a novel and accurate alternative to IMR.
Objective: This study aims to evaluate the predictive ability of caIMR for PMI in patients with stable coronary artery disease (CAD) undergoing percutaneous coronary intervention (PCI).
Methods: Consecutive patients with stable CAD undergoing elective PCI of a single lesion were recruited. caIMR was measured before and after revascularisation, and total creatine kinase-MB (CK-MB) and high-sensitivity troponin T (hsTnT) levels were measured before and within 24 h after PCI.
Results: A total of 65 patients were enrolled and 26 patients fulfilled the diagnostic criteria for PMI. Post-PCI caIMR values were significantly higher in the PMI group than in the control group (27.02 ± 3.70 vs. 15.91 ± 3.43U, $P < 0.001$). Pearson correlation analysis showed that increased post-PCI caIMR values had a significant positive correlation with peak hsTnT ($r = 0.803$, $P < 0.001$) and peak CK-MB ($r = 0.512$, $P = 0.001$). Multivariate logistic regression analysis showed that post-PCI caIMR was an independent predictor of PMI (OR,1.731; 95 % CI:1.348–2.023; $P < 0.001$).ROC analysis suggested that the best cut-off value of post-PCI caIMR was 25.17U to diagnose PMI (AUC = 0.951, sensitivity 88.5 %, specificity 97.1 %). During a median follow-up 16 months, patients with PMI had a higher incidence of major adverse cardiovascular events (MACE) (42.31 % vs 5.13 %, $P = 0.04$).
Conclusions: Post-PCI caIMR can accurately predict PMI and clinical outcomes in stable CAD patients undergoing elective PCI, which supports the use of caIMR in clinical practice.

1. Introduction

Perioperative myocardial injury (PMI) has a significant impact on the prognosis of patients with coronary artery disease (CAD) [1].

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Recent research has increasingly shown that coronary microvascular dysfunction (CMD) is common in CAD patients undergoing percutaneous coronary intervention (PCI) and is closely associated with PMI [2,3]. The index of microvascular resistance (IMR) has been shown to be a reliable measure of CMD [4]. However, the widespread adoption of pressure wire-based IMR measurement is hampered by its procedural complexity and significant cost [5].

In response to these challenges, an innovative approach to IMR assessment has been developed using angiography alone, without the need for a physiological wire and adenosine. This novel method, known as coronary angiography-derived IMR (caIMR), has been rigorously validated for accuracy against conventional wire-based IMR and has demonstrated a high degree of agreement [6,7]. In particular, caIMR offers a faster, more accessible and cost-effective alternative, paving the way for improved CMD research [8].

While previous studies have highlighted the accurate diagnostic capabilities of caIMR for CAD and its significant long-term prognostic value [9], the specific impact of caIMR on PMI in patients with stable CAD remains to be elucidated. This study aims to fill this gap by investigating the predictive ability of caIMR for PMI in stable CAD patients undergoing PCI.

2. Methods

2.1. Study population

This was a prospective, single-centre trial (registration number: ChiCTR2200064634, registered on October 13, 2022). Sixty-five consecutive patients with stable CAD, normal cardiac troponin T (cTnT) levels and scheduled for elective PCI were enrolled. Inclusion criteria included patients aged 18–75 years, with a single target lesion greater than 75 % diameter stenosis and Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow. Exclusion criteria included patients with a history of myocardial infarction, malignancy or coronary artery bypass graft surgery.

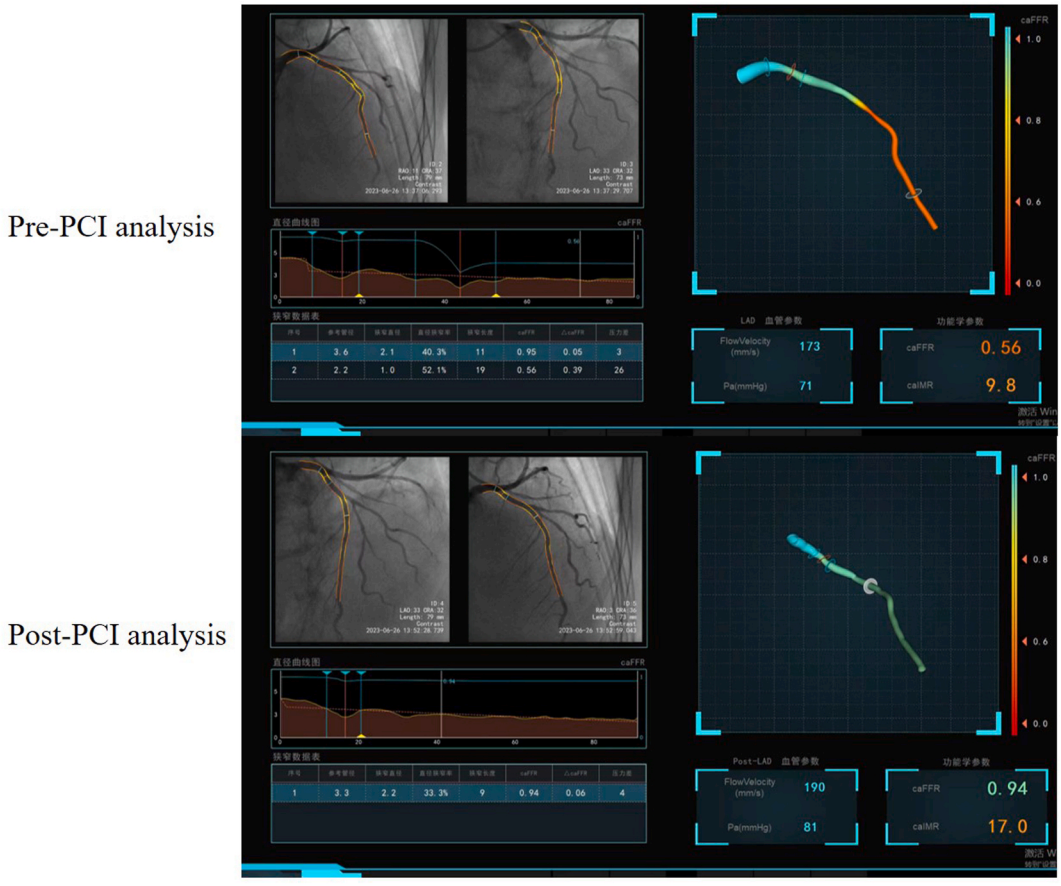

Fig. 1. A representative case of coronary angiogram and physiological measurements.
The graph displays coronary angiography-derived physiological measurements in left anterior descending coronary(LAD) artery lesion before and after PCI. PCI, percutaneous coronary intervention.

2.2. Baseline and data collection

We prospectively collected comprehensive baseline characteristics and procedural details for all participants during their hospitalisation. This included recording essential clinical information, medical history and laboratory results for each subject enrolled in the study. In addition, diagnostic and monitoring tools such as echocardiograms and coronary angiograms were used to collect cardiovascular data from all enrolled subjects. To ensure objectivity and unbiased analysis, all coronary angiograms were independently reviewed by two experienced cardiologists who were blinded to the experimental results. This meticulous approach was designed to ensure the integrity and reliability of the data collection process, which was essential for the subsequent analysis and interpretation of the study results.

2.3. Angiography-derived FFR and IMR measurements

For the measurement of coronary angiography-derived fractional flow reserve (caFFR) and coronary angiography-derived index of microvascular resistance (caIMR), we used a technique that used angiographic views at a minimum of 30° intervals. This approach facilitated the reconstruction of 3D mesh models of the coronary arteries using the commercial software FlashAngio (Rainmed Ltd, Suzhou, China), in accordance with the methods described in previous publications [10,11]. The caIMR assessments were performed by two experienced operators who were deliberately blinded to the clinical data to prevent bias. To illustrate the application of these angiographically derived physiological indices in a clinical setting, Fig. 1 provides a case example showing the changes in these measures before and after PCI.

2.4. Measurement of cardiac enzymes

Levels of total creatine kinase-MB (CK-MB) and high-sensitivity troponin T (hsTnT) were measured systematically at baseline, before coronary revascularisation and at 8, 16 and 24 h after PCI. According to current guidelines, PCI-related myocardial injury was identified when post-procedural cTnT levels exceeded the 99th percentile of the upper reference limit (URL) [12]. The peak value was defined as the highest measurement obtained after the procedure.

2.5. Coronary artery plaque composition analysis

Microcirculatory function is influenced by the morphological structure of the coronary plaque. Coronary plaque morphology was assessed by intravascular ultrasound (IVUS) or frequency domain optical coherence tomography (FD-OCT). The IVUS images were acquired with a 40-MHz rotating IVUS imaging catheter (Boston Scientific, Natick, MA, USA). The OCT examination was performed with a frequency domain OCT system (Ilumien Optis, Abbott Vascular, Santa Clara, CA, USA). Off-line IVUS or OCT analysis of all imaged segments was performed by two experienced operators, and disagreements were resolved by consensus with the involvement of a third operator blinded to the clinical data. Plaque components were classified as lipid plaque, fibrotic plaque, calcified plaque or mixed plaque [13].

2.6. Clinical outcomes

The primary outcome is the incidence of major adverse cardiovascular events (MACE) after PCI. MACE is defined as the composite endpoint of recurrent angina (Canadian Cardiovascular Society class III-IV), acute myocardial infarction, heart failure, target vessel revascularisation (PCI or bypass surgery), ischaemic stroke and cardiovascular mortality [14]. All patients were followed up individually by direct telephone contact or outpatient visits. Clinical data were confirmed every 6 months. Patients were censored at the time of the last follow-up visit or at the occurrence of the clinical endpoint.

2.7. Statistical analysis

Continuous variables were summarised as mean ± standard deviation(SD), while categorical data were presented as frequencies and percentages. Comparisons between groups were made using Student's t-test for normally distributed continuous variables and Mann-Whitney *U* test for non-normally distributed variables. The Fisher exact test or the $\chi 2$ test was used for the assessment of differences between groups for categorical variables. Pearson's correlation analysis was used to examine the relationship between caIMR and peak levels of CK-MB and hsTnT. A multivariable logistic regression model was performed to identify predictors of the primary outcome, with results presented as odds ratios (ORs) with 95 % confidence intervals (CIs). Variables considered clinically relevant to the outcome and showing statistical significance ($P < 0.05$) in the univariate analysis were selected as candidate predictors for the multivariate analysis.The accuracy and optimal cut-off of caIMR for predicting PMI were determined using receiver operating characteristic (ROC) curve analysis. The optimal cut-off was identified at the point where the sum of sensitivity and specificity was maximised. Statistical significance was set at a two-tailed *P* value of <0.05. All statistical procedures were performed using SPSS software, version 20.0 (IBM Corporation, Armonk, NY, USA).

3. Result

3.1. Clinical characteristics

In a total of 65 patients, 26 (40.0 %) had perioperative myocardial injury (PMI). Baseline clinical and laboratory characteristics of the study population were described in Table 1. Angiographic and coronary artery plaque type determined by intracoronary imaging were summarised in Table 2. There were no statistically significant differences in age, gender, body mass index (BMI), laboratory findings or medication use between the groups with and without PMI. Similarly, the prevalence of traditional CAD risk factors such as hypertension, diabetes, smoking history and dyslipidaemia did not differ significantly between the two groups. Echocardiography showed that left ventricular ejection fraction (LVEF) was comparable between the two groups. In addition, analyses of target vessel, coronary plaque type, maximum post-dilatation pressure and post-PCI TIMI flow grade showed no significant differences between the groups.

3.2. caIMR to predict PMI

In our analysis, baseline hsTnT levels were below the 99th percentile of the URL in all participants. We observed that peak levels of cardiac enzyme levels after PCI were significantly elevated in patients who developed PMI compared with those who did not. Specifically, peak hsTnT levels were 2.576 ± 1.086 ng/mL in the PMI group versus 0.122 ± 0.097 ng/mL in the non-PMI group ($P < 0.001$), and peak CK-MB levels were 19.23 ± 5.39 U/L in the PMI group versus 14.97 ± 3.65 U/L in the non-PMI group ($P < 0.01$).

There were no significant differences in pre-PCI caFFR or caIMR between the two groups. While post-PCI caFFR values remained similar between groups, post-PCI caIMR values were significantly increased in the PMI group compared to the non-PMI group (27.02 ± 3.70 vs. 15.9 ± 3.43 U, $P < 0.001$), as shown in Table 3. Notably, significant correlations were found between post-PCI caIMR and peak CK-MB levels ($r = 0.512$, $P = 0.001$)(Fig. 2A), and between post-PCI caIMR and peak hsTnT levels ($r = 0.803$, $P < 0.001$)(Fig. 2B).

ROC curve analysis showed that post-PCI caIMR has significant predictive value for PMI in patients with stable CAD undergoing PCI. The optimal post-PCI caIMR cut-off value for predicting PMI was identified as 25.17 U, giving a sensitivity of 88.5 % and a specificity of 97.1 % (area under the curve (AUC) = 0.951; 95 % confidence interval (CI) 0.905–1.000, $P = 0.001$)(Fig. 3).

Table 1
Baseline clinical data of patients with and without periprocedural myocardial injury.

Parameters	Total (n = 65)	No periprocedural MI (n = 39)	Periprocedural MI (n = 26)	*P* value
Age (years)	60.34 ± 10.23	58.62 ± 11.34	62.92 ± 8.25	0.097
Male (n,%)	48(73.85)	31 (79.49 %)	17 (65.38 %)	0.205
Body mass index (kg/㎡)	24.77 ± 3.52	25.06 ± 3.41	24.33 ± 3.70	0.417
Systolic blood pressure (mmHg)	136.37 ± 20.90	134.33 ± 21.23	139.42 ± 20.43	0.340
Diastolic blood pressure (mmHg)	81.83 ± 11.60	80.64 ± 13.29	83.62 ± 8.39	0.315
Heart rate (beats/min)	78.18 ± 12.26	76.87 ± 11.46	80.15 ± 13.35	0.294
Risk factors (n,%)				
Diabetes	16(24.62)	7 (17.95 %)	9 (34.62 %)	0.126
Hypertension	37(56.92)	23 (58.97 %)	14 (53.85 %)	0.683
Dyslipidemia	18(27.69)	11 (28.21 %)	7 (26.92 %)	0.910
Current smoking	26(40.0 %)	18 (46.15 %)	8 (30.77 %)	0.215
Medication use (n,%)				
Aspirin	60(92.31)	37 (94.88 %)	23 (88.46 %)	0.342
Clopidogrel	38(58.46)	24 (61.54 %)	14 (53.85 %)	0.758
Ticagrelor	24(36.92)	13 (33.33 %)	11 (42.31 %)	0.471
Beta-blocker	19(29.23)	12 (30.77 %)	7 (26.92 %)	0.738
Nitrate	16(24.62)	10 (25.65 %)	6 (23.08)	0.814
ACEI or ARB	15(23.08)	11 (28.21)	4 (15.38)	0.229
Statin	57(87.69)	34 (87.18)	23 (88.46)	0.878
Biochemical parameters				
Total cholesterol (mmol/L)	3.92 ± 0.89	3.80 ± 0.88	4.10 ± 0.81	0.182
LDL (mmol/L)	2.35 ± 0.67	2.29 ± 0.68	2.45 ± 0.70	0.384
Triglycerides (mmol/L)	1.46 ± 0.67	1.53 ± 0.71	1.35 ± 0.62	0.282
hs-CRP (mg/L)	2.46 ± 0.33	2.47 ± 0.72	2.45 ± 0.82	0.981
FBG (mmol/L)	6.75 ± 2.07	6.43 ± 1.67	7.23 ± 2.52	0.126
HbA1c (%)	6.37 ± 1.26	6.21 ± 0.85	6.62 ± 1.70	0.209
Creatinine (μmol/L)	72.32 ± 14.65	73.14 ± 16.42	71.08 ± 11.72	0.582
NT-proBNP (pg/ml)	186.74 ± 34.62	154.38 ± 36.95	235.26 ± 40.94	0.156
LVEF (%)	65.32 ± 7.01	66.41 ± 5.39	63.69 ± 8.75	0.126

Data are presented as Mean ± standard deviation(SD) for continuous variables and n (%) for categorical variables. **MI**: myocardial injury; **ACEI**: angiotensin-converting enzyme inhibitor; **ARB**: angiotensin II receptor blocker; **LDL-C**: low-density lipoprotein-cholesterol; **hs-CRP**: high-sensitivity C-reactive protein; **FBG**: fasting blood glucose; **HbA1c**: hemoglobin A1c; **NT-proBNP:** N-terminal pro-brain natriuretic peptide; **LVEF**: left ventricular ejection fraction.

Table 2
Angiographic and coronary plaque characteristics of patients with and without periprocedural myocardial injury.

Parameters	Total (n = 65)	No periprocedural MI (n = 39)	Periprocedural MI (n = 26)	*P* value
Target vessel (n,%)				0.440
LAD	48(73.85)	31(79.49 %)	17 (65.38)	
LCX	6(9.23)	3 (7.69 %)	3 (11.54)	
RCA	11(16.92)	5 (12.82 %)	6 (23.08)	
Lesion diameter stenosis (%)	86.74 ± 6.09	87.03 ± 6.20	86.31 ± 6.01	0.645
Lesion length (mm)	18.26 ± 1.49	17.59 ± 1.22	19.27 ± 1.45	0.380
Reference vessel size (mm)	3.18 ± 0.62	3.16 ± 0.12	3.25 ± 0.24	0.705
Plaque type assessed by intracoronary imaging (n, %)				0.889
Lipid plaque	19(29.23)	12 (30.77 %)	7 (26.92 %)	
fibrotic plaque	17(26.15)	11 (28.21 %)	6 (23.08 %)	
calcified plaque	5(7.69)	3 (7.69 %)	2 (7.69 %)	
mixed plaque	24(36.92)	13 (33.33 %)	11 (42.31 %)	
Plaque burden (%)	77.84 ± 9.22	77.63 ± 6.52	77.69 ± 4.58	0.997
MLA (mm)	1.91 ± 0.63	2.03 ± 0.53	1.72 ± 0.49	0.054
Procedural details				
Total stent length (mm)	22.48 ± 7.59	21.89 ± 6.91	23.31 ± 8.54	0.471
Coronary stents implantation pressure (atm)	11.11 ± 1.40	11.14 ± 1.33	11.08 ± 1.52	0.865
Maximal post-dilatation pressure (atm)	16.52 ± 1.93	16.29 ± 1.92	16.83 ± 2.01	0.301
Post-PCI TIMI flow grade (n,%)				0.392
0 or 1	0	0	0	
2	3(4.62)	2 (5.13 %)	1 (3.85)	
3	62(95.38)	37 (94.87 %)	25 (96.15 %)	

Data are presented as Mean ± standard deviation(SD) for continuous variables and n (%) for categorical variables. **MI**: myocardial injury; **LAD**: left anterior descending; **LCX**: left circumflex; **RCA**: right coronary artery; **MLA**: minimum lumen area; **PCI**: percutaneous coronary intervention; **TIMI**: thrombolysis in myocardial infarction.

Table 3
Coronary physiology and cardiac biomarkers changes in patients with and without periprocedural myocardial injury.

Parameters	Total (n = 65)	No periprocedural MI (n = 39)	Periprocedural MI (n = 26)	*P* value
Pre-PCI				
CaFFR	0.65 ± 0.12	0.64 ± 0.11	0.63 ± 0.10	0.662
CaIMR (U)	11.09 ± 2.97	11.39 ± 2.92	10.64 ± 3.06	0.323
Post-PCI				
CaFFR	8.61 ± 5.88	7.95 ± 5.87	9.60 ± 5.85	0.270
CaIMR (U)	19.55 ± 5.71	15.91 ± 3.43	27.02 ± 3.70	<0.001
Cardiac enzymes change				
Baseline CK-MB level (IU/L)	12.58 ± 3.17	12.59 ± 2.91	12.57 ± 3.60	0.981
Peak post-procedural CK-MB level (IU/L)	16.68 ± 4.87	14.97 ± 3.65	19.23 ± 5.39	<0.01
Baseline hs-cTnT level (ng/ml)	0.017 ± 0.014	0.015 ± 0.013	0.019 ± 0.015	0.220
Peak post-procedural hs-cTnT level (ng/ml)	1.104 ± 1.390	0.122 ± 0.097	2.576 ± 1.086	<0.001

Data are presented as Mean ± standard deviation(SD) for continuous variables. **MI**: myocardial injury; **PCI**: percutaneous coronary intervention; **FFR**: fractional flow reserve; **IMR**: index of microvascular resistance; **CK-MB**: creatine kinase-MB; **hs-cTnT**: high sensitivity troponin T.

3.3. Predictors of PMI in stable CAD patients undergoing elective PCI

Table 4 shows the effect of various potential confounders on the risk of PMI. Univariate and multivariate logistic regression analyses were performed. In this analysis, PMI was adjusted for factors such as post-PCI caIMR>25, age, sex, BMI, diabetes, hypertension, current smoking status, high-sensitivity C-reactive protein (hs-CRP) levels, LVEF, coronary stent implantation pressure, and maximum post-dilatation pressure.

Univariate logistic regression analysis showed that a post-PCI caIMR>25 was significantly associated with an increased risk of PMI (OR = 3.741; 95 % CI: 1.452–6.726; $P < 0.001$), along with age and maximum post-dilatation pressure. On further examination using multivariate logistic regression analyses, a post-PCI caIMR >25 remained independently associated with an increased risk of PMI (OR = 1.731; 95 % CI: 1.348–2.023; $P < 0.001$), underscoring its importance as a predictor of PMI in patients undergoing elective PCI for stable CAD.

3.4. Clinical outcomes and adverse events

The mean duration follow-up was 16 months (69.23 % of patients>12 months follow-up; 30.77 % of patients >6 months follow-up). During this period, ten patients (38.46 %) had recurrent angina pectoris, one patient (1.54 %) underwent target vessel revascularisation and one patient(1.54 %) had heart failure. Patients with PMI had a higher incidence of MACE (42.31 % vs 5.13 %, $P = 0.04$) and angina pectoris (38.46 % vs 2.56 %, $P = 0.03$). Table 5 shows all individual endpoints and their corresponding incidences.

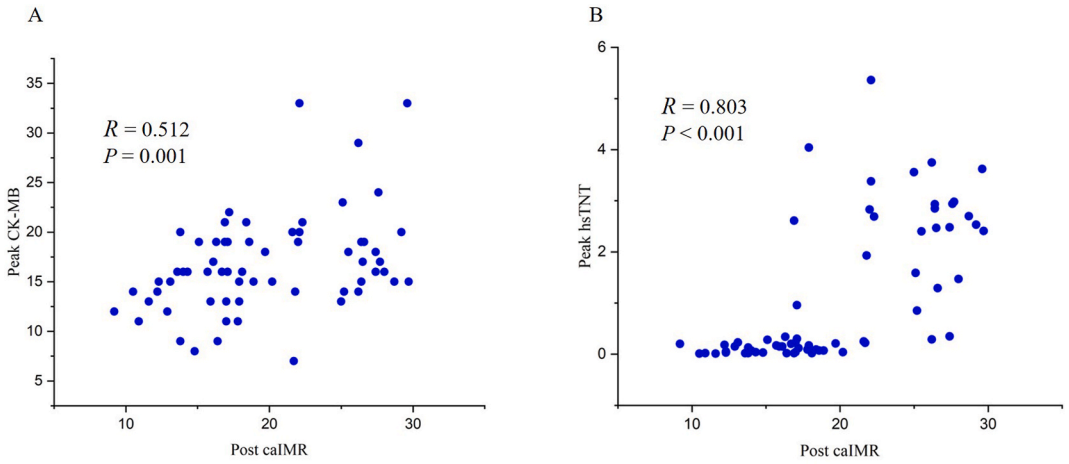

Fig. 2. The scatter plot shows the correlation of post-PCI caIMR values with peak CK-MB levels (U/L) (A) and with peak hsTnT concentration (ng/mL) (B) after PCI.
caIMR, coronary angiography-derived index of microvascular resistance; PCI, percutaneous coronary intervention; CK-MB, creatine kinase-MB; hsTnT, high sensitivity Troponin T.

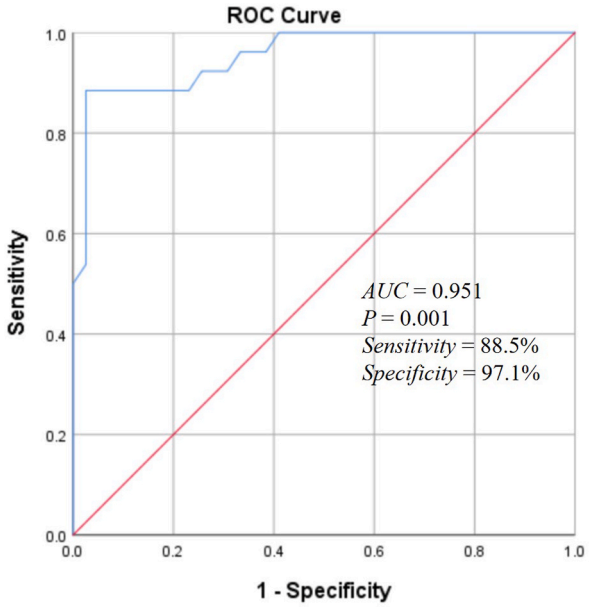

Fig. 3. Receiver operating characteristic curve of post-PCI caIMR values for prediction of periprocedural myocardial injury. AUC, area under the curve; PCI, percutaneous coronary intervention; caIMR, coronary angiography-derived index of microvascular resistance.

4. Discussion

The primary objective of this study was to assess the risk of PMI using caIMR in patients with stable CAD undergoing elective PCI. The key findings of this study include: (1) a significant association between elevated post-PCI caIMR and PMI in stable CAD patients; (2) even after adjustment for other confounding variables, post-PCI caIMR>25 U remained an independent risk factor for PMI.

Despite the effectiveness of PCI in achieving target vessel recanalisation, PMI remains a common complication. A previous study reported a 45.3 % incidence of PMI in stable CAD patients undergoing elective PCI [15]. Factors such as microvascular obstruction, inflammation and vasoconstriction are known to contribute to the development of PMI [16]. Previous research has shown that the IMR measured after PCI can be used to predict the PMI in patients with CAD [2,17]. However, the routine use of IMR has been limited by the need for special pressure-temperature sensor wires. Recent advances in functional assessment techniques have spurred efforts to calculate IMR using coronary angiography alone, eliminating the need for a coronary guidewire and pharmacological hyperemia [10]. Several studies in different patient populations have demonstrated the diagnostic and prognostic efficacy of caIMR. Hou C et al.,

Table 4
Univariate and multivariate analysis results for predictors of periprocedural myocardial injury.

Parameters	Univariable analysis		Multivariable analysis	
	OR (95 % CI)	*P* value	OR (95 % CI)	*P* value
Post-PCI caIMR >25	3.741(1.452–6.726)	<0.001	1.731(1.348–2.023)	<0.001
Age	1.953(1.073–3.059)	0.042	0.967(0.672–1.364)	0.812
Male	0.487(0.159–1.492)	0.209		
Body mass index	0.943(0.817–1.083)	0.412		
Diabetes mellitus	2.420(0.742–5.639)	0.132		
Hypertension	1.042(0.903–1.826)	0.205		
Current smoking	0.517(0.174–1.209	0.258		
LVEF	1.019(0.736–1.638)	0.167		
hs-CRP	1.358(0.935–1.804)	0.247		
Coronary stents implantation pressure	1.160(0.879–1.537)	0.291		
Maximal post-dilatation pressure	1.121(1.036–1.972)	0.016	1.014(0.831–1.648)	0.149

OR:odds ratio; **CI**: confidence interval; **PCI**: percutaneous coronary intervention; **caIMR**: coronary angiography-derived index of microvascular resistance; **LVEF**: left ventricular ejection fraction; **hs-CRP**: high-sensitivity C-reactive protein.

Table 5
Clinical outcomes of patients with periprocedural myocardial injury during follow up.

Characteristics	Total patients (n = 65)	Patients with post-PCI caIMR <25 (n = 39)	Patients with post-PCI caIMR >25 (n = 26)	*P* value
MACE (n,%)	13 (20.0)	2 (5.13)	11 (42.31)	0.04
Angina pectoris	11 (16.92)	1 (2.56)	10 (38.46)	0.03
target vessel revascularisation	1 (1.54)	0 (0.0)	1 (1.54)	0.004
acute myocardial infarction	0 (0.0)	0 (0.0)	0 (0.0)	–
heart failure	1 (1.54)	1 (2.56)	0 (0.0)	0.004
ischemic stroke	0 (0.0)	0 (0.0)	0 (0.0)	–
cardiovascular mortality	0 (0.0)	0 (0.0)	0 (0.0)	–

Data are presented as n (%) for categorical variables. **PCI**: percutaneous coronary intervention; **caIMR**: coronary angiography-derived index of microvascular resistance;**MACE**: major adverse cardiovascular events.

reported that caIMR values measured after PCI could accurately predict recovery of left ventricular function in patients with ST-segment elevation myocardial infarction (STEMI) [18]. Similarly, Dai N et al. found that post-PCI caIMR values were predictive of cardiac death or hospital readmission for heart failure in patients with CAD [11]. However, the prognostic significance of caIMR in relation to PMI in stable CAD patients has not been investigated. This study was therefore designed to investigate the utility and diagnostic value of caIMR for PMI in stable CAD patients undergoing PCI.

caFFR and caIMR is a novel approach to assess coronary physiology, based on the generation of angiographic projections by dedicated software [10]. In the present study, we found that a significant change in post-PCI caIMR values between the PMI and non-PMI groups, whereas no significant changes in post-PCI caFFR values were observed between the two groups. This can be attributed to the following reasons. caFFR incorporates epicardial coronary flow changes and can be considered a specific index of epicardial coronary stenosis resistance [19],whereas caIMR accounts for changes in microvascular resistance [6]. A previous study showed that the severity of epicardial CAD, as assessed by coronary angiography or FFR, was not collinear with the development of coronary microvascular dysfunction, as assessed by IMR [20]. A combination of caFFR and caIMR may improve the physiological assessment of macro- and microvascular disease in stable CAD patients undergoing elective PCI.

Many clinical trials have demonstrated coronary microvascular dysfunction associated with PMI in patients with stable CAD [2,9]. Our results showed that a post-PCI caIMR> 25U is indicative of PMI, with elevated post-PCI caIMR values showing a strong positive correlation with peak hsTnT ($r = 0.803$, $P < 0.001$) and CK-MB ($r = 0.512$, $P = 0.001$). These results are consistent with previous studies demonstrating the important role of coronary microcirculatory status in predisposing patients to PMI during elective PCI [3]. Therefore, caIMR measurements before and after PCI provide more convenient and reliable methods to assess PMI. These results have important implications for identifying patients at high risk of PMI and optimising their management.

After a median follow-up of 16 months, thirteen MACE events occurred in our study. Patients with caIMR≥25U had a higher rate of MACE than patients with caIMR <25U (42.31 % vs. 5.13 %, $P = 0.04$). Previous study shows that a high IMR is associated with an increased risk of adverse events in stable CAD patients [21]. Another study by *Zhou Y* et al. also reported that stable CAD patients with PMI had a higher incidence of cardiovascular events than those without PMI over an 18-month follow-up period [15].In addition, previous evidence has shown that high levels of post-PCI caIMR are associated with an increased risk of adverse events in patients with STEMI [22].Thus, caIMR is a promising alternative to IMR for assessing the prognosis of stable CAD patients undergoing elective PCI who are at risk of future adverse cardiovascular events.

In our study, nearly 40 % of the stable CAD patients without a history of myocardial infarction who received ticagrelor. This is because we are using cytochrome P450 2C19 (CYP2C19) genotype-guided selection of oral antiplatelet therapy in CAD patients

undergoing PCI in clinical practice. The choice of antiplatelet therapy in Asian populations for the treatment of CAD is complicated by the high prevalence of the CYP2C19 genetic polymorphism, which has been associated with reduced clopidogrel efficacy. Ticagrelor is a potent alternative antiplatelet agent that is not affected by the CYP2C19 polymorphism. Compared with clopidogrel, ticagrelor may also improve microvascular function [23].

4.1. Clinical practical implications

Our study suggests that post-PCI caIMR $\geq$25U accurately predicts PMI in stable CAD undergoing elective PCI. caIMR may provide clinicians with a faster and more convenient assessment of coronary microvascular function and facilitate risk stratification for PMI after PCI.

5. Limitations

Several limitations must be considered when interpreting our results. First, as a single-centre prospective observational cohort study with a relatively small sample size. In our future studies, a prospective and multicentre study would be conducted to validate the present results. Second, the lack of IMR measurements as a reference point for our enrolled patients is another limitation, although caIMR has been shown to have high diagnostic accuracy for assessing microvascular function. Third, reliance on a single caIMR measurement immediately after PCI may not adequately capture the full spectrum of PMI or provide a complete prognosis for the patient. Future research efforts should aim to integrate caIMR and cardiac magnetic resonance (CMR) to prevent missed diagnoses of PMI, and high-risk patients with PMI should have serial hs-cTnT measurements during the first 48–72 h after PCI. Despite these limitations, the current study provides initial and preliminary evidence that post-PCI caIMR may be a reliable assessment of coronary microvascular function immediately after stenting and a potential predictor of PMI and patient prognosis. Based on this encouraging finding, a further multicentre study with a larger sample size and longer follow-up is ongoing in our centre.

6. Conclusions

Our results indicate that post-PCI caIMR>25U is a strong predictor of PMI and clinical outcome in patients with stable CAD undergoing PCI. These findings suggest that the use of caIMR in clinical assessment may help to identify high-risk CAD patients and encourage earlier intervention.

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Ethics statement

This study was performed in line with the principles of the Declaration of Helsinki. This study was reviewed and approved by the Ethics Committee of The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China(approval number: 2022KY223). All participants provided written informed consent for the publication of their anonymised case details and images.

Data availability statement

Data associated with the study has not been deposited into a publicly available repository. Data are available from the corresponding author on reasonable request.

CRediT authorship contribution statement

BuChun Zhang: Writing – original draft, Funding acquisition, Data curation, Conceptualization. **Yi Zhang:** Project administration, Investigation, Data curation. **KaiJian Zhang:** Project administration, Investigation, Data curation. **Kang Hu:** Writing – original draft, Formal analysis. **Zhan Shi:** Investigation, Data curation. **LiKun Ma:** Supervision, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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